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Making Health Care Safer: A Critical Analysis of Patient Safety Practices

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Preface

The Agency for Healthcare Research and Quality (AHRQ), formerly the Agency for Health Care Policy and Research (AHCPR), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review prior to their release.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome written comments on this evidence report. They may be sent to: Director, Center for Practice and Technology Assessment, Agency for Healthcare Research and Quality, 6010 Executive Blvd., Suite 300, Rockville, MD 20852.

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Structured Abstract

Objectives: Patient safety has received increased attention in recent years, but mostly with a focus on the epidemiology of errors and adverse events, rather than on practices that reduce such events. This project aimed to collect and critically review the existing evidence on practices relevant to improving patient safety.

Search Strategy and Selection Criteria: Patient safety practices were defined as those that reduce the risk of adverse events related to exposure to medical care across a range of diagnoses or conditions. Potential patient safety practices were identified based on preliminary surveys of the literature and expert consultation. This process resulted in the identification of 79 practices for review. The practices focused primarily on hospitalized patients, but some involved nursing home or ambulatory patients. Protocols specified the inclusion criteria for studies and the structure for evaluation of the evidence regarding each practice. Pertinent studies were identified using various bibliographic databases (e.g., MEDLINE, PsycINFO, ABI/INFORM, INSPEC), targeted searches of the Internet, and communication with relevant experts.

Data Collection and Analysis: Included literature consisted of controlled observational studies, clinical trials and systematic reviews found in the peer-reviewed medical literature, relevant non-health care literature and "gray literature." For most practices, the project team required that the primary outcome consist of a clinical endpoint (i.e., some measure of morbidity or mortality) or a surrogate outcome with a clear connection to patient morbidity or mortality. This criterion was relaxed for some practices drawn from the non-health care literature. The evidence supporting each practice was summarized using a prospectively determined format. The project team then used a predefined consensus technique to rank the practices according to the strength of evidence presented in practice summaries. A separate ranking was developed for research priorities.

Main Results: Practices with the strongest supporting evidence are generally clinical interventions that decrease the risks associated with hospitalization, critical care, or surgery. Many patient safety practices drawn primarily from nonmedical fields (e.g., use of simulators, bar coding, computerized physician order entry, crew resource management) deserve additional research to elucidate their value in the health care environment. The following 11 practices were rated most highly in terms of strength of the evidence supporting more widespread implementation.

- Appropriate use of prophylaxis to prevent venous thromboembolism in patients at risk;
- Use of perioperative beta-blockers in appropriate patients to prevent perioperative morbidity and mortality;
- Use of maximum sterile barriers while placing central intravenous catheters to prevent infections;

- Appropriate use of antibiotic prophylaxis in surgical patients to prevent postoperative infections;
- Asking that patients recall and restate what they have been told during the informed consent process;
- Continuous aspiration of subglottic secretions (CASS) to prevent ventilator-associated pneumonia;
- Use of pressure relieving bedding materials to prevent pressure ulcers;
- Use of real-time ultrasound guidance during central line insertion to prevent complications;
- Patient self-management for warfarin (Coumadin™) to achieve appropriate outpatient anticoagulation and prevent complications;
- Appropriate provision of nutrition, with a particular emphasis on early enteral nutrition in critically ill and surgical patients; and
- Use of antibiotic-impregnated central venous catheters to prevent catheter-related infections.

Conclusions: An evidence-based approach can help identify practices that are likely to improve patient safety. Such practices target a diverse array of safety problems. Further research is needed to fill the substantial gaps in the evidentiary base, particularly with regard to the generalizability of patient safety practices heretofore tested only in limited settings and to promising practices drawn from industries outside of health care.

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Overview

Patient safety has become a major concern of the general public and of policymakers at the State and Federal levels. This interest has been fueled, in part, by news coverage of individuals who were the victims of serious medical errors and by the publication in 1999 of the Institute of Medicine's (IOM's) report *To Err is Human: Building a Safer Health System*. In its report, IOM highlighted the risks of medical care in the United States and shocked the sensibilities of many Americans, in large part through its estimates of the magnitude of medical-errors-related deaths (44,000 to 98,000 deaths per year) and other serious adverse events. The report prompted a number of legislative and regulatory initiatives designed to document errors and begin the search for solutions. But Americans, who now wondered whether their next doctor's or hospital visit might harm rather than help them, began to demand concerted action.

Three months after publication of the IOM report, an interagency Federal government group, the Quality Interagency Coordination Task Force (QuIC), released its response, *Doing What Counts for Patient Safety: Federal Actions to Reduce Medical Errors and Their Impact*. That report, prepared at the President's request, both inventoried on-going Federal actions to reduce medical errors and listed more than 100 action items to be undertaken by Federal agencies.

An action promised by the Agency for Healthcare Research and Quality (AHRQ), the Federal agency leading efforts to research and promote patient safety, was "the development and dissemination of evidence-based, best safety practices to provider organizations." To initiate the work to be done in fulfilling this promise, AHRQ commissioned the University of California at San Francisco (UCSF) – Stanford University Evidence-based Practice Center (EPC) in January 2001 to review the scientific literature regarding safety improvement. To accomplish this, the EPC established an Editorial Board that oversaw development of this report by teams of content experts who served as authors.

Defining Patient Safety Practices

Working closely with AHRQ and the National Forum for Quality Measurement and Reporting (the National Quality Forum, or NQF)—a public–private partnership formed in 1999 to promote a national health care quality agenda the EPC began its work by defining a patient safety practice as *a type of process or structure whose application reduces the probability of adverse events resulting from exposure to the health care system across a range of diseases and procedures.*

This definition is consistent with the dominant conceptual framework in patient safety, which holds that systemic change will be far more productive in reducing medical errors than will targeting and punishing individual providers. The definition's focus on actions that cut across diseases and procedures also allowed the research team to distinguish patient safety activities from the more targeted quality improvement practices (e.g., practices designed to increase the use of beta-blockers in patients who are admitted to the hospital after having a myocardial infarction). The editors recognize, however, that this distinction is imprecise.

This evidence-based review also focuses on hospital care as a starting point because the risks associated with hospitalization are significant, the strategies for improvement are better documented there than in other health care settings, and the importance of patient trust is paramount. The report, however, also considers evidence regarding other sites of care, such as nursing homes, ambulatory care, and patient self-management.

The results of this EPC study will be used by the NQF to identify a set of proven patient safety practices that should be used by hospitals. Identification of these practices by NQF will allow patients throughout the nation to evaluate the actions their hospitals and/or health care facilities have taken to improve safety.

Reporting The Evidence

As is typical for evidence-based reviews, the goal was to provide a critical appraisal of the evidence on the topic. This information would then be available to others to ensure that no practice unsupported by evidence would be endorsed and that no practice substantiated by a high level of proof would lack endorsement. Readers familiar with the state of the evidence regarding quality improvement in areas of health care where this has been a research priority (e.g., cardiovascular care) may be surprised and even disappointed, by the paucity of high quality evidence in other areas of health care for many patient safety practices. One reason for this is the relative youth of the field. Just as there had been little public recognition of the risks of health care prior to the first IOM report, there has been relatively little attention paid to such risks – and strategies to mitigate them – among health professionals and researchers.

Moreover, there are a number of methodologic reasons why research in patient safety is particularly challenging. Many practices (e.g., the presence of computerized physician order entry systems, modifying nurse staffing levels) cannot be the subject of double-blind studies because their use is evident to the participants. Second, capturing all relevant outcomes, including "near misses" (such as a nurse catching an excessive dosage of a drug just before it is administered to a patient) and actual harm, is often very difficult. Third, many effective practices are multidimensional, and sorting out precisely which part of the intervention works is often quite challenging. Fourth, many of the patient safety problems that generate the most concern (wrong-site surgery, for example) are uncommon enough that demonstrating the success of a "safety practice" in a statistically meaningful manner with respect to outcomes is all but impossible.

Finally, establishing firm epidemiologic links between presumed (and accepted) causes and adverse events is critical, and frequently difficult. For instance, in studying an intuitively plausible "risk factor" for errors, such as "fatigue," analyses of errors commonly reveal the presence of fatigued providers (because many health care providers work long hours and/or late at night). The question is whether or not fatigue is over-represented among situations that lead to errors. The point is not that the problem of long work-hours should be ignored, but rather that strong epidemiologic methods need to be applied before concluding that an intuitive cause of errors is, in fact, causal.

Researchers now believe that most medical errors cannot be prevented by perfecting the technical work of individual doctors, nurses, or pharmacists. Improving patient safety often involves the coordinated efforts of multiple members of the health care team, who may adopt strategies from outside health care. The report reviews several practices whose evidence came

from the domains of commercial aviation, nuclear safety, and aerospace, and the disciplines of human factors engineering and organizational theory. Such practices include root cause analysis, computerized physician order entry and decision support, automated medication dispensing systems, bar coding technology, aviation-style preoperative checklists, promoting a "culture of safety," crew resource management, the use of simulators in training, and integrating human factors theory into the design of medical devices and alarms. In reviewing these practices, the research team sought to be flexible regarding standards of evidence, and included research evidence that would not have been considered for medical interventions. For example, the randomized trial that is appropriately hailed as the "gold standard" in clinical medicine is not used in aviation, as this design would not capture all relevant information. Instead, detailed case studies and industrial engineering research approaches are utilized.

Methodology

To facilitate identification and evaluation of potential patient safety practices, the Editorial Board divided the content for the project into different *domains*. Some cover "content areas," including traditional clinical areas such as adverse drug events, nosocomial infections, and complications of surgery, but also less traditional areas such as fatigue and information transfer. Other domains consist of practices drawn from broad (primarily nonmedical) disciplines likely to contain promising approaches to improving patient safety (e.g., information technology, human factors research, organizational theory). Once this list was created—with significant input from patient safety experts, clinician–researchers, AHRQ, and the NQF Safe Practices Committee—the editors selected teams of authors with expertise in the relevant subject matter and/or familiarity with the techniques of evidence-based review and technology appraisal.

The authors were given explicit instructions regarding search strategies for identifying safety practices for evaluation (including explicit inclusion and exclusion criteria) and criteria for assessing each practice's level of evidence for efficacy or effectiveness in terms of study design and study outcomes. Some safety practices did not meet the inclusion criteria because of the paucity of evidence regarding efficacy or effectiveness but were included in the report because an informed reader might reasonably expect them to be evaluated or because of the depth of public and professional interest in them. For such high profile topics (such as bar coding to prevent misidentifications), the researchers tried to fairly present the practice's background, the experience with the practice thus far, and the evidence (and gaps in the evidence) regarding the practice's value.

For each practice, authors were instructed to research the literature for information on:

- prevalence of the problem targeted by the practice;
- severity of the problem targeted by the practice;
- the current utilization of the practice;
- evidence on efficacy and/or effectiveness of the practice;
- the practice's potential for harm;
- data on cost, if available; and
- implementation issues.

The report presents the salient elements of each included study (e.g., study design, population/setting, intervention details, results), and highlights any important weaknesses and

biases of these studies. Authors were *not* asked to formally synthesize or combine the evidence across studies (e.g., perform a meta-analysis) as part of their task.

The Editorial Board and the Advisory Panel reviewed the list of domains and practices to identify gaps in coverage. Submitted chapters were reviewed by the Editorial Board and revised by the authors, aided by feedback from the Advisory Panel. Once the content was finalized, the editors analyzed and ranked the practices using a methodology summarized below.

Summarizing the Evidence and Rating the Practices

Because the report is essentially an anthology of a diverse and extensive group of patient safety practices with highly variable relevant evidence, synthesizing the findings was challenging, but necessary to help readers use the information. Two of the most obvious uses for this report are: 1) to inform efforts of providers and health care organizations to improve the safety of the care they provide, and 2) to inform AHRQ, other research agencies, and foundations about potential fruitful investments for their research support. Other uses of the information are likely. In fact, the National Quality Forum plans to use this report to help identify a list of patient safety practices that consumers and others should know about as they choose among the health care provider organizations to which they have access.

In an effort to assist both health care organizations interested in taking substantive actions to improve patient safety and research funders seeking to spend scarce resources wisely, AHRQ asked the EPC to rate the evidence and rank the practices by opportunity for safety improvement and by research priority. This report, therefore, contains two lists.

To create these lists, the editors aimed to separate the practices that are most promising or effective from those that are least so on a range of dimensions, without implying any ability to calibrate a finely gradated scale for those practices in between. The editors also sought to present the ratings in an organized, accessible way while highlighting the limitations inherent in their rating schema. Proper metrics for more precise comparisons (e.g., cost-effectiveness analysis) require more data than are currently available in the literature.

Three major categories of information were gathered to inform the rating exercise:

- *Potential Impact of the Practice*: based on prevalence and severity of the patient safety target, and current utilization of the practice;
- *Strength of the Evidence Supporting the Practice*: including an assessment of the relative weight of the evidence, effect size, and need for vigilance to reduce any potential negative collateral effects of the practice; and
    - *Implementation*: considering costs, logistical barriers, and policy issues.

For all of these data inputs into the practice ratings, the primary goal was to find the best available evidence from publications and other sources. Because the literature has not been previously organized with an eye toward addressing each of these areas, most of the estimates could be improved with further research, and some are informed by only general and somewhat speculative knowledge. In the summaries, the editors have attempted to highlight those assessments made with limited data.

The four-person editorial team independently rated each of the 79 practices using general scores (e.g., High, Medium, Low) for a number of dimensions, including those italicized in the

section above. The editorial team convened for 3 days in June, 2001 to compare scores, discuss disparities, and come to consensus about ratings for each category.

In addition, each member of the team considered the totality of information on potential impact and support for a practice to score each of these factors on a 0 to 10 scale (creating a "Strength of the Evidence" list). For these ratings, the editors took the perspective of a leader of a large health care enterprise (e.g., a hospital or integrated delivery system) and asked the question, "If I wanted to improve patient safety at my institution over the next 3 years and resources were not a significant consideration, how would I grade this practice?" For this rating, the Editorial Board explicitly chose *not* to formally consider the difficulty or cost of implementation in the rating. Rather, the rating simply reflected the strength of the evidence regarding the effectiveness of the practice and the probable impact of its implementation on reducing adverse events related to health care exposure. If the patient safety target was rated as "High" impact and there was compelling evidence (i.e., "High" relative study strength) that a particular practice could significantly reduce (e.g., "Robust" effect size) the negative consequences of exposure to the health care system (e.g., hospital-acquired infections), raters were likely to score the practice close to 10. If the studies were less convincing, the effect size was less robust, or there was a need for a "Medium" or "High" degree of vigilance because of potential harms, then the rating would be lower.

At the same time, the editors also rated the usefulness of conducting more research on each practice, emphasizing whether there appeared to be questions that a research program might have a reasonable chance of addressing successfully (creating a "Research Priority" list). Here, they asked themselves, "If I were the leader of a large agency or foundation committed to improving patient safety, and were considering allocating funds to promote additional research, how would I grade this practice?" If there was a simple gap in the evidence that could be addressed by a research study or if the practice was multifaceted and implementation could be eased by determining the specific elements that were effective, then the research priority was high. (For this reason, some practices are highly rated on both the "Strength of the Evidence" and "Research Priority" lists.) If the area was one of high potential impact (i.e., large number of patients at risk for morbid or mortal adverse events) and a practice had been inadequately researched, then it would also receive a relatively high rating for research need. Practices might receive low research scores if they held little promise (e.g., relatively few patients are affected by the safety problem addressed by the practice *or* a significant body of knowledge already demonstrates the practice's lack of utility). Conversely, a practice that was clearly effective, low cost, and easy to implement would not require further research and would also receive low research scores.

In rating both the strength of the evidence and the research priority, the purpose was not to report precise 0 to 10 scores, but to develop general "zones" or practice groupings. This is important because better methods are available for making comparative ratings *when the data inputs are available*. The relative paucity of the evidence dissuaded the editors from using a more precise, sophisticated, but ultimately unfeasible, approach.

Clear Opportunities for Safety Improvement

The following 11 patient safety practices were the most highly rated (of the 79 practices reviewed in detail in the full report and ranked in the Executive Summary Addendum, AHRQ Publication No. 01-E057b) in terms of strength of the evidence supporting more widespread implementation. Practices appear in descending order, with the most highly rated practices listed first. Because of the imprecision of the ratings, the editors did not further divide the practices, nor indicate where there were ties.

- Appropriate use of prophylaxis to prevent venous thromboembolism in patients at risk;
- Use of perioperative beta-blockers in appropriate patients to prevent perioperative morbidity and mortality;
- Use of maximum sterile barriers while placing central intravenous catheters to prevent infections;
- Appropriate use of antibiotic prophylaxis in surgical patients to prevent perioperative infections;
- Asking that patients recall and restate what they have been told during the informed consent process;
- Continuous aspiration of subglottic secretions (CASS) to prevent ventilator-associated pneumonia;
- Use of pressure relieving bedding materials to prevent pressure ulcers;
- Use of real-time ultrasound guidance during central line insertion to prevent complications;
- Patient self-management for warfarin (Coumadin™) to achieve appropriate outpatient anticoagulation and prevent complications;
- Appropriate provision of nutrition, with a particular emphasis on early enteral nutrition in critically ill and surgical patients; and
- Use of antibiotic-impregnated central venous catheters to prevent catheter-related infections.

This list is generally weighted toward clinical rather than organizational matters, and toward care of the very, rather than the mildly or chronically ill. Although more than a dozen practices considered were general safety practices that have been the focus of patient safety experts for decades (i.e., computerized physician order entry, simulators, creating a "culture of safety," crew resource management), most research on patient safety has focused on more clinical areas. The potential application of practices drawn from outside health care has excited the patient safety community, and many such practices have apparent validity. However, clinical research has been promoted by the significant resources applied to it through Federal, foundation, and industry support. Since this study went where the evidence took it, more clinical practices rose to the top as potentially ready for implementation.

Clear Opportunities for Research

Until recently, patient safety research has had few champions, and even fewer champions with resources to bring to bear. The recent initiatives from AHRQ and other funders are a promising shift in this historical situation, and should yield important benefits.

In terms of the research agenda for patient safety, the following 12 practices rated most highly, as follows:

- Improved perioperative glucose control to decrease perioperative infections;
- Localizing specific surgeries and procedures to high volume centers;
- Use of supplemental perioperative oxygen to decrease perioperative infections;
- Changes in nursing staffing to decrease overall hospital morbidity and mortality;
- Use of silver alloy-coated urinary catheters to prevent urinary tract infections;
- Computerized physician order entry with computerized decision support systems to decrease medication errors and adverse events primarily due to the drug ordering process;
- Limitations placed on antibiotic use to prevent hospital-acquired infections due to antibiotic-resistant organisms;
- Appropriate use of antibiotic prophylaxis in surgical patients to prevent perioperative infections;
- Appropriate use of prophylaxis to prevent venous thromboembolism in patients at risk;
- Appropriate provision of nutrition, with a particular emphasis on early enteral nutrition in critically ill and post-surgical patients;
- Use of analgesics in the patient with an acutely painful abdomen without compromising diagnostic accuracy; and
- Improved handwashing compliance (via education/behavior change; sink technology and placement; or the use of antimicrobial washing substances).

Of course, the vast majority of the 79 practices covered in this report would benefit from additional research. In particular, some practices with longstanding success outside of medicine (e.g., promoting a culture of safety) deserve further analysis, but were not explicitly ranked due to their unique nature and the present weakness of the evidentiary base in the health care literature.

Conclusions

This report represents a first effort to approach the field of patient safety through the lens of evidence-based medicine. Just as *To Err is Human* sounded a national alarm regarding patient safety and catalyzed other important commentaries regarding this vital problem, this review seeks to plant a seed for future implementation and research by organizing and evaluating the relevant literature. Although all those involved tried hard to include all relevant practices and to review all pertinent evidence, inevitably some of both were missed. Moreover, the effort to grade and rank practices, many of which have only the beginnings of an evidentiary base, was admittedly ambitious and challenging. It is hoped that this report provides a template for future clinicians, researchers, and policy makers as they extend, and inevitably improve upon, this work.

In the detailed reviews of the practices, the editors have tried to define (to the extent possible from the literature) the associated costs—financial, operational, and political. However, these considerations were not factored into the summary ratings, nor were judgments made regarding the appropriate expenditures to improve safety. Such judgments, which involve complex tradeoffs between public dollars and private ones, and between saving lives by improving patient safety versus doing so by investing in other health care or non-health care practices, will obviously be critical. However, the public reaction to the IOM report, and the media and legislative responses that followed it, seem to indicate that Americans are highly concerned about the risks of medical errors and would welcome public and private investment to decrease them. It seems logical to infer that Americans value safety during a hospitalization just as highly as safety during a transcontinental flight.

Evidence Report

PART I. OVERVIEW

Chapter 1. An Introduction to the Report

1.1. General Overview

The Institute of Medicine's (IOM) report, *To Err is Human: Building a Safer Health System*,[1] highlighted the risks of medical care in the United States. Although its prose was measured and its examples familiar to many in the health professions (for example, the studies estimating that up to 98,000 Americans die each year from preventable medical errors were a decade old), the report shocked the sensibilities of many Americans. More importantly, the report undermined the fundamental trust that many previously had in the health care system.

The IOM report prompted a number of legislative and regulatory initiatives designed to document errors and begin the search for solutions. These initiatives were further catalyzed by a second IOM report entitled *Crossing the Quality Chasm: A New Health System for the 21st Century*,[2] which highlighted safety as one of the fundamental aims of an effective system. But Americans, who now wondered whether their next health care encounter might harm rather than help them, began to demand concerted action.

Making Health Care Safer represents an effort to determine what it is we might do in an effort to improve the safety of patients. In January 2001, the Agency for Healthcare Research and Quality (AHRQ), the Federal agency taking the lead in studying and promoting patient safety, commissioned the UCSF-Stanford Evidence-based Practice Center (EPC) to review the literature as it pertained to improving patient safety. In turn, the UCSF-Stanford EPC engaged 40 authors at 11 institutions around the United States to review more than 3000 pieces of literature regarding patient safety practices. Although AHRQ expected that this evidence-based review would have multiple audiences, the National Quality Forum (NQF)—a public-private partnership formed in the Clinton Administration to promote a national quality agenda—was particularly interested in the results as it began its task of recommending and implementing patient safety practices supported by the evidence.

A Definition of "Patient Safety Practices"

One of our first tasks was to define "patient safety practices" in a manner that would allow us and our reviewers to assess the relevant evidence. Given our task—producing a full report in less than six months—a complete review of all practices associated with improving health care quality was both impossible and off-point. Working closely with AHRQ and NQF, we chose the following definition:

> *A Patient Safety Practice is a type of process or structure whose application reduces the probability of adverse events resulting from exposure to the health care system across a range of diseases and procedures.*

A few elements of the definition deserve emphasis. First, our focus on processes and structure allowed us to emphasize changing the system to make it safer rather than targeting and removing individual "bad apples." We recognize that when individuals repeatedly perform poorly and are unresponsive to education and remediation, action is necessary. Nevertheless, there is virtual unanimity among patient safety experts that a focus on systemic change will be far more productive than an emphasis on finding and punishing poor performers.

Second, looking at crosscutting diseases and procedures allowed us to distinguish patient safety activities from more targeted quality improvement practices. Admittedly, this dichotomization is imprecise. All would agree that a practice that makes it less likely that a

patient will receive the wrong medication or have the wrong limb amputated is a patient safety practice. Most would also agree that practices designed to increase the use of beta-blockers in patients admitted to the hospital after myocardial infarction or to improve the technical performance of hernia repair would be quality improvement strategies rather than patient safety practices. When there was a close call, we generally chose to be inclusive. For example, we included practices designed to increase the rate of appropriate prophylaxis against venous thromboembolism, the appropriateness of pain management, and the ascertainment of patient preferences regarding end-of-life care. We recognize that these practices blur the line somewhat between safety and quality, but we believe that they are reasonable examples of ways to address potential patient safety hazards.

Third, we realized it would be impossible to review every potential safety practice and recognized that some gaps in the evidence were inevitable, so at times we reviewed illustrative examples that *might* be broadly generalizable. For example:

- Methods to avoid misread radiographs (Chapter 35); where the content could be relevant to analogous efforts to avoid misread electrocardiograms or laboratory studies
- Decreasing the risk of dangerous drugs (Chapter 9), where the focus was on anticoagulants, but similar considerations might be relevant for chemotherapy and other high-risk drugs
- Localizing care to specialized providers reviews geriatric units and intensivists (Chapters 30 and 38), but similar evidence may be relevant for the rapidly growing field of hospitalists[3-5]
- The use of ultrasound guidance for central line placement (Chapter 21); the premise (decreasing the risk of an invasive procedure through radiologic localization) may also be relevant for ultrasound guidance while performing other challenging procedures, such as thoracentesis

A Focus on Hospital Care

Most of the literature regarding medical errors has been drawn from hospital care.[6-22] For example, the two seminal studies on medical error[22,23] from which the oft-cited extrapolations of yearly deaths from medical error were derived, have highlighted the risks of inpatient care. We applaud recent studies examining the risks of errors in the ambulatory setting[24] but believe that the hospital is an appropriate initial focus for an evidence-based review because the risks associated with hospitalization are high, strategies for improvement are better documented, and the importance of patient trust is paramount.

That said, the reader will see that we allowed the evidence to take us to other sites of care. For example, although much of the literature regarding the occurrence and prevention of adverse drug events is hospital-based, more recent literature highlights outpatient issues and is included in this review. An example is the chapter on decreasing the risk of anticoagulant treatment (Chapter 9), in which two of the most promising practices involve outpatient anticoagulation clinics and patient self-monitoring at home. Similarly, strategies to prevent falls or pressure ulcers are relevant to nursing home patients as well as those in hospitals, and many studies that shed light on these issues come from the former setting.

The Evidence

Chapter 3 describes our strategy for evidence review. As in other evidence-based reviews, we set the bar high. One would not want to endorse a practice unsupported by evidence, nor withhold one substantiated by a high level of proof. In the end, we aimed to identify practices whose supporting evidence was so robust that immediate widespread implementation would lead to major improvements in patient safety. Additionally, we hoped to identify several practices whose promise merited a considerable investment in additional research, but whose evidentiary base was insufficient for immediate endorsement. The results of this effort are summarized in Part V of the Report.

Readers familiar with the state of the evidence regarding quality improvement in areas where this has been a research priority (eg, cardiovascular care) may be surprised and even disappointed by the paucity of high quality evidence for many patient safety practices. The field is young. Just as there had been little public recognition of the risks of health care prior to the first IOM report, there has been relatively little attention paid to such risks—and strategies to mitigate them—among health professionals and researchers. Nevertheless, we found a number of practices supported by high quality evidence for which widespread implementation would save many thousands of lives.

Moreover, there are important methodologic reasons why research in patient safety is particularly challenging. First is the problem of blinding. The physician who has begun to use a new computerized order entry system cannot be blinded to the intervention or its purpose. Second, it is sometimes difficult to measure important outcomes. As in aviation, enormous benefits can be reaped from analyzing "near misses" (with no ultimate harm to patients),[25,26] and yet these outcomes cannot be reliably counted in the absence of potentially obtrusive, and often very expensive observation. Third, many effective practices are multidimensional, and sorting out precisely which part of the intervention works is often quite challenging. Fourth, many of the patient safety problems that generate the most concern (wrong-site surgery, for example) are probably uncommon. This makes demonstrating the success of a "safety practice" in a statistically meaningful manner with respect to outcomes all but impossible.

Finally, establishing firm epidemiologic links between presumed (and accepted) causes and adverse events is critical, and frequently difficult. For instance, verbal orders from doctors to nurses are regarded as a cause of medication errors almost as matter of dogma, with many hospitals prohibiting or strongly discouraging this practice except in emergency situations.[27] Yet, the one study that we could identify that specifically and comprehensively addressed this issue[28] actually reported *fewer* errors among verbal medication orders compared with written medication orders. A similar relationship might be found studying other intuitively plausible "risk factors" for errors, such as "fatigue." Because many health care providers work long hours and/or late at night, analyses of errors will commonly reveal fatigued providers. The question is whether or not fatigue is over-represented among situations that lead to errors. As discussed in Chapter 46, the evidence supporting fatigue as a contributor to adverse events is surprisingly mixed. The point is not that the problem of long work-hours should be ignored, but rather that strong epidemiologic methods need to be applied before concluding that an intuitive cause of errors is in fact causal. These methodologic issues are further explored in Chapters 3 (methods for analyzing the individual practices) and 56 (methods for summarizing the overall evidence).

Improving patient safety is a team effort, and the playbook is often drawn from fields outside of health care. Most medical errors cannot be prevented by perfecting the technical work of individual doctors, nurses or pharmacists. Improving patient safety often involves the

coordinated efforts of multiple members of the health care team, who may adopt strategies from outside health care. Thus, our teams of authors and advisors included physicians, pharmacists, nurses, and experts from non-medical fields. The literature we reviewed was often drawn from journals, books, or Web sites that will not be on most doctors' reading lists. We reviewed several promising practices whose evidence came from the domains of commercial aviation, nuclear safety, and aerospace, and the disciplines of human factors engineering and organizational theory. In reviewing these practices, we tried to be flexible regarding standards of evidence. For example, the randomized trial that is appropriately hailed as the "gold standard" in health care is rarely used in aviation, which instead relies on analyses of detailed case studies and industrial engineering research approaches. (Examples and additional discussion of this issue can be found in Chapter 2.)

We also limited our discussion to the existing practices, recognizing that future technology may make the ones we reviewed obsolete. For example, much of the struggle to find safe ways to administer warfarin (Chapter 9) would be rendered moot by the development of a much safer, but equally effective oral anticoagulant that did not require monitoring. Similarly, the evidence regarding changing the flooring of rooms to decrease falls (Subchapter 26.4) indicated that present options may *decrease* the harm from falls but actually *increase* their rate. Clearly, a better surface would make falls *both* less likely and less harmful. Such a surface has not yet been tested.

Finally, we have tried to define (to the extent possible from the literature) the costs—financial, operational, and political—associated with the patient safety practices we considered. However, we have not made judgments regarding the appropriate expenditures to improve safety. These judgments, which involve complex tradeoffs between public dollars and private ones, and between saving lives by improving patient safety versus doing so by investing in other health care or non-health care practices, will obviously be critical. However, the public reaction to the IOM report, and the media and legislative responses that followed it, seem to indicate that Americans are highly concerned about the risks of medical errors and would welcome public and private investment to decrease them. It seems logical to infer that Americans value safety during a hospitalization just as highly as safety during a transcontinental flight.

The Decision to Include and Exclude Practices

The patient safety/quality interface was only one of several areas that called for judgments regarding which practices to include or exclude from the Report. In general (and quite naturally for an evidence-based review), we excluded those practices for which we found little or no supporting evidence. However, we recognize that patient safety is of great public and professional interest, and that the informed reader might expect to find certain topics in such a review. Therefore, we included several areas notwithstanding their relatively meager evidentiary base. For such high profile topics (such as bar coding to prevent misidentifications, Subchapter 43.1), we tried to fairly present the practice's background, the experience with the practice thus far, and the evidence (and gaps in the evidence) regarding its value. In many of these cases, we end by encouraging additional study or demonstration projects designed to prove whether the practices live up to their promise.

Conversely, another very different group of practices lacked evidence and were excluded from the review. These practices were characterized by their largely self-evident value (in epidemiologic terms, their "face validity"). For example, large randomized studies of the removal of concentrated potassium chloride from patient care floors surely are not necessary in order to recommend this practice as a sensible way of preventing egregious errors that should

never occur. Although some of these types of practices were not included in this "evidence-based" Report, the reader should not infer their exclusion as a lack of endorsement.

A cautionary note is in order when considering such "obviously beneficial" practices. Even an apparently straightforward practice like "signing the site" to prevent surgery or amputation of the wrong body part may lead to unexpected opportunities for error. As mentioned in Subchapter 43.2, some surgeons adopt the practice of marking the intended site, while others mark the site *to avoid*. The clinical research literature furnishes enough examples of practices that everyone "knew" to be beneficial but proved not to be (or even proved to be harmful) once good studies were conducted (antiarrhythmic therapy for ventricular ectopy[29] or hormone replacement therapy to prevent cardiac deaths,[30] for example) that it is reasonable to ask for high-quality evidence for most practices. This is particularly true when practices are expensive, complex to implement, or carry their own risks.

Other Content Issues

There may appear to some readers to be an inordinate focus on clinical issues versus more general patient safety practices. In this and other matters, we went where the evidence took us. Although more than a dozen chapters of the Report consider general safety practices that have been the focus of many patient safety experts for decades (ie, computerized order entry, simulators, crew resource management), most research on patient safety, in fact, has focused on more clinical matters. It is likely that some of this is explained by the previous "disconnect" between research in patient safety and its application. We are hopeful that the Report helps to bridge this gap. We also think it likely that clinical research has been promoted by the significant resources applied to it through Federal, foundation, and industry support. Until recently, patient safety research has had few champions, and even fewer champions with resources. The recent initiatives from AHRQ and other funders are a promising shift in this historical situation, and should yield important benefits.

The reader will notice that there is relatively little specific coverage of issues in pediatrics, obstetrics, and psychiatry. Most of the patient safety practices we reviewed have broad applicability to those fields as well as larger fields such as surgery and medicine. Much of the research in the former fields was too disease-specific to include in this volume. For example, practices to improve the safety of childbirth, although exceptionally important, were excluded because they focused on the care of patients with a single "condition," just as we excluded research focused specifically on the care of patients with pneumonia or stroke.

Readers may also be surprised by the relatively small portion of the Report devoted to the prevention of high-profile and "newsworthy" errors. Even if much of the national attention to patient safety stemmed from concerns about wrong-site surgery or transfusion mix-ups, in fact these are not the dominant patient safety problems today. If widespread use of hip protectors (Subchapter 26.5) leads to a marked decrease in injuries from patient falls, implementing this safety practice would be more important than preventing the few wrong-site surgeries each year, although the former seem far less likely to garner attention in a tabloid.

Conclusions

Making Health Care Safer represents a first effort to approach the field of patient safety through the lens of evidence-based medicine. Just as *To Err is Human* sounded a national alarm regarding patient safety and catalyzed other important commentaries regarding this vital problem, this review is a germinal effort to mine the relevant literature. Although we and the authors tried hard to include all relevant practices and to review all pertinent evidence, we

inevitably missed some of both. Moreover, our effort to rank practices (Part V), many of which have only the beginnings of an evidentiary base, was admittedly ambitious and challenging. We hope that the Report provides a template for future clinicians, researchers, and policy makers as they extend, and inevitably improve upon, our work.

1.2. How to Use this Report

Organizational Framework

This document is divided into five parts:

Part I – The overview introduces many of the methodologic, content, and policy issues.

Part II – We describe, and present the evidence regarding 2 practices that are used to report and respond to patient safety problems: incident reporting and root cause analysis. Since both these "practices" have relevance for all of the patient safety targets and practices covered in Part III, we neither grade them nor rank them.

Part III – In 45 chapters, we review the evidence regarding the utility of 79 patient safety practices. Each chapter is structured in a standard fashion, as follows:

- *Background* – of the patient safety problem and the practice;
- *Practice Description* – in which we try to present the practice at a level of detail that would allow a reader to determine the practice's applicability to their setting;
- *Prevalence and Severity of the Target Safety Problem* – Here, we try to answer the following questions: How common is the safety problem the practice is meant to address? How often does the problem lead to harm? How bad is the harm when it occurs?;
- *Opportunities for Impact* – In this section, we consider the present-day use of the patient safety practice. For example, we found that the use of "unit-dose" drug dispensing was quite common in US hospitals, and thus the opportunity to make an impact with wider dissemination of this practice was relatively low. Conversely, computerized physician order entry is still relatively uncommon, and therefore (assuming it is effective), its widespread implementation could have a far larger impact;
- *Study Designs* – We review the designs of the major studies evaluating the practice. Similarly, *Study Outcomes* looks at the kinds of outcomes (eg, adverse drug events, surgical complications, mortality) that were considered. Our criteria for grading the evidence related to both design and outcomes (more information on other methodologic issues appears in Chapter 3);
- *Evidence for Effectiveness of the Practice* – Here, the authors summarize the findings of the studies and comment on any methodologic concerns that might effect the strength of these findings. This section is often accompanied by tables summarizing the studies and their findings;

- *Potential for Harm* – Many practices that are effective in improving patient safety nonetheless carry the potential for harm. More widespread use of antibiotic prophylaxis or antibiotic-impregnated urinary or vascular catheters could prevent individual hospital-acquired infections yet breed antibiotic resistance. Increasing the use of barrier precautions could also prevent infections, but might lead caregivers to visit patients less often. These sections do not imply that harm is inevitable; rather they highlight the issues that require vigilance during the implementation of effective practices;
- *Costs and Implementation* – Here we consider the costs and other challenges of implementing the practice. We tried to uncover data related to the true costs of implementation (How much does an automatic drug dispensing machine cost a pharmacy?), but also considered some of the potential offsets when there were data available. We also considered issues of feasibility: How much behavior change would be necessary to implement the practice? Would there be major political concerns or important shifts in who pays for care or is compensated for providing it? We tried not to assign values to such issues, but rather to present them so that policy makers could consider them; and
- *Comment* – Here, the authors highlight the state of the evidence, elucidate key implementation issues, and define a potential research agenda.

Part IV – In many ways a mirror of Part II, Part IV considers the ways in which patient safety practices can be implemented. The evidence is reviewed, and some of the benefits and limitations of various strategies are analyzed. As with Part II, we neither grade nor rank these "practices" in Part V since each of these strategies can be applied to most of the patient safety targets and practices covered in Part III.

Part V – Here we analyze the practices. Using methods described in Chapter 56, we synthesize the evidence in Part III to grade and rank the patient safety practices across two major dimensions:

- *Does the evidence support implementation of the practice to improve patient safety?*
- *Does the evidence support additional research into the practice?*

Tips for Users of the Report

We envision that this evidence-based report of patient safety practices will be useful to a wide audience.

Policy makers may use its contents and recommendations to promote or fund the implementation of certain practices. Similarly, local *health care organization leaders* (including leaders of hospitals, medical groups, or integrated delivery systems) may use the data and analysis to choose which practices to consider implementing or further promoting at their institutions.

Researchers will identify a wealth of potential research opportunities. This document is, in many ways, a road map for future research into patient safety. Those who fund research, including (but not limited to) AHRQ, which sponsored this report, will find literally dozens of areas ripe for future studies. In some cases, such studies may be expensive randomized controlled trials, while other practices may require a simple meta-analysis or cost-effectiveness analysis to tip the scales toward or away from recommending a practice.

Clinicians and trainees will, we hope, find the material both interesting and relevant to their practices. One of the salutary consequences of the IOM's reports has been their impact on the attitudes of our future health care providers. We have noticed at our institutions that students and post-graduate trainees in medicine, nursing, and pharmacy are increasingly taking a systems approach to health care. Several of us have heard medical residents refer to issues as "patient safety problems" that beg for a "systems solution" over the past two years, terms that were absent from the medical ward a few years earlier. Clinicians must be part of the solutions to patient safety problems, and their increasing interest in the field is an exceedingly hopeful sign.

Finally, although not primarily written for *patients and their families*, we recognize the broad public interest in, and concern about patient safety and believe that much of the material will be compelling and potentially useful to the public. For years quality advocates have lamented the relatively small impact that "quality report cards" appear to have on patients' choices of health care providers and institutions. One study demonstrated that patients were more likely to respond to a newspaper report of an egregious error than such quality report cards.[31] These data indicate that patients may be interested in knowing whether their institutions, providers, and health plans are proactive in implementing practices that demonstrably decrease the risk of adverse events. Also, any general reader is likely to come away from this Report with heightened sensitivity to the unique challenges that the health care industry—which aims to provide compassionate, individualized care in a dynamic, organizationally and politically complex, and technologically fluid environment—faces in improving safety, and the significant strides that have already been made. Continued improvement will require the infusion of substantial resources, and the public debate about their source, quantity, and target is likely to be lively and very important.

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- **John W. Gosbee, MD, MS**, Director of Patient Safety Information Systems, Department of Veterans Affairs National Center for Patient Safety
- **Peter V. Lee, JD**, President and Chief Executive Officer, Pacific Business Group on Health
- **Arnold Milstein, MD, MPH**, Medical Director, Pacific Business Group on Health; National Health Care Thought Leader, William M. Mercer, Inc.
- **Karlene H. Roberts, PhD**, Professor, Walter A. Haas School of Business, University of California, Berkeley
- **Stephen M. Shortell, PhD**, Blue Cross of California Distinguished Professor of Health Policy and Management and Professor of Organization Behavior, University of California, Berkeley

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Chapter 2. Drawing on Safety Practices from Outside Health Care

The medical profession's previous inattention to medical error, along with other publicized deficiencies (such as a notable lag in adopting sophisticated information technologies) have invited unfavorable comparisons between health care and other complex industries.[1-5] The first of the two recent Institute of Medicine (IOM) reports on the quality of health care in America, *To Err is Human: Building a Safer Health System*,[3] states that "health care is a decade or more behind other high-risk industries in its attention to ensuring basic safety." Consequently, one of the goals of this project was to search these other industries for evidence-based safety strategies that might be applied to health care.

The relatively short timeline of this project necessitated a focused approach to the search for potentially applicable patient safety practices from non-health care writings. Fortunately, many relevant practices have received at least some analysis or empirical study in the health care literature. As a practical solution we present original articles from outside health care as foundational and background material, rather than as a primary source of evidence. Specific topics and practices reviewed in *Making Health Care Safer* that clearly derive from fields outside health care include:

- Incident reporting (Chapter 4)
- Root cause analysis (Chapter 5)
- Computerized physician order entry and decision support as a means of reducing medication errors (Chapter 6)
- Automated medication dispensing systems (Chapter 11)
- Bar coding technology to avoid misidentification errors (Subchapter 43.1)
- Aviation-style preoperative checklists for anesthesia equipment (Chapter 23 and Subchapter 41.3)
- Promoting a "culture of safety" (Chapter 40)
- Crew resource management, a model for teamwork training and crisis response modeled after training approaches in aviation (Chapter 44)
- Simulators (of patients or clinical scenarios) as a training tool (Chapter 45)
- Human factors theory in the design of medical devices and alarms (Chapter 41)

Many readers may still wonder at the relative paucity of safety practices drawn from non-health care sources. While the headline-grabbing assessments of medicine's safety have been criticized by researchers and likely overstate the hazard to patients,[6-8] it is undeniable that some industries, most notably commercial aviation, have safety records far superior to that of health care. One issue we faced in compiling this evidence-based review was the extent to which specific practices could be identified as playing a direct and measurable role in this achievement. Interestingly, the same issue—ascertaining a causative variable—arose in reviewing the literature on anesthesia, likely the one field of medicine with a safety record that rivals aviation's (see also Chapter 56).

As outlined in Chapter 24, significant complications attributable to anesthesia have decreased[9-12] to the point that major morbidity and mortality are now too rare to serve as practical endpoints for measuring the quality of anesthesia care, even in large multicenter studies.[13,14] In attempting to account for this decrease, however, it is very difficult to find evidence supporting a causative role for even the most plausible candidates, such as widely utilized intraoperative monitoring standards.[15] In other words, while the field of anesthesia has clearly made tremendous strides in improving patient safety over the past 50 years, it is hard to discern a particular, isolated practice that accounts for the clear and dramatic secular change in its safety. While at one level, a pragmatist might argue, "who cares, as long as it's safe," trying to adopt the lessons of anesthesia (or for that matter aviation) to the rest of health care is made more challenging by tenuous causality.

Some might argue that, rather than pinpointing specific practices to embrace from other industries, health care institutions should emulate organizational models that promote safety in complex, high-risk industries that manage to operate with high reliability.[16] Analysis of detailed and interesting case studies[17-22] have fueled a school of thought known as *high reliability theory*, whose proponents suggest a number of organizational features that likely reduce the risk of "organizational accidents" and other hazards. A cogently argued alternative position, often called *normal accident theory*, questions not only these prescriptions for organizational change, but fundamentally challenges the idea of high reliability in certain kinds of complex, "tightly coupled" organizations.[23,24] These competing schools of thought offer interesting and valuable insights into the ways that organizational strategies foster safety, while cautioning about the ever-present threat of new sources of error that come with increasingly complex human and technical organizations. Unfortunately, this rich literature does not permit ready synthesis within the framework of evidence-based medicine, even using the less stringent standards we adopted in evaluating non-medical literature (see Chapters 1 and 3).

Even the more engineering-oriented of the disciplines with potential relevance to patient safety yielded a surprising lack of empirical evaluation of safety practices. For instance, numerous techniques for "human error identification" and "error mode prediction" purport to anticipate important errors and develop preventive measures prospectively.[25-27] Their basic approach consists of breaking down the task of interest into component processes, and then assigning a measure of the likelihood of failure to each process. Many of the techniques mentioned in the literature have received little detailed description[25,26] and few have received any formal validation (eg, by comparing predicted failures modes with observed errors).[28,29] Even setting aside demands for validation, the impact of applying these techniques has not been assessed. Total quality management and continuous quality improvement techniques were championed as important tools for change in health care based on their presumed success in other industries, but evaluations of their impact on health care have revealed little evidence of success.[30-33]

In the end, we are left with our feet firmly planted in the middle of competing paradigms. One argues that an evidence-based, scientific approach has served health care well and should not be relaxed simply because a popular practice from a "safer" industry sounds attractive. The other counters that medicine's slavish devotion to the scientific and epidemiologic method has placed us in a patient safety straightjacket, unable to consider the value of practices developed in other fields because of our myopic traditions and "reality."

We see the merits in both arguments. Health care clearly has much to learn from other industries. Just as physicians must learn the "basic sciences" of immunology and molecular biology, providers and leaders interested in making health care safer must learn the "basic

sciences" of organizational theory and human factors engineering. Moreover, the "cases" presented on rounds should, in addition to classical clinical descriptions, also include the tragedy of the Challenger and the successes of Motorola. On the other hand, an unquestioning embrace of dozens of promising practices from other fields is likely to be wasteful, distracting, and potentially dangerous. We are drawn to a dictum from the Cold War era—"Trust, but verify."

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Chapter 3. Evidence-based Review Methodology

Definition and Scope

For this project the UCSF-Stanford Evidence-based Practice Center (EPC) defined a *patient safety practice* as "a type of process or structure whose application reduces the probability of adverse events resulting from exposure to the health care system across a range of conditions or procedures." Examples of practices that meet this definition include computerized physician order entry (Chapter 6), thromboembolism prophylaxis in hospitalized patients (Chapter 31), strategies to reduce falls among hospitalized elders (Chapter 26), and novel education strategies such as the application of "crew resource management" to train operating room staff (Chapter 44). By contrast, practices that are disease-specific and/or directed at the underlying disease and its complications (eg, use of aspirin or beta-blockers to treat acute myocardial infarction) rather than complications of medical care are not included as "patient safety practices." Further discussion of these issues can be found in Chapter 1.

In some cases, the distinction between patient safety and more general quality improvement strategies is difficult to discern. *Quality improvement practices* may also qualify as patient safety practices when the current level of quality is considered "unsafe," but standards to measure safety are often variable, difficult to quantify, and change over time. For example, what constitutes an "adequate" or "safe" level of accuracy in electrocardiogram or radiograph interpretation? Practices to improve performance to at least the "adequate" threshold may reasonably be considered safety practices because they decrease the number of diagnostic errors of omission. On the other hand, we considered practices whose main intent is to improve performance above this threshold to be quality improvement practices. An example of the latter might be the use of computer algorithms to improve the sensitivity of screening mammography.[1]

We generally included practices that involved acute hospital care or care at the interface between inpatient and outpatient settings. This focus reflects the fact that the majority of the safety literature relates to acute care and the belief that systems changes may be more effectively achieved in the more controlled environment of the hospital. However, practices that might be applicable in settings in addition to the hospital were not excluded from consideration. For example, the Report includes practices for preventing decubitus ulcers (Chapter 27) that could be applied in nursing homes as well as hospitals.

The EPC team received input regarding the scope of the Report from the Agency for Healthcare Research and Quality (AHRQ), which commissioned the report. In addition, the EPC team participated in the public meeting of the National Quality Forum (NQF) Safe Practices Committee on January 26, 2001. The NQF was formed in 1999 by consumer, purchaser, provider, health plan, and health service research organizations to create a national strategy for quality improvement. Members of the Safe Practices Committee collaborated with the EPC team to develop the scope of work that would eventually become this Report.

Organization by Domains

To facilitate identification and evaluation of potential patient safety practices, we divided the content for the project into different *domains*. Some cover "content areas" (eg, adverse drug events, nosocomial infections, and complications of surgery). Other domains involve identification of practices within broad (primarily "non-medical") disciplines likely to contain promising approaches to improving patient safety (eg, information technology, human factors research, organizational theory). The domains were derived from a general reading of the

literature and were meant to be as inclusive as possible. The list underwent review for completeness by patient safety experts, clinician-researchers, AHRQ, and the NQF Safe Practices Committee. For each domain we selected a team of author/collaborators with expertise in the relevant subject matter and/or familiarity with the techniques of evidence-based review and technology appraisal. The authors, all of whom are affiliated with major academic centers around the United States, are listed on page 9-13.

Identification of Safety Practices for Evaluation

Search Strategy

The UCSF-Stanford Evidence-based Practice Center Coordinating Team ("The Editors") provided general instructions (Table 3.1) to the teams of authors regarding search strategies for identifying safety practices for evaluation. As necessary, the Editors provided additional guidance and supplementary searches of the literature.

Table 3.1. Search strategy recommended by coordinating team to participating reviewers

a) Electronic bibliographic databases. All searches must include systematic searches of MEDLINE and the Cochrane Library. For many topics it will be necessary to include other databases such as the Cumulative Index to Nursing & Allied Health (CINAHL), PsycLit (PsycINFO), the Institute for Scientific Information's Science Citation Index Expanded**,** Social Sciences Citation Index**,** Arts & Humanities Citation Index, INSPEC (physics, electronics and computing), and ABI/INFORM (business, management, finance, and economics).
b) Hand-searches of bibliographies of retrieved articles and tables of contents of key journals.
c) Grey literature. For many topics it will necessary to review the "grey literature," such as conference proceedings, institutional reports, doctoral theses, and manufacturers' reports.
d) Consultation with experts or workers in the field.

To meet the early dissemination date mandated by AHRQ, the Editors did not require authors to search for non-English language articles or to use EMBASE. These were not specifically excluded, however, and authoring teams could include non-English language articles that addressed important aspects of a topic if they had translation services at their disposal. The Editors did not make recommendations on limiting database searches based on publication date. For this project it was particularly important to identify systematic reviews related to patient safety topics. Published strategies for retrieving systematic reviews have used proprietary MEDLINE interfaces (eg, OVID, SilverPlatter) that are not uniformly available. Moreover, the performance characteristics of these search strategies is unknown.[2,3] Therefore, these strategies were not explicitly recommended. The Editors provided authors with a search algorithm (available upon request) that uses PubMed, the freely available search interface from the National Library of Medicine, designed to retrieve systematic reviews with high sensitivity without overwhelming users with "false positive" hits.[4]

The Editors also performed independent searches of bibliographic databases and grey literature for selected topics.[5] Concurrently, the EPC collaborated with NQF to solicit information about evidence-based practices from NQF members, and consulted with the project's Advisory Panel (page 31), whose members provided additional literature to review.

Inclusion and Exclusion Criteria

The EPC established criteria for selecting which of the identified safety practices warranted evaluation. The criteria address the applicability of the practice across a range of conditions or procedures and the available evidence of the practices' efficacy or effectiveness.

Table 3.2. Inclusion/Exclusion criteria for practices

Inclusion Criteria
1. The practice can be applied in the hospital setting or at the interface between inpatient and outpatient settings AND can be applied to a broad range of health care conditions or procedures.
2. Evidence for the safety practice includes at least one study with a Level 3 or higher study design AND a Level 2 outcome measure. For practices not specifically related to diagnostic or therapeutic interventions, a Level 3 outcome measure is adequate. (See Table 3.3 for definition of "Levels").
Exclusion Criterion
1. No study of the practice meets the methodologic criteria above.

Practices that have only been studied outside the hospital setting or in patients with specific conditions or undergoing specific procedures were included if the authors and Editors agreed that the practices could reasonably be applied in the hospital setting and across a range of conditions or procedures. To increase the number of potentially promising safety practices adapted from outside the field of medicine, we included evidence from studies that used less rigorous measures of patient safety as long as the practices did not specifically relate to diagnostic or therapeutic interventions. These criteria facilitated the inclusion of areas such as teamwork training (Chapter 44) and methods to improve information transfer (Chapter 42).

Each practice's level of evidence for efficacy or effectiveness was assessed in terms of study design (Table 3.3) and study outcomes (Table 3.4). The Editors created the following hierarchies by modifying existing frameworks for evaluating evidence[6-8] and incorporating recommendations from numerous other sources relevant to evidence synthesis.[9-25]

Table 3.3. Hierarchy of study designs*

Level 1. Randomized controlled trials – includes quasi-randomized processes such as alternate allocation
Level 2. Non-randomized controlled trial – a prospective (pre-planned) study, with predetermined eligibility criteria and outcome measures.
Level 3. Observational studies with controls – includes retrospective, interrupted time series (a change in trend attributable to the intervention), case-control studies, cohort studies with controls, and health services research that includes adjustment for likely confounding variables
Level 4. Observational studies without controls (eg, cohort studies without controls and case series)
* Systematic reviews and meta-analyses were assigned to the highest level study design included in the review, followed by an "A" (eg, a systematic review that included at least one randomized controlled trial was designated "Level 1A")

Table 3.4. Hierarchy of outcome measures

Level 1. Clinical outcomes - morbidity, mortality, adverse events
Level 2. Surrogate outcomes - observed errors, intermediate outcomes (eg, laboratory results) with well-established connections to the clinical outcomes of interest (usually adverse events).
Level 3. Other measurable variables with an indirect or unestablished connection to the target safety outcome (eg, pre-test/post-test after an educational intervention, operator self-reports in different experimental situations)
Level 4. No outcomes relevant to decreasing medical errors and/or adverse events (eg, study with patient satisfaction as only measured outcome; article describes an approach to detecting errors but reports no measured outcomes)

Implicit in this hierarchy of outcome measures is that surrogate or intermediate outcomes (Level 2) have an established relationship to the clinical outcomes (Level 1) of interest.[26] Outcomes that are relevant to patient safety but have not been associated with morbidity or mortality were classified as Level 3.

Exceptions to EPC Criteria

Some safety practices did not meet the EPC inclusion criteria because of the paucity of evidence regarding efficacy or effectiveness, but were included in the Report because of their face validity (ie, an informed reader might reasonably expect them to be evaluated; see also Chapter 1). The reviews of these practices clearly identify the quality of evidence culled from medical and non-medical fields.

Evaluation of Safety Practices

For each practice, authors were instructed to research the literature for information on:

- prevalence of the problem targeted by the practice
- severity of the problem targeted by the practice
- the current utilization of the practice
- evidence on efficacy and/or effectiveness of the practice
- the practice's potential for harm
- data on cost if available
- implementation issues

These elements were incorporated into a template in an effort to create as much uniformity across chapters as possible, especially given the widely disparate subject matter and quality of evidence. Since the amount of material for each practice was expected to, and did, vary substantially, the Editors provided general guidance on what was expected for each element, with particular detail devoted to the protocol for searching and reporting evidence related to efficacy and/or effectiveness of the practice.

The protocol outlined the search, the threshold for study inclusion, the elements to abstract from studies, and guidance on reporting information from each study. Authors were asked to review articles from their search to identify practices, and retain those with the better study designs. More focused searches were performed depending on the topic. The threshold for study inclusion related directly to study design. Authors were asked to use their judgment in deciding whether the evidence was sufficient at a given level of study design or whether the evidence from the next level needed to be reviewed. At a minimum, the Editors suggested that there be at least 2 studies of adequate quality to justify excluding discussion of studies of lower level designs. Thus inclusion of 2 adequate clinical trials (Level 1 design) were necessary in order to exclude available evidence from prospective, non-randomized trials (Level 2) on the same topic.

The Editors provided instructions for abstracting each article that met the inclusion criteria based on study design. For each study, a required set of 10 abstraction elements (Table 3.5) was specified. Authors received a detailed explanation of each required abstraction element, as well as complete abstraction examples for the 3 types of study design (Levels 1A, 1, and 3; Level 2 was not included since the information collected was same as Level 1). Research teams were encouraged to abstract any additional elements relevant to the specific subject area.

Table 3.5. Ten Required Abstraction Elements

1. Bibliographic information according to AMA Manual of Style: title, authors, date of publication, source
2. Level of study design (eg, Level 1-3 for studies providing information for effectiveness; Level 4 if needed for relevant additional information) with descriptive material as follows:

   Descriptors

   For Level 1 Systematic Reviews Only

   (a) Identifiable description of methods indicating sources and methods of searching for articles.

   (b) Stated inclusion and exclusion criteria for articles: yes/no.

   (c) Scope of literature included in study.

   For Level 1 or 2 Study Designs (Not Systematic Reviews)

   (a) Blinding: blinded, blinded (unclear), or unblinded

   (b) Describe comparability of groups at baseline – ie, was distribution of potential confounders at baseline equal? If no, which confounders were not equal?

   (c) Loss to follow-up overall: percent of total study population lost to follow-up.

   For Level 3 Study Design (Not Systematic Reviews)

   (a) Description of study design (eg, case-control, interrupted time series).

   (b) Describe comparability of groups at baseline – ie, was distribution of potential confounders at baseline equal? If no, which confounders were not equal?

   (c) Analysis includes adjustment for potential confounders: yes/no. If yes, adjusted for what confounders?
3. Description of intervention (as specific as possible)
4. Description of study population(s) and setting(s)
5. Level of relevant outcome measure(s) (eg, Levels 1-4)
6. Description of relevant outcome measure(s)
7. Main Results: effect size with confidence intervals
8. Information on unintended adverse (or beneficial) effects of practice
9. Information on cost of practice
10. Information on implementation of practice (information that might be of use in whether to and/or how to implement the practice – eg, known barriers to implementation)

We present the salient elements of each included study (eg, study design, population/setting, intervention details, results) in text or tabular form. In addition, we asked authors to highlight weaknesses and biases of studies where the interpretation of the results might be substantially affected. Authors were not asked to formally synthesize or combine (eg, perform a meta-analysis) the evidence across studies for the Report.

Review Process

Authors submitted work to the Editors in 2 phases. In the first phase ("Identification of Safety Practices for Evaluation"), which was submitted approximately 6 weeks after authors were commissioned, authoring teams provided their search strategies, citations, and a preliminary list of patient safety practices to be reviewed. In the subsequent phase ("Evaluation of Safety Practices"), due approximately 12 weeks after commissioning, authors first submitted a draft chapter for each topic, completed abstraction forms, and—after iterative reviews and revisions—a final chapter.

Identification of Safety Practices for Evaluation

The Editors and the Advisory Panel reviewed the list of domains and practices to identify gaps in coverage. In addition, the Editors reviewed final author-submitted lists of excluded practices along with justifications for exclusion (eg, insufficient research design, insufficient outcomes, practice is unique to a single disease process). When there were differences in opinion as to whether a practice actually met the inclusion or exclusion criteria, the Editors made a final disposition after consulting with the author(s). The final practice list, in the form of a Table of Contents for the Report, was circulated to AHRQ and the NQF Safe Practices Committee for comment.

Evaluation of Safety Practices

Chapters were reviewed by the editorial team (The EPC Coordinating Team Editors and our Managing Editor) and queries were relayed to the authors, often requesting further refinement of the analysis or expansion of the results and conclusions. After all chapters were completed, the entire Report was edited to eliminate redundant material and ensure that the focus remained on the evidence regarding safety practices. Near the end of the review process, chapters were distributed to the Advisory Panel for comments, many of which were incorporated. Once the content was finalized, the Editors analyzed and ranked the practices using a methodology described in Chapter 56. The results of these summaries and rankings are presented in Part V of the Report.

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PART II. REPORTING AND RESPONDING TO PATIENT SAFETY PROBLEMS

Chapter 4. Incident Reporting

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Background

Errors in medical care are discovered through a variety of mechanisms. Historically, medical errors were revealed retrospectively through morbidity and mortality committees and malpractice claims data. Prominent studies of medical error have used retrospective chart review to quantify adverse event rates.[1,2] While collection of data in this manner yields important epidemiologic information, it is costly and provides little insight into potential error reduction strategies. Moreover, chart review only detects documented adverse events and often does not capture information regarding their causes. Important errors that produce no injury may go completely undetected by this method.[3-6]

Computerized surveillance may also play a role in uncovering certain types of errors. For instance, medication errors may be discovered through a search for naloxone orders for hospitalized patients, as they presumably reflect the need to reverse overdose of prescribed narcotics.[7,8] Several studies have demonstrated success with computerized identification of adverse drug events.[9-11]

Complex, high-risk industries outside of health care, including aviation, nuclear power, petrochemical processing, steel production, and military operations, have successfully developed incident reporting systems for serious accidents and important "near misses."[6] Incident reporting systems cannot provide accurate epidemiologic data, as the reported incidents likely underestimate the numerator, and the denominator (all opportunities for incidents) remains unknown.

Given the limited availability of sophisticated clinical computer systems and the tremendous resources required to conduct comprehensive chart reviews, incident reporting systems remain an important and relatively inexpensive means of capturing data on errors and adverse events in medicine. Few rigorous studies have analyzed the benefits of incident reporting. This chapter reviews only the literature evaluating the various systems and techniques for collecting error data in this manner, rather than the benefit of the practice itself. This decision reflects our acknowledgment that incident reporting has clearly played a beneficial role in other high-risk industries.[6] The decision also stems from our recognition that a measurable impact of incident reporting on clinical outcomes is unlikely because there is no standard practice by which institutions handle these reports.

Practice Description

Flanagan first described the *critical incident technique* in 1954 to examine military aircraft training accidents.[12] Critical incident reporting involves the identification of preventable incidents (ie, occurrences that could have led, or did lead, to an undesirable outcome[13]) reported by personnel directly involved in the process in question at the time of discovery of the event. The goal of critical incident monitoring is not to gather epidemiologic data *per se*, but rather to gather qualitative data. Nonetheless, if a pattern of errors seems to emerge, prospective studies can be undertaken to test epidemiologic hypotheses.[14]

Incident reports may target events in any or all of 3 basic categories: adverse events, "no harm events," and "near misses." For example, anaphylaxis to penicillin clearly represents an adverse event. Intercepting the medication order prior to administration would constitute a near miss. By contrast, if a patient with a documented history of anaphylaxis to penicillin received a penicillin-like antibiotic (eg, a cephalosporin) but happened not to experience an allergic reaction, it would constitute a no harm event, not a near miss. In other words, when an error does not result in an adverse event for a patient, because the error was "caught," it is a near miss; if the absence of injury is owed to chance it is a no harm event. Broadening the targets of incident reporting to include no harm events and near misses offers several advantages. These events occur 3 to 300 times more often than adverse events,[5,6] they are less likely to provoke guilt or other psychological barriers to reporting,[6] and they involve little medico-legal risk.[14] In addition, hindsight bias[15] is less likely to affect investigations of no harm events and near misses.[6,14]

Barach and Small describe the characteristics of incident reporting systems in non-medical industries.[6] Established systems share the following characteristics:

- they focus on near misses
- they provide incentives for voluntary reporting;
- they ensure confidentiality; and
- they emphasize systems approaches to error analysis.

The majority of these systems were mandated by Federal regulation, and provide for voluntary reporting. All of the systems encourage narrative description of the event. Reporting is promoted by providing incentives including:

- immunity;
- confidentiality;
- outsourcing of report collation;
- rapid feedback to all involved and interested parties; and
- sustained leadership support.[6]

Incident reporting in medicine takes many forms. Since 1975, the US Food and Drug Administration (FDA) has mandated reporting of major blood transfusion reactions, focusing on preventable deaths and serious injuries.[16] Although the critical incident technique found some early applications in medicine,[17,18] its current use is largely attributable to Cooper's introduction of incident reporting to anesthesia in 1978,[19] conducting retrospective interviews with anesthesiologists about preventable incidents or errors that occurred while patients were under their care. Recently, near miss and adverse event reporting systems have proliferated in single institution settings (such as in intensive care units (ICUs)[20,21]), regional settings (such as the New York State transfusion system[22]), and for national surveillance (eg, the National Nosocomial Infections Surveillance System administered by the Federal Centers for Disease Control and Prevention.)[23]

All of the above examples focus on types of events (transfusion events or nosocomial infections) or areas of practice (ICUs). Incident reporting in hospitals cuts a wider swath, capturing errors and departures from expected procedures or outcomes (Table 4.1). However, because risk management departments tend to oversee incident reporting systems in some capacity, these systems more often focus on incident outcomes, not categories. Few data describe the operation of these institution-specific systems, but underreporting appears endemic.[24]

In 1995, hospital-based surveillance was mandated by the Joint Commission on the Accreditation of Healthcare Organizations (JCAHO)[26] because of a perception that incidents resulting in harm were occurring frequently.[28] JCAHO employs the term *sentinel event* in lieu of critical incident, and defines it as follows:

> *An unexpected occurrence involving death or serious physical or psychological injury, or the risk thereof. Serious injury specifically includes loss of limb or function. The phrase "or the risk thereof" includes any process variation for which a recurrence would carry a significant chance of a serious adverse outcome.*[26]

As one component of its Sentinel Event Policy, JCAHO created a Sentinel Event Database. The JCAHO database accepts voluntary reports of sentinel events from member institutions, patients and families, and the press.[26] The particulars of the reporting process are left to the member health care organizations. JCAHO also mandates that accredited hospitals perform root cause analysis (see Chapter 5) of important sentinel events. Data on sentinel events are collated, analyzed, and shared through a website,[29] an online publication,[30] and its newsletter *Sentinel Event Perspectives*.[31]

Another example of a national incident reporting system is the Australian Incident Monitoring Study (AIMS), under the auspices of the Australian Patient Safety Foundation.[13] Investigators created an anonymous and voluntary near miss and adverse event reporting system for anesthetists in Australia. Ninety participating hospitals and practices named on-site coordinators. The AIMS group developed a form that was distributed to participants. The form contained instructions, definitions, space for narrative of the event, and structured sections to record the anesthesia and procedure, demographics about the patient and anesthetist, and what, when, why, where, and how the event occurred. The results of the first 2000 reports were published together, following a special symposium.[32]

The experiences of the JCAHO Sentinel Event Database and the Australian Incident Monitoring Study are explored further below.

Prevalence and Severity of the Target Safety Problem

The true prevalence of events appropriate for incident reporting is impossible to estimate with any accuracy, as it includes actual adverse events as well as near misses and no harm events. The Aviation Safety Reporting System (ASRS), a national reporting system for near misses in the airline industry,33,34 currently processes approximately 30,000 reports annually,35 exceeding by many orders of magnitude the total number of airline accidents each year.34 The number of reports submitted to a comparable system in health care would presumably number in the millions if all adverse events, no harm events, and near misses were captured.

By contrast, over 6 years of operation, the JCAHO Sentinel Event Database has captured only 1152 events, 62% of which occurred in general hospitals. Two-thirds of the events were self-reported by institutions, with the remainder coming from patient complaints, media stories and other sources.[29] These statistics are clearly affected by underreporting and consist primarily of serious adverse events (76% of events reported resulted in patient deaths), not near misses. As discussed in the chapter on wrong-site surgeries (Subchapter 43.2), comparing JCAHO reports with data from the mandatory incident reporting system maintained by the New York State Department of Health[36] suggests that the JCAHO statistics underestimate the true incidence of target events by at least a factor of 20.

Opportunities for Impact

Most hospitals' incident reporting systems fail to capture the majority of errors and near misses.[24] Studies of medical services suggest that only 1.5% of all adverse events result in an incident report[37] and only 6% of adverse drug events are identified through traditional incident reporting or a telephone hotline.[24] The American College of Surgeons estimates that incident reports generally capture only 5-30% of adverse events.[38] A study of a general surgery service showed that only 20% of complications on a surgical service ever resulted in discussion at Morbidity and Mortality rounds.[39] Given the endemic underreporting revealed in the literature, modifications to the configuration and operation of the typical hospital reporting system could yield higher capture rates of relevant clinical data.

Study Designs

We analyzed 5 studies that evaluated different methods of critical incident reporting. Two studies prospectively investigated incident reporting compared with observational data collection[24,39] and one utilized retrospective chart review.[37] Two additional studies looked at enhanced incident reporting by active solicitation of physician input compared with background hospital quality assurance (QA) measures.[40,41] In addition, we reviewed JCAHO's report of its Sentinel Event Database, and the Australian Incident Monitoring Study, both because of the large sizes and the high profiles of the studies.[13,26] Additional reports of critical incident reporting systems in the medical literature consist primarily of uncontrolled observational trials[42-44] that are not reviewed in this chapter.

Study Outcomes

In general, published studies of incident reporting do not seek to establish the benefit of incident reporting as a patient safety practice. Their principal goal is to determine if incident reporting, as it is practiced, captures the relevant events.[40] In fact, no studies have established the value of incident reporting on patient safety outcomes.

The large JCAHO and Australian databases provide data about reporting rates, and an array of quantitative and qualitative information about the reported incidents, including the identity of the reporter, time of report, severity and type of error.[13,26] Clearly these do not represent clinical outcomes, but they may be reasonable surrogates for the organizational focus on patient safety. For instance, increased incident reporting rates may not be indicative of an unsafe organization,[45] but may reflect a shift in organizational culture to increased acceptance of quality improvement and other organizational changes.[3,5]

None of the studies reviewed captured outcomes such as morbidity or error rates. The AIMS group published an entire symposium which reported the quantitative and qualitative data regarding 2000 critical incidents in anesthesia.[13] However, only a small portion of these incidents were prospectively evaluated.[14] None of the studies reviewed for this chapter performed formal root cause analyses on reported errors (Chapter 5).

Evidence for Effectiveness of the Practice

As described above, 6 years of JCAHO sentinel event data have captured merely 1152 events, none of which include near misses.[29] Despite collecting what is likely to represent only a fraction of the target events, JCAHO has compiled the events, reviewed the root cause analyses and provided recommendations for procedures to improve patient safety for events ranging from wrong-site surgeries to infusion pump-related adverse events (Table 4.2). This information may

prove to be particularly useful in the case of rare events such as wrong-site surgery, where national collection of incidents can yield a more statistically useful sample size.

The first 2000 incident reports to AIMS from 90 member institutions were published in 1993.[13] In contrast to the JCAHO data, all events were self-reported by anesthetists and only 2% of events reported resulted in patient deaths. A full 44% of events had negligible effect on patient outcome. Ninety percent of reports had identified systems failures, and 79% had identified human failures. The AIMS data were similar to those of Cooper[19] in terms of percent of incidents with reported human failures, timing of events with regard to phase of anesthesia, and type of events (breathing circuit misconnections were between 2% and 3% in both studies).[13,19] The AIMS data are also similar to American "closed-claims" data in terms of pattern, nature and proportion of the total number of reports for several types of adverse events,[13] which lends further credibility to the reports.

The AIMS data, although also likely to be affected by underreporting because of its voluntary nature, clearly captures a higher proportion of critical incidents than the JCAHO Sentinel Event Database. Despite coming from only 90 participating sites, AIMS received more reports over a similar time frame than the JCAHO did from the several thousand accredited United States hospitals. This disparity may be explained by the fact that AIMS institutions were self-selected, and that the culture of anesthesia is more attuned to patient safety concerns.[47]

The poor capture rate of incident reporting systems in American hospitals has not gone unnoticed. Cullen et al[24] prospectively investigated usual hospital incident reporting compared to observational data collection for adverse drug events (ADE logs, daily solicitation from hospital personnel, and chart review) in 5 patient care units of a tertiary care hospital. Only 6% of ADEs were identified and only 8% of serious ADEs were reported. These findings are similar to those in the pharmacy literature,[48,49] and are attributed to cultural and environmental factors. A similar study on a general surgical service found that 40% of patients suffered complications.[39] While chart documentation was excellent (94%), only 20% of complications were discussed at Morbidity and Mortality rounds.

Active solicitation of physician reporting has been suggested as a way to improve adverse event and near miss detection rates. Weingart et al[41] employed direct physician interviews supplemented by email reminders to increase detection of adverse events in a tertiary care hospital. The physicians reported an entirely unique set of adverse events compared with those captured by the hospital incident reporting system. Of 168 events, only one was reported by both methods. O'Neil et al[37] used e-mail to elicit adverse events from housestaff and compared these with those found on retrospective chart review. Of 174 events identified, 41 were detected by both methods. The house officers appeared to capture preventable adverse events at a higher rate (62.5% v. 32%, p=0.003). In addition, the hospital's risk management system detected only 4 of 174 adverse events. Welsh et al[40] employed prompting of house officers at morning report to augment hospital incident reporting systems. There was overlap in reporting in only 2.6% of 341 adverse events that occurred during the study. In addition, although the number of events house officers reported increased with daily prompting, the quantity rapidly decreased when prompting ceased. In summary, there is evidence that active solicitation of critical incident reports by physicians can augment existing databases, identifying incidents not detected through other means, although the response may not be durable.[37,40,41]

Potential for Harm

Users may view reporting systems with skepticism, particularly the system's ability to maintain confidentiality and shield participants from legal exposure.[28] In many states, critical

incident reporting and analysis count as peer review activities and are protected from legal discovery.[28,50] However, other states offer little or no protection, and reporting events to external agencies (eg, to JCAHO) may obliterate the few protections that do exist. In recognition of this problem, JCAHO's Terms of Agreement with hospitals now includes a provision identifying JCAHO as a participant in each hospital's quality improvement process.[28]

Costs and Implementation

Few estimates of costs have been reported in the literature. In general, authors remarked that incident reporting was far less expensive than retrospective review. One single center study estimated that physician reporting was less costly ($15,000) than retrospective record review ($54,000) over a 4-month period.[37] A survey of administrators of reporting systems from non-medical industries reported a consensus that costs were far offset by the potential benefits.[6]

Comment

The wide variation in reporting of incidents may have more to do with reporting incentives and local culture than with the quality of medicine practiced there.[24] When institutions prioritize incident reporting among medical staff and trainees, however, the incident reporting systems seem to capture a distinct set of events from those captured by chart review and traditional risk management[40,41] and events captured in this manner may be more preventable.[37]

The addition of anonymous or non-punitive systems is likely to increase the rates of incident reporting and detection.[51] Other investigators have also noted increases in reporting when new systems are implemented and a culture conducive to reporting is maintained.[40,52] Several studies suggest that direct solicitation of physicians results in reports that are more likely to be distinct, preventable, and more severe than those obtained by other means.[8,37,41]

The nature of incident reporting, replete with hindsight bias, lost information, and lost contextual clues makes it unlikely that robust data will ever link it directly with improved outcomes. Nonetheless, incident reporting appears to be growing in importance in medicine. The Institute of Medicine report, *To Err is Human*,[53] has prompted calls for mandatory reporting of medical errors to continue in the United States.[54-57] England's National Health Service plans to launch a national incident reporting system as well, which has raised concerns similar to those voiced in the American medical community.[58] While the literature to date does not permit an evidence-based resolution of the debate over mandatory versus voluntary incident reporting, it is clear that incident reporting represents just one of several potential sources of information about patient safety and that these sources should be regarded as complementary. In other industries incident reporting has succeeded when it is mandated by regulatory agencies or is anonymous and voluntary on the part of reporters, and when it provides incentives and feedback to reporters.[6] The ability of health care organizations to replicate the successes of other industries in their use of incident reporting systems[6] will undoubtedly depend in large part on the uses to which they put these data. Specifically, success or failure may depend on whether health care organizations use the data to fuel institutional quality improvement rather than to generate individual performance evaluations.

Table 4.1. Examples of events reported to hospital incident reporting systems[25-27]

Adverse Outcomes	Procedural Breakdowns	Catastrophic Events
• Unexpected death or disability • Inpatient falls or "mishaps" • Institutionally-acquired burns • Institutionally-acquired pressure sores	• Errors or unexpected complications related to the administration of drugs or transfusion • Discharges against medical advice ("AMA") • Significant delays in diagnosis or diagnostic testing • Breach of confidentiality	• Performance of a procedure on the wrong body part ("wrong-site surgery") • Performance of a procedure on the wrong patient • Infant abduction or discharge to wrong family • Rape of a hospitalized patient • Suicide of a hospitalized patient

Table 4.2. Sentinel event alerts published by JCAHO following analysis of incident reports[46]

- Medication Error Prevention – Potassium Chloride
- Lessons Learned: Wrong Site Surgery
- Inpatient Suicides: Recommendations for Prevention
- Preventing Restraint Deaths
- Infant Abductions: Preventing Future Occurrences
- High-Alert Medications and Patient Safety
- Operative and Postoperative Complications: Lessons for the Future
- Fatal Falls: Lessons for the Future
- Infusion Pumps: Preventing Future Adverse Events
- Lessons Learned: Fires in the Home Care Setting
- Kernicterus Threatens Healthy Newborns

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Chapter 5. Root Cause Analysis

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Background

Historically, medicine has relied heavily on quantitative approaches for quality improvement and error reduction. For instance, the US Food and Drug Administration (FDA) has collected data on major transfusion errors since the mid-1970s.[1,2] Using the statistical power of these nationwide data, the most common types of errors have been periodically reviewed and systems improvements recommended.[3]

These epidemiologic techniques are suited to complications that occur with reasonable frequency, but not for rare (but nonetheless important) errors. Outside of medicine, high-risk industries have developed techniques to address major accidents. Clearly the nuclear power industry cannot wait for several Three Mile Island-type events to occur in order to conduct valid analyses to determine the likely causes.

A retrospective approach to error analysis, called root cause analysis (RCA), is widely applied to investigate major industrial accidents.[4] RCA has its foundations in industrial psychology and human factors engineering. Many experts have championed it for the investigation of sentinel events in medicine.[5-7] In 1997, the Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) mandated the use of RCA in the investigation of sentinel events in accredited hospitals.[8]

The most commonly cited taxonomy of human error in the medical literature is based on the work of James Reason.[4,9,10] Reason describes 2 major categories of error: active error, which generally occurs at the point of human interface with a complex system, and latent error, which represents failures of system design. RCA is generally employed to uncover latent errors underlying a sentinel event.[6,7]

RCA provides a structured and process-focused framework with which to approach sentinel event analysis. Its cardinal tenet is to avoid the pervasive and counterproductive culture of individual blame.[11,12] Systems and organizational issues can be identified and addressed, and active errors are acknowledged.[6] Systematic application of RCA may uncover common root causes that link a disparate collection of accidents (ie, a variety of serious adverse events occurring at shift change). Careful analysis may suggest system changes designed to prevent future incidents.[13]

Despite these intriguing qualities, RCA has significant methodologic limitations. RCAs are in essence uncontrolled case studies. As the occurrence of accidents is highly unpredictable, it is impossible to know if the root cause established by the analysis is the cause of the accident.[14] In addition, RCAs may be tainted by hindsight bias.[4,15,16] Other biases stem from how deeply the causes are probed and influenced by the prevailing concerns of the day.[16,17] The fact that technological failures (device malfunction), which previously represented the focus of most accident analyses, have been supplanted by staffing issues, management failures, and information systems problems may be an example of the latter bias.[17] Finally, RCAs are time-consuming and labor intensive.

Despite legitimate concerns about the place of RCA in medical error reduction, the JCAHO mandate ensures that RCA will be widely used to analyze sentinel events.[8] Qualitative methods such as RCA should be used to supplement quantitative methods, to generate new hypotheses, and to examine events not amenable to quantitative methods (for example, those that occur rarely).[18] As such, its credibility as a research tool should be judged by the standards appropriate for qualitative research, not quantitative.[19,20] Yet, the outcomes and costs associated with RCA are largely unreported. This chapter reviews the small body of published literature regarding the use of RCA in the investigation of medical errors.

Practice Description

To be credible, RCA requires rigorous application of established qualitative techniques. Once a sentinel event has been identified for analysis (eg, a major chemotherapy dosing error, a case of wrong-site surgery, or major ABO incompatible transfusion reaction), a multidisciplinary team is assembled to direct the investigation. The members of this team should be trained in the techniques and goals of RCA, as the tendency to revert to personal biases is strong.[13,14] Multiple investigators allow triangulation or corroboration of major findings and increase the validity of the final results.[19] Based on the concepts of active and latent error described above, accident analysis is generally broken down into the following steps[6,7]:

1. *Data collection*: establishment of what happened through structured interviews, document review, and/or field observation. These data are used to generate a sequence or timeline of events preceeding and following the event;
2. *Data analysis*: an iterative process to examine the sequence of events generated above with the goals of determining the common underlying factors:
   (i) Establishment of how the event happened by identification of active failures in the sequence;
   (ii) Establishment of why the event happened through identification of latent failures in the sequence which are generalizable.

In order to ensure consideration of all potential root causes of error, one popular conceptual framework for contributing factors has been proposed based on work by Reason.[7] Several other frameworks also exist.[21,22] The categories of factors influencing clinical practice include institutional/regulatory, organizational/management, work environment, team factors, staff factors, task factors, and patient characteristics. Each category can be expanded to provide more detail. A credible RCA considers root causes in all categories before rejecting a factor or category of factors as non-contributory. A standardized template in the form of a tree (or "Ishikawa") may help direct the process of identifying contributing factors, with such factors leading to the event grouped (on tree "roots") by category. Category labels may vary depending on the setting.[23]

At the conclusion of the RCA, the team summarizes the underlying causes and their relative contributions, and begins to identify administrative and systems problems that might be candidates for redesign.[6]

Prevalence and Severity of the Target Safety Problem

JCAHO's 6-year-old sentinel event database of voluntarily reported incidents (see Chapter 4) has captured a mere 1152 events, of which 62% occurred in general hospitals. Two-thirds of the events were self-reported by institutions, with the remainder coming from patient

complaints, media stories and other sources.[24] These statistics are clearly affected by underreporting and consist primarily of serious adverse events (76% of events reported resulted in patient deaths), not near misses. The number of sentinel events appropriate for RCA is likely to be orders of magnitude greater.

The selection of events for RCA may be crucial to its successful implementation on a regular basis. Clearly, it cannot be performed for every medical error. JCAHO provides guidance for hospitals about which events are considered "sentinel,"[8] but the decision to conduct RCA is at the discretion of the leadership of the organization.[12]

If the number of events is large and homogeneous, many events can be excluded from analysis. In a transfusion medicine reporting system, all events were screened after initial report and entered in the database, but those not considered sufficiently unique did not undergo RCA.[25]

Opportunities for Impact

While routine RCA of sentinel events is mandated, the degree to which hospitals carry out credible RCAs is unknown. Given the numerous demands on hospital administrators and clinical staff, it is likely that many hospitals fail to give this process a high profile, assigning the task to a few personnel with minimal training in RCA rather than involving trained leaders from all relevant departments. The degree of underreporting to JCAHO suggests that many hospitals are wary of probationary status and the legal implications of disclosure of sentinel events and the results of RCAs.[12,26]

Study Designs

As RCA is a qualitative technique, most reports in the literature are case studies or case series of its application in medicine.[6,27-30] There is little published literature that systematically evaluates the impact of formal RCA on error rates. The most rigorous study comes from a tertiary referral hospital in Texas that systematically applied RCA to all serious adverse drug events (ADEs) considered preventable. The time series contained background data during the initial implementation period of 12 months and a 17-month follow-up phase.[13]

Study Outcomes

Published reports of the application of RCA in medicine generally present incident reporting rates, categories of active errors determined by the RCA, categories of root causes (latent errors) of the events, and suggested systems improvements. While these do not represent clinical outcomes, they are reasonable surrogates for evaluation. For instance, increased incident reporting rates may reflect an institution's shift toward increased acceptance of quality improvement and organizational change.[5,21]

Evidence for Effectiveness of the Practice

The Texas study revealed a 45% decrease in the rate of voluntarily reported serious ADEs between the study and follow-up periods (7.2 per 100,000 to 4.0 per 100,000 patient-days, $p<0.001$).[13] Although there were no fatal ADEs in the follow-up period, the small number of mortalities in the baseline period resulted in extremely wide confidence intervals, so that comparing the mortality rates serves little purpose.[13]

The authors of the Texas study attribute the decline in serious ADEs to the implementation of blame-free RCA, which prompted important leadership focus and policy changes related to safety issues. Other changes consisted of improvements in numerous aspects of the medication ordering and distribution processes (eg, the application of "forcing" and "constraining" functions that make it impossible to perform certain common errors), as well as more general changes in organizational features, such as staffing levels.

The significance of the decline in ADEs and its relationship to RCA in the Texas study is unclear. As the study followed a highly publicized, fatal ADE at the hospital, other cultural or systems changes may have contributed to the measured effect. The authors were unable to identify a control group, nor did they report data from serious ADEs in the year preceding the study. Their data may reflect underreporting, as there is no active surveillance for ADEs at the study hospital, leaving the authors to rely on voluntary reports. The decline in reported ADEs may actually call into question the robustness of their reporting system as other studies have found that instituting a blame-free system leads to large increases in event reporting.[5] On the other hand, it seems unlikely that serious ADEs would be missed in a culture of heightened sensitivity to error.

In a separate report, an event reporting system for transfusion medicine was implemented at 2 blood centers and 2 transfusion services.[25] Unique events were subjected to RCA, and all events were classified using a model adapted from the petrochemical industry.[21] There were 503 events reported and 1238 root causes identified. Human failure accounted for 46% of causes, 27% were due to technical failures, and 27% were from organizational failures. This distribution was very similar to that seen in the petrochemical industry, perhaps an indication of the universality of causes of error in complex systems, regardless of industry.

Potential for Harm

The potential for harm with the use of RCA has received only passing mention in the literature, but might result from flawed analyses.[31] The costs of pursuing absolute safety may be the implementation of increasingly complex and expensive safeguards, which in themselves are prone to systems failures.[4,16] Ill-conceived RCAs which result in little effective systems improvement could also dampen enthusiasm for the entire quality improvement process. Arguably the harm caused by pursuit of incorrect root causes must be offset by the costs of not pursuing them at all.

Costs and Implementation

No estimates of costs of RCA have appeared in the literature, but as it is a labor-intensive process they are likely significant. Counterproductive cultural norms and medico-legal concerns similar to those seen in incident reporting may hinder implementation of RCA.[12,26] The authors of the Texas study note the importance of clear expressions of administrative support for the process of blame-free RCA.[13] Other studies note the receptiveness of respondents to blame-free

investigation in the name of quality improvement, with one health system reporting a sustained 10-fold increase in reporting.[25,27]

Comment

Root cause analyses systematically search out latent or system failures that underlie adverse events or near misses. They are limited by their retrospective and inherently speculative nature. There is insufficient evidence in the medical literature to support RCA as a proven patient safety practice, however it may represent an important qualitative tool that is complementary to other techniques employed in error reduction. When applied appropriately, RCA may illuminate targets for change, and, in certain health care contexts, may generate testable hypotheses. The use of RCA merits more consideration, as it lends a formal structure to efforts to learn from past mistakes.

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PART III. PATIENT SAFETY PRACTICES & TARGETS

Section A. Adverse Drug Events (ADEs)

Section B. Infection Control

Section C. Surgery, Anesthesia, and Perioperative Medicine

Section D. Safety Practices for Hospitalized or Institutionalized Elders

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Section A. Adverse Drug Events (ADEs)

Chapter 6. Computerized Physician Order Entry (CPOE) with Clinical Decision Support Systems (CDSSs)

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Background

Medication errors and *adverse drug events* (ADEs) are common, costly, and clinically important problems.[1-7] Two inpatient studies, one in adults and one in pediatrics, have found that about half of medication errors occur at the stage of drug ordering,[2, 7] although direct observation studies have indicated that many errors also occur at the administration stage.[8] The principal types of medication errors, apart from missing a dose, include incorrect medication dose, frequency, or route.[2] ADEs are injuries that result from the use of a drug. Systems-based analysis of medication errors and ADEs suggest that changes in the medication ordering system, including the introduction of *computerized physician order entry* (CPOE) with *clinical decision support systems* (CDSSs), may reduce medication-related errors.[9]

Despite growing evidence and public mandates, implementation of CPOE has been limited. The Leapfrog Group, a consortium of companies from the Business Roundtable, has endorsed CPOE in hospitals as one of the 3 changes that would most improve patient safety in America (see also Chapter 55).[10] A Medicare Payment Advisory Commission report suggested instituting financial incentives for CPOE implementation.[11] US Senators Bob Graham (D-Fla.) and Olympia Snowe (R-Maine) recently introduced a bill, entitled the "Medication Errors Reduction Act of 2001," to establish an informatics system grant program for hospitals and skilled nursing facilities.[12] In addition, California recently enacted legislation stipulating that acute care hospitals implement information technology, such as CPOE to reduce medication-related errors.[13]

Practice Description

CPOE refers to a variety of computer-based systems of ordering medications, which share the common features of automating the medication ordering process. Basic CPOE ensures standardized, legible, complete orders by only accepting typed orders in a standard and complete format. Almost all CPOE systems include or interface with CDSSs of varying sophistication. Basic clinical decision support may include suggestions or default values for drug doses, routes, and frequencies. More sophisticated CDSSs can perform drug allergy checks, drug-laboratory value checks, drug-drug interaction checks, in addition to providing reminders about corollary orders (eg, prompting the user to order glucose checks after ordering insulin) or drug guidelines to the physician at the time of drug ordering (see also Chapter 53).

At times, CDSSs are implemented without CPOE. Isolated CDSSs can provide advice on drug selection, dosages, and duration. More refined CDSSs can incorporate patient-specific information (for example recommending appropriate anticoagulation regimens), or incorporate pathogen-specific information such as suggesting appropriate anti-infective regimens. After viewing such advice, the physician proceeds with a conventional handwritten medication order.

Prevalence and Severity of the Target Safety Problem

It is estimated that over 770,000 people are injured or die in hospitals from ADEs annually.[4, 5, 14] The few hospitals that have studied incidence rates of ADEs have documented rates ranging from 2 to 7 per 100 admissions.[2, 4, 15, 16] A precise national estimate is difficult to calculate due to the variety of criteria and definitions used by researchers.[17] One study of preventable inpatient ADEs in adults demonstrated that 56% occurred at the stage of ordering, 34% at administration, 6% at transcribing, and 4% at dispensing.[2] In this study, the drug class most commonly associated with preventable ADEs was analgesics, followed by sedatives and antibiotics. Even fewer studies have been conducted in the outpatient setting. One recent cross-sectional chart review and patient care survey found an ADE rate of 3% in adult primary care outpatients.[18]

Opportunities for Impact

Clear data do not exist about the prevalence of CPOE with CDSSs or isolated CDSSs. One survey of 668 hospitals indicated that 15% had at least partially implemented CPOE.[19] A slightly more recent survey of pharmacy directors at 1050 acute care hospitals in the United States (51% response rate) reported that 13% of hospitals had an electronic medication order-entry system in place, while an additional 27% stated they were in the process of obtaining such a sysytem.[20]

Study Designs

The 4 studies listed in Table 6.1 evaluated CPOE with CDSSs.[21-24] The first study, a randomized controlled trial evaluating the utility of CPOE in improving prescribing for corollary orders, was conducted by the Regenstrief Institute for Health Care (affiliated with the Indiana University School of Medicine).[21] The remaining 3 studies evaluated the CPOE system at Brigham and Women's Hospital (BWH).[22-24] Of note, both the Regenstrief and BWH systems are "home-grown" rather than "off-the-shelf" commercial systems. The first BWH study was a cross-sectional analysis comparing an intervention period of CPOE with CDSSs for adult inpatients on medical, surgical, and intensive care wards with a historical period.[22] The other 2 BWH studies were time series analyses of orders written for adult inpatients.[23, 24]

Table 6.2 lists 4 studies[25-28] that evaluated isolated CDSSs, 2 of which represent systematic reviews.[25, 26] Hunt et al[25] updated an earlier systematic review,[29] and included 68 studies that prospectively evaluated use of CDSSs in a clinical setting by a healthcare practitioner with a concurrent control. Importantly, Hunt et al included studies of outpatient settings in their review. Walton's review addressed 15 articles that studied computerized advice on drug dosage for inpatients.[26] Evans et al, at Latter Day Saints Hospital, performed the other 2 studies,[27, 28] again on a "home-grown" system. The first was a randomized controlled trial of empiric antibiotic selection using CDSSs.[27] The second study was a cross-sectional analysis comparing an intervention period of a computer-assisted management program for anti-infectives with a historical control period.[28] This second study[28] was likely excluded from the systematic review by Hunt et al[25] for methodologic reasons, as it did not have a concurrent control. The reasons for excluding the first study[27] remain unclear. Finally, it is important to emphasize again that of the primary studies that were included, 6 of 8 were performed at 3 institutions with sophisticated "home-grown" systems.

Study Outcomes

Adverse drug events (ADEs), (injuries that result from the use of drugs) by definition constitute clinical outcomes (Level 1). ADEs that are associated with a medication error are considered preventable, while those not associated with a medication error (eg, known medication side effects) are considered non-preventable. An example of a preventable ADE is the development of rash after the administration of ampicillin to a known penicillin-allergic patient. In contrast, a non-preventable ADE would be development of an ampicillin-associated rash in a patient with no known drug allergies. Non-intercepted serious medication errors include non-intercepted potential ADEs and preventable ADEs (ie, medication errors that either have the potential or actually cause harm to a patient).

Medication errors refer to errors in the processes of ordering, transcribing, dispensing, administering, or monitoring medications, irrespective of the outcome (ie, injury to the patient). One example is an order written for amoxicillin without a route of administration. Other medication errors have a greater potential for patient harm and so are often designated as "serious medication errors" or "potential ADEs" – eg, an order for amoxicillin in a patient with past anaphylaxis to penicillin.

Potential ADEs may or may not be intercepted before reaching the patient. An example of an intercepted potential ADE would be an order written for an acetaminophen overdose that is intercepted and corrected by a nurse before reaching the patient. An example of a non-intercepted potential ADE would be an administered overdose of acetaminophen to a patient who did not suffer any sequelae.

Medication errors include a mixture of serious medication errors with a significant potential for patient injury (Level 2) and other deviations from recommended practice that do not have a clear or established connection to adverse events (Level 3). Examples of the latter include failure to choose the optimal dosing schedule for a medication and many standards related to monitoring serum drug levels and routine electrolytes.

Only 2 studies (from a single institution) evaluating CPOE with CDSSs included ADEs as a secondary outcome (Level 1),[22] and even these studies primary outcomes were serious medication errors (Level 2) and non-intercepted medication errors.[23] The other studies reported a variety of other errors often involving mixtures of Level 2 and Level 3 outcomes – eg, "prescribing practices"[24] and "corollary orders."[21] *Corollary orders* refer to orders required to detect or ameliorate adverse reactions that may result from the trigger order - eg, checking the serum creatinine a minimum of 2 times per week in a patient receiving a nephrotoxic agent such as amphotericin. Many corollary orders capture Level 3 outcomes, as failure to prescribe these orders would in most cases have no clear impact on clinical outcomes – eg, failure to order daily tests for fecal occult blood in patients on heparin or screening audiometry for patients receiving vancomycin.[21]

The predominance of Level 2 and 3 outcomes in these studies is understandable, given the much higher frequency of these outcomes compared to actual ADEs and the enormous costs of conducting these studies.

Similarly, the studies evaluating CDSSs reported a mixture of outcomes from Levels 1-3. Hunt et al reviewed articles to determine changes in patient outcomes (Level 1) or physician performance (Levels 2 and 3, depending on the practice).[25] Walton et al evaluated a range of outcomes (Levels 1-3), including reductions in "adverse reactions and unwanted effects" (Level 1).[26] In one study, Evans et al determined rates of pathogen susceptibility to an antibiotic

regimen[27] (Level 2); another study by the same authors evaluated adverse drug events caused by anti-infectives as a main outcome (Level 1).[28]

Evidence for Effectiveness of the Practice

Of the 2 studies at BWH that addressed the impact of CPOE with CDSSs on medication errors and ADEs, the first demonstrated a 55% decrease in serious medication errors.[22] As a secondary outcome, this study found a 17% decrease in preventable ADEs, which was not statistically significant. The second study, a time series analysis, demonstrated marked reductions in all medication errors excluding missed dose errors and in non-intercepted serious medication errors.[23] The number of ADEs in this study was quite small – 25 in the baseline period and 18 in the third of the 3 periods with CPOE and CDSS. Correcting for the number of opportunities for errors, the total number of ADEs/1000 patient days decreased from 14.7 to 9.6 ($p=0.09$). For the sub-category of preventable ADEs, the reduction (from 5 to 2) achieved borderline statistical significance ($p=0.05$).

Overhage et al and Teich et al studied more focused aspects of the medication system. Overhage et al[21] studied computerized reminders for corollary orders (eg, entering a laboratory order to check electrolytes when ordering potassium for a patient) and showed a greater than 100% improvement in the rate of corollary orders ($p<0.0001$). Teich et al[24] studied a broad range of computerized clinical decision support tools utilized at BWH and demonstrated 5 prescribing improvements in types, doses, and frequencies of drug usage.

In summary, these studies provide some evidence that CPOE with CDSSs can substantially decrease medication errors in broad as well as in more focused areas. Despite the significant impact on medication errors, the reduction in ADEs did not achieve statistical significance in one study,[22] and achieved only borderline significance in one of the outcomes in the other study.[23] Furthermore, the systems evaluated in this relatively small literature were developed internally rather than purchased and installed, so the potential impact of commercially available systems remains somewhat speculative.

In the studies evaluating CDSSs, 2 were systematic reviews.[25, 26] In Hunt's review, which emphasized clinical performance, 6 of 14 studies reported improvements in patient outcomes and 43 of 65 studies showed improvement in physician performance.[25] This study concludes that CDSSs can enhance clinical performance for drug dosing, preventive care, and other aspects of medical care, but that the impact of CDSSs on patient outcomes remains unclear (see also Chapter 53). Walton's systematic review evaluated computerized drug dosage advice and found a 6% decrease in adverse drug reactions.[26] The authors concluded that there is some limited evidence that CDSSs for drug dosing are effective, however there are relatively few studies, many of which are of sub-optimal quality. They also suggest that further research is needed to determine if the CDSS benefits realized with specialist applications can be realized by generalist use. Evans et al performed the remaining 2 studies.[27, 28] The 1994 study evaluated the use of a computerized antibiotic selection consultant, and demonstrated a 17% greater pathogen susceptibility to an antibiotic regimen suggested by a computer consultant versus a physician ($p<0.001$).[27] The second study demonstrated a 70% decrease in ADEs caused by anti-infectives ($p=0.018$) through use of a computer based anti-infective management program. As with CPOE, these CDSSs studies demonstrate improvements in medication errors with statistical significance. In addition, both Walton's systematic review[26] and the latter study by Evans et al[28] demonstrated significant decreases in ADEs. Importantly, each of these CDSSs studies only addressed focal aspects of the medication system. In addition, relatively little information is available about the differences between systems.

Potential for Harm

Faulty decision support data, for example an incorrect default dosing suggestion, can lead to inappropriate ordering choices by physicians. The BWH time series analysis demonstrated an initial rise in intercepted potential ADEs due to the structure of the ordering screen for potassium chloride.[23] This structural error was identified and easily rectified, but underscores the importance of close scrutiny of all aspects of CPOE screens, both initially and on an ongoing basis.[23]

Also, analogously to writing an order in the wrong patient chart in a conventional system, a physician can electronically write an order in the wrong patient's record - eg, after walking away from the terminal, opening the wrong record from a personalized rounding list. In addition, it is critical that the trigger level for warnings appropriately balances alarm sensitivity and specificity. These systems must have thresholds set so that physicians receive warnings in situations with a potential for significant harm, without being overwhelmed by "false alarms." Another potential risk is hardware outage or software instability. For example, the reliability that is needed with CPOE is much higher than that required for systems that simply report laboratory results.

Costs and Implementation

Six of the studies described in this review evaluated "home-grown" rather than "off-the-shelf" systems. The present costs for purchasing commercial systems are substantially more than the previous costs of developing such systems. For BWH, the cost of developing and implementing CPOE in 1992 was estimated to be $1.9 million, with maintenance costs of $500,000 per year. In comparison, the cost of purchasing and implementing large commercial systems varies substantially, but may be on the order of tens of millions of dollars. Several studies demonstrate that only minimal resources are needed to introduce and/or maintain decision support programs into existing order entry programs.[21, 24, 30]

Relatively few data are available regarding the financial benefits of CPOE, although they extend well beyond medication-related events. The net savings of the BWH system are estimated at $5-10 million per year.[31] It is estimated that the costs to BWH for preventable ADEs are $2.8 million annually.[32] Evans et al reported a $100,000 per year cost avoidance with a computer-assisted antibiotic dosing program largely attributable to decreased antibiotic use and avoided ADEs.[33]

Importantly, healthcare systems must garner both financial and organizational support before introducing CPOE with CDSSs. CPOE requires a very large up-front investment with more remote, albeit substantial returns. In addition, CPOE impacts clinicians and workflow substantially. Its complexity requires close integration with multiple systems, such as the laboratory and pharmacy systems. Failure to attend to the impact of such a large-scale effort on organizational culture and dynamics may result in implementation failure.[34] Therefore, it is essential to have organizational support and integration for its successful implementation and use.

Comment

The literature supports CPOE's beneficial effect in reducing the frequency of a range of medication errors, including serious errors with the potential for harm. Fewer data are available regarding the impact of CPOE on ADEs, with no study showing a significant decrease in actual patient harm. Similarly, isolated CDSSs appear to prevent a range of medication errors, but with

few data describing reductions in ADEs or improvements in other clinical outcomes. Finally, the studied CDSSs address focused medication use (for example, antibiotic dosing) rather than more general aspects of medication use.

Further research should be conducted to compare the various types of systems and to compare "home-grown" with commercially available systems. Such comparisons are particularly important since the institutions that have published CPOE outcomes have generally been those with strong institutional commitments to their systems. Whether less committed institutions purchasing "off the shelf" systems will see benefits comparable to those enjoyed by "pioneers" with home-grown systems remains to be determined. Studying the benefits of such complex systems requires rigorous methodology and sufficient size to provide the power to study ADEs. Further research also needs to address optimal ways for institutions to acquire and implement computerized ordering systems.

Table 6.1. Studies of computerized physician order entry (CPOE) with clinical decision support systems (CDSSs)[*]

Study	Study Design	Study Outcomes	Results
Overhage, 1997.[21] Impact of faculty and physician reminders (using CPOE) on corollary orders for adult inpatients in a general medical ward at a public teaching hospital affiliated with the Indiana University School of Medicine	Level 1 (RCT with physicians randomized to receive reminders or not)	Levels 2 & 3 (errors of omission in corollary orders)	25% improvement in ordering of corollary medications by faculty and residents ($p<0.0001$)
Bates, 1998.[22] CPOE with CDSSs for adult inpatients on medical, surgical, and intensive care wards at BWH, a tertiary care center affiliated with Harvard University	Levels 2 & 3 (two study designs)	Level 1 (ADE rates) and Level 2 (serious medication errors)	55% decrease in non-intercepted serious medication errors ($p=0.01$) 17% decrease in preventable ADEs ($p=0.37$)
Bates, 1999.[23] CPOE with CDSSs for adult inpatients in 3 medical units at BWH	Level 3 (retrospective time series)	Level 1 (ADEs) and Level 2 (main outcome measure was medication errors)	81% decrease in medication errors ($p<0.0001$) 86% decrease in non-intercepted serious medication errors ($p=0.0003$)
Teich, 2000.[24] CPOE with CDSSs for all adult inpatients at BWH	Level 3 (retrospective before-after analysis)	Levels 2 & 3 (changes in 5 prescribing practices)	Improvement in 5 prescribing practices ($p<0.001$ for each of the 5 comparisons)

[*] ADE indicates adverse drug event; BWH, Brigham and Women's Hospital; and RCT, randomized controlled trial.

Table 6.2. Studies of clinical decision support systems (CDSSs)*

Study Setting	Study Design	Study Outcomes	Results
Hunt, 1998.[25] Use of CDSSs by healthcare practitioners in multiple inpatient and outpatient settings	Level 1A (systematic review of RCTs)	Levels 1 & 2 (a variety of measures related to patient outcomes and physician practice, not just ADEs and processes of care related to medication use.	6 of 14 studies showed improvement in patient outcomes 43 of 65 studies showed improvement in physician performance
Walton, 2001.[26] Use of CDSSs for drug dosage advice by healthcare practitioners for 1229 patients in multiple inpatient settings	Levels 1A-3A (systematic review of RCTs, interrupted time series analyses, and controlled before-after studies)	Level 1 (one main outcome measure was adverse drug reactions	Absolute risk reduction with CDSSs: 6% (95% CI: 0-12%)
Evans, 1994.[27] Use of a computerized antibiotic selection consultant for 451 inpatients at Salt Lake City's LDS Hospital, a 520-bed community teaching hospital and tertiary referral center	Level 1 (RCT with crossover design)	Level 2 (one of 5 primary outcomes was pathogen susceptibility to prescribed antibiotic regimens	17% greater pathogen susceptibility to an antibiotic regimen suggested by computer consultant versus physicians ($p<0.001$)
Evans, 1998.[28] Computer-based anti-infective management program for 1136 intensive care unit patients from a 12-bed ICU at LDS Hospital	Level 2 (prospective before-after analysis)	Level 2 (one primary outcome was ADEs due to anti-infective agents	70% decrease in ADEs caused by anti-infectives ($p=0.02$)

* ADE indicates adverse drug event; CI, confidence interval; ICU, intensive care unit; and RCT, randomized controlled trial.

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Chapter 7. The Clinical Pharmacist's Role in Preventing Adverse Drug Events

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Background

A large literature documents the multiple roles clinical pharmacists can play in a variety of health care settings.[1-8] Much of this literature focuses on measures of impact not directly relevant to this Report – eg, economic benefits,[4,8] patient compliance,[6] and drug monitoring.[2,3] More recently, systems-based analyses of medication errors and adverse drug events (ADEs) have drawn attention to the impact clinical pharmacists can exert on the quality and safety of medication use.[9-12] In this chapter, we review the evidence supporting the premise that direct participation of pharmacists' in clinical care reduces medication errors and ADEs in hospitalized and ambulatory patients.

Practice Description

Clinical pharmacists may participate in all stages of the medication use process, including drug ordering, transcribing, dispensing, administering, and monitoring. The specific activities of clinical pharmacists vary substantially in the studies reviewed in this chapter. In the hospital setting, one study evaluated the role of a senior pharmacist participating fully in intensive care unit rounds and available throughout the day in person or by page for questions.[13] Another study evaluated a ward pharmacy service that examined order sheets for new therapies and carried out checks that were formerly performed in the pharmacy.[14]

Pharmacists may also play a role at the time of discharge. One study reported the impact of clinical pharmacists' consultation for geriatric patients at the time of discharge,[15] with pharmacists serving as consultants to physicians and reinforcing patients' knowledge of their medication regimen. The roles of clinical pharmacists are similarly diverse in studies of ambulatory settings. Here they include the provision of consultative services,[16-18] patient education,[16-18] therapeutic drug monitoring,[3] and even follow-up telephone calls to patients.[3,16-18]

Prevalence and Severity of the Target Safety Problem

It is estimated that over 770,000 people are injured or die in hospitals from adverse drug events (ADEs) annually.[19-21] The few hospitals that have studied incidence rates of ADEs have documented rates ranging from 2 to 7 per 100 admissions.[11,19,22,23] A precise national estimate is difficult to calculate due to the variety of criteria and definitions used by researchers.[24] One study of preventable inpatient ADEs in adults demonstrated that 56% occurred at the stage of ordering, 34% at administration, 6% at transcribing, and 4% at dispensing.[22] In this study, the drug class most commonly associated with preventable ADEs was analgesics, followed by sedatives and antibiotics. Even fewer studies have been conducted in the outpatient setting. One recent cross-sectional chart review and patient care survey found an ADE rate of 3% in adult primary care outpatients.[25]

Opportunities for Impact

Although many hospital pharmacy departments offer clinical pharmacy consultation services,[26] the degree to which these services include rounding with clinicians[13] is unclear.

Hospital pharmacies provide support to a variable degree in different ambulatory settings (clinics, nursing homes, adult daycare),[26] but the precise nature of clinical pharmacists' activities in these settings is not uniformly characterized.

Study Designs

We identified 3 systematic reviews of clinical pharmacists in the outpatient setting.[5,17,18] We included only the most recent review,[18] as it followed the most rigorous methodology and included the bibliographies of the previous reviews.[5,17] We identified only one study[16] of the impact of clinical pharmacists on patient outcomes in the ambulatory setting that had not been included in this systematic review.[18] This study, a randomized controlled trial evaluating clinical pharmacists' participation in the management of outpatients with congestive heart failure,[16] was therefore also included.

For studies of clinical pharmacists in the hospital setting, an older review[2] did not meet the characteristics of a systematic review, but was a very thorough summary of the relevant literature. It included 8 studies evaluating pharmacists' roles in detecting and reporting ADEs in the hospital setting. Preliminary review of these studies revealed that the measured outcomes were Level 3 (detection of ADEs as an end in itself). Consequently, we did not include them. One older retrospective before-after analysis (Level 3)[14] did meet our inclusion criteria, as did 2 more recent studies of clinical pharmacists' roles in the inpatient setting: a prospective, controlled before-after study (Level 2)[13] and a randomized controlled trial (Level 1).[15]

We included an additional meta-analysis focusing on therapeutic drug monitoring by clinical pharmacists in the hospital and ambulatory settings.[3] The studies included in this meta-analysis consisted predominantly of controlled observational studies (Level 3) and non-randomized clinical trials (Level 2), but one randomized controlled trial was also included (Level 1-3A).

Table 7.1 lists the studies reviewed in this chapter and briefly describes their salient features. All of the listed studies involved adult patients, as the single pediatric study[9] identified by our literature search had no control group (Level 4 design) and was therefore excluded.

Study Outcomes

Level 1 outcomes reported in the included studies consisted of ADEs[13] and clinical events related to heart failure, including mortality.[16] One study used telephone interviews to solicit patient self-reports of adverse drug reactions.[13,27] This study was excluded since the systematic review of clinical pharmacists' roles in ambulatory settings[18] incorporated its findings in several of its analyses.

The distinction between Level 2 and 3 outcomes can be somewhat ambiguous in studies of prescribing practice, as the exact point at which choices of therapeutic agents or dosing patterns become not just sub-optimal but actually represent "errors" is difficult to define precisely. Even for objective outcomes, such as serum drug concentrations, the connection to patient outcomes is weak in some cases (eg, monitoring vancomycin levels[28,29]), and therefore more appropriately designated as Level 3 rather than Level 2. Acknowledging the subjectivity of this judgment in some cases, we included studies that contained a mixture of Level 2 and 3 outcomes, including "prescribing problems," (which included inappropriate choice of therapy, dosage errors, frequency errors, drug-drug interactions, therapeutic duplications, and allergies[15]), and serum drug concentrations for a broad range of medications.[3]

Evidence for Effectiveness of the Practice

In the inpatient setting, Leape's study[13] demonstrated a statistically significant 66% decrease in preventable ADEs due to medication ordering. The study of geriatric patients at the time of discharge demonstrated clinically and statistically significant decreases in medication errors.[15] The meta-analysis of the effect of clinical pharmacokinetics services on maintaining acceptable drug ranges indicated only modest effect sizes for the outcomes measured, and only 2 of the main results achieved statistical significance.[3]

The comprehensive review of clinical pharmacist services in ambulatory settings reported positive impacts for patients with hypertension, hypercholesterolemia, chronic heart failure, and diabetes.[18] However, the authors identify important limitations: these studies are not easily generalizable, only 2 studies compared pharmacist services with other health professional services, and both studies had important biases. Consequently, they emphasized the need for more rigorous research to document the effects of outpatient pharmacist interventions.[18] The additional study of outpatients demonstrated significant decreases in mortality and heart failure events,[16] but these results may reflect closer follow-up and monitoring (including telemetry) for the intervention group or the higher doses of angiotensin-converting enzyme (ACE) inhibitors the patients received. Generalizing this benefit to other conditions is difficult since most conditions do not have a single medication-related process of care that delivers the marked clinical benefits as do ACE inhibitors in the treatment of congestive heart failure.[30]

Potential for Harm

Introducing clinical pharmacists might potentially disrupt routine patient care activities. However, the 2 studies that assessed physician reactions to clinical pharmacists[13,27] found excellent receptivity and subsequent changes in prescribing behavior.

Costs and Implementation

Two studies examined resource utilization and cost savings in the inpatient setting. The intensive care unit study indicated that there could be potential savings of $270,000 per year for this hospital if the intervention involved re-allocation of existing pharmacists' time and resources.[13] McMullin et al studied all interventions made by 6 hospital pharmacists over a one-month period at a large university hospital and estimated annual cost savings of $394,000.[31]

A systematic review of outpatient pharmacists indicated that pharmacist interventions could lead to increased scheduled service utilization and decreased non-scheduled service utilization, specialty visits, and numbers and costs of drugs.[18]

Comment

At present, one study provides strong evidence for the benefit of clinical pharmacists in reducing ADEs in hospitalized intensive care unit patients.[13] One additional study provides modest support for the impact of ward-based clinical pharmacists on the safety and quality of inpatient medication use.[14] The evidence in the outpatient setting is less substantial, and not yet convincing. Given the other well-documented benefits of clinical pharmacists and the promising results in the inpatient setting, more focused research documenting the impact of clinical pharmacist interventions on medication errors and ADEs is warranted.

Table 7.1. Studies of clinical pharmacists' impact on ADEs and medication errors*

Study	Study Design	Study Outcomes	Results
Beney, 2000.[18] Systematic review of the roles and impacts of pharmacists in ambulatory settings; reviewed studies included 16,000 outpatients and 40 pharmacists	Level 1A (systematic review)	Levels 1-3 (variety of patient outcomes, surrogate outcomes, impacts on physician prescribing practices and measures of resource use)	Improvement in outcomes for patients with hypertension, hypercholesterolemia, chronic heart failure, and diabetes
Gattis, 1999.[16] 181 patients with heart failure due to left ventricular dysfunction followed in a general cardiology clinic	Level 1 (RCT)	Level 1 (mortality and other clinical outcomes related to heart failure)	16 versus 4 deaths or other heart failure events ($p<0.005$)
Leape, 1999.[13] Medical and cardiac intensive care unit patients at Massachusetts General Hospital, a tertiary care hospital in Boston	Level 2 (prospective before-after study with concurrent control)	Level 1 (ADEs)	66% decrease in the rate of preventable ADEs ($p<0.001$)
Leach, 1981.[14] 315 patients at Queen Elizabeth Hospital in Birmingham, England	Level 3 (retrospective before-after analysis)	Level 2 (various types of medication errors)	40-50% overall reduction in medication errors All 8 of the targeted error types decreased (results achieved statistical significance for 5 error types)
Lipton, 1992.[15] 236 geriatric patients discharged from the hospital on three or more medications	Level 1	Levels 2 & 3 ("prescribing problems")	Less likely to have a "prescribing problem" ($p=0.05$)
Ried, 1989.[3] Pooled patient population not reported, but review of articles indicates predominance of studies of (mostly adult) hospitalized patients	Level 1A-3A (meta-analysis predominantly included controlled observational studies and non-randomized trials)	Levels 2 & 3 (measures of peak, trough and toxic serum drug concentrations for a variety of medications)	More likely to have therapeutic peak and trough and less likely to have toxic peak and trough, but modest effect sizes (results achieved statistical significance for only 2 measures)

* ADE indicates adverse drug event; and RCT, randomized controlled trial.

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Chapter 8. Computer Adverse Drug Event (ADE) Detection and Alerts

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Background

Adverse drug events (ADEs) occur in both inpatient and outpatient settings.[1,2] Most institutions use spontaneous incident reporting to detect adverse events in general, and ADEs in particular. Spontaneous incident reporting relies exclusively on voluntary reports from nurses, pharmacists and physicians focused on direct patient care. However, spontaneous reporting is ineffective, identifying only one in 20 ADEs.[3] Efforts to increase the frequency of spontaneous reporting have had only a minor impact.

Several studies demonstrate the effectiveness of using computerized detection and alert systems (referred to as *computer "monitors")* to detect ADEs. In 1991, Classen et al[4] published information about a computerized ADE monitor that was programmed to identify signals—in effect mismatches of clinical information—that suggested the presence of an ADE. The signals included sudden medication stop orders, antidote ordering, and certain abnormal laboratory values.[4] The computerized signals were then evaluated by a pharmacist who determined whether an ADE had occured. Based on the rules of this study, Jha et al developed a similar monitor that identified approximately half the ADEs identified by chart review, at much lower cost.[5] Similarly, Bowman and Carlstedt used the Regenstrief Medical Record System to create a computerized inpatient ADE detection system.[6] Compared to the "gold standard" of chart review, the monitor had 66% sensitivity and 61% specificity, with a positive predictive value of 0.34. Finally, one community hospital implemented an ADE monitor with triggers that were reviewed by pharmacists who then contacted physicians to make appropriate regimen changes. This study identified opportunities to prevent patient injury at a rate of 64/1000 admissions.[7] These studies and others demonstrate the potential value of computer monitors, especially when linked to effective integrated information systems. While monitors are not yet widely used, they offer an efficient approach for monitoring the frequency of ADEs on an ongoing basis, and the Health Care Financing Administration is considering mandating them.[8]

Practice Description

Computerized ADE alert monitors use rule sets to search signals that suggest the presence of adverse drug events. The most frequently studied rule sets (or "triggers") are those that search for *drug names* (eg, naloxone, kayexalate), *drug-lab interactions* (eg, heparin and elevated PTT) or *lab levels alone* (eg, elevated digoxin levels) that frequently reflect an ADE. Simple versions can be implemented with pharmacy and laboratory data alone, although the yield and positive predictive value of signals is higher when the 2 databases are linked.

Further refinements include searches for International Classification of Diseases (ICD-9) codes, and text-searching of electronic nursing bedside charting notes or outpatient notes for *drug-symptom combinations* (eg, medication list includes an angiotensin converting enzyme inhibitor and the patient notes mention "cough"). Although these refinements do increase the yield of monitors, they require linkage to administrative databases or electronic medical records.

The information captured with computer monitors is used to alert a responsible clinician or pharmacist, who can then change therapy based on the issue in question. Systems are designed

to alert the monitoring clinician in various ways. Alerts can go to one central location (eg, hospital pharmacist) or to individual physicians. Monitoring pharmacists typically review the alert and contact the appropriate physician if they determine that the alert has identified a true event. The alert modality also varies based on the available technology, from printed out reports, to automatic paging of covering physicians, to display of alerts on computer systems (either in results or ordering applications). It should be emphasized that computerized physician order entry (Chapter 6) is not a requirement for these monitors. Thus, a simple version of this approach could be implemented in most US hospitals**.**

Prevalence and Severity of the Target Safety Problem

It is estimated that over 770,000 people are injured or die in hospitals from ADEs annually,[3,9,10] but variations in study criteria and definitions prevent precise national estimates.[11] Fewer data address the epidemiology of ADEs in the outpatient setting. One recent study found an ADE rate of 3% in adult primary care outpatients,[12] while an older study reported a similar rate of 5% among ambulatory patients attending an internal medicine clinic over a 1-year period.[2]

Detection and alerting interventions primarily target ADEs related to the medication ordering process. One study of preventable inpatient ADEs in adults demonstrated that 56% occurred at the stage of ordering.[13] Among the 6.5 ADEs per 100 admissions in this study, 28% were judged preventable, principally by changing the systems by which drugs are ordered and administered.[14] In one study of computerized ADE detection, the ADEs identified by computerized monitoring were significantly more likely to be classified as severe than those identified by chart review (51% vs. 42%, p=0.04).[5] Thus, monitors may capture a subset of events with the most potential for patient injury.

Injuries due to drugs have important economic consequences. Inpatients that suffer ADEs have increased lengths of stay of nearly 2 days and added hospital costs of more than $2000.[9,15] Bootman has estimated the annual cost of drug-related morbidity and mortality within the United States at $76.6 billion, with the majority ($47 billion) related to hospital admissions due to drug therapy or the absence of appropriate drug therapy.[16]

Opportunities for Impact

Unfortunately, there are no good data as to how many hospitals have integrated lab and medication systems, which are required for many of the triggers used in computerized ADE monitors.

Study Designs

We found 5 studies of computerized ADE alert systems that were Level 3 or better (see Table 8.1). Four studies[17-20] detected potential ADEs using computerized monitoring and then alerted physicians or pharmacists about the event. One additional study[21] both alerted the monitoring clinician and made recommendations for actions relating to the suspect condition. Four studies[17-20] were in the inpatient setting and one was in the ambulatory setting.[21]

Study Outcomes

All of the studies reported Level 1 or 2 outcomes. Level 1 outcomes were the rate of ADEs[18,19] and renal impairment (as reflected by rises in creatinine).[20] Level 2 outcomes included percent of time recommended actions were taken and time to respond to an event.[17-20]

Evidence for Effectiveness of the Practice

One study demonstrated significant decreases in adverse clinical outcomes with the alert systems.[18] This decrease included a surprisingly large reduction in allergic reactions (ones not previously known); it is not clear how the computer alert or decision support system could have contributed to this result.[18] The second study[19] showed no significant difference in the number of adverse events in the intervention and control groups. This study and 3 others revealed significant improvements in response times concerning lab values,[17-20] and one study found a significant decrease in the risk of serious renal impairment.[20] Finally, one study demonstrated significant changes in physician behavior/modification of therapy based on alerts with recommended actions.[21] The effect sizes shown in these studies are listed in Table 8.1.

Potential for Harm

None of the studies discuss any potential for harm associated with the monitor and alerts. It is certainly possible that alerts could be erroneous, but it is doubtful that this would lead to any direct patient harm. As in studies of safety in other industries, one possible source of harm could be too many false positives. Large numbers of clinically insignificant warnings for patients would interfere with routine care, and might result in providers ignoring all warnings, even clinically meaningful ones.

Costs and Implementation

In general, implementation of alert monitors requires computer systems that can link laboratory and medication information. Integrating this information requires the creation of interface between the drug and laboratory databases, with costs that will vary depending on the nature of the existing information systems. In addition, alert methods vary, with some applications directly contracting physicians (which requires further integration of coverage and pager databases) and others using pharmacist intermediaries. The cost of pharmacist review of triggers was less than 1 FTE per hospital in 2 studies[5,7]; one of them reported an annual cost savings of up to 3 million dollars by reducing preventable ADEs with this alerting technique.[7]

Studies thus far suggest that physicians view computerized alert systems favorably. Forty-four percent of physician-respondents receiving alerts indicated that the alerts were helpful and 65% wished to continue receiving them (although these alerts went to many physicians because it was unclear who the responsible doctor was). In another study in which alerts were sent only to the responsible physician, 95% of physician-respondents were pleased to receive them.[19]

The systems in these studies were all “homegrown” and contained idiosyncrasies that might undermine their implementation elsewhere. Clearly it is important that systems track which physicians are responsible for which patients. In addition, all 4 of the inpatient studies were conducted at tertiary care hospitals and the outpatient study was done at clinics affiliated with a tertiary care center. The translation of this alerting approach to community settings may be difficult. One community teaching hospital has reported success in detecting opportunities to prevent injury (64/1000 admissions) using computerized detection and alerting. This report had only a Level 4 design (no control group), so it was not included in the Table.[7]

Comment

Computerized real-time monitoring facilitates detection of actual and potential ADEs and notification of clinicians. This in turn may aid in the prevention of ADEs or decrease the chances that ADEs will cause harm. The monitors also yield improvements in secondary measures relating to the length of time until response and the quality of response.

The applications in these studies were all "homegrown." Future applications should be evaluated and refined further. In particular, it is important to quantify the yield of collecting these data in terms of patient outcomes, since the start-up costs are significant. If monitors do lead to important clinical benefits, they should become standard features of commercially available hospital computer systems. As this occurs, careful attention will need to be paid to optimizing the response process.

In addition, little has been done to translate these monitoring systems to the outpatient setting, largely because outpatient clinical information is often not computerized or resides in disparate systems. As integrated computerized outpatient records become more common, the systems developed in the inpatient setting should be translatable to the outpatient setting.

Table 8.1. Included studies of computerized systems for ADE detection and alerts*

Study Intervention	Study Design, Outcomes	Results†
Kuperman, 1999[19] Computerized alerts to physicians via paging system	Level 1, Level 1	Median time until initial treatment ordered: 1 vs. 1.6 hours (p=0.003) Median time until condition resolved: 8.4 vs. 8.9 hours (p=0.11) Number of adverse events: no significant difference
McDonald, 1976[21] Alerts to outpatient physicians with suggested responses to medication related events	Level 1, Level 2	Physicians performed recommended testing: 36% vs. 11% (p<0.00001) Physicians made changes in therapy: 28% vs. 13% (p<0.026)
Evans, 1994[18] Computerized monitor to detect ADEs (including drug/lab monitors and searches of nursing notes) and then computerized alerts to physicians	Level 3, Level 1	Type B ADEs (allergic or idiosyncratic) and severe ADEs: 0.1 vs. 0.5 per 1000 patient-days (p<0.002) Severe ADEs: 0.1 vs. 0.4 per 1000 patient-days (p<0.001)
Rind, 1994[20] Computerized alert system to physicians about rising serum creatinine values in patients receiving potentially nephrotoxic medications	Level 3, Level 1	Serious renal impairment: RR 0.45 (95% CI: 0.22-0.94) Mean serum creatinine lower after an event (0.16 mg/dL lower on Day 3, p<0.01) Dose adjusted or medication discontinued an average of 21.6 hours sooner after an event (p<0.0001)
Bradshaw, 1989[17] Computerized alerts integrated into result review and alerts by flashing light	Level 3, Level 2	Response time to alert condition: 3.6 (±6.5) vs. 64.6 (±67.1) hours

* ADE indicates adverse drug event; CI, confidence interval; and RR, relative risk.
† Results reported as rates with intervention vs. control (Level 1 study designs) or after intevention vs. before intervention (Level 3 study designs).

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Chapter 9. Protocols for High-Risk Drugs: Reducing Adverse Drug Events Related to Anticoagulants

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Background

Published studies of adverse drug events and multiple case reports have consistently identified certain classes of medications as particularly serious threats to patient safety.[1-3] These "high risk" medications include concentrated electrolyte solutions such as potassium chloride, intravenous insulin, chemotherapeutic agents, intravenous opiate analgesics, and anticoagulants such as heparin and warfarin. Analyses of some of the adverse events involving these mediations have led to important recommendations regarding their administration. Examples include the use of order templates for chemotherapeutic agents, removal of intravenous electrolyte solutions from general ward stock, and protocols for reviewing the settings of intravenous pumps delivering continuous or frequent doses of opiates.[2,4,5] While these recommendations have high face validity, they have generally not been subject to formal evaluation regarding their impact in reducing the targeted adverse events. By contrast, several practices relating to the management of patients receiving anticoagulants have been evaluated quite extensively, and therefore constitute the focus of this chapter.

Heparin and warfarin are medications whose use or misuse carry significant potential for injury. Subtherapeutic levels can lead to thromboembolic complications in patients with atrial fibrillation or deep venous thrombosis (DVT), while supratherapeutic levels can lead to bleeding complications. These medications are commonly involved in ADEs for a variety of reasons, including the complexity of dosing and monitoring, patient compliance, numerous drug interactions, and dietary interactions that can affect drug levels. Strategies to improve both the dosing and monitoring of these high-risk drugs have potential to reduce the associated risks of bleeding or thromboembolic events.

Practice Description

The practices reviewed in this chapter are all intended to reduce dosing and/or monitoring errors for heparin and warfarin, as follows:

- *Heparin dosing protocols ("nomograms")* typically involve a standard initial bolus and infusion rate, instructions for when to draw the first partial thromboplastin time (PTT), and orders for dosing adjustments in response to this and subsequent values (so nurses can adjust doses automatically). In some cases, the initial bolus and infusion rates are based on patient weight.

- *Inpatient anticoagulation services* for both heparin and warfarin (with or without dosing nomograms) typically consist of pharmacist-run services that provide daily pharmacy input on dosing and monitoring for patients on heparin and/or warfarin. (We excluded studies focusing solely on warfarin prophylaxis in orthopedic patients.[6])

- *Outpatient anticoagulation clinics* provide coordinated services for managing outpatient warfarin therapy. Services typically include anticoagulation monitoring and follow-up, warfarin dose adjustment, and patient education. These clinics are usually run by pharmacists or nurses operating with physician back-up, and sometimes following specific dosing nomograms.
- *Patient self-monitoring* using a home finger-stick device and self-adjustment of warfarin dosages using a nomogram. (The accuracy of these devices and the comparability of patients' and professional readings have been extensively evaluated.[7-11])

Prevalence and Severity of the Target Safety Problem

Intravenous heparin and oral warfarin are commonly used medications for cardiac disease and thromboembolism in the inpatient and outpatient settings. While in the aggregate they are highly beneficial (see Chapter 31), these drugs can have significant morbidities unless they are dosed and monitored appropriately. For example, inadequate therapeutic dosing of heparin can lead to increased length of stay and the potential for clot formation and/or propagation.[12] The risk of recurrent thromboembolism is reduced if the therapeutic effect of heparin is achieved quickly.[12] In addition, Landefeld et al[13] showed that the frequency of fatal, major, and minor bleeding during heparin therapy was twice that expected without heparin therapy. The effect with warfarin therapy was even more pronounced - approximately 5 times that expected without warfarin therapy. Consistent with this finding, anticoagulants accounted for 4% of preventable ADEs and 10% of potential ADEs in one large inpatient study.[1] Finally, careful drug monitoring in hospitals can reduce ADEs, suggesting that some events are due to inadequate monitoring of therapies and doses.[14] These studies highlight the clear need for safety-related interventions with respect to both the dosing and monitoring of these high-risk drugs in order to prevent thromboembolic and bleeding complications.

Opportunities for Impact

The number of hospitals using weight-based heparin nomograms, or that have established anticoagulation clinics or services is unknown. Although common in some European countries,[15] patient self-management of long-term anticoagulation with warfarin is unusual in the United States as many payers, including Medicare, do not currently cover the home testing technology.[15]

Study Designs

Heparin nomograms were evaluated in one randomized controlled trial (Level 1),[16] one prospective cohort comparison (Level 2)[17] and 4 controlled observational studies (Level 3).[18-21] Two of these studies involved weight-based nomograms.[16,21] A third study involving a weight-based nomogram[22] was included with the studies of anticoagulation services (see below), as clinical pharmacists actively managed the dosing protocol. We excluded one retrospective before-after analysis of a weight-based heparin protocol for cardiac intensive care patients,[23] because the method of selecting charts for review was never stated. Moreover, when the authors found an increase in the number of patients with excessive anticoagulation in the intervention group, they chose a second group of control patients (again with an unspecified selection method) for review, and in the end concluded that the difference was not significant.

All studies of *outpatient anticoagulation clinics* have been Level 3 studies, typically retrospective before-after analyses,[22,24-28] although one study might more appropriately be

regarded as a case-control study.[29] A comprehensive review of the literature on various forms of anticoagulation management[30] did not meet the criteria for a systematic review, but referenced all of the additional studies of anticoagulation clinics that we could identify[31-36] and used quantitative methods to pool their results. We use the pooled results from this article[30] in Table 9.2 in place of individual entries for each of these six Level 3 studies.

Two studies evaluated the impact of a coordinated *inpatient anticoagulation service* (with or without nomograms for dosing).[22,37]

Patient self-management of warfarin therapy has been evaluated in at least 3 randomized controlled trials[38-40] (Level 1) and one non-randomized clinical trial.[41] Because a number of higher-level studies exist, we did not include retrospective cohort analyses (Level 3) addressing this topic.[42-45]

Study Outcomes

Most studies did not evaluate bleeding complications or had insufficient numbers of patients to evaluate this outcome adequately. One recent study of an anticoagulation clinic's adverse events[25] focused on anticoagulation as the primary outcome (Level 1), as did the review that pooled results from 6 observational studies of anticoagulation clinics.[30] As shown in Tables 9.1-3, the rest of the studies reported Level 2 outcomes, consisting of various indicators of time to therapeutic anticoagulation and intensity or appropriateness of anticoagulation.

Evidence for Effectiveness of the Practice

- *Heparin nomograms:* As shown in Table 9.1, all studies showed a significant decrease (ie, improvement) in time to achievement of a therapeutic PTT and/or an increase in the proportion of patients in the therapeutic range.
- *Inpatient anticoagulation services*: As shown in Table 9.2, both Level 3 studies evaluating this practice showed significant improvements in relevant measures of anticoagulation.[22, 37]
- *Outpatient anticoagulation services for warfarin* (with and without dosing nomograms): the multiple Level 3 studies of this practice showed improvements in relevant measures of anticoagulation, with one exception.[28] This study took place in a semi-rural region of England, and the hospital-based anticoagulation clinic was staffed mainly by junior physician trainees rotating through the clinic. The one study that focused primarily on Level 1 outcomes[25] showed significant reductions in adverse events related to under- or over-anticoagulation.
- *Patient self-management*: Patient self-management achieved superior measures of anticoagulation on one Level 1 comparison with routine care.[22,37] More impressive is that two Level 1 studies[38,46] and one Level 2 study[41] reported equivalent or superior measures of anticoagulation for self-management compared with anticoagulation clinics.

Potential for Harm

Heparin nomograms are primarily intended to achieve PTT values within the therapeutic range as quickly as possible. Although none of the studies showed increased bleeding as a result

of aggressive anticoagulation, it is important to note that 4 of the 6 studies showed a significant increase in the proportion of patients with PTTs above the target range.[16,19-21]

Anticoagulation clinics carry the usual theoretical risk that increased fragmentation of care will introduce new hazards, but no study showed any significant cause for concern.

Patient self-monitoring clearly carries with it risks relating to the possibilities of patient misunderstanding of, or non-compliance with dosing and monitoring protocols. No increases in adverse events were observed in the studies reviewed, but the patients evaluated in these studies, even if randomized, were still chosen from a group of relatively compliant and motivated patients.

Costs and Implementation

For anticoagulation clinics, one study showed reduced costs of $162,058 per 100 patients annually, primarily through reductions in warfarin-related hospitalizations and emergency room visits.[25] Other studies indicate potential cost-savings due to reduced hospitalizations from anticoagulation-related adverse events, or show that the anticoagulation was revenue neutral.[19,24,29] Considering without these offsetting potential savings, however, anticoagulant clinics often require institutional subsidy since professional fee or laboratory payments do not fully cover costs.

Heparin nomograms may increase lab costs due to more frequent monitoring, but one study calculated that lab costs were offset by the need for fewer heparin boluses.[22]

For patient self-management of warfarin, one study showed that the cost of self-monitoring was $11/international normalized ratio (INR) value and postulated that this would be cost-effective if it reduced the number of clinic visits.[39] Other studies have suggested that the capillary blood testing devices themselves[47] and the overall practice of patient self-management are cost-effective.[48,49] In the United States, the home monitoring devices sell for approximately $1000. Factoring in the price of cartridges and assuming the devices operate without requiring repair for 5 years, one source estimated an annual cost of approximately $600.[40]

Implementation of a heparin nonogram appears feasible, and was well received by physicians and nurses.[18] Physician/staff education about the protocols was important to its success.[23,24] One study showed a high level of physician and patient satisfaction with an anticoagulation clinic.[24] In addition, multiple studies reveal that patients who self-manage warfarin have significantly higher levels of satisfaction and experience less anxiety.[9,10,38,39]

Comment

The primary purpose of heparin nomograms is the timely achievement of therapeutic anticoagulation, and their superiority in this regard (compared with routine care) has been convincingly established. While none of the studies showed adverse consequences of this focus on timely anticoagulation, the trend toward increases in excessive anticoagulation presents safety concerns. Studies powered to detect significant differences in bleeding complications in patients being managed with heparin dosing protocols may be warranted.

The literature on anticoagulation clinics consists entirely of observational studies with important possible confounders. Nonetheless, with one exception[28] they are consistently shown to achieve superior measures of anticoagulation, and in one study,[25] superior clinical outcomes.

Among the practices reviewed in this chapter, the literature on patient self-management is perhaps the most impressive. Three randomized trials and one non-randomized clinical trial show that patient control of anticoagulation is at least equivalent, if not superior, to management by usual care or an anticoagulation clinic. Additional observational studies reach the same results.[42-45] Thus, a relatively substantial literature supports patient self-management for outpatient warfarin therapy for motivated patients able to comply with the monitoring and dosing protocols. These studies clearly involved select groups of patients,[9] so that a larger randomized trial with intention-to-treat analysis would be helpful.

Many insurance carriers in the United States, including Medicare, do not currently subsidize the home testing technology or provide only partial coverage.[15] Despite the relatively high cost of the home testing devices, this practice may nonetheless be cost-effective due to reduced use of other clinical services.[48,49] A larger US study or detailed cost-effectiveness analysis appears warranted, especially given the higher level of patient satisfaction with this approach as compared with outpatient anticoagulation.

Table 9.1. Studies focused primarily on heparin or warfarin nomograms*

Study	Study Design, Outcomes	Results†
Raschke, 1993[16] Weight-based heparin nomogram for patients with venous thromboembolism or unstable angina	Randomized controlled trial (Level 1) Various markers of adequate anticoagulation (Level 2)	PTT in therapeutic range within 24 hours: 97% vs. 77% ($p<0.002$) Mean time to therapeutic PTT: 8.2 vs. 20.2 hours ($p<0.001$) PTT exceeding the therapeutic range: at 24 hours, 27% vs. 7% ($p<0.001$) at 48 hours, 18% vs. 8% ($p<0.001$)
Elliott, 1994[17] Use of heparin nomogram for patients with acute proximal deep venous thrombosis	Non-randomized clinical trial (Level 2) Time to therapeutic PTT (Level 2)	Time to therapeutic PTT: less with use of nomogram (values not given, $p=0.025$)
Brown, 1997[21] Weight-based heparin nomogram for ICU patients requiring acute anticoagulation with unfractionated heparin	Retrospective before-after analysis (Level 3) Time to therapeutic PTT (Level 2)	Mean time to therapeutic PPT: 16 vs. 39 hours ($p<0.05$) Supratherapeutic PTTs were more common after implementation of the nomogram, but there was no observed increase in bleeding
Cruickshank, 1991[18] Heparin nomogram for patients with acute venous thromboembolism	Retrospective before-after analysis (Level 3) Time to first therapeutic PTT, time to correct subsequent PTTs, time outside the therapeutic range (Level 2)	PTT in therapeutic range at 24 hours, 66% vs. 37% ($p<0.001$) PTT in therapeutic range at 48 hours, 81% vs. 58% ($p<0.001$)

Table 9.1. Studies focused primarily on heparin or warfarin nomograms* (cont.)

Study	Study Design, Outcomes	Results†
Hollingsworth, 1995[19] Heparin nomogram for hospitalized patients with acute venous thromboembolism	Retrospective before-after analysis (Level 3) Primary outcome of the study was length of hospital stay (Level 3) but time to therapeutic PTT was a secondary outcome (Level 2)	Time to therapeutic PTT: 17.9 vs. 48.8 hours ($p<0.001$) PTTs were sub-therapeutic less often: 28% vs. 56% ($p<0.001$) Proportion of patients with supra-therapeutic PTTs was significantly increased in the intervention group. There was no increase in bleeding complications associated with this finding, but the study was underpowered to detect such a difference.
Phillips, 1997[20] Inpatient heparin and warfarin nomograms and monitoring charts	Retrospective before-after analysis (Level 3) Measures of under- and over-anticoagulation (Level 2)	Heparin nomogram • Time spent under-anticoagulated: 18.5% vs, 32.7% ($p<0.0001$) • Time spent above the therapeutic range: 35.6% vs. 24.4% ($p<0.01$) Warfarin nomogram: • Time spent over-anticoagulated: 5.4% vs. 2.7% ($p<0.001$, but questionable clinical significance)

* PTT indicates partial thromboplastin time.
† Results reported as rates with intervention vs. control (Level 1 & 2 study designs) or after intevention vs. before intervention (Level 3 study designs).

Table 9.2. Inpatient anticoagulation services and outpatient anticoagulation clinics*

Study	Study Design, Outcomes	Results
Ansell, 1996[30] Pooled comparison of anticoagulation clinics and routine medical care	Pooled results from 6 Level 3 study designs comparing anticoagulation clinics with routine medical care[31-36] (Level 3A) Major bleeding and thromboembolic events (Level 1)	Major bleeding events per patient-year: anticoagulation clinic, 0.028 (95% CI: 0-0.069) vs. routine care, 0.109 (95% CI: 0.043-0.268) Thromboembolic events per patient-year: anticoagulation clinic, 0.024 (95% CI: 0-0.08) vs. routine care, 0.162 (95% CI: 0.062-0.486)
Hamby, 2000[29] Analysis of adverse events related to outpatient warfarin therapy among 395 patients followed at a Veterans Affairs Hospital, with 306 enrolled in an anticoagulation clinic and 89 patients receiving usual care	Case-control study (Level 3) Adverse events related to under- or over-anticoagulation (Level 1)	Among the 12 patients with preventable adverse events related to anticoagulation, 8 were not enrolled in the anticoagulation clinic Patients receiving usual care had 20 times the relative risk (95% CI: 6-62) of an adverse event compared with patients in the anticoagulation clinic.
Lee, 1996[26] Comparison of pharmacist-managed anticoagulation clinic with patient receiving usual care	Retrospective cohort comparison (Level 3) Hospital admissions related to under- or over-anticoagulation – ie, thromboembolic or bleeding events (Level 1)†	Patients in anticoagulation clinic had non-significant reductions in hospital admissions related to thromboembolic or bleeding events compared with control group‡
Ellis, 1992[37] Pharmacy-managed inpatient anticoagulation service (flow sheet for monitoring, but no nomogram) for monitoring patients receiving warfarin for a variety of indications	Retrospective before-after analysis (Level 3) Anticoagulation "stability" at discharge and odds of therapeutic anticoagulation at first outpatient visit (Level 2)	Patients receiving the intervention were more likely to have PT "stability" at discharge: 61.5% vs. 42.3% (p=0.02) Odds of having therapeutic PT at first outpatient clinic visit with intervention: OR 5.4 (95% CI: 1.87-15.86)

Table 9.2. Inpatient anticoagulation services and outpatient anticoagulation clinics* (cont.)

Study	Study Design, Outcomes	Results
Gaughan, 2000[24] Anticoagulation clinic for outpatients receiving warfarin for atrial fibrillation (managed by nurse practitioner using warfarin dosing nomogram)	Retrospective before-after analysis (Level 3) Percentage of patients in the desired range for anticoagulation (Level 2) was evaluated as a secondary outcome	Minor increase in percentage of patients with INR in desired range: 53.7% vs. 49.1% ($p<0.05$, but questionable clinical significance)
Radley, 1995[27] Performance of pharmacist-run hospital-based outpatient anticoagulation clinic in England compared with historical control (management by rotating physician trainees)	Retrospective before-after analysis (Level 3) Proportions of INR measurements "in" or "out" of the therapeutic range	No significant difference for patients with stable INR in the baseline period, but patients with an INR result "out" of range were more likely to return to "in" range under anticoagulation clinic management compared with routine physician management
Rivey, 1993[22] Pharmacy-managed inpatient anticoagulation service (using weight-based heparin protocol) for medicine inpatients compared with older fixed-dose protocol without any active management by pharmacists	Before-after analysis (Level 3) Time to therapeutic PTT (Level 2)	Time to therapeutic PTT was less with nomogram protocol: 40 vs. 20 hours ($p<0.05$) Fewer supra-therapeutic PTTs with protocol: 1.7 vs. 5.5 ($p<0.05$) Bleeding rates: no difference but numbers were small

* CI indicates confidence interval; INR, international normalized ratio; OR, odds ratio; PT, prothrombin time; and PTT, partial thromboplastin time.

† We counted this outcome as Level 1, but it is important to note that authors did not capture all of the designated clinical events, just those that resulted in admissions to the study hospital.

‡ Using the results reported in the study, we calculated the 95% CIs for admissions related to thromboembolic events (intervention, 0.2-18.5%; usual care, 12.7-42.5%) and bleeding events (inervention, 1.1-22.8%; usual care, 7-33.4%).

Table 9.3. Outpatient self-management using home testing devices and dosing nomograms*

Study	Study Design, Outcomes	Results
Cromheecke, 2000[38] Oral anticoagulation self-management with home monitoring and dose adjustment compared with anticoagulation clinic (Netherlands)	Randomized trial with crossover comparison (Level 1) Adequacy of anticoagulation (Level 2)	Percent of self-managed measurements within 0.5 INR units of therapeutic target did not differ (55% vs. 49%, p=0.06). However, 29 patients (60%) during self-management spent >50% of time in target range, compared with 25 (52%) during clinic management (p<0.05).
Sawicki, 1999[39] Oral anticoagulation self-management with home monitoring and dose adjustment compared with routine care (Germany)	Single blind, multicenter randomized controlled trial (Level 1) Adequacy of anticoagulation (Level 2)	Intervention group more often had INRs within target range (p<0.01), and had significantly fewer deviations from target range and 6 months
White, 1989[40] Oral anticoagulation self-management with home monitoring and dose adjustment compared with anticoagulation clinic (United States)	Randomized prospective comparison (Level 1) Adequacy of anticoagulation (Level 2)	Self-management group had significantly greater proportion of patients in target INR range (93% vs. 75%, p<0.01)
Watzke, 2000[41] Self-management compared with anticoagulation clinic (Austria)	Prospective cohort comparison (Level 2) Various measures of adequacy of anticoagulation (Level 2)	Non-significant trends towards more INR values within the therapeutic range for self-management group compared with anticoagulation clinic, both for standard therapeutic range of INR 2.0-3.0 (82.2% vs. 68.9%) and for more intense anticoagulation targeted to INR range of 2.5-4.5 (86.2% vs. 80.1%)

* INR indicates international normalized ratio.

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Chapter 10. Unit-Dose Drug Distribution Systems

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Background

Medication errors are especially likely when health professionals engage in multiple tasks within a short time span. This situation occurs repeatedly in hospitals when pharmacists and technicians load unit-dose carts, and when nurses administer medications. Unit-dose carts are prepared daily, often manually, by technicians and then checked by pharmacists. These carts, containing thousands of patient-specific dosages of drugs, are sent to the wards daily, for nurses to administer medications to patients. Dosing frequencies vary widely, ranging from regular intervals around the clock to "stat" doses given to control acute pain or other symptoms. Medication administration alone is an enormous task for nurses, and one in which they are repeatedly interrupted. It is not surprising that the administration phase of medication use is particularly vulnerable to error.[1]

Unit-dose dispensing of medication was developed in the 1960s to support nurses in medication administration and reduce the waste of increasingly expensive medications. Most of the investigations of medication errors and unit-dose dispensing took place from 1970 to 1976. Now, unit-dose dispensing of medications is a standard of practice at hospitals in the United States. This chapter reviews the evidence supporting this practice.

Practice Description

In unit-dose dispensing, medication is dispensed in a package that is ready to administer to the patient.[2] It can be used for medications administered by any route, but oral, parenteral, and respiratory routes are especially common. When unit-dose dispensing first began, hospital pharmacies equipped themselves with machines that packaged and labeled tablets and capsules, one pill per package. They also purchased equipment for packaging liquids in unit-doses. As the popularity of this packaging increased, the pharmaceutical industry began prepackaging pills in unit-of-use form. Many hospitals now purchase prepackaged unit-dose medications. However, it is still common for hospital pharmacies to purchase bulk supplies of tablets and capsules from manufacturers and repackage them in the central pharmacy into unit-dose packages.[2] It is important to note that hospitals vary in the proportion of their wards covered by a unit-dose system.

There are many variations of unit-dose dispensing. As just one example, when physicians write orders for inpatients, these orders are sent to the central pharmacy (by pharmacists, nurses, other personnel, or computer). Pharmacists verify these orders and technicians place drugs in unit-dose carts. The carts have drawers in which each patient's medications are placed by pharmacy technicians—one drawer for each patient. The drawers are labeled with the patient's name, ward, room, and bed number. Before the carts are transported to the wards, pharmacists check each drawer's medications for accuracy. Sections of each cart containing all medication drawers for an entire nursing unit often slide out and can be inserted into wheeled medication carts used by nurses during their medication administration cycles. A medication administration recording form sits on top of the cart and is used by the nurse to check-off and initial the time of each administration of each medication. The next day, the carts are retrieved from the wards and

replaced by a fresh and updated medication supply. Medications that have been returned to the central pharmacy are credited to the patient's account.

A 1999 national survey of drug dispensing and administration practices indicated that three-fourths of responding hospitals had centralized pharmacies, 77% of which were not automated.[2] Larger hospitals and those affiliated with medical schools were more likely to have some component of decentralized pharmacy services. About half of the surveyed hospitals reported drug distribution "systems" that bypassed the pharmacy, including hospitals that reported using floor stocks, borrowing other patients' medications, and hidden drug supplies.

Studies often compare unit-dose dispensing to a *ward stock system*. In this system, nurses order drugs in bulk supplies from the pharmacy; the drugs are stored in a medication room on the ward. Nurses prepare medication cups for each patient during medication administration cycles. The correct number of pills must be taken out of the correct medication container for each cycle and taken to the patient for administration. Liquids must be poured by the nurse from the appropriate bottle and each dose carefully measured. Nurses are responsible for any necessary labeling. Any medications taken from stock bottles and not administered to patients are generally disposed of.

Prevalence and Severity of the Target Safety Problem

The targets of the safety problem for unit-dosing are drug dispensing[3] and administration.[4,5] Improving these stages probably carries the greatest opportunity to reduce medication errors.

Bates et al[6] identified 530 medical errors in 10,070 written orders for drugs (5.3 errors/100 orders) on 3 medical units observed for 51 days. Of the 530 errors, 5 (0.9%) resulted in an adverse drug event. The most common reason for an error was a missing dose of medication, which occurred in 53% of orders. In a systems analysis of 334 errors causing 264 adverse drug events over 6 months in 2 tertiary care hospitals, 130 errors (39%) resulted from physician ordering, 40 (12%) involved transcription and verification, 38 (11%) reflected problems with pharmacy dispensing, and 126 (38%) were from nursing administration.[4] In other words, 164 (49%) of the errors in the above-cited study[4] were in the dispensing and administration stages. In further research, the investigators found that errors resulting in preventable adverse drug events were more than likely to be those in the administration stage (34%) than those in the dispensing stage (4%) of the medication use process.[1]

Opportunities for Impact

Because unit-dose dispensing now constitutes a standard for approval by the Joint Commission for Accreditation of Healthcare Organizations (JCAHO)[7,8] and is closely linked to the increasingly common use of automated dispensing devices (see Chapter 11), there is likely little opportunity for further implementation of this practice in US hospitals. In a 1994 survey of pharmacy directors, 92% of acute care hospitals reported using unit-dose dispensing.[7] Use of unit-dose dispensing is extremely common on general medical and surgical wards, but less so in other locations such as intensive care units, operating rooms, and emergency departments. In these areas, bulk medication stock systems are still found. In a 1999 survey of pharmacy directors, 80% reported that unit-dose dispensing was used for 75% or more of oral doses, and 52% of injectable medications dispensed in their hospitals.[9]

Study Designs

The 5 studies meeting inclusion criteria for this review (Table 10.1) included 4 Level 3 studies, and one prospectively designed before-after observation (Level 2 design). We excluded the following studies for the reasons outlined:

- Read[10] conducted a study of a unit-dose system applied to respiratory therapy solutions that was focused primarily on measures of efficiency. Volume/concentration errors in preparing respiratory solutions were also discussed, but the method of detection was not stated nor were specific error data provided for the study period.
- Reitberg et al[11] conducted a prospective before-after study with a concurrent comparison floor as a control (Level 2 design) in which medication errors represented the main outcomes (Level 2). During period 1 when both wards used the ward stock system, total errors were 4.7% on the ward that remained on ward stock and 34.2% on the ward that used the modified dispensing system. During period 2, the ward stock system had 5.1% error, while the intervention ward (unit-dose) exhibited a significantly *increased* 18% error rate. Excluding administration-time errors resulted in error rates of 5.1% (conventional system) and 4.8% (unit-dose), which are not significantly different. The greater number of errors on the modified dispensing ward before and after the intervention were attributed by the authors to factors other than the dispensing systems. Because of this problem, and the fact that this study took place in a skilled nursing facility rather than an acute care hospital, we excluded this study.
- Shultz et al[12] conducted a prospective before-after study (Level 2) involving a somewhat complicated comparison. In the baseline period, approximately 50% of wards used a unit-dose system. During the study period, some wards switched to a unit-dose system in which nurses still administered the medications, while other wards adopted an experimental system, in which pharmacists and pharmacy technicians handled all aspects of the mediation dispensing and administration process. The authors report an error rate of 0.64% for complete unit-dose plus pharmacy technician medication system compared to 5.3% in the more conventional unit-dose system in which nurses continue to administer medications ($p<0.001$ for this comparison). The authors repeated their observations 2 years later, and show a persistent marked reduction in the "complete unit-dose system" compared to the nurse-administered unit-dose system. Unfortunately, nowhere do the authors report the error rate in the baseline period in the wards without a unit-dose system. Thus, none of the results reported by the authors relate specifically to the conversion from a multi-dose to a unit-dose system.

In addition, 2 of the relevant references identified[13,14] almost certainly reported the same data. The 2 papers have only one author in common, but they come from the same institution, involve study wards of the same size and observation periods of the same duration, and report identical error rates for the main comparison. The data from these 2 papers were combined to produce a single entry in Table 10.1.

Lastly, we were unable to obtain one of the original studies of the unit-dose system within the timeline of the project. The data from this study appears to have been published only as a technical report.[15] Other publications related to this study and which we were able to obtain[16-18] did not provide sufficient detail on the aspects of the study relating to medication errors to permit abstraction or inclusion in this chapter. The published reports of a study conducted in a private hospital similarly did not contain sufficient detail about the study methods or results to permit abstraction and inclusion.[19,20]

Study Outcomes

Studies reported errors measured by direct observation using a methodology that was first described by Barker.[21] All of these studies involved Level 2 outcomes.

Evidence for Effectiveness of the Practice

Though the practice of unit-dose dispensing is generally well accepted and has been widely implemented, the evidence for its effectiveness is modest. Most of the published studies reported reductions in medication errors of omission and commission with unit-dose dispensing compared with alternative dispensing systems such as ward stock systems. One exception was the international study by Dean,[22] which compared a United States hospital using unit-dose and transcription of medication orders with a United Kingdom hospital using ward stock and no transcription of orders. The results of this study indicated that the United Kingdom hospital had less than half the errors of the United States hospital. The study groups were often difficult to compare because of differing cultures, hospitals, or nursing care units. Moreover, co-interventions undoubtedly confounded the results. Each study is summarized in Table 10.1.

Potential for Harm

Unit-dosing shifts the effort and distraction of medication processing, with its potential for harm, from the nursing ward to central pharmacy. It increases the amount of time nurses have to do other tasks but increases the volume of work within the pharmacy. Like the nursing units, central pharmacies have their own distractions that are often heightened by the unit-dose dispensing process itself, and errors do occur.[3]

Overall, unit-dose appears to have little potential for harm. The results of most of the Level 2 observational studies seem to indicate that it is safer than other forms of institutional dispensing. However, the definitive study to determine the extent of harm has not yet been conducted.

A major advantage of unit-dose dispensing is that it brings pharmacists into the medication use process at another point to reduce error.[3] Yet, as pointed out in the Practice Description above, about half of the hospitals in a national survey bypass pharmacy involvement by using floor stock, borrowing patients' medications, and hiding medication supplies.[2]

Costs and Implementation

The cost considerations of unit-dose dispensing are mainly a trade-off between pharmacy and nursing personnel. The pharmacy personnel involved are mainly technicians who load unit-dose ward carts for the pharmacists to check and may package some medications that are commercially unavailable in unit-dose form. The pharmacist must verify that the correct medication and dosage of each medication is sent to the ward for the nurse to administer. Nursing time to maintain a drug inventory is reduced, allowing more time for other nursing activities. A variable cost of unit-dose dispensing is the cost of equipment and supplies to those

hospitals that wish to do much of the packaging themselves instead of purchasing medications pre-packaged as unit-doses.

Comment

The studies evaluating the practice of unit-dosing contain important methodologic problems and, although yielding somewhat heterogeneous results, are overall relatively consistent in showing a positive impact on error reduction. In contrast to other practices related to medication use, none of the studies evaluated Level 1 outcomes, such as actual adverse drug events. Nonetheless, unit-dose dispensing or some form of automated dispensing of unit-doses (see Chapter 11) has become ubiquitous in American hospitals and a standard of care in the delivery of pharmacy services. Consequently, it is unlikely that more rigorous studies could now be conducted.

Table 10.1. Studies evaluating the impact of unit-dose dispensing on medication errors*

Study	Study Design, Outcomes†	Results: Error Rates (95% CI)
Hynniman, 1970[23]	Cross-sectional comparison between study hospital and non-randomly selected "comparison" hospitals (Level 3) Errors of commission and omission (Level 2) among doses ordered	Unit-dose system: 3.5% (3.1-4.0%) Conventional distribution systems at 4 hospitals: 8.3% (7.1-9.7%) 9.9% (8.0-12.2%) 11.4% (9.9-13.2%) 20.6% (18.4-22.9%)
Means, 1975[13] Simborg, 1975[14]‡	Cross-sectional comparison of 2 wards within a single hospital over a 60-day period (Level 3) Errors of commission (Level 2) among doses administered during randomly chosen observation periods	Unit-dose ward: 1.6% (1.0-2.5%) Multi-dose ward: 7.4% (6.1-8.9%)§
Schnell, 1976[24]	Prospective before-after study (Level 2) at four Canadian hospitals Errors observed during medication preparation and administration (Level 2)	Before vs. after implementation of unit-dose system: 37.2 vs. 38.5%; 42.9 vs. 23.3%; 20.1% vs. 7.8%; 38.5% vs. 23.1%¶
Dean, 1995[22]	Cross-sectional comparison (Level 3) of US and UK hospitals with different pharmacy distribution systems Errors observed during medication administration (Level 2)	84 errors among 2756 observations in UK hospital using traditional ward stock system: 3.0% (2.4-3.7%) 63 errors among 919 observations in US hospital using unit-doses and automated dispensing: 6.9% (5.2-8.5%) Absolute difference: 3.9% (2.1-5.7%)
Taxis, 1998[25]	Cross-sectional comparison (Level 3) of 2 hospitals in Germany and one hospital in the UK Errors observed during medication administration	UK hospital using traditional ward stock system: 8.0% (6.2-9.8%) German hospital using traditional ward stock system: 5.1% (4.4-5.8) German hospital using unit-dose system: 2.4% (2.0-2.8%) Omission was the most common type of error

* CI indicates confidence interval.
† Errors of commission include administration of wrong dose or wrong or unordered drug, whereas errors of omission include missed doses for inclusion in a patient's unit-dose drawer or a dose not administered.
‡ As outlined in the text, the similarities in study setting, time, design and results suggest that these 2 references contain data from the same study; information from these references was therefore combined and treated as a single study.
§ The 95% CIs shown in the table were calculated using the reported data: 20 errors in 1234 observed doses on the unit-dose ward vs. 105 errors in 1428 observed doses on the multidose ward.

¶ When wrong time errors were omitted, the above results changed so that the change to a unit-dose was associated with a significant increase in errors at the first hospital, a non-significant decrease in errors at the second hospital, and significant decreases in errors at the other two hospitals.

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Chapter 11. Automated Medication Dispensing Devices

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Background

In the 1980s, automated dispensing devices appeared on the scene, a generation after the advent of unit-dose dispensing (Chapter 11). The invention and production of these devices brought hopes of reduced rates of medication errors, increased efficiency for pharmacy and nursing staff, ready availability of medications where they are most often used (the nursing unit or inpatient ward), and improved pharmacy inventory and billing functions.[1-4] Although the capacity of such systems to contribute to patient safety appears great, surprisingly few studies have evaluated the clinical impact of these devices.

Practice Description

Automated dispensing systems are drug storage devices or cabinets that electronically dispense medications in a controlled fashion and track medication use. Their principal advantage lies in permitting nurses to obtain medications for inpatients at the point of use. Most systems require user identifiers and passwords, and internal electronic devices track nurses accessing the system, track the patients for whom medications are administered, and provide usage data to the hospital's financial office for the patients' bills.

These automated dispensing systems can be stocked by centralized or decentralized pharmacies. Centralized pharmacies prepare and distribute medications from a central location within the hospital. Decentralized pharmacies reside on nursing units or wards, with a single decentralized pharmacy often serving several units or wards. These decentralized pharmacies usually receive their medication stock and supplies from the hospital's central pharmacy.

More advanced systems provide additional information support aimed at enhancing patient safety through integration into other external systems, databases, and the Internet. Some models use machine-readable code for medication dispensing and administration. Three types of automated dispensing devices were analyzed in the studies reviewed here, the McLaughlin dispensing system, the Baxter ATC-212 dispensing system, and the Pyxis Medstation Rx. Their attributes are described below.

- The McLaughlin dispensing system[5] includes a bedside dispenser, a programmable magnetic card, and a pharmacy computer. It is a locked system that is loaded with the medications prescribed for a patient. At the appropriate dosing time, the bedside dispenser drawer unlocks automatically to allow a dose to be removed and administered. A light above the patient's door illuminates at the appropriate dosing time. Only certain medications fit in the compartmentalized cabinet (such as tablets, capsules, small pre-filled syringes, and ophthalmic drops).
- The Baxter ATC-212 dispensing system [6] uses a microcomputer to pack unit-dose tablets and capsules for oral administration. It is usually installed at the pharmacy. Medications are stored in calibrated canisters that are designed specifically for each medication. Canisters are assigned a numbered location, which is thought to reduce mix-up errors upon dispensing. When an order is sent to the microcomputer, a tablet is dispensed from a particular canister. The

drug is ejected into a strip-packing device where it is labeled and hermetically sealed.

- The Pyxis Medstation, Medstation Rx, and Medstation Rx 1000 are automated dispensing devices kept on the nursing unit.[7-9] These machines are often compared to automatic teller machines (ATMs). The Medstation interfaces with the pharmacy computer. Physicians' orders are entered into the pharmacy computer and then transferred to the Medstation where patient profiles are displayed to the nurse who accesses the medications for verified orders. Each nurse is provided with a password that must be used to access the Medstation. Pharmacists or technicians keep these units loaded with medication. Charges are made automatically for drugs dispensed by the unit. Earlier models had sufficient memory to contain data for about one week, and newer models can store data for longer periods.

Studies reviewed did not include the automated dispensing systems manufactured by Omnicell, which produces point-of-use systems that can be integrated into a hospital's information system.[10] Omnicell systems are also capable of being integrated into external support systems that support machine-readable code, drug information services, and medication error reporting systems.

Prevalence and Severity of the Target Safety Problem

Medication errors within hospitals occur with 2% to 17% of doses ordered for inpatients.[5,7,11-14] It has been suggested that the rate of inpatient medication errors is one per patient per inpatient day.[15] The specific medication errors targeted by automated dispensing systems are those related to drug dispensing and administration. Even with the use of unit-doses (see Chapter 11) errors still occur at the dispensing[16] and administration stages[3,17] of the medication use process. For instance, in one large study of 530 medical errors in 10,070 written orders for drugs (5.3 errors/100 orders),[18] pharmacy dispensing accounted for 11% of errors and nursing administration 38%.[3]

Opportunities for Impact

Automated dispensing devices have become increasingly common either to supplement or replace unit-dose distribution systems in an attempt to improve medication availability, increase the efficiency of drug dispensing and billing, and reduce errors. A 1999 national survey of drug dispensing and administration practices indicated that 38% of responding hospitals used automated medication dispensing units and 8.2% used machine-readable coding with dispensing.[19] Three-fourths of respondents stated that their pharmacy was centralized and of these centralized pharmacies, 77% were not automated. Hospitals with automated centralized pharmacies reported that greater than 50% of their inpatient doses were dispensed via centralized automated systems. Half of all responding hospitals used a decentralized medication storage system. One-third of hospitals with automated storage and dispensing systems were linked to the pharmacy computer. Importantly, about half of the surveyed hospitals reported drug distributions that bypassed the pharmacy including floor stock, borrowing patients' medications, and hidden drug supplies.

Study Designs

There were no true randomized trials. One crossover study of the McLaughlin dispensing system randomized nurses to work with the intervention medication system or the control

system.[5] We classified this as a Level 2 study, since, from the patient perspective, the design is that of a non-randomized trial. Other studies included in this review consisted of retrospective observational studies with before-after[6-8] or cross-sectional design[11] (Level 3). The reviewed studies described dispensing systems for orally administered medications, and were published between 1984 and 1995 (see Table 12.1).

Study Outcomes

All studies measured rates of medication errors (Level 2 outcome). Four studies[5,7,8,11] detected errors by direct observation using a methodology that was first described by Barker.[5] Direct observation methods have been criticized because of purported Hawthorne effect (bias involving changed behavior resulting from measurements requiring direct observation of study subjects). However, proponents of the method state that such effects are short-lived, dissipating within hours of observation.[15] Dean and Barber have recently demonstrated the validity and reliability of direct observational methods to detect medication administration errors.[20] Another study, a Level 3 design, determined errors by inspecting dispensed drugs.[6]

Evidence for Effectiveness of the Practice

The evidence provided by the limited number of available, generally poor quality studies does not suggest that automated dispensing devices reduce medication errors. There is also no evidence to suggest that outcomes are improved with the use of these devices. Most of the published studies comparing automated devices with unit-dose dispensing systems report reductions in medication errors of omission and scheduling errors with the former.[7,9] The studies suffer from multiple problems with confounding, as they often compare hospitals or nursing care units that may differ in important respects other than the medication distribution system.

Potential for Harm

Human intervention may prevent these systems from functioning as designed. Pharmacists and nurses can override some of the patient safety features. When the turn around time for order entry into the automated system is prolonged, nurses may override the system thereby defeating its purpose. Furthermore, the automated dispensing systems must be refilled intermittently to replenish exhausted supplies. Errors can occur during the course of refilling these units or medications may shift from one drawer or compartment to another causing medication mix-ups. Either of these situations can slip past the nurse at medication administration.

The results of the study of the McLaughlin dispensing system indicated that though overall errors were reduced compared to unit-dose (10.6% vs. 15.9%), errors decreased for 13 of 20 nurses but increased for the other 7 nurses.[5] In a study of Medstation Rx vs. unit-dose,[8] errors decreased in the cardiovascular surgery unit, where errors were recorded by work measurement observations. However, errors increased over 30% in 6 of 7 nurses after automated dispensing was installed in the cardiovascular intensive care unit, where incident reports and medication error reports were both used for ascertaining errors, raising the question of measurement bias. Finally, in a study primarily aimed at determining differences in errors for ward and unit-dose dispensing systems,[11] a greater error prevalence was found for medications dispensed using Medstation Rx compared with those dispensed using unit-dose or non-automated floor stock (17.1% vs. 5.4%).

Costs and Implementation

The cost of automated dispensing mainly involves the capital investment of renting or purchasing equipment for dispensing, labeling, and tracking (which often is done by computer). A 1995 study revealed that the cost of Medstation Rx to cover 10 acute care units (330 total beds) and 4 critical care units (48 total beds) in a large referral hospital would be $1.28 million over 5 years. Taking into account costs saved from reduced personnel and decreased drug waste, the units had the potential to save $1 million over 5 years. Most studies that examine economic impact found a trade-off between reductions in medication dispensing time for pharmacy and medication administration time for nursing personnel. A common complaint by nurses is long waiting lines at Pyxis Medstations if there are not enough machines. Nurses must access these machines using a nurse-specific password. This limited access to drugs on nursing units decreases drug waste and pilferage.

Comment

Although the implementation of automated dispensing reduces personnel time for medication administration and improves billing efficiency, reduction in medication errors have not been uniformly realized. Indeed, some studies suggest that errors may increase with some forms of automation. The results of the study of the McLaughlin Dispensing System by Barker et al[5] showed considerable nurse-to-nurse variability in the error rate between the automated system and conventional unit dose. Qualitative data aimed at determining the reason for this variability would be useful. The study by Klein et al[6] indicated little difference in the accuracy of medication cart filling by the Baxter ATC-212 (0.65%) versus filling by technicians (0.84%). Borel and Rascati found that medication errors, largely those related to the time of administration, were fewer after implementation of the Pyxis Medstation Rx (10.4%) compared with the historical period (16.9%).[7] These results are consistent with a more recent study by Shirley, that found a 31% increase in the on-time administration of scheduled doses after installation of the Medstation Rx 1000.[9] In contrast, errors were greater after Medstation Rx in the study by Schwarz and Brodowy,[8] increasing on 6 of 7 nursing units by more than 30%. Finally, Dean et al found half the errors in a ward-based system without automation in the United Kingdom (3.0%, 95% CI: 2.4-3.7%) compared with an automated unit-dose medication distribution system in the United States (6.9%, 95% CI: 5.2-8.5%).[11]

The practical limitations of the systems were illustrated by a variety of process deviations observed by Borel and Rascati.[7] These included nurses waiting at busy administration times, removal of doses ahead of time to circumvent waiting, and overriding the device when a dose was needed quickly. These procedural failures emphasize an often-raised point with the introduction of new technologies, namely that the latest innovations are not a solution for inadequate or faulty processes or procedures.[2]

Although automated dispensing systems are increasingly common, it appears they may not be completely beneficial in their current form. Further study is needed to demonstrate the effectiveness of newer systems such as the Omnicell automated dispensing devices. If the standard, namely unit-dose dispensing, is to be improved, such improvements will likely derive from robotics and informatics. To document impact of automated dispensing devices on patient safety, studies are needed comparing unit-dose dispensing with automated dispensing devices. Until the benefits of automated dispensing devices become clearer, the opportunities for impact of these devices is uncertain.

Table 11.1. Six studies reviewing automated drug dispensing systems*

Study	Study Design	Study Outcomes	N	Results
Barker, 1984[5]	Prospective controlled clinical trial (Level 2)	Errors of omission and commission among number of ordered and unauthorized doses. (Level 2)	1775	96 errors among 902 observations (10.6%) using the McLaughlin dispensing system vs. 139 errors among 873 observations (15.9%) using unit-dose dispensing (control)
Klein, 1994[6]	Prospective comparison of two cohorts (Level 2)	Dispensing errors in unit-dose drawers to be delivered to nursing units (Level 2)	7842	34 errors found among 4029 doses (0.84%) filled manually by technicians vs. 25 errors among 3813 doses (0.66%) filled by automated dispensing device
Borel, 1995[7]	Prospective before-after study (Level 2)	Errors observed during medication administrationin medications administered (Level 2)	1802	148 errors among 873 observations (16.9%) before vs. 97 errors among 929 observations (10.4%) after Medstation Rx ($p<0.001$). Most errors were wrong time errors.
Schwarz, 1995[8]	Prospective before-after study (Level 2)	Errors in medications administered (Level 2)	NA†	Medication errors decreased after automated dispensing on the cardiovascular surgery unit but increased on the cardiovascular intensive care unit.
Dean, 1995[11]	Cross-sectional comparison (Level 3) of US and UK hospitals with different pharmacy distribution systems	Errors in medications administered (Level 2)	3675	63 errors among 919 observations (6.9%, 95% CI: 5.2-8.5%) in the US hospital using unit doses and automated dispensing vs. 84 errors among 2756 observations (3.0%; 95% CI, 2.4-3.7%) in the UK hospital using ward stock. The absolute difference in error rates was 3.9% (95%CI: 2.1-5.7%).

* CI indicates confidence interval.
† Study used various denominator data.

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Section B. Infection Control

Chapter 12. Practices to Improve Handwashing Compliance

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Background

Hospital-acquired infections exact a tremendous toll, resulting in increased morbidity and mortality, and increased health care costs.[1,2] Since most hospital-acquired pathogens are transmitted from patient to patient via the hands of health care workers,[3] handwashing is the simplest and most effective, proven method to reduce the incidence of nosocomial infections.[4] Indeed, over 150 years ago, Ignaz Semmelweis demonstrated that infection-related mortality could be reduced when health care personnel washed their hands.[5] A recent review summarized the 7 studies published between 1977 and 1995 that examined the relationship between hand hygiene and nosocomial infections.[6]

Most of the reports analyzed in this study reveal a temporal relation between improved hand hygiene and reduced infection rates.[6] Despite this well-established relationship, compliance with handwashing among all types of health care workers remains poor.[7-11] Identifying effective methods to improve the practice of handwashing would greatly enhance the care of patients and result in a significant decrease in hospital-acquired infections.

Practice Description

This chapter focuses on practices that increase compliance with handwashing, rather than the already proven efficacy of handwashing itself.[4] The term "handwashing" defines several actions designed to decrease hand colonization with transient microbiological flora, achieved either through standard handwashing or hand disinfection.[4] Standard *handwashing* refers to the action of washing hands in water with detergent to remove dirt and loose, transient flora. *Hand disinfection* refers to any action where an antiseptic solution is used to clean the hands (ie, medicated soap or alcohol). Handwashing with bland soap (without disinfectant) is inferior to handwashing with a disinfecting agent.[12] *Hygienic hand rub* consists of rubbing hands with a small quantity (2-3mL) of a highly effective and fast acting antiseptic agent. Because alcohols have excellent antimicrobial properties and the most rapid action of all antiseptics, they are the preferred agents for hygienic hand rub (also called waterless hand disinfection). Also, alcohols dry very rapidly, allowing for faster hand disinfection.[4]

Given health care workers' documented low compliance with recommended handwashing practices,[7-9] improving compliance represents a more pressing patient safety concern than does the choice of different disinfectants, or attention to other specific issues such as choice of drying method, removal of rings, etc. Of the 14 studies reviewed in this chapter (Table 12.1), all study sites utilized hygienic hand rub and/or another method of hand disinfection as standard practice. However, only 2 studies assessed the specific characteristics of handwashing practice (eg, duration of washing, method of drying) according to established hospital guidelines,[13,14] while the other 12 studies assessed only whether or not handwashing occurred after patient contact.

Prevalence and Severity of the Target Safety Problem

Nosocomial infections occur in about 7-10% of hospitalized patients[1] and account for approximately 80,000 deaths per year in the United States.[15] Although handwashing has been proven to be the single most effective method to reduce nosocomial infections, compliance with recommended hand hygiene practices is unacceptably low.[7-9] Indeed, a recent review of 11 studies noted that the level of compliance with basic handwashing ranged from 16% to 81%.[4] Of these 11 studies, only 2 noted compliance levels above 50%.[4] One reason for poor handwashing compliance may be that the importance of this simple protocol for decreasing infections is routinely underestimated by health care workers.[2] Recent surveys demonstrate that although most health care workers recognize the importance of handwashing in reducing infections, they routinely overestimate their own compliance with this procedure.[10] A survey of approximately 200 health care workers noted that 89% recognized handwashing as an important means of preventing infection.[10] Furthermore, 64% believed they washed their hands as often as their peers, and only 2% believed that they washed less often than their peers did.[10]

Opportunities for Impact

Given these findings, opportunities for improvement in current practice are substantial, and efforts to improve current practice would have vast applicability. Many risk factors for non-compliance with hand hygiene guidelines have been identified, including professional category (eg, physician, nurse, technician), hospital ward, time of day or week, and type and intensity of patient care.[8] These results suggest that interventions could be particularly targeted to certain groups of health care workers or to particular locations, to increase the likelihood of compliance. Importantly, this study demonstrates that the individuals with the highest need for hand hygiene (ie, those with the greatest workloads) were precisely the same group least likely to wash their hands. Finally, another recent study noted that approximately 75% of health care workers surveyed reported that rewards or punishments would not improve handwashing, but 80% reported that easy access to sinks and availability of hand washing facilities would lead to increased compliance.[10]

Study Designs

A structured search of the PubMed database (including MEDLINE) and review of the bibliographies of relevant articles identified 14 studies that have examined methods to improve handwashing compliance (Table 12.1). Three studies were non-randomized controlled trials (Level 2) that directly compared separate units, or parts of units, in which one area received the intervention and another did not.[14,16,17] Eleven studies were before-after studies (Level 3), in which baseline data regarding handwashing rates were obtained during an initial observation period, and then measured again in the time period after a particular intervention. Regardless of the type of study design, details regarding the comparability of the groups under observation were reported in only 4 studies.[13,16,18,19]

Study Outcomes

All of the studies reported changes in percent compliance with handwashing, assessing whether or not handwashing took place (Table 12.1). While 13 studies assessed handwashing through observation of health care worker behavior (Level 2), one study assessed soap usage as an indicator of handwashing frequency (Level 3).[20] Two studies also assessed changes in the quality of handwashing.[13,14] Several studies reported results of surveys conducted following

interventions to assess effectiveness and potential adverse events related to the interventions.[14,20,21] One study also assessed changes in 2 clinical outcomes (incidence of nosocomial infections and newly detected cases of methicillin-resistant *Staphylococcus aureus*) as a result of interventions (Level 1).[18]

Evidence for Effectiveness of the Practice

Since many different risk factors have been identified for non-compliance with handwashing, it is not surprising that a variety of different interventions have been studied in an effort to improve this practice. While most of the reviewed studies demonstrated significant improvement in handwashing compliance,[9,13,17,18,20-22] some did not.[14,19,23,24] No single strategy has consistently been shown to sustain improved compliance with handwashing protocols.[11] In fact, of the studies which assessed longer-term results following intervention,[16,21,25] all 3 found that compliance rates decreased from those immediately following the intervention, often approaching pre-intervention levels.

Potential for Harm

While no harm is likely to befall a patient as a result of handwashing, one potential adverse effect of handwashing for health care workers is skin irritation. Indeed, skin irritation constitutes an important barrier to appropriate compliance with handwashing guidelines.[27] Soaps and detergents can damage the skin when applied on a regular basis. Alcohol-based preparations are less irritating to the skin, and with the addition of emollients, may be tolerated better.[6]

Another potential harm of increasing compliance with handwashing is the amount of time required to do it adequately. Current recommendations for standard handwashing suggest 15-30 seconds of handwashing is necessary for adequate hand hygiene.[28] Given the many times during a nursing shift that handwashing should occur, this is a significant time commitment that could potentially impede the performance of other patient care duties. In fact, lack of time is one of the most common reasons cited for failure to wash hands.[11] Since alcohol-based handrubs require much less time, it has been suggested that they might resolve this concern. In fact, a recent study which modeled compliance time for handwashing as compared with alcoholic rubs, suggested that, given 100% compliance, handwashing would consume 16 hours of nursing time per standard day shift, while alcohol rub would consume only 3 hours.[29]

Costs and Implementation

Interventions designed to improve handwashing may require significant financial and human resources. This is true both for multifaceted educational/feedback initiatives, as well as for interventions that require capital investments in equipment such as more sinks, automated sinks, or new types of hand hygiene products. The costs incurred by such interventions must be balanced against the potential gain derived from reduced numbers of nosocomial infections. Only one study addressed the cost implications of handwashing initiatives.[20] The implementation of a patient education campaign, when compared to the estimated $5000 per episode cost of each nosocomial infection, would result in an annual savings of approximately $57,600 for a 300-bed hospital with 10,000 admissions annually.[20] As others have estimated that the attributable cost of a single nosocomial bloodstream infection is approximately $40,000 per survivor,[30] the potential cost savings of interventions to improve handwashing may be even greater.

Comment

While many studies have investigated a variety of interventions designed to improve compliance with handwashing, the results have been mixed. Even when initial improvements in compliance have been promising, long-term continued compliance has been disappointing. Future studies should focus on more clearly identifying risk factors for non-compliance, and designing interventions geared toward sustainability. Some investigators postulate that better understanding of behavior theory, and its application to infection control practices, might result in more effectively designed interventions.[26] In addition, any intervention must target reasons for non-compliance at all levels of health care (ie, individual, group, institution) in order to be effective. A more detailed study of the cost (and potentially cost savings) of handwashing initiatives would also foster greater enthusiasm among health care institutions to support such initiatives.

Table 12.1. Fourteen studies of practices to improve handwashing compliance*

Study Setting; Practice	Study Design, Outcomes	Handwashing Compliance (unless otherwise noted)†
All medical staff in a neurologic ICU and a surgical ICU in a 350-bed tertiary care teaching hospital in Washington, DC, 1983-84; multifaceted intervention (education, automatic sinks, feedback)[16]	Level 2, Level 2	69% vs. 59% (p=0.005)
Medical staff in 2 ICUs in a university teach hospital in Philadelphia; increase number of available sinks[17]	Level 2, Level 2	76% vs. 51% (p<0.01)
Medical staff in a 6-bed post-anesthesia recovery room and a 15-bed neonatal ICU in a tertiary care hospital in Baltimore, 1990; automatic sink compared with standard sink[14]	Level 2, Level 2	Mean handwashes per hour: 1.69 vs. 1.21 on unit 1; 2.11 vs. 0.85 on unit 2; (p<0.001)
All staff at a large acute-care teaching hospital in France, 1994-97; hand hygiene campaign including posters, feedback, and introduction of alcohol-based solution[18]	Level 3, Level 1	Noscomial infections: 16.9% vs. 9.9% Handwashing: 66.2% vs. 47.6% (p<0.001)
Medical staff in a 6-bed pediatric ICU in a large academic medical center in Virginia, 1982-83; mandatory gowning[19]	Level 3, Level 2	29.6% vs. 30.7%
Medical staff in 2 ICUs in a community teaching hospital in Tennessee, 1983-84; sequential interventions of lectures, buttons, observation, and feedback[24]	Level 3, Level 2	29.9% vs. 22% (p=0.071)
Medical staff in an 18-bed ICU in a tertiary care hospital in Australia; introduction of chlorhexidine-based antiseptic handrub lotion[9]	Level 3, Level 2	45% vs. 32% (p<0.001)
12 nurses in a 12-bed ICU in Mississippi, 1990; education/feedback intervention[31]	Level 3, Level 2	92% vs. 81%
Medical staff in an 18-bed pediatric ICU in a children's teaching hospital in Melbourne, 1994; 5-step behavioral modification program[25]	Level 3, Level 2	Handwashing rates after patient contact: 64.8% vs. 10.6%
Medical staff in a 3000-bed tertiary care center in France, 1994-95; 13-step handwashing protocol [13]	Level 3, Level 2	18.6% vs. 4.2% (p<0.0001)

Table 12.1. Fourteen studies of practices to improve handwashing compliance (cont.)

Medical staff in two ICUs at a teaching hospital in Virginia, 1997; 6 education/feedback sessions followed by introduction of alcohol antiseptic agent[22]	Level 3, Level 2	Baseline 22%; Education/feedback 25%; Alcohol antiseptic 48%; ($p<0.05$)
Medical staff in a 14-bed ICU in a tertiary care hospital in France, 1998; introduction of alcohol-based solution[21]	Level 3, Level 2	60.9% vs. 42.4% ($p=0.0001$)
All staff in a medical ICU and step-down unit in a large teaching hospital in Virginia; installation of alcohol-based solution[23]	Level 3, Level 2	52% vs. 60% ($p=0.26$)
Medical staff on 2 general inpatient floor at each of 4 community hospitals in New Jersey; patient education intervention[20]	Level 3, Level 3	Soap usage (as an indicator of handwashing) increased by 34% ($p=0.021$)

* ICU indicates intensive care unit.
† Results are reported as intervention group vs. control group.

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Chapter 13. Impact of Barrier Precautions in Reducing the Transmission of Serious Nosocomial Infections

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Background

Many nosocomial infections are easily transferable from patient-to-patient, either via the hands of health care workers,[1,2] or through the contamination of inanimate objects, including clothing and equipment.[3,4] For some infections, the threat to other patients is considered serious enough that many institutions employ special barrier precautions, such as the use of gloves, gowns and disposable equipment for all patient contact, in caring for patients colonized or infected with these pathogens. Vancomycin-resistant enterococci (VRE)[5] and *Clostridium difficile*[6] represent 2 typical examples of nosocomial pathogens that may trigger such precautions.

Although adherence to barrier precautions to prevent the spread of particularly concerning nosocomial pathogens has obvious face validity, the utility of specific interventions and the optimal forms they should take remain unclear. This uncertainty may in part reflect the impact of particular aspects of the epidemiology of the targeted nosocomial pathogens – ie, the benefit of a given strategy may vary in different settings and with different organisms. Consequently, this chapter contrasts with the review of handwashing (Chapter 13), a practice for which the benefit was regarded as sufficiently established to warrant focusing on strategies for improving compliance. While compliance with barrier precautions is also an important topic and likely plays a significant role in the efficacy of such interventions, this chapter analyzes the literature evaluating the benefit of the barrier precautions themselves.

Practice Description

Barrier precautions include any activity designed to prevent the spread of nosocomial pathogens from patient to patient. This chapter reviews the following 3 practices:

- *Use of gowns and gloves for all contact with patients colonized or infected with VRE and/or C. difficile:* Health care workers typically don gloves and gowns when entering the room of an infected or colonized patient, and remove them upon exiting (followed immediately by handwashing) to reduce the likelihood of clothing or equipment contamination that could transmit pathogens to other patients;
- *Use of dedicated or disposable examining equipment for patients colonized or infected with VRE and/or C. difficile*: Hospital equipment (ie, blood pressure cuffs, thermometers) remains in a patient's room and is not carried from room to room; and
- *Patient and/or staff cohorting for patients colonized or infected with VRE and/or C. difficile*: Patients colonized or infected with similar pathogens are admitted to specific floors of the hospital where designated health care workers care only for patients colonized or infected with these pathogens.

Prevalence and Severity of the Target Safety Problem

Nosocomial infections, including *C. difficile*-associated diarrhea and VRE, significantly increase the morbidity and mortality of hospitalized patients.[5,6] Both infections are also associated with increased hospital costs. Recent evidence also suggests there may be a relationship between *C. difficile* and VRE, with *C. difficile* infection identified as a risk factor for VRE infection.[7] The increased incidence of both VRE and *C. difficile* can be attributed to spread from patient to patient.[5,6] Failure to recognize these dissemination patterns may result in an inability to contain outbreaks when they occur in the hospital.

C. difficile has been identified as the major, if not only, important cause of infectious diarrhea that develops in patients after hospitalization, occurring in up to 30% of adult hospitalized patients who developed diarrhea.[5] One study found an acquisition rate of 13% for patients hospitalized 1-2 weeks, which increased to 50% for patients hospitalized >4 weeks.[8] In addition, the incidence of *C. difficile* infection has increased in recent years, with one study reporting a 5-fold increase in clinical infection between 1993 and 1996.[9] *C. difficile* infection increases lengths of stay, often to as long as 18-30 days[10,11] and, when fulminant, can lead to exploratory and therapeutic surgical procedures.[12] Mortality attributable to *C. difficile*, while reported, occurs in fewer than 5% of patients.[13] The costs associated with *C. difficile* diarrhea, while not well described, may be as high as $10,000 per patient.[14]

VRE, first described in 1988, currently accounts for greater than 25% of all nosocomial enterococci.[6] Early national data suggested that infections with VRE were associated with mortality rates of over 36%, more than double that of patients with vancomycin-susceptible (VSE) infections.[15] While later studies called some of these results into question,[16,17] the most recent studies have again suggested that vancomycin-resistance carries an independent effect on mortality.[18] VRE infections are also associated with significantly higher hospital costs than those due to VSE.[18]

Although *C. difficile* and VRE are among the most common nosocomial pathogens that have significant effects on morbidity, mortality, and cost, there are a number of other nosocomial pathogens which could also be studied. These include pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum beta-lactamase (ESBL) producing *Enterobacteriaceae*, *Acinetobacter* species, and *Pseudomonas aeruginosa*. While these are all important nosocomial pathogens, *C. difficile* and VRE were chosen as examples because they are extremely common, and they represent both antibiotic-susceptible (*C. difficile*) and antibiotic-resistant (VRE) pathogens. Additionally, (unlike MRSA and *P. aeruginosa*) the epidemiology of both pathogens is complex, representing both person-to-person spread and association with prior antibiotic use, allowing for a more comprehensive discussion of the relative merits of both antimicrobial use interventions and barrier precaution interventions (see Chapter 15 for more discussion regarding other antimicrobial intervention practices) and their general application to other pathogens.

Opportunities for Impact

As noted above, both VRE and *C. difficile* affect a large proportion of hospitalized patients. Improvements in barrier precaution interventions against these pathogens would have a tremendous impact. There are few data regarding the percentage of hospitals that employ any one of a number of barrier precautions (eg, gowns, gloves, disposable thermometers).[19] In addition, while standard practice is to apply barrier precautions for patients with nosocomial pathogens with demonstrated horizontal spread, compliance with precautions is frequently

poor,[20] often below 50%.[21] Purported reasons for this lack of compliance include lack of resources and busy staff workload.[20] Regardless, these results suggest that the opportunity for improvement in these practices is great.

Study Designs

A structured search of the PubMed database (including MEDLINE) and review of the bibliographies of relevant articles identified 19 studies that have examined the implementation of barrier precaution practices designed to impact the incidence of VRE and/or *C. difficile* infection (Table 13.1, 13.2, 13.3). All studies found on literature search were included in this review except for those reporting very small outbreaks (defined as fewer than 10 cases of *C. difficile* or VRE). Sixteen of the reviewed studies were before-after observational cohort studies (Level 3), in which baseline data regarding incidence of VRE or *C. difficile* were obtained during an observational period and compared to a second period after implementation of an intervention. Crude comparability data on the before and after groups (eg, total admissions, patient census) were provided in 2 reports[22,23] while only one study statistically compared the before and after groups to assess comparability.[24] Three reports[25-27] detailed unblinded comparative studies (Level 2) in which patients on different wards were assigned different interventions. Each of these studies assessed the comparability of the study groups on the basis of underlying demographic variables.

Study Outcomes

All of the studies reviewed reported changes in the incidence or prevalence of either VRE or *C. difficile* as a result of barrier precaution interventions (Level 1). For studies investigating *C. difficile*, all outcomes were reported in terms of clinical infections. For studies investigating VRE, outcomes were reported as VRE colonization and/or infection rates.

Evidence for Effectiveness of the Practice

As both VRE and *C. difficile* have clearly been shown to be transferable from patient-to-patient, interventions designed to improve barrier precautions yield significant reductions in the incidence of infection with these two pathogens. All studies that examined the effect of enhanced barrier precautions on *C. difficile* infection demonstrated benefit, suggesting that barrier precaution interventions are effective in controlling its emergence. Most studies employed a multifaceted approach including several different barrier precaution components. For example, one study combined use of vinyl gloves and ongoing educational interventions,[26] another included cohorting, culture screening, and daily room disinfection,[28] while another combined reinforcement of enteric precautions, replacement of electronic thermometers, and institution of closed paper towel dispensers.[29] Given the varied components of barrier precaution interventions instituted in different studies, it is difficult to determine the specific effect of any individual component.

The evidence of effectiveness of barrier precautions for VRE is somewhat less clear-cut. All but 4[27,30-32] of the studies examining the effect of barrier precautions on VRE demonstrated a benefit, but study design differences and particular epidemiologic trends may account for the inconsistent findings.

One of the 4 studies that noted no significant effect compared glove use to glove and gown use.[27] The second [30] noted that the emergence of VRE at the study institution was due to multiple genetically-unrelated strains, suggesting that person-to-person spread was less important at that site. It is thus not surprising that barrier precautions would have less of an

effect. In the third study,[32] routine rectal swab surveillance and contact precautions were instituted in response to a clinical outbreak of VRE and surveillance was continued for only 6 months. Since surveillance was not conducted prior to institution of precautions, it is impossible to say what the colonization prevalence had been prior to the intervention. Furthermore, as the authors point out, it may be that the outbreak would have been much worse had the precautions not been put in place. Finally, no determination of genetic relatedness (and hence spread) was made in this study. In the fourth study,[31] while there was a reduction in the isolation of VRE, there was not complete eradication. According to the authors, the most likely reason for this less-than-optimal response was poor compliance with contact precaution guidelines.

Thus, it appears that enhanced barrier precautions are generally effective in reducing the incidence of VRE but that various aspects of both the epidemiology of the VRE outbreak and the implementation of guidelines may temper the effectiveness of interventions. Similar to the studies investigating response of *C. difficile* to barrier precautions, most studies of VRE employed several components of barrier precautions as part of a multifaceted approach (Table 13.1). It is thus difficult to determine the specific effect of any individual component.

Potential for Harm

None of the reviewed studies reported any assessment of possible harm as a result of the barrier precaution interventions. In fact, the implementation of barrier precautions is unlikely to result in harm to the patient. One potential concern is that time necessary to comply with the interventions (eg, gowning, gloving), might make health care workers less likely to complete tasks necessary to provide acceptable patient care. Indeed, it has recently been noted that health care workers were half as likely to enter the rooms of patients on contact isolation.[33] Furthermore, while contact precautions appeared to have little effect on patient examination by resident physicians, attending physicians were 50% less likely to examine a patient on contact precautions compared to a patient not on precautions.[34] Future studies should address these concerns by documenting the time required to adhere to barrier precautions, and determining the potential impact of precautions on patient care.

Another potentially harmful consequence of barrier precaution interventions is the psychological effect that contact precautions may have on the isolated patient. While research has examined the effects of sensory deprivation and social isolation, a recent review of the literature noted little progress in the investigation of the psychological effects of contact isolation.[35]

Costs and Implementation

It seems apparent that the more complicated an intervention, the less likely health care workers will adhere to it. While 2 studies noted compliance with barrier precautions at close to 90%,[21,24] others noted levels closer to 70%.[31] One study actually noted compliance levels to be significantly higher in those health care workers who used both gowns and gloves compared to those using only gowns.[27] This somewhat counterintuitive finding suggests that other factors may be at play in influencing compliance. Of the reviewed studies that reported compliance levels, all did so relatively shortly after the initial implementation of interventions. Future studies should assess compliance with guidelines over a longer period.

Four studies reported the costs of specific interventions. Implementation of use of disposable thermometers was estimated at $14,055 per year at a 343-bed institution.[22] Another study of the impact of disposable thermometers estimated that the cost per prevented *C. difficile* infection would be approximately $611.[25] A study using a multifaceted approach estimated that

the annual expenses due directly to increased demand for gowns and gloves were approximately $11,000.[31] Finally, a multifaceted intervention at a 254-bed long-term care facility which included education, gowns and gloves for resident contact, no sharing of personal equipment, and daily double cleaning of resident rooms and wheelchairs, estimated the total cost of the intervention to be $12,061 Canadian (approximately $8000 US).[36]

The costs of implementing a program to enhance barrier precaution practices must be balanced against the potential cost savings due to decreased incidence of nosocomial infections. Both VRE and *C. difficile* infections have been associated with significantly increased length of hospital stay.[5,6] Preventing even a small number of these infections is likely to have a significant financial impact. While several of the reviewed studies documented costs associated with various interventions,[22,25,26,31,36] no study systematically compared these costs to the potential cost savings of infections prevented.

Comment

The majority of reviewed studies demonstrated a significant reduction in the incidence of VRE or *C. difficile* following barrier precaution interventions. The fact that not all studies found a benefit suggests that future studies should identify those scenarios (eg, outbreak, endemic colonization, etc.) in which attention to barrier precautions is most likely to be beneficial. In addition, it is possible that a combined intervention involving both enhanced barrier precautions as well as antibiotic formulary interventions might be needed in order to effect the greatest possible change in VRE and *C. difficile* infection rates. While these studies, much like those that examined the impact of antibiotic use practices, demonstrated short-term success, future studies should determine the efficacy of such interventions over the long term. Finally, the cost-effectiveness of such strategies should be investigated.

Table 13.1. Studies of multifaceted approaches with and without "cohorting"*

Study Setting	Compliance	Study Design, Outcomes	Change in *C. difficile* or VRE
725-bed academic medical center in Philadelphia in 1987-88: before-after study of impact of multifaceted intervention (isolation precautions, clindamycin restriction) on *C. difficile*[37]	NA	Level 3, Level 1	Cases of *C. difficile* decreased from 1.47 cases/100 hospital discharges in 1987 to 0.74 cases/100 hospital discharges by the second half of 1988
350-bed acute care hospital in Virginia in 1987-96: before-after study of impact of multifaceted intervention on *C. difficile* infections[23]	NA	Level 3, Level 1	Mean annual new cases of *C. difficile* decreased from 155/year in the before period to 67/year in the after period ($p<0.05$).
840-bed tertiary care center in Brussels in 1989-90: impact of a multifaceted infection control intervention, including cohorting, on incidence of *C. difficile*[28]	NA	Level 3, Level 1	Incidence of *C. difficile* decreased from 1.5 cases/1000 admissions to 0.3 cases/1000 admission (protective efficacy 73%, 95% CI: 46-87%)
Bone marrow transplant unit of a large academic medical center in Texas in 1995: impact of multifaceted infection control intervention on *C. difficile* attack rate[29]	NA	Level 3, Level 1	Attack rate for third week in May was 60%. Following intervention, rate dropped to 17% for remainder of May, 21% for June, and 7% for July ($p<0.05$)
Tertiary-care Veterans Affairs Medical Center in Brooklyn in 1991-95: impact of multifaceted infection control intervention on VRE rates[30]	NA	Level 3, Level 1	Incidence of VRE cases per 1000 admissions was 0.6 in 1991, 3.3 in 1992. Following intervention, the rates were 8.0 in 1993 and 9.2 in 1994
22-bed oncology unit in a 650-bed tertiary care hospital in New York in 1993-95: impact of multifaceted infection control program, including cohorting, on VRE infection and colonization[24]	91.7% of persons who entered room used gowns and gloves appropriately	Level 3, Level 1	Incidence of VRE bloodstream infection (patients per 1000 patient-days) decreased from 2.1 to 0.45 ($p=0.04$). VRE colonization decreased from 20.7 to 10.3 ($p<0.001$).
375-bed community hospital in Indianapolis in 1995-96: impact of cohorting on VRE prevalence[21]	Compliance with recom-mendations rose from 22% to 88% ($p<0.001$)	Level 3, Level 1	VRE prevalence decreased from 8.1% to 4.7% ($p=0.14$). VRE among patients whose VRE status was unknown before cultures were obtained decreased from 5.9% to 0.8% ($p=0.002$).

254-bed long-term care facility in Toronto in 1996-97: impact of barrier precautions including cohorting on prevalence of VRE[36]	NA	Level 3, Level 1	4/85 (4.7%) patients initially screened were VRE colonized. No patients in subsequent screenings were positive.

Table 13.1. Studies of multifaceted approaches with and without "cohorting" (cont.)

23-bed oncology unit in a 1300-bed teaching hospital in South Africa in 1998: impact of barrier precautions including cohorting on VRE prevalence[39]	NA	Level 3, Level 1	VRE colonization decreased from 19/34 (55%) patients to 1/14 (7%) following implementation of infection control interventions
347-bed tertiary care medical center in Massachusetts in 1993: impact of a multifaceted infection control intervention including cohorting on VRE infection and colonization[31]	Overall hand-washing compliance was 71%	Level 3, Level 1	In the year prior interventions, 116 patients were colonized or infected with VRE, compared with 126 in the year after implementation.

* NA indicates not applicable; VRE, vancomycin-resistant enterococci.

Table 13.2. Studies of barrier precaution interventions*

Study Setting	Compliance	Study Design, Outcomes	Change in *C. difficile* or VRE
370-bed academic medical center in Massachusetts in 1991-92: before-after study of impact of infection control interventions on *C. difficile* incidence[38]	NA	Level 3, Level 1	Incidence of *C. difficile* increased from 0.49% to 2.25% from 1989 to 1993. Following interventions, incidence of *C. difficile* decreased to 1.32%
Veterans Administration Medical Center in Minnesota in 1986-87: impact of universal glove use on incidence of *C. difficile*[26]	Mean glove use/100 pts: 4539 on glove ward; 3603 on control ward (p=NS)	Level 2, Level 1	Incidence of *C. difficile* on glove wards decreased from 7.7/1000 patients discharges to 1.5/1000 (p=0.015). No significant change in incidence on the control wards
8-bed combined medical and surgical ICU in a 235-bed acute care hospital in New York City in 1990-91: impact of barrier precautions on VRE colonization[1]	NA	Level 3, Level 1	16 patients infected or colonized with VRE identified over 6 months period. No new VRE infection or colonization in the 2 months after intervention.
250-bed university-affiliated hospital in Rhode Island in 1991-92: impact of sequential barrier precaution intervention on VRE[40]	NA	Level 3, Level 1	13 patients with VRE identified over 8 month period. In the 3 months after the first intervention (private room + gloves) 20 patients were found to have VRE. In the 6 months after the second intervention (gowns added), 4 patients were VRE positive.
181 consecutive patients admitted to the medical ICU in a 900-bed urban teaching hospital in Chicago in 1994-95: comparison of impact of gown and glove vs. glove on incidence of VRE colonization[27]	Compliance in glove and gown group, 79%; glove group, 62% (p<0.001)	Level 2, Level 1	24 (25.8%) of the glove and gown group acquired VRE in the ICU compared to 21 (23.9%) of those patients in the gown only room (p=NS)
550-bed tertiary teaching hospital in Minneapolis in 1993-94: impact of barrier precautions on VRE colonization[32]	NA	Level 3, Level 1	Weekly rectal swab surveillance performed. Rates of VRE colonization remained at 7-9% throughout 6 month study period

* ICU indicates intensive care unit; NA, not applicable; NS, not statistically significant; and VRE, vancomycin-resistant enterococci.

Table 13.3. Studies of use of dedicated or disposable examining equipment*

Study Setting	Compliance	Study Design, Outcomes	Change in *C. difficile* or VRE
343-bed acute hospital and 538-bed skilled nursing facility in New York: before-after study of impact of replacing electronic thermometers with disposable thermometers on *C. difficile* infection rate[22]	100% replacement of electronic thermo-meters	Level 3, Level 1	Incidence of *C. difficile* decreased from 2.71 to 1.76 cases per 1000 patients in the acute hospital ($p<0.01$) Incidence of *C. difficile* decreased from 0.41 to 0.11 cases per 1000 patient days in the skilled nursing facility ($p<0.01$)
20 inpatient units in a 700-bed university hospital in Virginia: randomized crossover trial of impact of disposable thermometers for prevention of *C. difficile*[25]	100% compliance with use of specific types of ther-mometers	Level 2, Level 1	Incidence of *C. difficile* was 0.16 cases/1000 patient days in the intervention group compared to 0.37/1000 patient days in controls (RR 0.44, 95% CI: 0.21-0.93; p=0.026]
343-bed acute care facility in New York in 1992: impact of change to tympanic thermometers on VRE incidence[22]	100% switch to tympanic thermo-meters	Level 3, Level 1	Tympanic thermometer use resulted in risk reduction for VRE of 60% (RR 0.41, 95% CI: 0.31-0.55)

* CI indicates confidence interval; RR, relative risk; and VRE, vancomycin-resistant enterococci.

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Chapter 14. Impact of Changes in Antibiotic Use Practices on Nosocomial Infections and Antimicrobial Resistance – *Clostridium Difficile* and Vancomycin-resistant Enterococcus (VRE)

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Background

As discussed in the chapters on handwashing and barrier precautions (Chapters 12 and 13), hospital infection control has historically focused on preventing the transmission of nosocomial pathogens—either from patient to patient or from provider to patient. The potential role of overseeing hospital-wide antibiotic use as an infection control measure has also been recognized for many years.[1] With the widespread emergence of nosocomial antibiotic-resistant infections over the past 10-15 years, institutional efforts to control antibiotic use have become a priority for infection control.[2,3]

The practices reviewed in this chapter involve institutional efforts to control antibiotic use as a means of controlling complications of antibiotic overuse or misuse. In evaluating the potential benefits of these practices, the focus is on the impacts of antibiotic use on infections with vancomycin-resistant enterococci (VRE)[4] and *Clostridium difficile.*[5] These pathogens represent two of the most important nosocomial pathogens with relationships to inappropriate antibiotic use. Moreover, as suggested by recent evidence, infection with *C. difficile* may represent a risk factor for infection with VRE.[6]

Practice description

Interventions designed to limit the use of antibiotics may take many forms. Specific practices reviewed in the chapter include:

- *Infectious diseases physician approval*[7] – all requests for an antibiotic are discussed with an infectious diseases physician who decides whether use is appropriate
- *Monitoring of antibiotic use by pharmacy service*[8] – pharmacists monitor the use of certain antibiotics and make recommendations for changes to the prescriber
- *Guidelines for antimicrobial use*[8] – dissemination to physicians of guidelines describing appropriate and inappropriate use
- *Therapeutic substitution*[9] – use of one agent replaced by another agent with similar spectrum of activity
- *Computer-assisted prescribing*[10] – computer-based restriction of agent with extra prompts requesting documentation of indication for agent
- *Antibiotic-management program (AMP)*[11] – continuation of antibiotic after a specific duration requires approval from either an infectious diseases physician or pharmacist on the AMP

Prevalence and Severity of the Target Safety Problem

This chapter focuses on 2 of the most important nosocomial pathogens: VRE and *C. difficile*. VRE currently accounts for greater than 25% of all nosocomial enterococci[4] and confers an increased risk of death, independent of comorbid conditions that may have initially led to the infection.[12] VRE infections are also associated with significantly higher hospital costs than those due to vancomycin-sensitive enterococci (VSE)[12] (see Chapter 13). *C. difficile* represents the major, if not only, important infectious cause of nosocomial diarrhea.[5] Although death attributable to *C. difficile* occurs in less than 5% of patients,[17] the impact of *C. difficile* infection remains significant. Patients may require substantially longer lengths of hospital stay—upwards of 18-30 days,[18,19] with exploratory and therapeutic surgical procedures required in severe cases.[20] It has also been suggested that more debilitated patients (eg, in rehabilitation centers or long-term care facilities) may be at even greater risk for increased morbidity and mortality due to *C. difficile* infection.[21] The costs associated with *C. difficile* diarrhea, while not well described, are estimated to be as high as $10,000 per patient[22] (see Chapter 13).

Opportunities for Impact

Over half of all hospitalized patients are treated with antibiotics.[23] The antibiotics represent a significant portion of overall health care costs, accounting for between 20% and 50% of total hospital drug expenditures.[23] It has been estimated that 50% of all antibiotics prescribed are either at the wrong dose, the wrong drug, or taken for the wrong duration.[24,25] These findings suggest that there is significant room for improvement in antibiotic prescribing practices.

Most hospitals employ formulary restrictions for certain medications (particularly expensive agents, selecting one drug from a group of equivalent agents). However, only a minority of hospitals uses formulary restrictions to limit the use of entire antibiotic classes or specific agents. Those hospitals that do employ antimicrobial formulary restrictions most often do so as a means of controlling costs, rather than as an infection control measure.[26] Thus, there remain substantial opportunities to expand upon these existing formulary programs to control the emergence of antimicrobial resistance.

Study Designs

A structured search of the PubMed database (including MEDLINE) and review of the bibliographies of relevant articles identified 10 studies that have examined methods to change antibiotic use with respect to VRE and/or *C. difficile* infection (Table 14.1). All of these studies were before-after observational cohort studies (Level 3) in which baseline data regarding incidence of VRE or *C. difficile* were obtained during an observational period and compared with a second time period after an intervention had been implemented. Data on baseline comparability of the before and after groups were not reported in 6 studies.[8-11,21,27] Two studies only reported similar admission and census rates during the before and after time periods,[7,28] while 2 studies compared patients in the 2 time periods on the basis of numerous variables.[29,30]

Study Outcomes

All of the studies reviewed reported changes in the clinical incidence or prevalence of either VRE or *C. difficile* as a result of antibiotic practice interventions (Level 1). Studies investigating *C. difficile* measured clinical infections. Studies investigating VRE examined VRE infection[11] or VRE colonization.[8-10,27]

Evidence for Effectiveness of the Practice

Of the 10 studies listed in Table 14.1, all but 3[8,11,21] showed significant reductions in the incidence of *C. difficile* or VRE following practice changes. Several possibilities may explain the negative findings of these 3 studies. First, the interventions analyzed might not have produced significant alterations in antibiotic use, so that infection rates with the target pathogens remained unchanged. Second, it is possible that patient-to-patient spread of these pathogens limited the efficacy of the interventions, as this mode of transmission is well known to occur for both VRE and *C. difficile*, usually via the hands of health care workers (see also Chapter 13).[31,32] Third, since environmental contamination occurs with both these pathogens, successful control of these organisms may require enhanced disinfection procedures in some cases.[33,34] Targeting antibiotic use may not be sufficient to reduce incidence of these pathogens since a significant number of infected or colonized patients may serve as reservoirs. Under this scenario, the argument for barrier precautions as an adjunct measure to prevent spread of organisms from patient to patient becomes more persuasive (see Chapter 13). Indeed, although changes in antibiotic use practice were the primary intervention in all of the studies reviewed here, one study included a component of enhanced barrier precautions in the intervention.[21] Future studies should investigate the impact of such multifaceted interventions, both for VRE and *C. difficile* as well as for other nosocomial pathogens.

Other Potential Benefits

Although not the focus of this chapter, the practices reviewed here may have a beneficial impact on other emerging nosocomial pathogens strongly associated with inappropriate antibiotic use, such as extended-spectrum beta-lactamase (ESBL) producing *Enterobacteriaceae.*[35] In addition, although we have focused on control of VRE as an end in itself, a primary motivation to achieve this goal is the need to delay the emergence of vancomycin-resistance in *Staphylococcus aureus*.[36,37] As *S. aureus* represents the most common nosocomial infection,[38] the development of high-level vancomycin resistance among staphylococci would constitute a public health disaster.[39]

Thus, practices that decrease the prevalence of VRE may play an important, albeit indirect, role in preventing or delaying this occurrence.

Potential for Harm

Few of the reviewed studies reported any assessment of possible harm as a result of the antibiotic use practice interventions. One potential result of interventions designed to reduce the use of one antibiotic, or antibiotic class, is the subsequent increase in the use of another class of agents to compensate. In fact, one reviewed study[7] noted an increase in the use of other anti-anaerobic agents as clindamycin use decreased. Whether changes in antibiotic use results in changes in antimicrobial susceptibilities, either in the pathogen under study (eg, VRE, *C. difficile*) or in other nosocomial pathogens, it is a fertile ground for future study.

Finally, efforts to decrease use of certain antibiotics might increase infection rates due to inappropriate withholding of appropriate antibiotics. However, one reviewed study [10] noted no increase in rates of surgical site infections following decrease in the use of vancomycin for preoperative prophylaxis (see also Subchapter 20.1).

Costs and Implementation

The costs of implementing a program to alter antibiotic use practices must be balanced against potential cost savings. Sources of savings may be reduced antibiotic use, use of less expensive agents rather than the more expensive newer agents, and potentially, reduced costs due to decreased incidence of nosocomial infections as a result of interventions. Although several studies reported cost savings due only to decreased antibiotic use,[10,11,29] analyses taking into account costs related to subsequent infections (or infections prevented) have been sparse. One study noted that cost savings from decreased use of clindamycin offset the expenditures due to increased use of other antibiotics.[7] The authors suggested that if each case of *C. difficile* resulted in a cost of $2000, the savings to the hospital of the intervention could approach $162,000 annually based on the number of cases averted.[7]

Another cost of antibiotic use interventions is the expense of ongoing monitoring of antibiotic use and antimicrobial susceptibilities of nosocomial pathogens. Effective recommendation of certain antimicrobial agents over others requires access to (and financial and logistic support for) routine antimicrobial susceptibility testing. Monitoring institutional resistance patterns is vital in order to make required formulary changes in response to emerging resistance patterns and to determine the most effective agents given prevailing susceptibility patterns.

Comment

Given the strong association between antibiotic use and subsequent infection (demonstrated for both *C. difficile* and VRE), it is not surprising that changes in antibiotic use practices can reduce the incidence of infection with these 2 pathogens. The majority of reviewed studies demonstrated a significant reduction in the incidence of VRE or *C. difficile* following interventions to change antibiotic use practice. While these studies all demonstrated short-term success, future studies should confirm the efficacy of such interventions over the long term. In addition, the effectiveness and feasibility of combining antibiotic practice strategies with efforts to enhance barrier precautions (Chapter 13) should be investigated. Finally, the cost-effectiveness of such strategies (taking into account both the costs associated with monitoring and maintaining sound antibiotic use practices and the costs associated with nosocomial antibiotic-resistant infections) should be investigated.

Table 14.1. Before-after studies of practices to improve antibiotic use*

Study Setting and Intervention	Outcomes	Results: before vs. after practice
Elderly care unit of a large teaching hospital in England, 1984-85; Changes in empiric antibiotic regimens[29]	Level 1	*C. difficile* infections decreased from 37 to 16 cases (p=0.002).
Chronic care facility in Baltimore, 1985-86; multifaceted intervention[21]	Level 1	Patients with *C. difficile* toxin decreased from 28% to 24% (p=NS); Patients with *C. difficile* culture increased from 33% to 42% (p=NS)
Veterans Affairs Medical Center in Arizona, 1990-92; restriction of clindamycin use[28]	Level 1	*C. difficile* infections decreased from 7.7 to 1.9 cases/month (p<0.001)
660-bed Veterans Affairs hospital in California, 1992-94; removal of antibiotic restrictions[30]	Level 1	Monthly incidence of *C. difficile* infections per 1,000 admissions increased from 3.4 to 6.2 (p<0.05)
703-bed Veterans Affairs Medical Center in Virginia, 1993-94; restriction of clindamycin use[7]	Level 1	*C. difficile* infections decreased from 11.5 to 3.33 cases/month (p<0.001)
557-bed academic medical center in Maryland, 1994; restriction of vancomycin use[8]	Level 2	Mean monthly prevalence of VRE decreased from 26% to 25% (p=NS)
35-bed hematologic malignancy unit in a large medical center in England, 1994-95; sequential antimicrobial formulary changes[9]	Level 2	VRE colonization for phases 1, 2, and 3 were 57%, 19%, 36%, respectively (p<0.001 for phase 1 vs. 2; p=0.08 for phase 2 vs. 3)
Large academic medical center in Virginia, 1994-95; computer-based restriction of vancomycin use[10]	Level 2	VRE colonization decreased (p<0.001, test for trend)
310-bed Veterans Affairs medical center in New York, 1995; restriction of multiple antibiotics[27]	Level 2	Point prevalence of VRE decreased from 42% to 15% (p<0.001)
725-bed teaching hospital in Philadelphia, 1995-96; restriction of vancomycin use[11]	Level 2	Incidence of VRE was unchanged at 30% (p=NS)

* NS indicates not statistically significant; VRE, vancomycin-resistant entercocci.

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Chapter 15. Prevention of Nosocomial Urinary Tract Infections

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Background

Many hospitalized patients require the placement of indwelling urinary catheters for days or even weeks at a time.[1] Only a minority of patients develop urinary tract infections because of the presence of these devices,[2,3] but the frequency of their use produces substantial overall morbidity for patients and costs to the health care system. Urinary tract infections (UTIs) account for up to 40% of nosocomial infections,[4,5] with urinary catheter-related infections causing the vast majority of nosocomial UTIs.[6] Each hospital-acquired UTI adds approximately $675 to the costs of hospitalization. When bacteremia develops, this additional cost increases to at least $2800.[2]

Because of the substantial complications and costs associated with the use of urinary catheters, a number of practices have been evaluated in an effort to reduce the incidence of urinary catheter-related infections. This chapter reviews the evidence supporting the use of silver alloy coated urinary catheters, and, because of its similarity, the recently described practice of using urinary catheters impregnated with the antibiotic combination of minocycline and rifampin. Subchapter 15.2 reviews the evidence supporting the use of suprapubic catheters as an alternative to urethral catheters.

Subchapter 15.1. Use of Silver Alloy Urinary Catheters

Practice Description

Silver is a highly effective antibacterial substance, which can be applied to various types of catheters. (See Subchapter 16.2 for a discussion of intravascular catheters coated with a combination of silver sulfadiazine and chlorhexidine). Multiple studies have suggested that silicone urethral catheters coated with hydrogel and silver salts reduce the risk of developing bacteriuria, compared with standard latex urethral catheters (Foley catheters). As shown in a recent meta-analysis, this benefit applies to catheters coated with silver alloy (which are coated on both internal and external surfaces of the catheter), but not silver oxide (which are coated on the external catheter surface only). Consequently, this chapter focuses only on studies evaluating silver alloy catheters, and the use of catheters coated with antimicrobials.[8]

Prevalence and Severity of the Target Safety Problem

Almost one million episodes of nosocomial UTI occur annually in the United States.[9] Each year approximately 96 million urethral catheters are sold worldwide. Of these, nearly 25% are sold in the United States.[3] The daily rate of bacteriuria in catheterized patients ranges from 3 to 10%, with the incidence directly related to the duration of catheterization.[4] Among patients with bacteriuria, 10 to 25% will develop symptoms of local urinary tract infection,[2,10] such as suprapubic or flank pain. The development of catheter-related bacteriuria carries with it a 2.8-fold increased risk of death, independent of other co-morbid conditions and disease severity.[11,12] Bacteremia results from catheter-related bacteriuria in approximately 3% of patients, and invariably represents a serious complication.[2,3]

Beyond the morbidity and mortality associated with indwelling catheters, catheter-related infection results in substantially increased health care costs. Data suggest that each episode of

hospital-acquired symptomatic catheter-related UTI costs an additional $676, and each episode of catheter-related nosocomial bacteremia costs a minimum of $2836.[2]

Estimates from one university hospital, based on data from almost 20 years ago, were that hospital-acquired UTI led to approximately $204,000 in additional expenses per year.[13] More recent data are unavailable, but the institutional costs attributable to catheter-related infection are clearly substantial.

Opportunities for Impact

Since catheter-related UTI is the leading cause of nosocomial infection in the United States and is associated with increased morbidity and costs, any intervention that reduces the incidence of catheter-related UTI is potentially important. Currently, it is unknown what proportion of patients with indwelling catheters receives silver alloy catheters, however it is likely to be the minority.

Study Designs

As shown in Table 15.1.1, a meta-analysis[7] which included 4 randomized clinical trials,[14-17] compared the efficacy of silver catheters with standard, non-coated catheters. Five additional studies[18-22] have appeared since publication of this meta-analysis. In 3 of these studies,[18,20,22] the patient represented the unit of analysis. Another study employed a randomized crossover design (Level 1), randomizing wards rather than individual patients.[19] The final study used a prospective, before-after design at 5 different hospitals (Level 2).[21]

The patient populations for these studies included patients on various hospital services including urology, internal medicine, neurology, and the intensive care unit. In general, the studies included patients expected to be catheterized for at least 2 days. Since the patients resided in acute care hospitals rather than extended care centers, most were catheterized for 10 days or less. Several studies specified that patients given concomitant antibiotics were excluded.[15-18]

Study Outcomes

The individual trials and the meta-analysis focused primarily on the surrogate outcome of bacteriuria (Level 2). The definition of bacteriuria varied somewhat in the studies. However, low-level growth from a catheterized specimen (ie, 10^2 colony forming units (CFU) /mL) usually progresses within days to concentrations of greater than 10^4 CFU/mL unless antibiotic therapy is given.[23] Unfortunately, none of the studies was adequately powered to detect a significant difference in the clinically more important outcomes of catheter-related bacteremia or death. Though bacteriuria is a surrogate endpoint,[24] it is probably appropriate to use since it is a component of the only causal pathway in the disease process between catheterization and an important clinical outcome (eg, symptomatic UTI or catheter-related bacteremia). One study did report differences in secondary bloodstream infections.[19]

Evidence for Effectiveness of the Practice

The 4 clinical trials[14-17] of silver alloy catheters included in the meta-analysis[7] all showed a significant reduction in the development of catheter-associated bacteriuria. As shown in Table 15.1.1, studies published after the meta-analysis have reported more mixed results. Several of the studies have shown a statistically significant benefit of silver alloy catheters, but with a smaller relative risk reduction compared to that reported in the meta-analysis.[19,21,22] However, one study failed to find a significant benefit associated with silver alloy catheters,[20] and another found benefit from silver alloy catheters in those given such catheters for about 5 days, but not in those given the catheter for 14 days.[18] A formal update of the previous meta-analysis would be helpful, but is beyond the scope of the current report.

Potential for Harm

There is likely minimal harm from the use of silver alloy urinary catheters. The one theoretical harm involves the development of antimicrobial resistance. However, since silver is not used systemically in the form of an antimicrobial agent for treatment, the clinical significance of antimicrobial resistance to silver is unclear.

Costs and Implementation

Each silver alloy urinary catheter tray costs about $5.30 more than a standard, non-coated urinary catheter tray. However, a recent economic evaluation indicates that when all the clinical and economic costs are accounted for, silver alloy urinary catheters may provide both clinical and economic benefits in patients receiving indwelling catheterization for 2 to 10 days.[3] It should be noted that one of the major assumptions made in the economic evaluation is that a certain proportion of patients with bacteriuria develop the clinically important (Level 1) outcomes of symptomatic UTI or bacteremia. The economic analysis did not assign any costs to bacteriuria but did assign costs if patients developed these clinically important outcomes. Additionally, several of the very recent efficacy studies of silver alloy catheters[19,21,22] were not included in the economic analysis. A clinical study, adequately powered to detect both meaningful clinical and economic endpoints, would confirm the results of this economic evaluation that relied on modeling techniques. The overall cost of universal implementation of silver alloy catheters is unclear.

Comment

The data supporting the use of silver alloy urinary catheters to reduce urinary catheter-related bacteriuria is reasonably strong. As noted, the incidence of bacteriuria, while not extremely high, carries a high morbidity. It remains unclear whether silver alloy urinary catheters will also lead to decreases in the clinically more important outcomes of catheter-related bacteremia and mortality. Continuing investigation into the impact of silver alloy catheters on these important outcomes and their effect on the emergence of antibiotic resistance should be pursued.

Of note, catheters coated with antibacterial substances other than silver have also been evaluated. A recent randomized study[8] found that patients who received antimicrobial-impregnated catheters coated with minocycline and rifampin had significantly lower rates of gram-positive bacteriuria than a control group given standard, non-coated catheters (7.1% vs. 38.2%; $p < 0.001$). Both control and intervention groups had similar rates of gram-negative bacteriuria and candiduria (Table 15.1.1). However, the theoretical risk of developing antimicrobial resistance to minocycline and/or rifampin (2 agents occasionally used systemically) may limit the use of catheters coated with these antibiotics.

Table 15.1.1. Studies of silver alloy and antibiotic-impregnated urethral catheters*

Study	Description	Design, Outcomes	Results: Odds or Risk of Bacteriuria† (unless otherwise noted)
Saint, 1998[7]	Meta-analysis of 4 randomized controlled trials (n=453) of silver alloy vs. uncoated urinary catheters	Level 1A, Level 2	OR 0.24 (95% CI: 0.11-0.52)
Maki, 1998[22]	Prospective, randomized, double-blind trial of silver alloy (n=407) vs. standard Foley (n=443) catheters	Level 1, Level 2	RR 0.74 (95% CI: 0.56-0.99)
Verleyen, 1999[18]	Prospective, randomized study of medium-term catheterization with silver alloy (n=18) vs. silicone (n=17) catheters after radical prostatectomy	Level 1, Level 2	After 14 days, 50.0% vs. 53.3% (p=NS)
	Prospective, randomized study of short-term catheterization with silver alloy (n=79) vs. latex (n=101) catheters	Level 1, Level 2	On day 5, 6.3% vs. 11.9% (p<0.003)
Bologna, 1999[21]	Prospective, blinded study of silver alloy vs. standard latex Foley catheters in 5 hospitals. Baseline period ranged from 3-12 months (mean, 8 months); intervention period ranged from 7-19 months (mean, 10 months)	Level 2, Level 1	Unadjusted infection rate: 4.5 vs. 7.1 infections per 1000 catheter days (p<0.01) Adjusted infection rate: 4.9 vs. 8.1 infections per 1000 catheter days (p=0.13)
Karchmer, 2000[19]	12-month randomized crossover trial of catheter-associated urinary tract infections in patients with silver-coated and uncoated catheters. The ward was the unit of analysis. A cost analysis was also conducted.	Level 1, Level 1	Infection rate: 2.66 vs. 3.35 infections per 1000 patient-days, RR 0.79 (95% CI: 0.63-0.99) Infection rate: 1.10 vs. 1.36 infections per 100 patients, RR 0.81 (95% CI: 0.65-1.01) Infection rate: 2.13 vs. 3.12 infections per 100 catheters, RR 0.68 (95% CI: 0.54-0.86) Estimated hospital cost savings with silver-coated catheters: $14,456 to $573,293
Thibon, 2000[20]	Multicenter, prospective, randomized, double-blind trial of silver alloy (n=90) vs. standard (n=109) catheters in patients	Level 1, Level 2	After 10 days, 10% vs. 11.9% OR 0.82 (95% CI, 0.30-2.20)

	requiring catheterization for >3 days		
Darouiche, 1999[8]	Multicenter, prospective, randomized, blinded trial of medium-term catheterization (mean, 14 days) with minocycline-rifampin impregnated (n=56) vs. silicone (n=68) catheters after radical prostatectomy	Level 1, Level 2	Patients took longer to develop bacteriuria with antimicrobial-impregnated catheters than control catheters (p=0.006 by the log-rank test) Overall bacteriuria at day 7: 15.2% vs. 39.7% (p<0.05) Overall bacteriuria at day 14: 58.5% vs. 83.5% (p<0.05) Gram-positive bacteriuria: 7.1% vs. 38.2% (p<0.001) Gram-negative bacteriuria: 46.4% vs. 47.1% (p=NS) Candiduria: 3.6% vs. 2.9% (p=NS)

* CI indicates confidence interval; NS, not statistically significant; OR, odds ratio; and RR, relative risk.

† Results are reported as intervention group (silver alloy or minocycline/rifampin catheter) vs. control group.

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Subchapter 15.2. Use of Suprapubic Catheters

Background

As discussed in Subchapter 15.1, the use of indwelling urethral catheters results in substantial morbidity and mortality. Given the medical and social morbidity associated with urethral catheters, many clinicians have considered suprapubic catheterization as an alternative

to catheterization via the urethra. Suprapubic catheters are inserted in the lower abdomen, an area with less bacterial colonization than the periurethral region, so that the risk for infection is thought to be lower than with urethral catheters. Furthermore, although the suprapubic placement of urinary catheters represents a minor surgical procedure, patients may find the result more comfortable[89] and, as reviewed below, the development of infectious complications is reduced. Subchapter 15.1 discusses the use of silver alloy urinary catheters. The focus of this chapter is the use of suprapubic catheters as compared with standard urethral indwelling catheters in adults.

Practice Description

Suprapubic catheterization typically involves the percutaneous placement of a standard urinary catheter directly into the bladder. The procedure is performed by urologists using sterile technique. It is generally performed in the operating room and is considered minor surgery.

Prevalence and Severity of Target Problem

In addition to the infectious complications (and their associated costs) discussed in Subchapter 15.1, the use of urethral catheters causes substantial patient discomfort. In a recent study at a Veteran Affairs Medical Center, 42% of catheterized patients surveyed reported that the indwelling catheter was uncomfortable, 48% complained that it was painful, and 61% noted that it restricted their activities of daily living.[7] Restricted activity reduces patient autonomy and may promote other nosocomial complications, such as venous thromboembolism and pressure ulcers. In addition, 30% of survey respondents stated that the catheter's presence was embarrassing, and in unsolicited comments that supplemented the structured questionnaires several noted that it "hurts like hell."[7]

Opportunities for Impact

Since catheter-related urinary tract infection (UTI) is the leading cause of nosocomial infection in the United States and is associated with increased morbidity and costs, any intervention that reduces the incidence of catheter-related UTI is potentially important. Currently, it is unknown what proportion of patients who require indwelling urinary catheters receive suprapubic catheters, however, this practice is uncommon.

Study Design

There have been twelve prospective studies,[8,9,11-17] all but one randomized,[15] comparing the efficacy of suprapubic catheters with standard, non-coated catheters (Table 15.2.1). In all of these studies, the patient was the unit of analysis. The patient populations for these studies varied but generally included patients with acute urinary retention and those undergoing various surgical procedures. Since most of the patients evaluated resided in acute care hospitals, the average duration of catheterization was generally less than 14 days.

Study Outcomes

All the trials focused on the outcome of bacteriuria. Several of the studies also assessed patient satisfaction and the incidence of mechanical complications. The definition of bacteriuria varied somewhat in the studies. However, low-level growth from a catheterized specimen (ie, 10^2 colony forming units (CFU)/mL) usually progresses within days to concentrations of greater than 10^4 CFU/mL, unless antibiotic therapy is given.[18] Unfortunately, none of the studies was adequately powered to detect a significant difference in the clinically more important outcomes of catheter-related bacteremia or death. Though bacteriuria is a surrogate endpoint,[19] it is

probably appropriate to use since it is a component of the only causal pathway in the disease process between suprapubic catheterization and an important clinical outcome (eg, symptomatic UTI or catheter-related bacteremia).

Evidence for Effectiveness of the Practice

As shown in Table 15.2.1, studies comparing suprapubic catheterization with urethral catheterization have produced mixed results.[8,9,11-17,20-22] Six trials reported lower rates of bacteriuria in patients with suprapubic catheters,[11,13,15,16,21,22] and 4 trials indicated greater patient satisfaction with suprapubic as opposed to urethral catheters.[8,13,16,20] In 3 of the studies, however, mechanical complications were higher in those receiving suprapubic catheters.[12,15,16] Of note, 3 studies found that patients given suprapubic catheters have significantly decreased incidence of urethral strictures compared with patients who received urethral catheters.[15,23,24] However, the use of prophylactic antibiotics in patients receiving urethral catheters for transurethral resection of the prostate has been shown to significantly reduce the incidence of strictures in the anterior urethra.[25]

Potential for Harm

As stated above, the primary problem associated with suprapubic catheter use involves mechanical complications associated with insertion, most commonly catheter dislodgement or obstruction, and failed introduction. The safe insertion of suprapubic indwelling urinary catheters depends on trained personnel.

Costs and Implementation

The cost of each suprapubic urinary catheter tray is comparable to the cost of each standard, non-coated urethral catheter tray. However, the overall initial costs of using suprapubic catheters will no doubt be greater since procedure-related costs are substantially higher for suprapubic than urethral catheters. Nurses are able to place urethral catheters at the bedside, but urologists must place suprapubic catheters, and the procedure typically occurs in the operating room. Additionally, it is unclear whether urologists are currently proficient at the insertion of suprapubic catheters given how infrequently they are used. If suprapubic catheters are shown to be effective, they may have a positive impact on patient care. The cost of training individuals in inserting and maintaining the suprapubic catheter is likely to be substantial.

Comment

When compared with standard urethral indwelling catheters, suprapubic urinary catheters may reduce urinary catheter-related bacteriuria. Additionally, patient satisfaction may be greater with suprapubic catheters, although there is also evidence that patients placed with suprapubic catheters more frequently experience certain mechanical complications. On the other hand, urethral catheters are likely to lead to a higher incidence of urethral strictures. Given these mixed results, conclusions regarding the overall benefit of routine suprapubic catheterization cannot currently be made. However, it would be reasonable to consider conducting a formal meta-analysis of the published trials to answer the question, “Compared with urethral indwelling catheters, are suprapubic catheters less likely to lead to UTI (as measured by bacteriuria) and more likely to lead to enhanced patient satisfaction?” Using explicit inclusion criteria and accepted quantitative methods, a meta-analysis[26-28] can often help clarify the features of individual studies that have divergent results.[29] In addition, a possible interaction between gender of the patient and type of catheter is of interest since different pathophysiologic mechanisms

underlie the development of urethral catheter-related infection in men and women.[30] The possibility of adequately evaluating effects within subgroups (eg, those undergoing certain surgical procedures) because of an increased sample size is one of the benefits of meta-analysis.[31]

If formal meta-analysis suggests that suprapubic catheters are less likely to lead to urinary tract infection and more likely to enhance patient satisfaction, at least in some clinical settings, then these catheters should be considered in the management of certain patients. On the other hand, if the meta-analysis finds that urethral catheters are superior to suprapubic catheters, then use of suprapubic catheters, albeit currently quite limited, should be further reduced.

Table 15.2.1. Prospective studies comparing suprapubic with urethral catheters

Study	Design, Outcomes	Patient Population*	Bacteriuria (%)†		Odds Ratio (95% CI)‡	Comments§
			Suprapubic	Urethral		
Shapiro, 1982[16]	Level 1, Level 2	General surgical patients with urinary retention	2/25 (8)	21/31 (68)	0.04 (0.01-0.24)	Pseudorandomized (urethral catheters used in every third patient) study; suprapubic group had less pain but more mechanical complications
Andersen, 1985[13]	Level 1, Level 2	Women undergoing vaginal surgery	10/48 (21)	20/44 (45)	0.32 (0.11-0.86)	Patients rated acceptability of suprapubic catheters greater
Ichsan, 1987[9]	Level 1, Level 2	Patients with acute urinary retention	3/29 (10)	11/37 (30)	0.27 (0.04-1.22)	None of the suprapubic group complained of discomfort compared with 17 of the patients given urethral catheters
Sethia, 1987[11]	Level 1, Level 2	General surgical patients requiring urine output monitoring	2/32 (6)	16/34 (47)	0.08 (0.01-0.41)	Decrease in bacteriuria was more significant in women than in men
Schiotz, 1989[12]	Level 1, Level 2	Women undergoing vaginal surgery	8/38 (21)	5/40 (12)	1.87 (0.48-8.01)	26% of suprapubic group versus 5% of urethral group had mechanical complications
Horgan, 1992[15]	Level 2, Level 2	Men with acute urinary retention due to prostatic enlargement	10/56 (18)	12/30 (40)	0.33 (0.11-0.99)	21% of suprapubic group versus 3% of urethral group had dislodgement; 0% of suprapubic group versus 17% of urethral group developed urethral strictures
O'Kelley, 1995[8]	Level 1, Level 2	General surgical patients requiring abdominal surgery	3/28 (11)	3/29 (10)	1.04 (0.13-8.51)	Study design unclear, but probably not randomized; suprapubic catheters caused significantly fewer days of catheter-related pain
Ratnaval, 1996[14]	Level 1, Level 2	Men undergoing colorectal surgery	1/24 (4)	3/26 (12)	0.33 (0.01-4.60)	Suprapubic group had fewer voiding difficulties

Bergman, 1987[21]	Level 1, Level 2	Women undergoing vaginal surgery for stress incontinence	4/24 (17)	17/27 (63)	0.26 (0.10-0.68)	Length of hospital stay was significantly less (by 1 day) in the suprapubic catheter group
Abrams, 1980[20]	Level 1, Level 2	Men with urinary retention	21/52 (40)	13/50 (26)	1.6 (0.88-2.75)	12% of suprapubic catheter group found catheter uncomfortable compared with 64% in the standard urethral catheter group ($p<0.001$)
Vandoni, 1994[22]	Level 1, Level 2	Patients requiring surgery for various indications	0/19 (0)	6/24 (25)	0 (0-0.95)	All patients given pre-catheterization antibiotics; slight decrease in pain and discomfort in suprapubic group but not significant (authors do not provide actual satisfaction data)
Perrin, 1997[17]	Level 1, Level 2	Patients undergoing rectal surgery	12/49 (24)	29/59 (49)	0.34 (0.13-0.83)	12% of suprapubic group reported catheter discomfort compared with 29% of urethral group

* Studies enrolled both men and women unless otherwise noted.
† Indicates the ratio of patients who developed bacteriuria to the total number of participants assigned to each group.
‡ Odds of developing bacteriuria in the suprapubic versus urethral catheter groups; CI indicates confidence interval.
§ Mechanical complications consisted of failed introduction of catheter, and catheter dislodgement or obstruction.

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Chapter 16. Prevention of Intravascular Catheter-Associated Infections

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Background

Central venous catheters inserted for short-term use have become common and important devices in caring for hospitalized patients, especially the critically ill.[1] While they have important advantages (eg, ability to administer large volumes of fluid), short-term vascular catheters are also associated with serious complications, the most common of which is infection. Intravascular catheters are one of the most common causes of nosocomial bacteremia;[2] and catheter-related bloodstream infection (CR-BSI) affects over 200,000 patients per year in the United States.[3] This chapter focuses primarily on short-term central venous catheters. Two relatively recent reviews address prevention of infection due to other types of vascular catheters.[4,5] We review use of maximum barrier precautions (Subchapter 16.1), central venous catheters coated with antibacterial or antiseptic agents (Subchapter 16.2), and use of chlorhexidine gluconate at the insertion site (Subchapter 16.3). We review several promising practices, as well as some common ineffective practices (Subchapter 16.4).

Definitions and Microbiology

Catheter-related infections can be subdivided into those that are local and those that are bacteremic. Local infection involves only the insertion site and manifests as pericatheter skin inflammation. *Local infection* is usually diagnosed when there is evidence of an insertion-site infection (eg, purulence at the exit site). *Catheter colonization* is defined by growth of an organism from the tip or the subcutaneous segment of the removed catheter. Growth of greater than 15 colony-forming units (CFU) using the semiquantitative roll-plate culture technique is often used to define catheter colonization.[6] Alternatively, the presence of more than 1000 CFUs per catheter tip segment by quantitative culture using a method such as sonication indicates evidence of catheter colonization.[7] Signs of local infection may or may not be present when there is significant catheter colonization; evidence of local infection is observed in at least 5% of patients with catheter colonization.

Bacteremic catheter-related infection (often also referred to as CR-BSI) is defined as a positive blood culture with clinical or microbiologic evidence that strongly implicates the catheter as the source of infection.[1] This includes: 1) evidence of local infection with isolation of the same organism from both pus around the site and bloodstream; or 2) positive cultures of both the catheter tip (using either semi-quantitative or quantitative methods) and bloodstream with the same organism; or 3) clinical evidence of sepsis (eg, fever, altered mental status, hypotension, leukocytosis) that does not respond to antibiotic therapy, but resolves once the catheter is removed.[1,5] Some have proposed additional methods of diagnosing CR-BSI, including paired blood cultures (drawn from both the central venous catheter and from a noncatheterized vein)[8] and a technique in which time to culture positivity for blood drawn from the central venous catheter is compared with that for the blood drawn from percutaneous venipuncture.[9]

The most common organisms causing catheter-related infections are staphylococci, gram negative rods, and *Candida* species.[10,11] The pathophysiology of these infections include several mechanisms, the most important of which involve the skin insertion site and the catheter hub.[1] Bacteria migrate from the insertion site on the skin along the external surface of the catheter and

then colonize the distal tip.[12,13] The hub can also lead to infection when bacteria are introduced via the hands of medical personnel. These organisms then migrate along the internal surface of the lumen and may result in bacteremia.[14]

Less commonly, catheter-related infection can result from hematogenous seeding of the catheter from another focus[15] or from contaminated infusates.[16]

Prevalence and Severity of the Target Safety Problem

A recent quantitative review found that of patients in whom standard, non-coated central venous catheters are in place on average for 8 days, 25% can be expected to develop catheter colonization and 5% will develop CR-BSI.[17] The risk of CR-BSI from this estimate is similar to the rate reported by the Federal Centers for Disease Control and Prevention (CDC). The CDC has reported an average CR-BSI rate of 2.8 to 12.8 infections per 1000 catheter-days for all types of intensive care units and average rates of 4.5 to 6.1 infections per 1000 catheter-days for medical/surgical intensive care units.[18]

CR-BSI is associated with an increased risk of dying, but whether this association is causal remains controversial.[17] Some argue that hospitalized patients who develop CR-BSI may differ in their clinical and physiologic characteristics, and thus may have a higher risk of dying due to intrinsic factors. Proponents of this view believe that the development of CR-BSI is primarily a marker of severe underlying disease or deficient immunity rather than an independent risk factor for dying. Unfortunately, the few studies evaluating attributable mortality due to CR-BSI have conflicting results.

Pittet and colleagues estimated that the attributable mortality of CR-BSI was 25% in a matched case-control study.[19,20] Another matched study estimated that the attributable mortality was 28%.[21] Other investigators have found a much smaller attributable mortality associated with CR-BSI. DiGiovine et al, in a matched case-control study of 136 medical intensive care unit patients, found a non-significant attributable mortality of CR-BSI (4.4%; p=0.51).[22] A recent, carefully matched cohort study of 113 patients by Soufir and colleagues also failed to detect a statistically significant increase in mortality associated with CR-BSI.[23] Nevertheless, given the small sample size, these authors concluded that their findings are consistent with a 10% to 20% increased mortality due to CR-BSI.[23] Further research to clarify the mortality associated with CR-BSI is needed, but the available data are consistent with an attributable mortality of CR-BSI ranging between 4% and 20%.

Central venous catheter related infection also leads to increased health care costs. Though there is substantial variability in the economic estimates, a recent review estimates that an episode of local catheter-related infection leads to an additional cost of approximately $400, while the additional cost of CR-BSI ranges from about $6005 to $9738.[17] Some have estimated that each episode leads to even higher costs, approximately $25,000 per episode.[19,20]

Prevention

Unnecessarily prolonged catheterization should be avoided. Because of the increased risk of infection with prolonged catheterization, many clinicians attempt to reduce this risk with routine changes of the catheter, either over a guidewire or with a new insertion site. However, the available data do not support this practice.[24] Eyer et al[25] randomized 112 surgical patients receiving a central venous, pulmonary arterial, or systemic arterial catheter for more than 7 days into three groups: a) weekly catheter change at a new site; or b) weekly guidewire exchange at the same site; or c) no routine weekly changes. No significant difference was noted in the incidence of local or bacteremic infection.[25] Cobb and colleagues[26] randomized 160 patients with central venous or pulmonary arterial catheters to either replacement every 3 days at a new site or over a guidewire, or replacement only when clinically indicated. In those with replacement catheters at new sites, the risk of infectious complications was not decreased and the number of mechanical complications was increased. Those undergoing routine replacement via a guidewire exchange showed a trend towards a higher rate of bloodstream infections compared with those who had catheter replacement only when clinically indicated.[26] A recent meta-analysis has confirmed that routine changes of central venous and systemic arterial catheters appear unnecessary;[24] attempts should be made, however, to limit the duration of catheterization. Strict adherence to proper handwashing and use of proven infection control principles is crucial (see Chapters 13 and 14).[27,28]

Subchapter 16.1. Use of Maximum Barrier Precautions During Central Venous Catheter Insertion

Practice Description

Catheter-related infections often result from contamination of the central venous catheter during insertion. Maximum sterile barrier (MSB) precautions may reduce the incidence of catheter contamination during insertion and thus reduce the rate of CR-BSI. MSB precautions consist of the use of sterile gloves, long-sleeved gowns, and a full-size drape as well as a non-sterile mask (and often a non-sterile cap) during central venous catheter insertion.

Opportunities for Impact

The proportion of patients receiving central venous catheters in whom maximum barrier precautions are employed is not currently known. If maximum barrier precautions are not used, then the standard insertion technique involves the use of only sterile gloves and a sterile small drape. Given the additional time required to employ MSB, it is likely that many patients are not receiving maximum barrier precautions during catheter insertion.

Study Designs

One randomized and one non-randomized study have evaluated the use of maximum barrier precautions (Table 16.1.1). The clinical trial randomized 176 patients to catheter insertion using MSB and 167 patients to control (use of sterile gloves and sterile small drape).[29] A non-randomized before-after observational evaluation assessed the effect of a 1-day course on infection control practices and procedures on physician compliance with MSB use and incidence of catheter-infection.[30]

Study Outcomes

Both studies evaluated rates of catheter-related infection (Level 1), including local and bloodstream infection.

Evidence for Effectiveness of the Practice

There is moderately strong evidence that use of maximum barrier precautions decrease the risk of catheter-related infection (Table 16.1.1). Furthermore, the evidence that health care providers—specifically physicians-in-training—can be taught proper use of barrier precautions and thereby decrease the incidence of infection is reasonably strong.

Potential for Harm

There is virtually no harm associated with this intervention.

Costs and Implementation

The use of maximum barrier precautions will cost more than not using this technique in both materials and time. Additionally, teaching health care providers how to properly use maximum barrier precautions is also time-consuming and expensive. Sherertz and colleagues estimated the overall cost of their educational program and supplies to be $74,081.[30] However, when the costs of preventing catheter-related infection are also included, use of MSB has been estimated to be cost-saving in simplified "back-of-the-envelope" cost studies.[29,30] Formal economic evaluation is required to fully assess the economic consequences of full adoption of maximum barrier precautions.

Comments

Use of MSB appears to be a reasonable method of preventing catheter-related infection. Though achieving full compliance with this method of catheter insertion is likely to be challenging, a relatively simple educational intervention has demonstrated effectiveness in improving adherence and reducing infection rates. Given the excellent benefit-to-harm ratio of this patient safety practice, it seems reasonable to strongly consider employing MSB for all patients requiring central venous catheters. The economic consequences of full implementation of this practice are still not entirely clear.

Table 16.1.1. Studies of vascular catheter-related infection*

Study Description; Intervention	Study Design, Outcomes	Results (p-value or 95% CI)†
343 patients in a 500-bed cancer referral center; catheters inserted under maximal sterile barrier precautions (mask, cap, sterile gloves, gown, and large drape) vs. control precautions (sterile gloves and small drape only)[29]	Level 1, Level 1	CR-BSI per 1000 catheter days: 0.08 vs. 0.5, (p=0.02) Catheter colonization: 2.3% vs. 7.2% (p=0.04)
6 ICUs and a step-down unit in an academic medical center in NC; 1-day course for physicians-in-training on the control of vascular catheter infection, emphasizing use of full-size sterile drapes[30]	Level 2‡, Level 1	Primary bloodstream infection and catheter-related infection decreased 28% (p<0.01) Use of full-size sterile drapes increased from 44% to 65% (p<0.001)
Meta-analysis of 12 RCTs (2611 catheters) comparing central venous catheters coated with chlorhexidine/silver sulfadiazine with standard, non-coated catheters[44]	Level 1A, Level 1	Odds of CR-BSI with chlorhexidine/silver sulfadiazine catheter vs. standard catheter: OR 0.56 (0.37-0.84)
High-risk adult patients at 12 university-affiliated hospitals in whom central venous catheters were expected to remain in place for • 3 days; minocycline/rifampin vs. chlorhexidine/silver sulfadiazine catheters[46]	Level 1, Level 1	Incidence of CR-BSI: minocycline/rifampin 0.3% vs. chlorhexidine/silver sulfadiazine 3.4% (p<0.002) Both types of catheters had similar efficacy for approximately the first 10 days
Meta-analysis of 7 RCTs (772 catheters) comparing tunneling with standard placement of short-term central venous catheters[61]	Level 1A, Level 1	Catheter-related septicemia: RR 0.56 (0.31-1); excluding 1 study of placement in internal jugular: RR 0.71 (0.36-1.43) Catheter colonization: RR 0.61 (0.39-0.95); excluding 1 study of placement in internal jugular: RR 0.59 (0.32-1.10)
Meta-analysis of 12 RCTs comparing prophylactic heparin use (in different forms) with no heparin use on the following outcomes: central venous catheter colonization (3 trials), CR-BSI (4 trials), and catheter-related deep venous thrombosis (7 trials)[59]	Level 1A, Level 1	CR-BSI: RR 0.26 (0.07-1.03) Catheter colonization: RR 0.18 (0.06-0.60) Catheter-related deep venous thrombosis: RR 0.43 (0.23-078)

Meta-analysis of 12 RCTs (918 patients, • 1913 catheters) assessing the effect of guidewire exchange and a prophylactic replacement strategy (change every 3 days) on central venous catheter-related colonization (8 trials), exit site infection (4 trials), bacteremia (8 trials), and mechanical complications (9 trials) in critically ill patients[24]	Level 1A, Level 1	Catheter colonization: RR 1.26 (0.87-1.84) Exit site infection: RR 1.52 (0.34-6.73) Bacteremia: RR 1.72 (0.89-3.33) Mechanical complications: RR 0.48 (0.12-1.91) Prophylactic catheter replacement every 3 days was not found to be better than as-needed replacement

* CI indicates confidence interval; CR-BSI, catheter-related bloodstream infection; OR, odds ratio; RCT, randomized controlled trial; and RR, relative risk.

† Results are reported as intervention group vs. control (standard or usual care) group.

‡ Prospective before-after study design.

Subchapter 16.2. Use of Central Venous Catheters Coated with Antibacterial or Antiseptic Agents

Practice Description

Recent studies have indicated that central venous catheters coated with antimicrobial agents reduce the incidence of catheter-related bloodstream infection (CR-BSI). Implementing use of these catheters would be simple, primarily involving the replacement of standard, non-coated vascular catheters. However, these catheters, such as chlorhexidine/silver sulfadiazine-impregnated catheters and minocycline/rifampin-coated catheters, are more expensive than standard catheters. Thus, the cost-effectiveness of these catheters needs to be considered by decision makers.

Opportunities for Impact

Currently, it is not known precisely what proportion of patient who require central venous catheterization receive an antimicrobial catheter, however, it is probably the minority of patients.

Study Designs

Multiple randomized trials have compared chlorhexidine/silver sulfadiazine central venous catheters with standard, non-coated central venous catheters.[31-43] In addition, a recent meta-analysis used a fixed effects model to combine the results of these chlorhexidine/silver sulfadiazine trials.[44] A large, multicenter study has compared minocycline/rifampin coated catheters with non-coated, standard catheters.[45] Additionally, a recent multicenter randomized trial of minocycline/rifampin versus chlorhexidine/silver sulfadiazine catheters has also been reported.[46] The majority of the patients enrolled in the individual studies cited above had a central venous catheter in place for 8 days on average (range of average duration, 5 to 11 days). Details of the characteristics and results of the trials comparing central venous catheters coated with chlorhexidine/silver sulfadiazine to control catheters are in Tables 16.2.1 and 16.2.2.

Study Outcomes

Most studies reported the incidence of catheter colonization and CR-BSI. Though the precise outcome definitions in some of the studies varied, in general the definition of catheter colonization and CR-BSI used in most of these studies was explicit and appropriate.

Evidence for Effectiveness of the Practice

The evidence for the efficacy of chlorhexidine/silver sulfadiazine catheters is fairly substantial. The recent meta-analysis found a statistically significant decrease in the incidence of CR-BSI (odds ratio 0.56, 95% CI: 0.37-0.84).[44] There is also reasonable evidence that minocycline-rifampin catheters reduce the risk of CR-BSI compared with standard, non-coated catheters. The recent randomized trial of minocycline/rifampin versus chlorhexidine/silver sulfadiazine catheters found a significant and clinically important decrease in the incidence of CR-BSI in the group of patients using minocycline/rifampin compared with chlorhexidine/silver sulfadiazine catheters (0.3% vs. 3.4%, $p<0.002$).[46] Of note, both types of coated catheters had similar efficacy for approximately the first 10 days of catheterization.

Potential for Harm The potential for occurrence of immediate hypersensitivity reaction in association with the use of chlorhexidine/silver sulfadiazine impregnated catheters is of

concern. Although there have been no reports of hypersensitivity reactions to chlorhexidine/silver sulfadiazine impregnated central venous catheters in the United States (out of more than 2.5 million sold), 13 cases of immediate hypersensitivity reactions have been reported in Japan, including one potentially associated death.[47] There were 117,000 antiseptic-impregnated catheters sold in Japan before their use was halted because of these cases.[47] It is not clear why there have been no reports of hypersensitivity reactions in the U.S; this heterogeneity may be caused by a higher previous exposure of patients in Japan to chlorhexidine or by a genetic predisposition.

Minocycline and rifampin are both occasionally used as systemic antimicrobial agents; thus, their use on catheters raises the important theoretical issue of increased antimicrobial resistance. At this time, there has been no conclusive evidence that antimicrobial resistance has or will increase due to the use of these catheters.

Costs and Implementation

Formal and informal economic analyses indicate that central venous catheters coated with antibacterial agents (such as chlorhexidine/silver sulfadiazine or minocycline/rifampin) are likely to lead to both clinical and economic advantages in selected patients. In terms of formal economic comparisons, a recent analysis compared chlorhexidine/silver sulfadiazine catheters to standard catheters and found that chlorhexidine/silver sulfadiazine catheters lead to both clinical and economic advantages in patients receiving central venous catheterization for 2 to 10 days and who were considered high risk for infection (ie, critically ill or immunocompromised patients). Specifically, the chlorhexidine/silver sulfadiazine catheters led to a significant decrease in the incidence of CR-BSI and death, and a cost savings of approximately $200 per catheter used.[47] Importantly, the risk of hypersensitivity reaction to the chlorhexidine/silver sulfadiazine catheters was considered in the analysis, but had little effect on the overall clinical and economic outcomes.[47]

However, given the recently demonstrated efficacy of the minocycline/rifampin catheter compared with the chlorhexidine/silver sulfadiazine catheter,[46] a formal cost-effectiveness analysis comparing these two types of coated catheters is necessary. This is especially important since the minocycline/rifampin catheter costs about $9 more per catheter than the chlorhexidine/silver sulfadiazine catheter.

Implementation of either of these catheters would be straightforward. Stocking the appropriate antimicrobial catheter in areas of the hospital that are likely to require such catheters (eg, intensive care unit, operative room, hematology-oncology floor) would be a relatively simple way of translating the research findings into actual practice.

Comment

In light of the substantial clinical and economic burden of catheter-related infection, hospital personnel should adopt proven cost-effective methods to reduce this common and important nosocomial complication. The bulk of the evidence supports the use of either chlorhexidine/silver sulfadiazine or minocycline/rifampin central venous catheters rather than standard (non-coated) catheters in high-risk patients requiring short-term central venous catheterization (eg, for 2 to 10 days). Choosing between the 2 antimicrobial catheters requires a formal cost-effectiveness analysis since the minocycline/rifampin catheter costs significantly more than the chlorhexidine/silver sulfadiazine catheter. There are 2 primary issues that should be addressed when comparing these catheters: the expected duration of catheterization and the risk of antibiotic resistance to the patient, the hospital, and society. Though each minocycline/rifampin catheter costs more than the chlorhexidine/silver sulfadiazine catheter, using minocycline/rifampin catheters may actually result in cost-savings for at least some patient populations given their improved overall efficacy. Of note, the improved efficacy of the minocycline/rifampin catheters may be a result of coating both the internal and external surfaces with these substances; the chlorhexidine/silver sulfadiazine catheters evaluated to date have only had the external surface coated with the antiseptic combination.

Table 16.2.1. Characteristics of trials comparing central venous catheters coated with chlorhexidine/silver sulfadiazine to control catheters*

Study Description	Number of Catheters (Treatment, Control)	Mean Catheter Duration in Days (Treatment, Control)	Catheter Colonization†	Catheter-Related Bloodstream Infection†
Tennenberg[31]: 282 hospital patients (137 treatment, 145 control) in variety of settings; double- and triple-lumen catheters without exchanges over guidewires	137, 145	5.1, 53	SQ (IV, SC, >15 CFU)	SO (IV, SC, site), CS, NS
Maki[32]: 158 ICU patients (72 treatment, 86 control); triple-lumen catheters with catheter exchanges over guidewires	208, 195	6.0, 6.0	SQ (IV, >15 CFU)	SO (>15 CFU, IV, hub, inf)‡
van Heerden[33]§: 54 ICU patients (28 treatment, 26 control); triple-lumen catheters without catheter exchanges over guidewires	28, 26	6.6, 6.8	SQ (IV, >15 CFU)	NR
Hannan[34]: ICU patients; triple-lumen catheters	68, 60	7, 8	SQ (IV, $>10^3$ CFU) ¶	SO (IV, $>10^3$ CFU), NS
Bach[35]§: 26 ICU patients (14 treatment, 12 control); triple-lumen catheters without catheter exchanges over guidewires	14, 12	7.0, 7.0	QN (IV, $>10^3$ CFU)	NR
Bach[36]§: 133 surgical patients (116 treatment, 117 control); double- and triple-lumen cathetes without exchanges over guidewires	116, 117	7.7, 7.7	QN (IV, $>10^3$ CFU)	SO (IV)
Heard[37]§: 111 SICU patients (107 treatment, 104 control); triple-lumen catheters with exchanges over guidewires	151, 157	8.5, 9	SQ (IV, SC, >14 CFU)	SO (IV, SC, >4 CFU)
Collin[38]: 119 ER/ICU patients (58 treatment, 61 control); single-, double-, and triple-lumen catheters with exchanges over guidewires	98, 139	9.0, 7.3	SQ (IV, SC, >15 CFU)	SO (IV, SC)
Ciresi[39]§: 191 patients receiving TPN (92 treatment, 99 control); triple-lumen catheters with exchanges over guidewires	124, 127	9.6, 9.1	SQ (IV, SC, >15 CFU)	SO (IV, SC)
Pemberton[40]: 72 patients receiving TPN (32 treatment, 40 control); triple-lumen catheters without exchanges over guidewires	32, 40	10, 11	NR	SO (IV), Res, NS

Ramsay[41]§: 397 hospital patients (199 treatment, 189 control) in a variety of settings; triple-lumen catheters without exchanges over guidewires	199, 189	10.9, 10.9	SQ (IV, SC, >15 CFU)	SO (IV, SC)
Trazzera[42]§: 181 ICU/BMT patients (99 treatment, 82 control); triple-lumen catheters with exchanges over guidewires	123, 99	11.2, 6.7	SQ (IV, >15 CFU)	SO (IV, >15 CFU)
George[43]: Transplant patients; triple-lumen catheters without exchanges over guidewires	44, 35	NR	SQ (IV, >5 CFU)	SO (IV)

* BMT indicates bone marrow transplant; CFU, colony forming units; CS, clinical signs of systemic infection; ER, emergency room; ICU, intensive care unit; IV, intravascular catheter segment; inf, catheter infusate; NR, not reported; NS, no other sources of infection; QN, quantitative culture; Res, resolution of symptoms upon catheter removal; SC, subcutaneous catheter segment; SICU, surgical intensive care unit; site, catheter insertion site; SO, same organism isolated from blood and catheter; SQ, semi-quantitative culture; and TPN, total parenteral nutrition.

† Catheter segments (or site) cultured and criteria for a positive culture are given in parenthesis

‡ Organism identity confirmed by restriction-fragment subtyping

§ Additional information provided by author (personal communications, 1/98-3/98)

¶ Culture method reported as semiquantitative; criteria for culture growth suggests quantitative method

Table 16.2.2. Results of trials comparing central venous catheters coated with chlorhexidine/silver sulfadiazine to control catheters*

Study	Catheter Colonization			Catheter-related Bloodstream Infection		
	No. (%) Positive		Odds Ratio (95% CI)	No. (%) Positive		Odds Ratio (95% CI)
	Treatment	Control		Treatment	Control	
Tennenberg[31]	8 (5.8%)	32 (22.1%)	0.22 (0.10-0.49)	5 (3.6%)	9 (6.2%)	0.57 (0.19-1.75)
Maki[32]	28 (13.5%)	47 (24.1%)	0.49 (0.29-0.82)	2 (1.0%)	9 (4.6%)	0.20 (0.04-0.94)
van Heerden[33]†	4 (14.3%)	10 (38.5%)	0.27 (0.07-1.00)	–	–	–
Hannan[34]	22 (32.4%)	22 (36.7%)	0.83 (0.40-1.72)	5 (7.4%)	7 (11.7%)	0.60 (0.18-2.00)
Bach[35]†	0 (0%)	4 (33.3%)	0 (0-0.65)	–	–	–
Bach[36]†	2 (1.7%)	16 (13.7%)	0.11 (0.02-0.49)	0 (0%)	3 (2.6%)	0 (0-1.28)
Heard[37] †	60 (39.7%)	82 (52.2%)	0.60 (0.38-0.95)	5 (3.3%)	6 (3.8%)	0.86 (0.26-2.89)
Collin[38]	2 (2.0%)	25 (18.0%)	0.10 (0.02-0.41)	1 (1.0%)	4 (2.9%)	0.35 (0.04-3.16)
Ciresi[39]†	15 (12.1%)	21(16.5%)	0.69 (0.34-1.42)	13 (10.5%)	14 (11.0%)	0.95 (0.43-2.10)
Pemberton[40]	–	–	–	2 (6.3%)	3 (7.5%)	0.82 (0.13-5.24)
Ramsay[41]†	45 (22.6%)	63 (33.3%)	0.58 (0.37-0.92)	1 (0.5%)	4 (2.1%)	0.23 (0.03-2.11)
Trazzera[42] †	16 (13.0%)	24 (24.2%)	0.47 (0.23-0.94)	4 (3.3%)	5 (5.1%)	0.63 (0.17-2.42)
George[43]	10 (22.7%)	25 (71.4%)	0.12 (0.04-0.33)	1 (2.3%)	3 (8.6%)	0.25 (0.02-2.50)

* CI indicates confidence interval.
† Additional information provided by author (personal communications, 1/98-3/98)

Subchapter 16.3. Use of Chlorhexidine Gluconate at the Central Venous Catheter Insertion Site

Practice Description

Microbial populations on the skin are routinely suppressed with antiseptic agents prior to catheter insertion. Using an antiseptic solution for skin disinfection at the catheter insertion site helps to prevent catheter-related infections. The physician uses an agent that has antimicrobial properties to thoroughly cleanse the skin just prior to insertion of a central venous catheter. In the United States, povidone-iodine (PI) is overwhelmingly the most commonly used agent for this purpose. Recently, several studies have compared the efficacy of PI and chlorhexidine gluconate (CHG) solutions in reducing vascular catheter-related infections.

Opportunities for Impact

If PI is the most commonly used agent for site disinfection in the United States even though CHG may be superior, substantial opportunity exists for impact by switching to CHG.

Study Designs

The study characteristics of 6 randomized trials[48-53] comparing any type of CHG solution with PI solution for vascular catheter site care are shown in Table 16.3.1. The mean duration of catheterization for the CHG and PI groups was comparable in most of the studies. There was no significant difference in the sites at which catheters were inserted between the CHG and PI groups. Several formulations of CHG were used, including[9,12-14] an alcoholic solution and an aqueous solution. All studies used 10% PI solution for the control arm.

Study Outcomes

All studies[48-53] evaluated catheter colonization (Level 2 outcome) and all but one[52] evaluated CR-BSI (Level 1 outcome). All studies evaluating CR-BSI as an outcome required the recovery of the same microbial species from both the catheter segment and a blood culture.

Evidence for Effectiveness of the Practice

Most clinical trials have revealed that the use of CHG solution results in a significant decrease in catheter colonization, but the evidence is not clear for CR-BSI (Table 16.3.2). Most of the individual trials showed a trend in reducing CR-BSI incidence in patients using CHG solution. The lack of significant results may be a result of insufficient statistical power in the individual studies. A formal meta-analysis of the published trials would be valuable in assessing the comparative efficacy of PI versus CHG for central venous catheter site disinfection. Using explicit inclusion criteria and accepted quantitative methods, a meta-analysis[54-56] can often help clarify the features of individual studies that have divergent results[57] and increase statistical power since several small studies can be pooled.[58]

Potential for Harm

Only one study reported adverse effects from the use of either antiseptic solution. Maki et al[48] found erythema at the insertion site in 28.3% of catheters in the PI group and in 45.3% of catheters in the CHG group (p=0.0002). However, there was no statistically significant difference in erythema among these 2 groups and those patients whose site was disinfected with alcohol. Hypersensitivity reactions to chlorhexidine-silver sulfadiazine impregnated central

venous catheters and to use of CHG for bathing have been reported. Hypersenstivity reactions were not reported in any of the studies, but clinicians should be aware of such potential side effects. Another concern is the development of bacterial resistance. However, there have been few reports of bacterial resistance to CHG despite its widespread use for several decades.

Costs and Implementation

The cost of CHG is approximately twice that of PI with an absolute difference of $0.51 (approximately $0.92 versus $0.41 for a quantity sufficient to prepare a central venous catheter insertion site). If meta-analysis suggests that CHG use is effective in reducing the risk of CR-BSI, a formal economic evaluation of this issue is required.

Comment

The use of chlorhexidine gluconate rather than povidone-iodine solution for catheter site care may be an effective and simple measure for improving patient safety by reducing vascular catheter-related infections. Formal meta-analysis and economic evaluations are required before strongly recommending that CHG replace PI for central venous catheter site disinfection in appropriate patient populations.

Table 16.3.1. Characteristics of studies comparing chlorhexidine gluconate (CHG) and povidone-iodine (PI) solutions for vascular catheter site care*

Study Description†	Number of Catheters (Treatment, Control)	Mean Catheter Duration in Days (Treatment, Control)	Catheter Colonization‡	Catheter-Related Bloodstream Infection‡
Maki[48]: 441 ICU patients (2% aqueous CHG solution in 214, PI in 227)	214, 227	5.3, 5.3	SQ (>15 CFU)	CX, NoSource, Sx
Sheehan[49]: 189 ICU patients (2% aqueous CHG solution in 94, PI in 95)	169,177	NA	SQ (>15 CFU)	CX, NoSource, Sx
Meffre[50]: 1117 hospital patients (CHG solution of 0.5% alcohol 70% in 568, PI in 549)	568, 549	1.6, 1.6	SQ (>15 CFU) or QN (>10^3 CFU/mL)	[Local or Sx] or [CX, NoSource]
Mimoz[51]: ICU patients (Biseptine®§ vs. PI)	170, 145	4.5, 3.9	QN (>10^3 XFU/mL)	CX, Sx
Cobett and LeBlanc[52]: 244 hospital patients (0.5% alcohol 70% in 8, PI in 161)	83, 161	1.6, 1.7	SQ (>15 CFU)¶	NA
Humar et al[53]: 3374 ICU patients (0.5% alcohol in 193 and 181/193	193, 181	5.3, 6.	SQ (>15 CFU)	CX, Molec, NoSource

* CFU indicates colony forming units; CX, same organism or species matched between blood and catheter segment culture; ICU: intensive care units; Local: local signs of infection; Molec: same organism confirmed by molecular subtyping; NA:not available; NoSource: no other source of infection; QN: quantitative; Sx: clinical symptoms of bloodstream infection; SQ: semiquantitative.

† All studies used 10% povidone-iodine solution.

‡ Catheter segments (or site) cultured and criteria for a positive culture are given in parenthesis.

§ Biseptine® consists of 0.25% chlorhexidine gluconate, 0.025% benzalkonium chloride, 4% benzyl alcohol.

¶ Required one of the following symptoms: fever, erythema, heat at the site, and pain.

Table 16.3.2. Results of Studies Comparing Chlorhexidine Gluconate (CHG) and Povidone-iodine (PI) Solutions for Vascular Catheter Site Care *

	Catheter Colonization (Positive Cultures)		RR (95% CI) CHG vs. PI	Catheter Related Bloodstream Infection		RR (95% CI) CHG vs. PI
	CHG Solution	PI Solution		CHG Solution	PI Solution	
Maki[48]	5/214	21/227	0.25 (0.10,0.66)	1/214	6/227	0.18 (0.02,1.46)
Sheehan[9]	3/169	12/177	0.22 (0.06,0.75)	1/169	1/177	1.05 (0.07,16.61)
Meffre[50]	9/568	22/549	0.40 (0.18,0.85)	3/568	3/549	0.97 (0.20,4.77)
Mimoz[51]	12/170	24/145	0.43 (0.22,0.82)	3/170	4/145	0.64 (0.15,2.81)
Cobett and LeBlanc[52]†	6/83	23/161	0.49 (0.31,0.77)	-	-	-
Humar[53]	36/116	27/116	1.33 (0.87,2.04)	4/193	5/181	0.75 (0.20,2.75)

* CI indicates confidence interval; RR, relative risk.
† Additional information was provided by authors

Subchapter 16.4. Other Practices

Practices That Appear Promising

Use of heparin with central venous catheters. Because an association has been shown between thrombus formation and catheter-related infection, clinicians usually use heparin, in a variety of forms: 1) as flushes to fill the catheter lumens between use; 2) injected subcutaneously; or 3) bonded on the catheter. A meta-analysis of 12 randomized trials evaluating prophylactic use of heparin in patients using central venous catheters has shown that prophylactic heparin decreases catheter-related venous thrombosis (Level 2 outcome; RR 0.43, 95% CI: 0.23-078) and bacterial colonization (Level 2 outcome; RR 0.18, 95% CI: 0.06-0.60) and may decrease CR-BSI (Level 1 outcome; RR 0.26, 95% CI: 0.07-1.03).[59] Since subcutaneous heparin also offers benefit in reducing venous thromboembolism in certain patient populations (see Chapter 31), this is likely to be a reasonable strategy even though CR-BSIs have not definitely been shown to be reduced. However use of heparin is associated with several side effects, such as heparin-induced thrombocytopenia and bleeding.

Tunneling short-term central venous catheters. Since the primary site of entry for microorganisms on the central venous catheter is the site of cutaneous insertion,[60] tunneling the catheter through the subcutaneous tissue may decease the incidence of infection. Several trials have evaluated the effect of tunneling on catheter-related infection. A recent meta-analysis has summarized the potential benefit.[61] The meta-analysis included 7 trials and found that compared with patients receiving standard catheter placement, tunneling decreased bacterial colonization (Level 2 outcome; RR 0.61, 95% CI: 0.39-0.95) and decreased CR-BSI (Level 1 outcome; RR 0.56, 95% CI: 0.31-1).[61] However, the benefit of tunneling came primarily from one trial using the internal jugular as the site of catheter placement; the reduction in CR-BSI no longer reached statistical significance when data from the several subclavian catheter trials were pooled (RR 0.71; 95% CI 0.36-1.43).[61] The authors concluded appropriately that current evidence does not

support the routine use of tunneling central venous catheters. This could change if the efficacy of tunneling is clearly demonstrated at different placement sites and relative to other interventions (eg, antiseptic coated catheters).[61]

Ineffective Practices

Intravenous antimicrobial prophylaxis. There is no evidence to support the systemic use of either vancomycin[62] or teicoplanin[63] during insertion of central venous catheters. The randomized studies evaluating the use on intravenous vanomycin or teicoplanin have failed to demonstrate that this intervention reduces CR-BSI (Level 1 outcome).[62, 63] Given the theoretical risk of developing resistance to the antimicrobial agents used for prophylaxis, this practice is not recommended.

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Final Comment to Chapter 16

Infections due to central venous catheters are common and lead to substantial morbidity and health care costs. Several practices will likely reduce the incidence of this common patient safety problem, including the use of maximum sterile barrier precautions during catheter insertion, use of catheters coated with antibacterial or antiseptic agents, and use of chlorhexidine gluconate at the insertion site. Additionally, use of heparin and tunneling of the central venous catheter may prove to be effective in reducing CR-BSI. However, the relative efficacy of these interventions is unclear. Also, a clear and formal delineation of the economic consequences of combining several of these patient safety practices is necessary.

Chapter 17. Prevention of Ventilator-Associated Pneumonia

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Introduction

Ventilator-associated pneumonia (VAP) is a leading cause of morbidity and mortality in the intensive care unit (ICU).[1] The incidence of VAP varies greatly, ranging from 6 to 52% of intubated patients depending on patient risk factors. The cumulative incidence is approximately 1-3% per day of intubation. Overall, VAP is associated with an attributable mortality of up to 30%. Attributable mortality approaches 50% when VAP is caused by the more virulent organisms that typify late-onset VAP (occurring 4 or more days into mechanical ventilation). The cost per episode of VAP is substantial, although specific data are lacking. The average cost per episode of nosocomial pneumonia is estimated at $3000 to $6000, and the additional length of stay for patients who develop VAP is estimated at 13 days.[1,2]

VAP is typically categorized as either early-onset VAP (occurring in the first 3-4 days of mechanical ventilation) or late-onset VAP. This distinction is important microbiologically. Early-onset VAP is commonly caused by antibiotic-sensitive community-acquired organisms (eg, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Staphylococcus aureus*). Late-onset VAP is commonly caused by antibiotic-resistant nosocomial organisms (eg, *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus*, *Acinetobacter* species, and *Enterobacter* species). Most episodes of ventilator-associated pneumonia (VAP) are thought to develop from the aspiration of oropharyngeal secretions containing potentially pathogenic organisms. Aspiration of gastric secretions may also contribute, though likely to a lesser degree. Tracheal intubation interrupts the body's anatomic and physiologic defenses against aspiration, making mechanical ventilation a major risk factor for VAP.

This chapter reviews 4 practices that carry the potential to reduce the incidence of VAP in patients receiving mechanical ventilation. They are: variation in patient positioning, continuous aspiration of subglottic secretions, selective digestive tract decontamination, and the use of sucralfate.

Subchapter 17.1. Patient Positioning: Semi-recumbent Positioning and Continuous Oscillation

Background

Aspiration of gastric secretions likely contributes to the development of VAP.[1] Semi-recumbent positioning of mechanically ventilated patients may help reduce the incidence of gastroesophogeal reflux and lead to a decreased incidence of VAP. Immobility in critically ill patients leads to atelectasis and decreased clearance of bronchopulmonary secretions. Both of these sequelae may lead to increased risk of VAP. Continuous rotation and movement of critically ill patients (termed continuous oscillation) may thus help prevent such changes.

Semi-recumbent positioning

Practice Description

Semi-recumbent positioning is generally defined as elevation of the head of the bed to 45 degrees. This is generally achieved in a hospital bed with patients' feet remaining parallel to the floor (ie, the entire bed is not tilted) but this is not explicitly described in the published trials. Semi-recumbency is generally continued for the duration of mechanical ventilation.

Opportunities for Impact

Outside of select medical centers that have studied this practice, semi-recumbent positioning has not been widely adopted as the standard of care. Thus, such an intervention would have enormous opportunity for impact should it prove beneficial.

Study Designs

There have been three trials of semi-recumbent patient positioning and its effect on the incidence of VAP.[3-5] Two of these studies measured aspiration events using nuclear medicine techniques, the other was a randomized trial with the primary outcome being VAP. In the one randomized trial, 86 patients were randomized at the time of intubation to semi-recumbent body position (45 degrees) or supine body position (0 degrees).[3] All patients received the same general critical care (eg, sterile endotracheal suctioning, stress ulcer prophylaxis with sucralfate if tolerating oral medications, no ventilator tubing changes, no selective digestive tract decontamination).

Study Outcomes

In the one randomized clinical trial, VAP was clinically defined as a new and persistent infiltrate on chest radiography, plus two of the following: temperature of >38.3C, leukocyte count >12,000/mm^3 or <4000/mm^3, purulent tracheal secretions.[3] Microbiologic confirmation required the above criteria be met and the isolation of pathogenic bacteria from an endotracheal aspirate or bronchoscopic procedure. Mortality was reported at time of discharge from the ICU. Both studies of the frequency of aspiration measured radioisotope counts (counts per minute) of endotracheal aspirates at various time points before during and after semi-recumbent positioning.[4,5]

Evidence for Effectiveness of the Practice

Only one randomized clinical trial of semi-recumbent patient positioning in mechanically ventilated patients has been published to date (see Table17.1.1). Semi-recumbent positioning was associated with a statistically significant reduction in both clinically and microbiologically-diagnosed VAP.[3] There was no significant difference in mortality. These findings corroborate earlier studies that demonstrated decreased frequency of gastroesophogeal reflux with semi-recumbent positioning,[4,5] and an independent association of supine positioning with the development of VAP.[6]

Potential for Harm

No adverse effects were observed in patients randomized to semi-recumbent positioning.[3] However, patients were excluded if they had any of the following conditions: recent abdominal or neurologic surgery (<7 days), shock refractory to vasoactive therapy, and previous recent endotracheal intubation (<30 days).

Costs and Implementation

The cost of semi-recumbent positioning is negligible and implementation is simple but will require health care provider education.

Continuous oscillation

Practice Description

Continuous oscillation utilizes mechanical beds that employ either rotating platforms or alternating inflation/deflation of mattress compartments to turn patients from side to side. These beds achieve 40 to 60 degrees of tilt and can cycle every 5-30 minutes as programmed. In general, in published trials, continuous oscillation was started within 24 hours of admission to the ICU and continued until discharge.

Opportunities for Impact

Continuous oscillation is infrequently applied to critically ill patients. Thus, this intervention would have significant opportunity for impact should it prove beneficial.

Study Designs

A meta-analysis of six randomized controlled trials evaluated the effect of continuous oscillation on clinical outcomes, including pneumonia, in critically ill patients.[7] The vast majority of patients were mechanically ventilated but the absolute percentage is not reported in most trials. Five of the six trials included were limited to surgical and/or neurologic patients. A subsequent randomized controlled trial included 103 medical and surgical patients.[8] In most cases, continuous oscillation was compared to standard critical care practice of rolling patients every two hours.

Study Outcomes

The definition of VAP varied among trials but was generally clinical and required a new infiltrate on chest radiography, fever, and leukocytosis. Microbiologic confirmation was not consistently obtained. Mortality was recorded at time of ICU discharge.

Evidence for Effectiveness of the Practice

The role of continuous oscillation in the prevention of VAP is unclear (see Table 17.1.1). A meta-analysis of six randomized controlled trials on this subject found a statistically significant reduction in the risk of pneumonia.[7] Five of these studies were limited to surgical and/or neurologic patients. The sixth study, which included primarily medical patients, failed to find any significant effect.[9] A subsequent randomized controlled trial of medical and surgical patients also failed to find any benefit.[8]

Potential for Harm

There were no significant risks of continuous oscillation in any of the randomized trials. Inadvertent disconnection of intravenous lines, increased ventricular ectopy, and patient intolerance were reported, but not quantified. Conscious patients tolerated the procedure poorly.

Costs and Implementation

The incremental cost of specialized beds capable of continuous oscillation has been estimated at approximately $100 per day.[9] A significant reduction in VAP incidence and length of stay could result in cost savings.

Comment

Both semi-recumbent positioning and continuous oscillation are relatively low-cost, low-risk interventions. The one randomized trial to date of semi-recumbent positioning shows it to be an effective method of reducing VAP. While it has not proven to provide a mortality benefit, semi-recumbent positioning is a safe and straightforward intervention whose effectiveness should be confirmed by additional randomized clinical trials. Continuous oscillation is less clearly beneficial, although it may be effective in certain subgroups of patients (eg, surgical, neurologic). It also deserves continued study.

Table 17.1.1. Patient positioning*

Study Design	Study Design, Outcomes	Pneumonia or Aspiration	Mortality
Semi-recumbent positioning			
Randomized controlled trial of semi-recumbent patient positioning in 86 mechanically ventilated patients. Primary outcome was VAP. (Drakulovic, 1999)[3]	Level 1, Level 1	RR 0.24 (p=0.003)	RR 0.64 (p=0.289)
Two-period crossover trial of semi-recumbent patient positioning in 15 mechanically ventilated patients. Primary outcome was pulmonary aspiration. (Orozco-Levi, 1995)[4]	Level 3, Level 2	RR 0.65 (p<0.01)	–
Randomized two-period crossover trial of semi-recumbent patient positioning in 15 mechanically ventilated patients. Primary outcome was pulmonary aspiration. (Torres, 1992)[5]	Level 3, Level 2	RR 0.23 (p=0.036)	–
Continuous oscillation			
Randomized controlled trial of continuous oscillation in 103 critically ill medical and surgical patients (90% mechanically ventilated). Primary outcomes included pneumonia. (Traver, 1995)[8]	Level 1, Level 1	RR 0.62 (p=0.21)	RR 0.85 (p>0.05)
Meta-analysis of 6 randomized controlled trials of continuous oscillation in critically ill surgical or stroke patients (majority mechanically ventilated). (Choi, 1992)[7]	Level 1A, Level 1	RR 0.50 (p=0.002)	No significant difference (data not reported)
Randomized controlled trial of continuous oscillation in 86 critically ill medical patients (majority mechanically ventilated). Primary outcomes included pneumonia. (Summer, 1989)[9]	Level 1, Level 1	RR 0.57 (p=0.40)	RR 0.93 (p>0.05)

* RR indicates relative risk; VAP, ventilator-associated pneumonia.

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Subchapter 17.2. Continuous Aspiration of Subglottic Secretions

Background

Ventilator-associated pneumonia (VAP) frequently develops from the aspiration of oropharyngeal secretions containing potentially pathogenic organisms.[1] Tracheal intubation interrupts the body's anatomic and physiologic defenses against aspiration, making mechanical ventilation a major risk factor for VAP. The accumulation of contaminated oropharyngeal secretions above the endotracheal tube cuff may contribute to the risk of aspiration.[1] Removal of these pooled secretions through suctioning of the subglottic region, termed continuous aspiration of subglottic secretions (CASS), may reduce the risk of developing VAP.

Practice Description

Continuous aspiration of subglottic secretions requires intubation with specially designed endotracheal tubes (see Figure 17.2.1). These endotracheal tubes contain a separate dorsal lumen that opens into the subglottic region, allowing for aspiration of any pooled secretions. The amount of secretions is monitored (usually daily) and the patency of the suction lumen is tested frequently (every few hours). In studies of the impact of this practice, aspiration has been applied from time of intubation to time of extubation. One of the studies tested manual aspiration performed hourly instead of continuous mechanical aspiration.[2]

Opportunities for Impact

Continuous aspiration of subglottic secretions is an uncommon practice. The opportunities for impact are therefore significant should this practice prove beneficial in lowering rates of VAP.

Study Designs

There have been three randomized controlled trials of CASS to date.[2-4] (Table 17.2.1) Two have included both medical and surgical patients requiring mechanical ventilation for greater than 72 hours and one included only post-cardiac surgery patients. All three studies randomized patients to CASS or standard care. Attempts were made to control for additional, potentially effective preventive strategies such as patient positioning, frequency of ventilator circuit changes, type of stress ulcer prophylaxis used, and administration of antibiotics.

Study Outcomes

All trials reported development of VAP and mortality at the time of extubation, ICU or hospital discharge. VAP was generally defined as a new radiographic infiltrate plus two of the following: fever, leukocytosis/leukopenia, or purulent tracheal aspirate. Microbiologic confirmation was not consistently obtained. Time to development of VAP was also reported. Mortality was reported at time of discharge from the hospital.

Evidence for Effectiveness of the Practice

One of the three trials found a statistically significant decrease in the incidence of VAP with CASS when compared to standard treatment, while a second study showed a strong trend (See Table 17.2.1).[2,3] All three trials reported a statistically significant delay in the time to development of VAP, ranging from 48 hours to 8 days. Two trials found a decreased incidence of VAP caused by *Staphylococcus aureus* and *Hemophilus influenzae*, but no change was observed in the incidence of VAP caused by *Pseudomonas aeruginosa* or *Enterobacteriaceae*.[3,4] No difference in mortality was observed in any of the trials.

Potential for Harm

There is minimal potential for harm to patients from the application of CASS and no adverse patient events were reported in over 150 patients.[4]

Costs and Implementation

The cost and cost-effectiveness of CASS have not been examined. The direct costs appear minimal. Hi-Lo Evac tubes cost approximately 25% more than standard endotracheal tubes, putting the estimated cost of each unit at less than $1.[2] The cost-savings per episode of VAP prevented could therefore be substantial. Implementation would largely be a matter of making the specialized endotracheal tubes available and providing staff training. The mechanical suctioning apparatus would require frequent monitoring by nursing or respiratory therapy to insure adequate function.

Comment

Continuous aspiration of subglottic secretions is a promising strategy for the prevention of VAP. Two randomized controlled trials have suggested a decrease in the rate of VAP in patients requiring prolonged (>3 days) mechanical ventilation (only one trial was statistically

significant). The third trial showed no difference, but the patient population in this trial included many short-term intubations (mean duration of 36 hours) and was restricted to patients undergoing cardiac surgery. Larger randomized controlled trials are needed to address the impact of CASS more definitively.

Another interesting observation is the delay in the development of VAP and the decreased incidence of *Staphylococcus aureus* and *Hemophilus influenzae*. This suggests that CASS may provide most of its benefit by preventing early VAP caused by community-acquired organisms, and its use could therefore be targeted to those patients requiring mechanical ventilation for intermediate periods of time (ie, those at greatest risk for early VAP).

Figure 17.2.1. Diagram of continuous aspiration of subglottic secretions (copied with permission)[3]

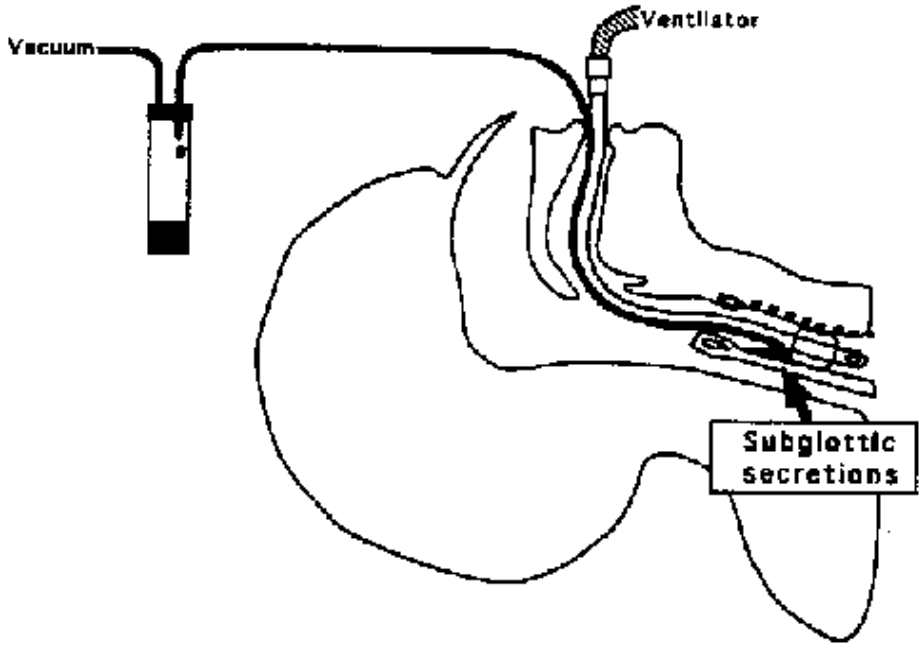

Table 17.2.1. Randomized trials of continuous aspiration of subglottic secretions*

Study Description	Study Outcomes	Relative Risk of Pneumonia (95% CI)	Relative Risk of Mortality (95% CI)
Kollef, 1999[4]: 343 patients undergoing cardiac surgery and requiring mechanical ventilation	Level 1	0.61 (0.27-1.40)	0.86 (0.30-2.42)
Valles, 1995[3]: 153 patients requiring prolonged mechanical ventilation	Level 1	0.47 (0.21-1.06)	1.09 (0.72-1.63)
Mahul, 1992[2]: 145 patients requiring mechanical ventilation for more than 3 days	Level 1	0.46 (0.23-0.93)	1.14 (0.62-2.07)

* CI indicates confidence interval.

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Subchapter 17.3. Selective Digestive Tract Decontamination

Background

Selective digestive tract decontamination (SDD) involves the use of non-absorbable antibiotics topically applied to the gastrointestinal tract in an effort to sterilize the oropharynx and stomach. The goal is to decrease the pathogenicity of aspirated secretions and thereby reduce the incidence of VAP.

Practice Description

Most studies have used a combination of topical polymixin, tobramycin or gentamicin, and amphotericin applied to the oropharynx (by hand) and the stomach (by nasogastric tube).[1] About half of the studies also included a short (3-4 day) course of systemic intravenous antimicrobial therapy, most commonly ceftriaxone. In general, topical antibiotics were applied several times daily from the time of intubation until extubation (or shortly thereafter).

Opportunities for Impact

SDD is not widely used in the United States.[1] The Centers for Disease Control and Prevention and the American Thoracic Society's guidelines published in the 1990s do not recommend its routine use.[2,3] Given the frequency and morbidity of VAP, if the practice is beneficial substantial opportunity for patient safety enhancement exists.

Study Designs

There have been over 30 randomized controlled trials and seven meta-analyses of SDD (see Table 17.3.1).[4-10] A representative meta-analysis identified 33 randomized trials of SDD using a structured search of the literature that met the authors' methodologic inclusion criteria: measurement of clinical outcomes (including VAP and mortality), inclusion of unselected patient populations, and mechanical ventilation in at least half of patients.[1] As with several of the other meta-analyses, individual trials in this particular meta-analysis were grouped into those that used topical antibiotics only and those that used topical and systemic antibiotics. This meta-analysis was unique in that the investigators obtained individual patient data for the majority of patients (4343 (76%) of the 5727 patients involved).[1]

Study Outcomes

All meta-analyses reported risk of VAP and mortality at hospital or ICU discharge. Individual study outcomes also included number of days intubated, length of ICU stay, duration of antibiotic therapy, time to onset of VAP, and cost. Several meta-analyses performed subgroup analysis to assess the importance of statistical methods (eg, quality of randomization, blinding, VAP definition) and clinical factors (eg, Acute Physiology and Chronic Health Evaluation (APACHE) score).

Evidence for Effectiveness of the Practice

All seven meta-analyses report substantial reduction in the risk of VAP with the use of SDD (see Table 17.3.1). Four of seven meta-analyses report a statistically significant reduction in mortality.[4-6,8] Four of seven meta-analyses separately analyzed trials using topical antibiotics only and those using topical and systemic antibiotics.[4,6,8,9] All four revealed a statistically significant mortality benefit with combined topical and systemic prophylaxis and no mortality benefit with topical prophylaxis alone.[1,6,8,9] However, these four meta-analyses did reveal a significant decrease in VAP incidence in those given topical antibiotics only compared to the placebo group.[4,6,8,9] Several of the meta-analyses included subgroup analyses to assess the benefit of SDD in patients categorized by type of illness (surgical, medical) and severity of illness (APACHE score), with conflicting results.[4,6]

Potential for Harm

There were no significant adverse events reported in most trials, although allergic reactions to the antibiotic preparations have been uncommonly noted. The primary long-term concern with the widespread use of SDD is the development of antibiotic resistance.[11-13] The data are unclear regarding the impact of SDD on the emergence of resistant organisms, and no study has demonstrated an impact of increased bacterial resistance on morbidity or mortality.

Costs and Implementation

The cost of implementing SDD appears minimal in most trials, but there have been no in depth reviews of the subject. Several trials have found that patients receiving SDD had lower

total antibiotic costs.[14-16] Overall hospital costs also may be lower, mediated through the decreased rate of VAP.[17]

Comment

SDD is a very promising method of reducing VAP and ICU-related mortality. The data supporting a significant reduction in risk of VAP and short-term mortality with SDD using topical and short-term intravenous antibiotics are strong. SDD is a relatively non-invasive intervention and the additional financial cost is minimal. What remains to be determined is the long-term effect of SDD on antibiotic resistance patterns, and the impact of such effect on morbidity and mortality. Research into the impact of SDD on the emergence of antibiotic resistance should be strongly encouraged.

Table 17.3.1. Meta-analyses of selective digestive tract decontamination*

Study Design	Pneumonia (95% CI)	Mortality (95% CI)
Nathens, 1999[6]: 21 randomized controlled trials of antibiotic prophylaxis used to decrease nosocomial respiratory tract infections; dual analysis of medical and surgical patients	Medical: OR 0.45 (0.33-0.62) Surgical: OR 0.19 (0.15-0.26)	Medical Overall: OR 0.91 (0.71-1.18) Topical/IV: OR 0.75 (0.53-1.06) Topical: OR 1.14 (0.77-1.68) Surgical Overall: OR 0.70 (0.52-0.93) Topical/IV: OR 0.60 (0.41-0.88) Topical: OR 0.86 (0.51-1.45)
D'Amico, 1998[1]: 33 randomized controlled trials from of antibiotic prophylaxis used to decrease nosocomial respiratory tract infections; dual analysis of topical and systemic antibiotics combined and topical antibiotics alone	Overall: not reported Topical/IV: OR 0.35 (0.29-0.41) Topical: OR 0.56 (0.46-0.68)	Overall: OR 0.88 (0.78-0.98) Topical/IV: OR 0.80 (0.69-0.93) Topical: OR 1.01 (0.84-1.22)
Hurley, 1995[5]: 26 randomized controlled trials of antibiotic prophylaxis used to decrease nosocomial respiratory tract infections	Overall: OR 0.35 (0.30-0.42)	Overall: OR 0.86 (0.74-0.99)
Kollef, 1994[7]: 16 randomized controlled trials of antibiotic prophylaxis used to decrease nosocomial respiratory tract infections	Overall: RD 0.145 (0.116-0.174)	Overall: RD 0.019 (-0.016-0.054)
Heyland, 1994[8]: 25 randomized controlled trials of antibiotic prophylaxis used to decrease nosocomial respiratory tract infections; performed subgroup analyses	Overall: RR 0.46 (0.39-0.56) Topical/IV: RR 0.48 (0.39-0.60) Topical: RR 0.43 (0.32-0.59)	Overall: RR 0.87 (0.79-0.97) Topical/IV: RR 0.81 (0.71-0.95) Topical: RR 1.00 (0.83-1.19)
SDD Trialists' Collaborative Group, 1993[9]: 22 randomized controlled trials of antibiotic prophylaxis used to decrease nosocomial respiratory tract infections; performed subgroup analyses	Overall: OR 0.37 (0.31-0.43) Topical/IV: OR 0.33 (0.27-0.40) Topical: OR 0.43 (0.33-0.56)	Overall: OR 0.90 (0.79-1.04) Topical/IV: OR 0.80 (0.67-0.97) Topical: OR 1.07 (0.86-1.32)
Vandenbroucke-Grauls, 1991[10]: 6 randomized controlled trials of antibiotic prophylaxis used to decrease nosocomial respiratory tract infections	Overall: OR 0.12 (0.08-0.19)	Overall: OR 0.70 (0.45-1.09)

* CI indicates confidence interval; RD, risk difference, RR, relative risk; and OR, odds ratio.

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Subchapter 17.4. Sucralfate and Prevention of VAP

Background

Aspiration of gastric secretions may contribute to the development of VAP. It has been observed that gastric colonization by potentially pathogenic organisms increases with decreasing gastric acidity, leading to the hypothesis that pH-altering drugs may cause increased rates of VAP.[1] H_2-antagonist therapy, widely used in mechanically-ventilated patients for stress ulcer prophylaxis (see Chapter 34), significantly elevates gastric pH. Sucralfate, an alternative prophylactic agent that does not affect gastric pH, may allow less gastric colonization with potentially pathogenic organisms than H_2-antagonists and therefore prevent some cases of VAP.

Practice Description

In general, 1 g of sucralfate suspension is given through a nasogastric tube every four to six hours. When H_2-antagonists are used, their dosing and frequency vary. A representative study used 50 mg of ranitidine intravenously every eight hours, dose adjusted for creatinine clearance.[2] Stress ulcer prophylaxis is usually started upon initiation of mechanical ventilation and continued until extubation (Chapter 34).

Opportunities for Impact

Stress ulcer prophylaxis is usually given to critically ill ventilated patients. A large cohort study of over 2000 critically ill patients suggests that the majority receive H_2-antagonists (71.8%) followed by sucralfate (7.0%) and combination therapy (15.4%) or other single agents (omeprazole, antacids, prostaglandins).[3] There is, therefore, significant opportunity for impact should sucralfate prove to lower rates of VAP and improve survival.

Study Designs

There have been over 20 randomized controlled trials of stress ulcer prophylaxis using sucralfate, H_2-antagonists, and other therapies in critically ill patients. Seven meta-analyses have been published to date.[2,4-10] The individual trials and meta-analyses have significant variation in methodology. In general, the individual trials randomized critically ill patients to sucralfate, H_2-antagonists, other agents such as antacids and pirenzepine, or placebo. The majority of patients included in these studies required mechanical ventilation. Various drug-drug, drug-placebo combinations were compared, and the rates of VAP and mortality were recorded.

Study Outcomes

Most trials report development of VAP and mortality as primary endpoints. There is significant variation in the definition of VAP used in these trials. In the largest and most recent randomized trial, VAP was defined as a new radiographic infiltrate plus two of the following: temperature of >38.5°C or <35.0°C, leukocyte count >10,000/mm^3 or <3000/mm^3, purulent sputum, and isolation of pathogenic bacterial from an endotracheal aspirate.[8] Mortality was reported at time of discharge from the ICU.

Evidence for Effectiveness of the Practice

The results of the seven meta-analyses and one recent large randomized controlled trial are inconclusive (see Table 17.4.1). The two largest meta-analyses to date suggest a decreased incidence of VAP with sucralfate compared to H_2-antagonists,[4,6] and one reports a statistically significant mortality benefit with sucralfate.[6] A recent randomized controlled trial of 1200 ventilated patients reports no significant difference between the two therapies in terms of VAP or mortality.[8]

Potential for Harm

Sucralfate therapy has been associated with a statistically significant increased risk of clinically important gastrointestinal bleeding when compared to H_2-antagonists.[8] Clinically important bleeding developed in 3.8% of patients receiving sucralfate compared with 1.7% of patients receiving H_2-antagonists (relative risk for H_2-antagonist = 0.44, 95% CI: 0.21-0.92).[8] Gastrointestinal bleeding in critically ill patients has an attributable mortality of approximately 12.5%.[8] While previous meta-analyses have suggested little difference in rates of gastrointestinal bleeding between the various prophylactic agents,[6] these results from a large randomized trial are convincing. There are very few adverse effects from sucralfate therapy aside from constipation, rare nausea and vomiting and very rare bezoar formation and aluminum intoxication.[11] Sucralfate administration has been associated with transmission of vancomycin resistant enterococcus, likely due to increased manipulation of patients' nasogastric tubes.[12] Unlike parenteral H_2-blockers, sucralfate mandates nasogastric tube placement in intubated patients. The drug can also lead to decreased absorption of other medications.

Costs and Implementation

Several studies have looked at the cost-effectiveness of stress ulcer prophylaxis.[13,14] Based on decision analysis, the cost per episode of gastrointestinal bleeding averted in high-risk patients is several thousand dollars greater with H_2-antagonists than with sucralfate.[13] This cost difference remains significant even if H_2-antagonists are assumed to be 50% more effective. There are no reliable data comparing overall costs from the actual clinical trials. The mean cost, largely driven by prolonged length of stay, is significantly higher for patients who bleed than for those who do not ($70,000 vs. $15-20,000), implying that in patients at high risk for GI bleeding (eg, mechanically ventilated patients, those with a coagulopathy), stress ulcer prophylaxis may be cost-neutral or even cost-saving (see also Chapter 34).[14] Implementation of sucralfate use would be largely an issue of staff education as administration is relatively uncomplicated.

Comment

The data supporting stress ulcer prophylaxis with sucralfate instead of H_2-antagonists to prevent VAP are inconclusive, and the theoretical contribution of increased gastric colonization with potentially pathogenic organisms to the development of VAP is unproven. There are data both supporting and refuting a decreased incidence of VAP with sucralfate. Most investigators have found at least a trend toward decreased incidence of VAP with sucralfate, and larger studies are warranted. The greatest benefit from sucralfate may be the prevention of late-onset VAP in patients requiring long-term ventilation.[15] Any increased risk of gastrointestinal bleeding with sucralfate therapy in these patients may be offset by the decreased risk of VAP. Until the data are more definitive, however, when stress ulcer prophylaxis is deemed appropriate (Chapter 34), the

use of H_2-blockers seems preferable to sucralfate because of the former's superiority in preventing clinically important gastrointestinal bleeding.

Table 17.4.1. Studies of stress ulcer prophylaxis

Study Design	Design, Outcomes	Pneumonia* (95% CI)	Mortality* (95% CI)
Meta-analysis of randomized controlled trials comparing ranitidine with placebo, sucralfate with placebo and ranitidine with sucralfate for the prevention of pneumonia in critically ill patients. (Messori, 2000)	Level 1A, Level 1	ranitidine vs. sucralfate: 1.35 (1.07-1.70) ranitidine vs. placebo: 0.98 (0.56-1.72) sucralfate vs. placebo: 2.21 (0.86-5.65)	not reported
Multicenter randomized, blinded, placebo-controlled trial of sucralfate with ranitidine in 1200 critically ill mechanically ventilated patients. Endpoints were gastrointestinal bleeding, VAP and mortality. (Cook, 1998)	Level 1, Level 1	ranitidine vs. sucralfate: 1.18 (0.92-1.51)	ranitidine vs. sucralfate: 1.03 (0.84-1.26)
27 randomized trials of stress ulcer prophylaxis in critically ill patients. The majority of patients were mechanically ventilated. Endpoints were gastrointestinal bleeding, pneumonia and mortality. (Cook, 1996)	Level 1A, Level 1	sucralfate vs. H_2-antagonist: 0.77 (0.60-1.01) H_2-antagonist vs. placebo: 1.25 (0.78-2.00)	sucralfate vs. H_2-antagonist: 0.73 (0.54-0.97)
14 randomized trials of stress ulcer prophylaxis in critically ill patients. (Tryba, 1995)	Level 1A, Level 1	sucralfate vs. H_2-antagonist/ antacid: 0.67 ($p<0.05$)	not reported
6 (outcome VAP) and 7 (outcome mortality) randomized trials of stress ulcer prophylaxis in critically ill patients. (Cook, 1995)	Level 1A, Level 1	sucralfate vs. H_2-antagonist/ antacid: 0.50 (0.21-0.79)	sucralfate vs. H_2-antagonist: 0.71 (0.49-1.04) sucralfate vs. antacid: 0.70 (0.52-0.94)
14 randomized trials of stress ulcer prophylaxis in critically ill patients. Endpoints were gastrointestinal bleeding and pneumonia. (Tryba. 1991)	Level 1A, Level 1	sucralfate vs. H_2-antagonist: 0.50 (0.32-0.78) sucralfate vs. antacid: 0.40 (0.24-0.69)	sucralfate vs. H_2-antagonist/ antacid: 0.81 (NA)

Table 17.4.1. Studies of stress ulcer prophylaxis (cont.)

9 randomized trials of stress ulcer prophylaxis in critically ill patients. (Tryba, 1991)	Level 1A, Level 1	sucralfate vs. H_2-antagonist/ antacid: 0.48 ($p<0.05$)	sucralfate vs. H_2-antagonist/ antacid: 0.72 ($p<0.05$)
8 randomized trials of stress ulcer prophylaxis in critically ill patients studying the rate of pneumonia with different drug regimens. (Cook, 1991)	Level 1A, Level 1	sucralfate vs. H_2-antagonist/ antacid: 0.55 (0.28-1.06) H_2-antagonist/antacid vs. placebo: 0.42 (0.17-1.11)	not reported

* Point estimates reflect odds ratio or relative risk.

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Final Comment to Chapter 17

Ventilator-associated pneumonia is common, costly, and morbid. This chapter confirms that there are several low-risk interventions that carry the potential to reduce the frequency of this complication. Further research will be needed to confirm the benefit of promising practices (eg, semi-recumbency or continuous aspiration of subglottic secretions) or fully allay concerns regarding practices that have potential for harm (eg, antibiotic resistance with selective decontamination).

Section C. Surgery, Anesthesia, and Perioperative Medicine

Chapter 18. Localizing Care to High-Volume Centers

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Background

The extent to which experience in caring for illness—as represented by a higher volume of cases—impacts outcomes has been well studied over the last 20 years. An extensive literature covering a broad range of conditions and procedures documents superior outcomes for hospitals and physicians with higher patient volumes.[1-6] Drawing on such evidence, various investigators have projected substantial reductions in mortality from regionalizing certain high-risk procedures with established volume-outcome relationships.[4-6]

When volume-outcomes relationships reflect a "practice makes perfect" effect, it may be reasonable to use volumes to assess quality of care. However, such relationships may also reflect "selective referral,"[7-10] when anecdotal knowledge of the superior quality of high volume centers exists in the community.[11] In such cases, direct measurements of processes or outcomes may represent more appropriate quality measures than volume alone.[12,13]

In an era of cost containment and a growing need for accountability for quality of care, any connection between site or physician-specific experience and patient outcomes has far reaching implications for patients, payers, and governmental agencies.[14] In fact, the Leapfrog Group (a consortium of major purchasers and purchasing coalitions) has made patient volume one of their criteria for quality, and has recently begun a project examining evidence-based referrals to high-volume centers (see also Chapter 55).[15]

The Institute of Medicine (IOM) recently sponsored a workshop to examine the evidence supporting this relationship,[16] part of which included a systematic review of investigations of the volume-outcome association.[17] This chapter summarizes the evidence supporting volume-outcomes relationships, drawing heavily on the IOM's systematic review and the workshop's findings.

Practice Description

The use of information regarding volume and its proven or potential relationship with better outcomes may result in several actions. Simply providing patients with volume data may result in preferential selection of high-volume centers or providers. Patients might also be incentivized to choose high-volume centers (eg, through reduced co-payments). Alternatively, payers may elect to contract only with high-volume centers, or provide higher payments to these sites. Finally, low-volume centers (eg, a hospital failing to meet a minimum threshold of bypass operations) or providers (eg, a cardiologist failing to perform a minimum number of angioplasties) might be restricted from continuing to perform the practice, through some combination of credentialing, accreditation, or regulatory actions (see Chapter 56).

Opportunities for Impact

Assuming that a feasible method could be developed to localize care to high-volume centers, a significant effect on patient safety and outcomes is likely. A recent study suggested that more than 500 deaths could be avoided annually in California alone if care for disorders with established volume-outcomes relationships were localized to more experienced centers. Extrapolating nationally, such localization would save 4000 lives.[6] In the case of acute myocardial infarction, transferring the care of these patients from hospitals in the lowest volume

quartile to those in the highest would save 2.3 lives per 100 patients.[4] The corresponding "number needed to treat" (NNT) of 50 falls within the range of many accepted therapeutic interventions.

Little information exists to assess differences in quality of care or rates of adverse events in high or low-volume sites. For example, the extent to which increasing volume leads to fewer medical errors or other direct impacts on patient safety (as opposed to specific improvement in care processes for discrete procedures, which would fall outside our definition of patient safety practices (Chapter 1)) is unknown. Ongoing prospective initiatives such as those proposed by the Leapfrog Group[15] may better quantify the various impacts of localizing care to high-volume centers.

Study Designs

We analyzed one large systematic review of 88 studies examining the relationship between volume and outcomes.[17] Using a structured MEDLINE search, this review included studies that examined health outcomes as the dependent variable with hospital and/or physician volume as an independent variable. The IOM review included medical and surgical conditions such as coronary artery bypass grafting, pediatric cardiac surgery, carotid endarterectomy, abdominal aortic aneurysm repair, cancer surgery, coronary angioplasty, acute myocardial infarction, AIDS, and multiple procedures. This chapter reviews the relationship for surgical illnesses only.

The source studies of the IOM review were entirely observational in nature. Close attention was paid to risk adjustment and statistical methods in assessment of results, and criteria for inclusion in the review selected for population or community-based samples. Thus, the level of the design is classified as Level 3A.

Study Outcomes

The IOM systematic review examined health outcomes as related to hospital or physician volume. The primary outcome of interest was mortality. Other clinical outcomes were chosen based on complications specific to the surgical procedure (eg, stroke following carotid endarterectomy).

Evidence for Effectiveness of the Practice

Results of the systematic review are outlined in Table 18.1. The studies reviewed were of variable design and analytic sophistication, with more recent investigations generally being of higher quality. For all procedures, there was a consistent trend toward an association between improved outcomes and higher hospital or physician-specific volume.* The evidence supporting the volume-outcomes relationship was similar when looking at hospital volume (78% of studies

* This trend has one major exception, a study of volume-outcome relationships for 8 major surgical procedures at Veterans Affairs hospitals across the country (Khuri SF, et al. Relation of surgical volume to outcome in eight common operations: results from the VA National Surgical Quality Improvement Program. *Ann Surg*. 1999;230:414-429). This comprehensive national study found no significant volume-outcome relationship for any of the 8 procedures analyzed. While it is tempting to attribute these negative findings to unique aspects of the VA system, this is also one of the few studies to employ robust risk-adjustment using clinical and not administrative data. The authors of the IOM review take particular note of the superior methodologic features and negative findings of this study.

showed an association) and physician volume (74% showed an association); the former was the more frequently analyzed variable.

The impact of volume on outcomes varied across procedures and diagnoses. The effect was most marked for complex cancer surgeries (ie, esophagectomy, pancreatoduodenectomy), with numbers needed to treat (NNT) between 7 and 17. For commonly performed surgeries such as coronary artery bypass grafting, the NNT was generally larger, but still within the range of other accepted therapies. Carotid endarterectomy appeared to have a much higher NNT, but this may be because the major adverse outcome of this surgery (ie, stroke) is often an indication for surgery as well as a complication of it. This relationship cannot be discerned from administrative data, and the studies upon which the NNT is based reported mortality, a less frequent complication of carotid surgery than stroke, as a primary outcome. The few studies that collected primary data (and would have been able to determine this important difference) were generally small and of lower quality design, making their findings suspect.

The authors of the IOM systematic review conclude that the volume-outcomes relationship exists, but they raise some caveats when interpreting the literature as a whole. They first note that the literature describing the relationship in greatest detail come from a few single-State databases (63% of studies coming from New York State alone), possibly limiting the generalizability of their results. Although few studies employed rigorous risk adjustment methodologies using clinical data, the relationship between volume and outcomes was consistent in these studies. Also, they raise a note of caution in interpreting this relationship because of the possibility that publication bias (ie, studies that fail to demonstrate a volume-outcome relationship might be less likely to be submitted or accepted for publication) has affected this literature. Finally, they point out that the precise mechanism by which outcomes are improved has yet to be elucidated; no study has reported the independent effects of ancillary personnel expertise or hospital system factors on patient outcomes. For example, in interpreting the improved outcomes of high volume centers in coronary artery bypass grafting, we do not presently know what the relative contributions are of the surgeon, cardiac bypass team, cardiac anesthesiologist, and hospital resources (eg, dedicated cardiothoracic intensive care units).

Potential for Harm

In the summary accompanying the IOM workshop's proceedings, several potential pitfalls of localizing care to high volume settings were noted, as follows[16]:

- The focus on high volume providers may be a “distracting priority,” and similar improvements in care may be achieved through more traditional local quality improvement measures.
- Hospitals with high volumes may use that data to misrepresent their experience in the absence of true outcomes data.
- High volume centers may achieve too much contractual leverage, leading to price inflation.
- Counting procedures may lead to perverse incentives to perform procedures that are not appropriate.
- Requiring high volumes will impede entry of new competitors into the marketplace.
- Narrowing the choice of providers may negatively impact patient satisfaction and override patients’ preferences for care (for example, if patients are forced to travel long distances to receive care at a high volume center).

Several of these concerns have been borne out in published studies. In a study of pediatric trauma centers, Tepas et al suggested that increases in volume may strain provider resources and worsen patient outcomes.[18] Even assuming potential improvements in patient outcomes, diverting patients to large referral centers has important health policy implications[14] and may decrease patient satisfaction.[19]

Costs and Implementation

The major barriers to implementing a selective referral program based on hospital volume include the potential harms listed above, as well as several additional factors. These may include patients' preference for care near home, lack of resources to travel, inability to transfer unstable patients to high-volume centers, loss of access to care in areas where low-volume services are discontinued (particularly rural areas), and resistance by providers to quality measurement activities. Finally, existing high volume centers may lack the capacity to accept additional patients. When they do not, further increases in volume could lead to increased rates of adverse events due to over-stressing the system, as was noted for pediatric trauma.[18]

Costs of this practice are not explicitly addressed in the IOM report, but widespread implementation of selective referrals would depend on the collection of detailed and accurate data (risk adjustment, process, and outcomes data), at substantial cost. Additionally, a nationwide systematic referral model may require augmenting capability of high-volume hospitals through additional construction or other major infrastructure investments. Finally, the travel and inconvenience costs of having patients obtain care at institutions outside the local community will be borne by either the system or the patients themselves—a cost which may be compounded further by patients' and families' lost productivity.

Comment

Changing practice patterns based on the compelling data linking volume and improved outcomes is a complex task involving patients, hospitals and communities, as well as payers and employers. Actually closing hospitals or designating specific health care centers as "magnet" sites for care of specific illnesses would require, in addition to a wholesale change in health care systems, major infusions of resources and difficult political choices. For these reasons alone, this policy decision seems unlikely. Alternatively, hospitals or medical groups may use physician-specific outcomes information to make decisions about staffing needs (eg, hiring a lower number of surgeons to ensure that all operators have high volumes), although this too seems unlikely unless meeting volume thresholds become mandatory or are strongly incentivized.

The Leapfrog Group's efforts represent one of the first major initiatives to use empiric data to direct selective referrals using volume data. As an initiative begun and carried out within a specific employer/health care purchaser system it may be limited in its generalizability. However, prospective evaluation of the effort will yield important information regarding the costs and outcomes of such a referral system and its impact on patient satisfaction with care.

Outside of the Leapfrog effort, the widespread publication of outcomes, especially mortality data, has been proposed as a way to help consumers to make more informed health care choices. A recent systematic review of this paradigm or "strategy" suggests that its impact has been mixed.[20] There are no data to suggest that patients or payers will make major changes in health care purchasing decisions when provided with volume data alone. To date, press reports of particularly noteworthy errors seem to have more of an impact on patients' choices of care than information about volume or even outcomes of care.[20,21]

In addition to the potential use of volume data to guide health care purchasing decisions, the IOM workshop and authors of the systematic review recommend using volume as one of several quality measures to initiate local or regional quality improvement efforts. This data may motivate or inform care improvement efforts at low-volume sites (or those with worse-than-expected outcomes) through use of site visits, feedback of risk-adjusted outcomes information, and assessment of care processes. This collaborative approach to quality improvement has been used successfully in the VA National Surgical Quality Improvement Project[22] and in several projects in New York State.[23,24] However, it seems likely that as the volume-outcome relationship becomes better defined and understood, its influence on the health care choices of both patients and payers is likely to grow.

Table 18.1. Summary of findings from IOM systematic review [17] of volume-outcome relationship*

Condition	Number of Studies Reviewed	Comments
Coronary artery bypass grafting	9	All studies used appropriate risk adjustment VOR for both physicians and hospital: 7 studies Absolute difference in mortality between high- and low-volume centers and surgeons was 3-10% (NNT 10-33) Some evidence to suggest that centers and surgeons with good outcomes experienced increasing volumes over time ("selective referrals")
Carotid endarterectomy	19	Only 9 studies performed adequate risk adjustment Most studies employed administrative data, making accurate ascertainment of postoperative stroke impossible VOR found for surgeon: 9 studies VOR found for hospital: 7 studies Absolute difference in mortality between high- and low-volume hospital/surgeon was 0.2-0.9% (NNT 100-500)
Cancer surgery	20	Risk adjustment methods variable, most are dependent on administrative data only VOR most marked for rare cancers/procedures such as pancreatic resection and esophageal surgery VOR unclear for common surgery such as colectomy and pneumonectomy For esophagectomy, absolute difference in mortality between high- and low-volume hospitals was 11-13.9% (NNT 7-9) For pancreatic resection, difference in mortality between high- and low-volume hospitals gives NNT 10-15
Abdominal aortic aneurysm repair	12	11 studies performed adequate risk adjustment VOR for hospitals and physicians noted Absolute reduction in mortality due to surgeon or hospital volume was 5-9% (NNT 11-20) "Selective referrals" noted
Pediatric cardiac surgery	3	All studies used appropriate risk adjustment VOR found for both hospital and surgeon volume Absolute difference in mortality due to surgeon or hospital volume was 3% (NNT 33) Possibly greater benefit for more complex/sicker patients

* NNT indicates number needed to treat; VOR, volume-outcome relationship

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Chapter 19. Learning Curves for New Procedures – the Case of Laparoscopic Cholecystectomy

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Background

Minimal access surgery began in the early 1980s with the introduction of laparoscopic fallopian tube ligation. The first laparoscopic cholecystectomy was performed 7 years later, and was rapidly embraced as the preferred method for cholecystectomy despite a lack of evidence to support the safety of the new technique.[1-6] In response to several deaths and complications associated with laparoscopic cholecystectomy, the New York State Department of Health issued guidelines for the credentialing of surgeons who wished to perform the procedure.[7,8] At the same time, a National Institutes of Health Consensus conference published recommendations regarding indications for laparoscopic cholecystectomy.[1]

Clinical trials comparing the laparoscopic procedure with other approaches eventually revealed that the newer procedure to be less morbid than traditional open cholecystectomy, or even mini-laparotomy.[9-16] Importantly, though, it also became clear that acquiring the skills to perform this new procedure involved a substantial surgical "learning curve."[17-22] This learning curve no longer affects patients undergoing laparoscopic cholecystectomy, as training has become a required part of all surgical residency programs, with graduating surgery residents typically having performed more than 50 laparoscopic cholecystectomies.[23,24] However, the growth of laparoscopic cholecystectomy has been followed by equally rapid development and application of minimal access procedures in virtually every surgical specialty. This chapter considers the patient safety issues that arise with the diffusion of a new procedurally-based technology. It highlights the "learning curve" inherent in any new procedure, as competence invariably grows with practice (see Chapter 18). Because it is so widely performed and has the largest literature describing its record, this chapter focuses on lessons learned from the introduction of laparoscopic cholecystectomy.

Practice Description

Although there are a wide variety of procedure-specific techniques in minimal access surgery, all operations utilize videoscopic or digital imaging in conjunction with remote manipulation. In general, the operator works from two-dimensional, magnified video images of the operative field while manipulating long narrow instruments placed into the operating cavity from outside the body. To become proficient in minimal access techniques, the surgeon must develop skills in interpreting a three-dimensional environment as a two-dimensional image, and learn how to do familiar tasks (eg, suture) with familiar instruments in an unfamiliar manner. Importantly, the surgeon never actually touches the tissue being moved with his or her hands.[21,25] This loss of tactile input is the major factor in making minimal access techniques difficult to learn.

Prevalence and Severity of the Target Safety Problem

Complications from minimal access procedures fall into 2 general categories: those directly resulting from the laparoscopic intervention (ie, trocar injuries, dissection injuries, insufflation-associated events)[26] and those associated with the operation itself (eg, bile duct injury with cholecystectomy, gastric injury with fundoplication).*[17-22] For laparoscopic cholecystectomy, a survey of 1750 surgery department chairpersons reported that bowel and vascular injuries (laparoscopic-specific injury) occurred in 0.14% and 0.25% of cases respectively, while the rate of bile duct injuries (procedure-specific) was 0.6%.[3] The bile duct injury rate was lower at institutions that had performed more than 100 cases. Although this study was large, as a survey it likely underestimates the true rate of complications. Other multi-institutional reports of laparoscopic cholecystectomy in the United States have noted a similar bile duct injury rate and report mortality rates of 0.04% to 0.1%.[5,21,25,29] Although undoubtedly underestimated, even these rates are higher than those associated with open cholecystectomy.

Opportunities for Impact

As set forth above, laparoscopic cholecystectomies is a standard part of surgical residency training.[23,24] Nearly all general surgeons who did not train in the current era have received postgraduate training in basic laparoscopic techniques. This training often takes the form of a 2-3 day course involving hands-on experience with animal models and laboratory-skills sessions, then observation or assisting with cases primarily performed by another surgeon, finally, performing cases supervised by an experienced laparoscopist, and finally performing cases independently.[6,24,30]

Proficiency in traditional techniques does not automatically translate to minimal access methods. We identified one study investigating whether the level of surgical training (attending surgeon versus chief resident) affected the performance of cholecystectomy.[17] This study suggested that, despite operating on more complex patients, the adverse event rate for surgical chief residents learning laparoscopic cholecystectomy was similar to that of attending physicians (who had far more operative experience).

Similarly, skills obtained with one minimal access procedure do not transfer to others. The operation of laparoscopic fundoplication for gastroesophageal reflux disease entered into surgical practice after laparoscopic cholecystectomy. Therefore, most surgeons who performed it had basic laparoscopic skill sets. Studies investigating its implementation suggest a threshold of 25-30 cases before surgeons attain proficiency,[31-34] in contrast to a threshold of about 15-20 cases for laparoscopic cholecystectomy.[25,29,30,35] In recognition of this lack of transferability, performing laparoscopic cholecystectomies does not qualify a surgeon to perform laparoscopic colon resection without first undergoing additional training specifically in laparoscopic colon techniques.[6,36] The need for specific new training has been seen with other procedures as well.[37-41]

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* A third problem concerns the potential adverse effects at the population. While the procedure itself may be less morbid, the rate at which this 'safer' procedure is performed may increase substantially to the point that the complications experienced by the patient population as a whole do not decrease.[27] This problem has been documented with laparoscopic cholecystectomy,[12,28] but processes for improved patient selection have not received sufficient testing to permit review of a particular safety practice relating to procedure "appropriateness."

Thus, determination of a minimum number of cases required to become proficient (as an aid to credentialing or proctoring activities), or determining methods to shorten the time needed to attain this level of skill will have a clear impact on patients undergoing minimal access procedures. This impact is likely to become greater as the breadth and complexity of procedures approached through minimal access techniques grows.

Study Designs

Using a structured MEDLINE search, we sought to identify papers that either reported a threshold number of cases required to attain proficiency, or explicitly compared training techniques for laparoscopic cholecystectomy in terms of patient outcomes. Our literature search found a large number of reports describing retrospective analyses or reports from procedure registries. These studies did not report training protocols, specific physician characteristics or surgeon-specific volumes, and were therefore excluded from our review. In addition, we found several review articles.[42-44] The first of these reviews focused primarily on statistical techniques for documenting and analyzing learning curves,[42] and the other two[43,44] did not meet criteria for systematic reviews. Nonetheless, the bibliographies of all 3 articles were scanned for relevant studies.

Study Outcomes

All studies reported clinical outcomes (Level 1), most commonly bile duct injury. Other complications (eg, insufflation or trocar injuries) were very unusual, and mortality was rare.

Evidence for Effectiveness of the Practice

Three studies specifically addressed the relationship between surgical experience in the performance of laparoscopic cholecystectomy and a well-defined adverse outcome, bile duct injury. The first reported 15 bile duct injuries in over 8000 laparoscopic cholecystectomies.[30] Multivariate analysis showed that the only significant factor in predicting this adverse event was the experience of the surgeon ($p=0.001$). Rapidity of learning was not significantly related to a surgeon's age, size of practice, or hospital setting. Ninety percent of injuries were predicted to occur during a surgeon's first 30 cases. Gigot et al[35] reported the incidence of bile duct injury was 1.3% when the surgeon had performed fewer than 50 cases and 0.35% afterwards ($p<0.001$). However, bile duct injuries still occurred with surgeons who had performed >100 cases.[35] Similar results have been observed in other studies of bile duct injury with laparoscopic cholecystectomy,[45] suggesting that something beyond the learning curve accounts for many laparoscopic errors. Examination from error analysis suggests that these events occur because of visual and perceptual difficulties involved in the operator/equipment interface.[46,47]

We identified one prospective cohort study from Japan that compared the effectiveness of 2 training courses for laparoscopic cholecystectomy.[2] In this study, one group of 8 surgeons was assigned to 10 supervised laparoscopic cholecystectomies as part of their initial training; a second group of 8 surgeons had only 2 observed training sessions. Complications that occurred over 21 months after completion of the 4 months of training were assessed by means of a questionnaire sent to all participants. The surgeons who had trained with 10 supervised procedures had 0.5% major complications (bleeding, bile duct injury or bile leakage) versus 2% for the surgeons trained with only 2 procedures ($p=0.03$). The incidence of major complications occurring during the initial 10 operations was higher among unsupervised surgeons ($p=0.005$).

Outside of laparoscopic cholecystectomy, we identified one study examining complication rates of urologic laparoscopic surgeons after completing a 2-day training seminar.[48]

Because the study relied on surveys of participants at 3 and 12 months after course completion, it is likely biased toward underestimating the incidence of adverse events. Nevertheless the study showed that surgeons who performed procedures without additional training were 3 times more likely to have at least one complication compared with surgeons who sought additional training. Additionally the presence of skilled associates and the development of a surgical team impact favorably on reducing the number of complications.[48,49]

Potential for Harm

It is unlikely that the specific introduction of training and requirements for a baseline of surgical experience in minimal access surgery procedures will lead to adverse events.

Costs and Implementation

In the initial introduction of laparoscopic cholecystectomy most surgeons attended at least one didactic and hands-on course in operative technique and instrument manipulation. Some of these experiences included operative procedures in animals and utilization of static training boxes and devices that may speed the acquisition of perceptual and motor skills. The need for practice in the development of technical skills is vital, and laboratory courses, training devices and simulators (Chapter 45) are being tested for their ability to improve operator skills.[50-55] There is insufficient evidence to make a recommendation of the superiority of one training method over any other and costs are presently undetermined.

After sufficient laboratory experience and practice, it is recommended that the procedure be performed initially in only carefully selected patients under the supervision of an experienced surgeon.[56-58] How practicing groups of providers obtain an experienced consultant is variable.[59,60] Surgical training fellowships in minimal access surgery have been established and graduates of these programs have the requisite expertise to supervise others. Unfortunately, such fellowship graduates are in short supply. Telemedicine may play a role in the mentoring and technical support for surgeons performing new techniques as it provides a means for remote performance of a procedure with real-time expert supervision and guidance.[61,62]

Comment

Minimal access surgery has become extraordinarily popular largely in response to market forces. The single most important predictor of adverse events in minimal access procedures is the experience of the provider with the specific operation. Surgeons must acquire the necessary technical skills and expertise before performing new procedures on patients. Hospitals and payers should help ensure that providers possess the requisite experience before allowing procedures to be performed in their facilities or paying for them, since patients alone will generally be unable to determine surgeon competency.

A number of governing bodies and surgical societies have published guidelines that outline standards for training for postgraduate surgeons for skill acquisition in minimal access surgery,[1,56-58,63-66] but these recommendations are based more on common sense and clinical experience than rigorous evidence. It is not known how influential these guidelines are in the granting of privileges. Continued research is needed to determine the threshold for safe performance of this and other procedures, the most effective training methods to ensure competence, and strategies to minimize patient harm while proceduralists gain the experience they need to be competent and to train others.

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Chapter 20. Prevention of Surgical Site Infections

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Subchapter 20.1. Prophylactic Antibiotics

Background

Surgical site infections (SSI) include superficial incisional infections, infections of the deep incision space and organ space infections.[1,2] A large body of evidence supports the premise that SSIs can be prevented through administration of appropriate prophylactic antibiotics. Two national organizations, the Federal Centers for Disease Control and Prevention (CDC) and the American Society for Health System Pharmacists (ASHP), have recently synthesized this vast literature to produce comprehensive guidelines regarding the administration of prophylactic antibiotics across a broad range of procedures.[3,4] Because of the breadth of this literature, we limited the focus of this review of strategies to prevent SSIs to adult surgery and procedures that typically occur in the operating room (as opposed to procedures such as endoscopy, interventional cardiology, or radiology procedures).

Practice Description

Antimicrobial prophylaxis refers to a brief course of an antimicrobial agent administered just before an operation begins in order to reduce intraoperative microbial contamination to a level that will not overwhelm host defenses and result in infection.[4] To maximize the benefits of antimicrobial prophylactic, the agent used should be safe, inexpensive, and bactericidal with an *in vitro* spectrum that covers the most probable contaminants for the operation.[4] Administration, usually by intravenous infusion, should be timed so that a bactericidal concentration is present in serum and tissues by the time the skin is incised.[5] This practice is now standard of care and recommended by professional societies.[6] Therapeutic levels in serum and tissues should be maintained until, at most, a few hours after the incision is closed in the operating room.[4]

Prevalence and Severity of the Target Safety Problem

Surgical site infections are a common complication of care, occurring in 2-5% of patients after clean extra-abdominal surgeries (eg, thoracic and orthopedic surgery) and in up to 20% of patients undergoing intra-abdominal procedures.[7-12] Studies following patients into the post-discharge period have reported even higher rates of postoperative infection.[13-16] These complications increase morbidity for patients and consume substantial additional resources.[17-21]

Opportunities for Impact

Approximately 80-90% of surgical patients receive some kind of antibiotic prophylaxis, though recent studies have shown that choice of regimen, timing of administration or duration of prophylaxis is inappropriate in approximately 25-50% of cases.[22-27]

Study Designs and Outcomes

As previously noted, the literature on prophylactic antibiotics is extensive. Therefore, the review was limited to evidence from Level 1A study designs. We identified 9 relevant studies examining the use of prophylactic antibiotics to prevent surgical site infections: 7 meta-analyses and 2 systematic reviews.[28-36] (Tables 20.1.1 and 20.1.2) These reviews were of high quality and limited their source material to randomized controlled trials. Although additional randomized trials have been published since these reviews were performed, updating the results of each review was beyond the scope of this project. All studies examined measured rates of site infection directly (Level 1), using previously published definitions to allow comparability. In addition, the rates of sepsis, length of stay, and physiologic measures were reported. One meta-analysis [31] and one systematic review [33] combined rates of several relevant infectious outcomes.

Evidence for Effectiveness of the Practice

All studies showed a marked reduction in the odds or relative risk of SSI when antibiotic prophylaxis was employed. None of the meta-analyses reviewed explicitly examined the timing of prophylaxis, although many studies pooled data from investigations of antibiotic regimens administered in the immediate preoperative period, (ie, within minutes to an hour of initial incision). Two meta-analyses in our review[29,31] suggested a trend towards lower rates of infection with use of broader-spectrum antibiotic prophylaxis, such as third generation cephalosporins. When compared with single dose prophylaxis, multiple dose prophylaxis generally did not result in significant additional benefit.[29,30,35] In fact, Tanos et al found the odds of SSI were significantly less with single dose prophylaxis.[31] Gillespie et al reported a greater relative risk of infection with single dose prophylaxis with a short-acting antibiotic when compared with multiple dose prophylaxis.[36] However, the risk of infection with single dose prophylaxis using long-acting antibiotics did not differ significantly from that seen with multiple-dose regimens.

Potential for Harm

None of the meta-analyses analyzed reported rates of adverse events (such as allergic reactions or nosocomial infections) associated with antibiotic prophylaxis of any type or duration. Both of the systematic reviews[33,36] noted a trend towards more frequent adverse events with the use of antibiotic prophylaxis. Authors of both systematic reviews observed that these events were reported rarely and that variation in the definition of "adverse events" across studies made pooling results difficult.

Infection with *Clostridium difficile* affects a large number of hospitalized patients and has significant clinical and economic implications. As many as 16% of *C. difficile* colitis cases in surgical patients can be attributed to prophylaxis alone,[37] with higher risk for this complication among patients receiving broad-spectrum antibiotics or prolonged courses of therapy. Shortening the duration of antibiotic administration may reduce potential risks of prophylaxis (see Chapter 14). Emergence of other types of resistant pathogens is an additional theoretical concern of inappropriate antibiotic prophylaxis; our literature search found no data describing effect of antibiotic prophylaxis on population-level incidence of these pathogens.

Costs and Implementation

A number of studies have evaluated strategies for improving compliance with recommended practices for perioperative antibiotic prophylaxis. These include chart audit with feedback,[38] computerized decision support,[23, 39-42] dissemination of guidelines,[43] total quality management (TQM) and continuous quality improvement (CQI) techniques,[44-47] provider education programs,[48,49] and comprehensive efforts by an infection control team.[50] Another promising and easily implemented method is to delegate the administration of prophylactic antibiotics to the anesthesia team or the holding room nursing staff.[22, 25, 48]

Costs for systems to increase appropriate use of antibiotics will likely be offset by savings due to prevented infections. However formal analyses of the cost-effectiveness of specific programs to improve prophylaxis have not been reported.

Comment

For many surgical procedures there is clear evidence supporting the use of antibiotic prophylaxis, administered in a timely manner, to prevent surgical site infections. The reviews suggest that broader spectrum antibiotics may be superior to limited-spectrum antibiotics for intra-abdominal or gynecologic surgeries. In addition, single-dose antibiotic prophylaxis appears to be at least as effective as multiple-dose regimens for a broad range of surgical procedures and may pose less risk to patients in terms of adverse events (eg, *C. difficile* colitis) and less risk to the population in terms of microbial resistance.

Future research will continue to address what prophylactic regimens are most effective for various surgical procedures. Investigation should also focus on methods to improve compliance. The optimal strategies for implementation will likely vary from institution to institution.

Table 20.1.1. Meta-analyses examining antibiotic prophylaxis*

Study	Trials Included	Surgical Procedures, Antibiotics	Results: Odds Ratio or Relative Risk of Infection (95% CI)
Kreter, 1992[35]	28	Cardiothoracic surgery; cephalosporins	▪ Cefazolin vs. placebo: OR 0.2 (0.10-0.48). ▪ Cefazolin vs. cefuroxime or cefamandole: OR 1.6 (1.03-2.45) • Single dose vs. multiple dose regimen: no significant difference
McDonald, 1998[30]	28	Multiple types of surgery; multiple antibiotics	▪ Single dose vs. multiple dose antibiotics (all studies): OR 1.06 (0.89-1.25) ▪ Duration of multiple dose regimen <24 hours: OR 1.02 (0.79-1.32) • Duration of multiple dose regimen >24 hours: OR 1.08 (0.86-1.36)
Meijer, 1990[29]	42	Biliary surgery; cephalosporins	▪ Antibiotic vs. placebo: OR 0.30 (0.23-0.38) ▪ Cephalosporin I vs. cephalosporin II or III: OR 1.18 (0.69-2)† • Single dose vs. multiple dose regimen: OR 0.80 (0.4-1.6)
Mittendorf, 1993[28]	25	Abdominal hysterectomy; multiple antibiotics	▪ Antibiotic vs. placebo (all studies): OR 0.35 (0.27-0.5); p<0.00001‡ ▪ Cefazolin vs. placebo: OR 0.32 (0.18-0.6); p=0.0002‡ • Metronidazole vs. placebo: OR 0.24 (0.08-0.8); p=0.015 ‡
Sharma, 2000[34]	6	Percutaneous gastrostomy; multiple antibiotics	▪ Antibiotic vs. placebo (all studies): RR 0.73, NNT 5.7 • Single dose regimens: RR 0.78, NNT 6.1
Tanos, 1994[31]	17	Abdominal hysterectomy; cephalosporins	▪ Antibiotic vs. placebo (all studies): OR 0.35 (0.3-0.4) ▪ Cephalosporin I vs. placebo: OR 0.4 (0.3-0.5) ▪ Cephalosporin II vs. placebo: OR 0.37 (0.2-0.8) ▪ Cephalosporin III vs. placebo: OR 0.26 (0.1-0.5)

			• Single dose vs. multiple dose regimen: OR 0.37 (0.3-0.5)
Wilson, 1992[51]	21	Multiple types of surgery; multiple antibiotics	▪ Amoxicillin-clavulanic acid vs. other antibiotics (all studies): OR 0.84 (0.68-1.04) ▪ Trend favoring amoxicillin-clavulanic acid for biliary and gynecologic surgery

* CI indicates confidence interval; NNT, number needed to treat; OR, odds ratio, and RR, relative risk.
† Roman numerals I, II, III indicate generation of cephalosporin antibiotics.
‡ P values were reported in article; OR were approximated based on figures.

Table 20.1.2. Systematic reviews of antibiotic prophylaxis*

Study	Trials Included	Surgical Procedures; Antibiotics	Results: Relative Risk of Infection (95% CI)
Gillespie, 2000[36]	48	Long bone fractures; multiple antibiotics	<u>Single dose antibiotic vs. placebo</u> Deep wound infection: RR 0.40 (0.24-0.67) Superficial wound infection: RR 0.69 (0.50-0.95) Urinary tract infection: RR 0.63 (0.53-0.76) Pneumonia: RR 0.46 (0.33-0.65) <u>Multiple dose antibiotic vs. placebo:</u> Deep wound infection: RR 0.36 (0.21-0.65) Superficial wound infection: RR 0.48 (0.28-0.81) Urinary tract infection: RR 0.66 (0.4-1.0) Pneumonia: RR 0.81 (0.41-1.63) Adverse events: RR 1.83 (0.96-3.50) <u>Single dose short-acting antibiotic vs. multiple doses same agent up to 24 hours after surgery</u> Deep wound infection: RR 7.98 (1.01-62.0) Superficial wound infection: RR 4.82 (1.08-21.6) Urinary tract infection: RR 1.81 (1.01-3.23) <u>Single dose long-acting antibiotic vs. any multiple dose regimen lasting more than 24 hours</u> Deep wound infection: RR 1.10 (0.22-5.34) Superficial wound infection: RR 0.57 (0.17-1.93) <u>Multiple doses administered over 24 hours or less vs. longer therapy</u> Deep wound infection: RR 1.1 (0.22-5.34) Superficial wound infection: RR 0.57 (0.17-1.93) <u>Oral vs. parenteral prophylaxis</u> Insufficient data (single underpowered study)
Smaill, 2000[33]	66	Cesarean section; multiple antibiotics	<u>Impact of antibiotic prophylaxis on …</u> <u>-Combined outcomes of fever, wound infection, sepsis and endometritis:</u> Elective Cesarean section: RR 0.25 (0.11-0.55) Emergent Cesarean section: RR 0.39 (0.33-0.46) Unspecified/nonelective: RR 0.37 (0.32-0.42)

			All Cesarean section: RR 0.37 (0.33-0.42) -Maternal side effects: RR 1.96 (0.86-4.49) -Length of stay: 0.34 fewer days in hospital (0.17-0.52)

* CI indicates confidence interval; RR, relative risk.

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Subchapter 20.2. Perioperative Normothermia

Background

The body temperature of patients may fall by 1 to 1.5°C during the first hour of general anesthesia.[1] Regional anesthesia also typically causes core hypothermia.[2] Intraoperative hypothermia impairs immune function (especially oxidative killing by neutrophils) and results in dermal vasoconstriction and reduced blood flow to surgical sites, which further increases the risk of surgical site infection by lowering tissue oxygen tension.[3] Hypothermia also results in reduced platelet function, shivering associated with patient discomfort and activation of the sympathetic nervous system, and adverse cardiac events.[2]

Practice Description

Normal core temperature can be maintained during surgery through use of active measures including warmed intravenous fluids and inspired gases, as well as forced air warming. The latter involves an air blanket placed over the patient that circulates air warmed to 40°C. Water blankets may also be used, but are not as effective in maintaining body temperature.[4] Patient temperature is monitored using conventional thermometer probes, with active measures adjusted to maintain core temperature near 36.5°C. Any method or combination of methods that maintains the target core temperature appears to have the same effect.[2]

Prevalence and Severity of the Target Safety Problem

See Subchapter 20.1.

Opportunities for impact

Attention to patient temperature is standard of care in intraoperative anesthesia management.* However, there are no data on the extent to which active warming measures are currently used perioperatively.

* The American Society of Anesthesiologists' *Standards for Basic Anesthesia Monitoring* notes "Every patient receiving anesthesia shall have temperature monitored when clinically significant changes in body temperature are intended, anticipated or suspected."[5]

Study Designs and Outcomes

We identified one randomized controlled trial[3] and one retrospective cohort study[6] evaluating the effect of active warming interventions on the rate of wound infection (Level 1 outcome). (Table 20.2.1). Wound infection was either defined as "suppuration requiring removal of sutures"[3] or as in previously published definitions.[7]

Evidence for Effectiveness of the Practice

Kurz et al performed a randomized controlled trial of active warming in the intraoperative care of patients undergoing elective colectomy. All patients received aggressive perioperative hydration and intravenous opioids for pain relief, in an effort to maximize wound perfusion. Patients in the normothermia arm experienced a 68% reduction in the rate of wound infection, lower wound infection scores (as defined by the elements of the acronym ASEPSIS: **A**dditional treatment, **S**erous discharge, **E**rythema, **P**urulent exudate, **S**eparation of deep tissues, **I**solation of bacteria, and duration of inpatient **S**tay), and shorter length of hospitalization.[3] While the relatively high infection rate (19% of control group in this university-based population with a substantial degree of underlying disease) and suboptimal antibiotic prophylaxis (antibiotics continued for about 4 days postoperatively; see Subchapter 20.1) do not invalidate the study results, they do limit their generalizability.

In a retrospective cohort study based on chart reviews of 150 patients undergoing elective colectomy, Barone et al noted no independent association between intraoperative hypothermia (defined as temperature less than <34.3ºC) and the incidence of wound infections, or the length of stay. Explanation for differences in the findings of the two studies may relate to confounding due to the retrospective design of the study by Barone, or in differences in defining wound infections by the authors (suppuration requiring removal of sutures).[8]

Other potential benefits of maintaining perioperative normothermia have been reported in randomized controlled trials. Frank et al found the risk of morbid cardiac events (combined outcome of angina, myocardial ischemia or infarction, and ventricular arrhythmia) was significantly decreased among patients in the normothermia group (1% intervention vs. 6% control, p=0.02).[9] Maintaining normothermia has also been associated with decreased blood loss and transfusion requirements among patients undergoing elective colectomy[3] and hip arthroplasty.[10,11] Postoperative shivering, thermal discomfort, time to extubation, and duration of post-anesthesia recovery are all significantly reduced.[2,12]

Potential for Harm

None of these studies reported an adverse effect directly related to these practices. Sigg et al observed a higher rate of wound bacterial colonization with the reuse of forced air coverlets.[13]

Costs and Implementation

Equipment for monitoring temperature is readily available in operating rooms. Kruz et al estimated the direct cost of fluid and forced air warming at $30 per case.[9] Studies have not formally assessed all relevant costs, including additional physician time required. It is likely that added costs are largely offset by savings due to reduced surgical site infections and associated decreases in length of stay.

Comment

Given the evidence of effectiveness, the low potential for harm, and the simplicity of the intervention (including the ready availability of the equipment), maintenance of perioperative normothermia seems a promising practice to improve patient safety. The methodologically stronger of the 2 studies reviewed showed clear benefits. However, some of its benefits may not be generalizable to patient populations undergoing other procedures. For example, intraoperative hypothermia may have little impact on wound infections in patients undergoing cesarean section.[14] Thus, additional study of the practice is needed in other settings. Furthermore, for some procedures hypothermia is likely to protect patients. Core temperature is often intentionally reduced to protect the myocardium and central nervous system during certain cardiac and neurosurgical procedures.[2,12,15] In such cases the potential benefits of normothermia may not outweigh the associated risks.

Table 20.2.1. Summary of studies reporting effectiveness of perioperative normothermia*

Study	Study Population; Intervention	Study Design, Outcomes	Results
Kurz, 1996[3]	200 patients (104 normothermia, 96 hypothermia) undergoing, elective colectomy in multicenter study; warmed gases, fluids and forced arm during operation vs. usual care	Level 1, Level 1	Wound infection rate: 6% vs. 19% (p=0.009) ASEPSIS score: 7 vs. 13 (p=0.002) Days to sutures out: 9.9 vs. 10.9 (p=0.002) Taking nutrition orally: 5.6 vs. 6.5 days (p=0.006) Length of stay: 12 vs. 15 days (p=0.001)
Barone, 1999[6]	150 patients (101 normothermia, 49 hypothermia) undergoing elective colectomy at a single community hospital; no formal intervention (retrospective chart review, warming devices were used in 90% of patients)	Level 3, Level 1	Wound infection rate: 12% in both groups Multivariate models: no significant association between hypothermia and wound infection or length of stay

* ASEPSIS indicates **A**dditional treatment, **S**erous discharge, **E**rythema, **P**urulent exudate, **S**eparation of deep tissues, **I**solation of bacteria, and duration of inpatient **S**tay.[7]

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Subchapter 20.3. Supplemental Perioperative Oxygen

Background

Low oxygen content in devitalized tissues predisposes them to bacterial colonization, which is thought to be a key pathophysiologic step in the initiation of surgical site infections.[1] Administration of high concentrations of oxygen increases wound oxygen tension, allowing for more effective neutrophil function and the potential for reduced infection rates.[2]

Practice Description

The practice of perioperative oxygen supplementation involves administration of 80% oxygen and 20% nitrogen by endotracheal tube intraoperatively and by sealed mask and manifold system or conventional non-rebreather mask for the first two hours of recovery. Oxygen is increased to 100% immediately before extubation, with the concentration returned to 80% as soon as deemed safe by the anesthesiologist.[3]

Prevalence and Severity of the Target Safety Problem

See Subchapter 20.1.

Opportunities for Impact

Administration of oxygen is a routine part of perioperative care. However the frequency with which high oxygen concentrations (as described above) are administered is not known.

Study Designs and Outcomes

We identified one randomized controlled trial evaluating the effect of high concentration oxygen supplementation on surgical site infections (Table 20.3.1).[3] The primary outcome was incidence of wound infection within 15 days after surgery (Level 1). Wounds were considered infected when bacteria were cultured from pus expressed from the incision or aspirated from a loculated collection within the wound.[3]

Evidence for Effectiveness of the Practice

The clinical characteristics of the intervention and control groups were similar at baseline, including risk of infection as assessed by a modified Study on the Efficacy of Nosocomial Infection Control (SENIC) score (p=0.8) and National Nosocomial Infection Surveillance System (NNISS) score (p=0.86). The incidence of wound infection was significantly less in the intervention group (13/250, 5%) than in the control group (28/250, 11%, p=0.014). The results remain statistically significant when the study definition of "infection" is broadened to include wounds with pus but no bacterial growth on culture (7% vs. 14%, p=0.012). Perioperative administration of high levels of oxygen was associated with a 54% relative risk reduction (95% CI: 12%-75%) of wound infection within 15 days of surgery. ASEPSIS (**A**dditional treatment, **S**erous discharge, **E**rythema, **P**urulent exudate, **S**eparation of deep tissues, **I**solation of bacteria, and duration of inpatient **S**tay[4]) scores were also significantly better with high levels of oxygen (3 vs. 5, p=0.01). Although longer follow-up might have identified additional wound infections, the authors argue that it was unlikely that these events would take place preferentially in one group as the proposed therapeutic effect of oxygen appears limited to the immediate perioperative period.[3] Admission to the intensive care unit and death were less frequent in the intervention group, but the difference failed to achieve statistical significance.

Two additional randomized controlled trials of perioperative supplemental oxygen were identified.[5,6] Both found a significant reduction in postoperative nausea and vomiting, but neither study evaluated the effect on wound infections.

Potential for Harm

The study by Greif et al reported no adverse affects related to the intervention. Several potential risks of high oxygen concentrations should be noted. High oxygen concentrations may present a fire hazard when heated surgical instruments (eg, lasers) are introduced into the airway.[7-11] Such concentrations can also induce lung injury in certain vulnerable patients[12] or precipitate atelectasis in patients at risk.[3,13,14] Hyperoxic mixtures may increase oxidative myocardial injury in patients undergoing cardiopulmonary bypass.[15] Finally, patients who undergo resuscitation with 100% oxygen may have worsened neurologic outcomes, possibly also as a result of increased oxygen free-radical generation.[16,17]

Costs and Implementation

The incremental direct costs associated with administering high oxygen concentrations are minimal, as oxygen delivery systems are elements of routine perioperative care and employ equipment readily available in operating rooms.

Comment

Administration of perioperative oxygen in high concentrations seems a promising adjunctive therapy: the practice is simple, the equipment needed is readily available, and a multicenter randomized trial has demonstrated its efficacy.

However, there are significant questions about the generalizability of the approach to expanded populations of surgical patients. All patients in the Grief et al study had core temperature maintained at 36ºC, were aggressively hydrated, and had postoperative pain treated with opioids in order to maximize wound perfusion. To what degree the effectiveness of the practice is affected by changes in these "co-interventions" has not been assessed. There is reason for concern regarding use of high concentrations of oxygen in patients undergoing procedures associated with low blood flow (eg, cardiopulmonary bypass), or in whom local production of oxygen free radicals may cause further organ injury (eg, patients with head trauma).

Additionally, questions remain regarding whether modifications to the protocol used would impart similar or greater benefit. For example, would oxygen administration by nasal cannula at 10 LPM be as effective as oxygen delivered by a sealed mask? Would longer duration of therapy impart additional benefit? These questions should be answered in future trials.

Table 20.3.1. Randomized controlled trial of supplemental perioperative oxygen*

Study	Study Population	Intervention	Results†
Greif, 2000[3]	500 patients undergoing colorectal resection; multicenter study, 1996-98	80% oxygen, 20% nitrogen during surgery and the first 2 hours of recovery	Wound infection: ARR 0.06 (95% CI, 0.018-0.102) RR 0.46 (95% CI, 0.25-0.88) ASEPSIS§ score: 3 vs. 5 (p=0.01) ICU admission: 2.0% vs. 4.8% (p=0.14) Mortality: 0.4% vs. 2.4% (p=0.13)

* ARR indicates absolute risk reduction; CI, confidence interval; ICU, intensive care unit; and RR, relative risk. The ASEPSIS scoring system incorporates **A**dditional treatment, **S**erous discharge, **E**rythema, **P**urulent exudate, **S**eparation of deep tissues, **I**solation of bacteria, and duration of inpatient **S**tay[4].

† Outcomes within 15 days of surgery, expressed as rates in intervention vs. control groups.

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Subchapter 20.4. Perioperative Glucose Control

Background

Diabetes is a well-known risk factor for perioperative medical complications. Poor glucose control is an independent risk factor for surgical site infections[1-5] in a range of surgical procedures. Increased risk for infection is thought to result from a combination of clinically apparent effects of longstanding hyperglycemia (eg, macro- and microvascular occlusive disease) and subtle immunologic defects, most notably neutrophil dysfunction.[6-12] Hyperglycemia may also impair the function of complement and antibodies, reducing the opsonic potential of these factors and impairing phagocytosis, further reducing barriers to infection.[13,14] Although many of the clinically apparent manifestations of diabetes are not easily reversed in the perioperative period, there is a small literature that suggests that improving glucose control can improve immunologic function and reduce the incidence of surgical site infections (SSI).[6-8,12]

Perioperative management of glucose for diabetic patients commonly includes withholding or administering a reduced dose of the patients' usual hypoglycemic agent(s) and commencing a low-rate intravenous glucose infusion while patients are NPO prior to surgery. The infusion is continued postoperatively until the patient is able to eat and resume outpatient diabetes therapy. Often a sliding scale insulin regimen, a schedule of subcutaneous regular insulin dosage contingent on capillary blood glucose measurements, is also continued through the perioperative period. However, use of a sliding scale may result in wide variations in serum glucose,[15] opening the rationale of this method to question.[16-18]

Practice description

Aggressive glucose control in the perioperative period can be achieved using a *continuous intravenous insulin infusion* (CII). Nursing staff monitor fingerstick (or arterial line drop-of-blood sample) glucose measurements and adjust the infusion rate based on a protocol intended to maintain serum glucose within a certain range. For example, the target range for the original Portland Protocol was between 151 and 200 mg/dL.[16,19,20] In the most recent version, the range is between 125 and 175 mg/dL.[21]

Prevalence and Severity of the Target Safety Problem

Little evidence exists to describe the practice of CII in prevention of surgical site infections in broad surgical practice. The small amount of evidence available describes its use in patients undergoing cardiac surgery, primarily coronary artery bypass grafting (CABG). Diabetes is a well-described risk factor for sternal wound infections, a catastrophic complication of median sternotomy.[19,22-25] Sternal wound infections occur in 0.8% to 2% of unselected patients undergoing median sternotomy and CABG.[20,22,23] Diabetic patients, who comprise between 17 and 20% of all patients undergoing CABG, have been reported to have an incidence of sternal wound infections as high as 5.6%.[26] Such infections are associated with marked increases in morbidity and costs. Furnary et al reported that patients with sternal wound infections had an average increased length of stay of 16 days and a higher mortality rate (19% vs. 3.8% in patients without sternal wound infections).[20] (See also Subchapter 20.1).

Opportunities for Impact

More than 700,000 Americans underwent open-heart surgery in 1998 alone.[27] Up to 20% of these patients may be candidates for continuous insulin infusion. Although CII is included in the recent ACC/AHA Guidelines for CABG Surgery,[28] there are no data on the extent to which the measure is currently used during cardiac or other surgical procedures.

Study Designs and Outcomes

We identified one prospective before-after study that compared rates of deep sternal wound infections (DSWI) in diabetic patients undergoing CABG before and after implementation of an aggressive CII protocol.[20] DSWI included infections involving the sternum or mediastinal tissues, including mediastinitis. An older study from the same authors was not reviewed as it reported findings at an earlier point in the same trial.[19] Additional studies examined the use of CII in perioperative patients but did not report Level 1 clinical outcomes relevant to patient safety (eg, mortality, wound infection) and were also not reviewed.[29]

Evidence for Effectiveness of the Practice

Furnary et al found that aggressive glucose control with CII was associated with a reduction in deep sternal wound infections.[20] The effect of the intervention remained statistically significant in a logistic regression model adjusting for multiple potential confounding variables. Furthermore, the demographic characteristics were generally biased against the CII group, which had a significantly higher percentage of patients with hypertension, renal insufficiency, and obesity but fewer patients with congestive heart failure. However, the authors did not adjust for long-term markers of glucose control such as glycosylated hemoglobin, nor did they describe other changes in patient care systems that resulted from changing patients to insulin infusions. Continuous insulin infusions require closer attention by nursing staff both for monitoring of infusion equipment and for frequent measurements of blood glucose. It is possible that the improved outcomes were due to closer overall attention to the patient. Although 74% of DSWI occurred after initial discharge (raising the concern that the shorter length of stay in the sliding scale insulin group may have resulted in some infection not being detected), the authors reported that they directly followed-up all diabetic patients for one year from the time of surgery.[30] The personnel, equipment, surgical techniques, and use of prophylactic antibiotics were similar throughout the study period.[31] Nonetheless, it is likely that secular trends in the care of patients undergoing cardiac surgery account for some of the impact attributed to CII.

Potential for Harm

Hypoglycemic episodes are the most concerning adverse event associated with intensive glucose management with intravenous insulin. These episodes result in a range of medical complications, from delirium to myocardial infarction resulting from increased sympathetic activity. Furnary noted that, using the standardized protocol in their study, no cases of symptomatic hypoglycemia occurred in either group of patients.[30] However, CII protocols intended to maintain normoglycemia in surgical patients have been associated with high rates (40%) of postoperative hypoglycemia requiring treatment (<60 mg/dL glucose).[32]

Costs and Implementation

The equipment and personnel required to administer intravenous insulin are readily available. Although a formal cost-effectiveness analysis of the practice has not yet been performed, limited data are available. Furnary et al estimate the additional expense of CII at $125-150 per patient.[33] While this likely includes direct costs of CII such as infusion equipment and additional nursing care for more frequent monitoring of glucose and adjustment of insulin infusion rates, it may underestimate the true costs of the practice at other sites, particularly during early phases of implementation. Furnary reported that the practice required a significant period of time for staff to gain familiarity and expertise with CII, and that by the end of the study they had in place a system that required no significant changes in care patterns for CII to be administered.[34] In early phases of implementation there may be additional costs related to excess time spent by patients in ICU or high-level care areas (ie, stepdown units) rather than regular wards. The start-up costs in terms of training and system changes, and whether the approach is easily adaptable to sites that lack the capability to administer CII in numerous inpatient settings, have yet to be determined.

It seems likely that savings from averted infections may substantially compensate for the incremental direct costs of CII. Based on Furnary's findings and cost assumptions, the average DSWI was associated with $26,000 in additional charges (not costs). Of 1499 patients in the

intervention group, the number of DSWIs prevented was 10 (95% CI: 4-21) and the average cost to prevent one DSWI was approximately $21,000 (95% CI: $10,000-$52,500). Of course, these figures do not incorporate the potential effects of the intervention on other sites of infection, mortality, adverse events, and patients' preferences (utilities) for these possible health states.

Comment

An increasing body of evidence demonstrates that tight control of blood glucose improves overall outcomes of patients with diabetes.[35-37] Emerging data, coupled with an increasing appreciation of the deleterious effects of hyperglycemia on immune function, strongly support the supposition that aggressive control of perioperative glucose reduces the incidence of surgical site infections. Although the practice has been implemented at a number of institutions and is also being used in diabetic patients undergoing non-cardiac surgeries,[34] studies of its effectiveness in these settings have not yet been published. Until additional evidence is available, preferably from blinded randomized controlled trials, the intervention can be considered promising but not yet proven to be causally associated with improved outcomes.

Table 20.4.1. Prospective, before-after study of aggressive perioperative glucose control*

Study	Study Population	Comparison Groups	Results†
Furnary, 1999[20]	2467 diabetic patients undergoing cardiac surgery at a community hospital	968 patients treated with sliding scale SQ insulin (1987-91) 1499 patients treated with CII to target glucose of 150-200 mg/dL until POD 3 (1991-97)	Deep surgical wound infections Unadjusted: 1.9% vs. 0.8% (p=0.011) Adjusted RR 0.34 (95% CI: 0.14-0.74) Mortality: 6.1% vs. 3.0% (p=0.03) Length of Stay: 10.7d vs. 8.5d (p<0.01)

* CI indicates confidence interval; CII, continuous intravenous insulin; POD, postoperative day; and RR, relative risk.
† Results reported as pre-intervention (sliding scale SQ insulin) vs. post-intervention (CII).

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Chapter 21. Ultrasound Guidance of Central Vein Catheterization

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Background

The multiple indications for central venous catheters (CVCs) include parenteral nutrition, intravascular depletion, access for vasoactive medications, hemodynamic monitoring, cardiopulmonary arrest, difficult peripheral intravenous (IV) access and long-term IV access for medications, such as antibiotics.[1,2] While these catheters can be life saving, they are also associated with significant risks.[3] These risks increase in association with several characteristics, including patient anatomy (eg, morbid obesity, cachexia, or local scarring from surgery or radiation treatment), patient setting (eg, patients receiving mechanical ventilation or during emergencies such as cardiac arrest) and co-morbidities (eg, bullous emphysema or coagulopathy).[3-5]

CVCs are placed by clinicians whose training and experience may vary greatly. The procedure takes place in a variety of hospital settings including intensive care units, emergency departments, operating rooms, pre- and post-anesthesia care units, hemodialysis units, cardiac catheterization units and other inpatient settings. Outpatient placement of CVCs has also become commonplace, occurring in hemodialysis centers and oncology centers providing outpatient chemotherapy.

Percutaneous insertions of CVCs are usually performed by "blind" techniques that rely on anatomic landmarks – ie, palpable or visible structures with known relationships to the desired vein. For example, the infraclavicular approach to the subclavian vein requires correct localization of the clavicle reference site, suprasternal notch and sternocleidomastoid-clavicular triangle landmarks, proper positioning of the patient and operator and correct venipuncture point depth, direction and insertion angle. Analogously, the various approaches to the internal jugular vein require thorough knowledge of this vein's course in relation to the sternocleidomastoid muscle and carotid artery.[1]

Newer technologies, such as portable ultrasound (US) devices, provide bedside imaging of the central veins during catheter placement. The advantages associated with US guided CVC placement include detection of anatomic variations and exact vessel location, avoidance of central veins with pre-existing thrombosis that may prevent successful CVC placement, and guidance of both guidewire and catheter placement after initial needle insertion. This review assesses the impact of real-time ultrasound guidance on improving the safety of CVC insertions.

Practice Description

Real-time ultrasound guidance of CVC insertion provides the operator with visualization of the desired vein and the surrounding anatomic structures prior to and during insertion of the needle, guidewire and catheter. Previous studies of US location of vessels *followed* by subsequent catheter placement with landmark techniques found no advantages over standard landmark techniques.[3] Real-time US guidance, on the other hand, appears to improve the success rate and decrease the complication rate associated with CVC placement.

Two types of real-time ultrasound guidance are described. The Doppler US guidance method include audio-guided Doppler,[6] fingertip pulsed Doppler[7] and probe-in-the-needle

technology.[6,8-10] The non-Doppler US guidance methods (subsequently referred to as US guidance) includes US with needle guidance[11,12] or without needle guidance.[13-15]

Prevalence and Severity of the Target Safety Problem

The annual number of all CVCs insertions in the United States is not known, but is estimated at "several million" for subclavian-vein catheters.[3] When aggregated with the various types of catheters placed into the central venous circulation and the increasing utilization of CVCs among routine surgical patients, critically ill patients (in both emergency departments and intensive care units), and for the management of many patients undergoing hemodialysis or chemotherapy, the total number of CVC placements may be many times greater than estimates for subclavian CVCs alone.[3]

Unsuccessful insertion of CVCs may occur in up to 20% of cases.[3-5] The hazards associated with attempted CVC insertion (whether successful or not) include arterial puncture, hematoma, pneumothorax, hemothorax, chylothorax, brachial plexus injury, arrhythmias, air embolus, catheter malposition and catheter knotting.[3-5] Other complications associated with CVCs, such as infection, thrombosis, arterial-venous fistula and vascular or cardiac erosion, are not usually associated with needle insertion but occur after catheter placement.[3-5]

The frequency of complications associated with CVC placement is quite variable, largely due to differences among selected venous insertion sites, the degree of prior operator experience and the presence of previously described risk factors. In general, the rate of major CVC complications (eg, pneumothorax or vessel laceration requiring repair) and minor complications (eg, arterial puncture without significant hemorrhage, transient catheter malposition) is between 0.5 and 10%.[3-5]

In addition to complications, several quality-of-care issues are associated with problems in CVC insertion. For example, a CVC insertion that requires multiple attempts may engender considerable patient anxiety and discomfort. More importantly, a prolonged insertion process may delay the infusion of life-saving fluids or medications during an emergency.

Opportunities for Impact

The majority of CVC insertions are placed using the landmark method. As set forth above, the number of catheters placed annually and the proportion currently inserted without US guidance is not known. Also unknown is the proportion of catheters placed in those patients who may benefit most from the US technique—those with multiple risk factors, those in high risk settings such as the intensive care unit, or those undergoing catheter placement by inexperienced operators.

There are a variety of catheters that require access to the central veins. These include single and multi-lumen CVCs, tunneled and non-tunneled catheters, and larger, more rigid catheter introducers that permit passage of thinner, more flexible devices (eg, pulmonary artery catheters, diagnostic cardiac catheters and temporary transvenous pacemakers). All centrally-placed catheters require an initial needle insertion into the vein, followed by a guidewire to permit passage of the catheter.

Study Designs

One meta-analysis and 10 original studies were analyzed. Among the 10 original studies, 9 were randomized control studies and 1 study was a quasi-randomized control trial (see Table 21.1).[11] The meta-analysis[16] includes 6 references cited in this chapter.[6,8,10,12-14] Four articles cited in this chapter were not cited in the 1996 meta-analysis, including 3 that were published

after 1996[9,15,17] and one that included a quasi-randomized design.[17] Two studies included in the meta-analysis were not included in this chapter because they were from non-English language journals.[7,18]

All of the studies analyzed for this chapter were prospective, non-blinded and randomized, with the exception of a quasi-randomized design involving alternate week allocation of patients to receive the intervention.[11] Randomization was at the patient (rather than physician) level in all studies.

The 10 original studies include 5 using an ultrasound guidance technique without Doppler and 5 using the Doppler US technique. Sites of catheterization included the internal jugular (IJ) veins in 6 studies, the subclavian (SC) veins in 3 studies and the femoral veins in 1 study. The study populations are diverse and include intensive care unit patients, surgical patients both preoperatively and intraoperatively, cardiac patients in both the catheterization and coronary care units, emergency department patients in cardiopulmonary arrest and oncology center outpatients.

Examples of studies excluded from analysis are studies lacking comparison control groups,[19-27] studies of US use but without real-time guidance,[3,28] and simulations of CVC placement rather than completed procedures.[29]

Study Outcomes

Studies included for review reported a combination of clinical outcomes. These outcomes include Level 1 complications that resulted in increased patient morbidity (eg, pneumothorax) and Level 2 complications that represent potential adverse events (eg, unwanted arterial puncture without sequelae). Most studies also reported the number of venipuncture attempts to achieve successful CVC placement as well as the time required to complete successful CVC insertions. These are considered Level 2 outcomes because increased venipuncture attempts are associated with increased complication rates.[4]

Evidence for Effectiveness of the Practice

The 1996 meta-analysis[16] estimated that real-time US guidance for CVC insertion is associated with a significant reduction in placement failures as compared with the usual landmark techniques (relative risk 0.32, 95% CI: 0.18-0.55). In addition, this review estimated that US guidance results in decreased complications during attempted CVC placements (relative risk 0.22, 95% CI: 0.10-0.45), corresponding to a relative risk reduction of 78%.[16] The mean number of attempted venipunctures till successful CVC insertion was significantly reduced with real-time US guidance (relative risk 0.60, 95% CI: 0.45-0.79), corresponding to a relative risk reduction of 40%.[16]

Two of the 3 studies reviewed for this chapter and not included in the meta-analysis (because they were published subsequently) deserve mention because of contrary findings. Both 1998 studies[9,17] included operators with significant prior experience placing CVCs by the usual landmark method. The overall failure rate for both landmark and US guidance techniques was very low in one study.[17] The other study found statistically insignificant negative results associated with US guidance, owing to a high failure rate during the initial learning period for the newly-introduced US guidance technique, and a very low (1.3%) overall complication rate for CVC placement.[9]

With the exception of femoral venous catheterization during cardiopulmonary resuscitation,[15] the studies reviewed for this chapter did not find reductions in insertion time when using real-time US guidance. With 2 exceptions,[910] the cited studies reached statistical

significance for at least one of the 3 outcome measures (morbidity, potential adverse events, and number of venipuncture attempts). The most favorable outcomes associated with real-time US guidance were found in studies of inexperienced operators.[6,12,13]

Potential for Harm

The additional equipment and manipulation associated with real-time US guidance for CVC insertion may increase the rate of catheter-related infections, but published studies have not included these complications. In emergency settings, the increased length of time required to place CVCs under US guidance (usually an additional 30 seconds to several minutes) may result in unacceptable delays. Potential harmful consequences resulting from real-time US guidance for CVC placement relate to changes in training and subsequent dependence on this technology. Supporters of this technology argue that increased competence and anatomic knowledge gained with US guidance will enhance performance of customary, unaided CVC placement. It is unclear if trainees who have performed CVC placement only with US assistance will have different complication rates when placing CVCs in practice settings without US equipment. Therefore, for certification of qualification, trainees may need to demonstrate competence with both US and non-US guided CVC placement.

Costs and Implementation

The major impediments to the widespread implementation of US guidance for CVC insertion are the purchase costs of the US machines. A typical machine costs $11,000-16,000 (including the probes), with a single machine able to serve most critical care units. Depending on the layout of units placing CVCs, an average 400-bed hospital would require 1-3 machines for use outside of the operating room. (Departments of Anesthesia may require only one or two machines, as experienced anesthesiologists can continue to place most CVCs without US guidance). Hospitals in which nurses place *peripherally inserted central catheter* (PICC) lines using US guidance typically facilitate this function with a single machine, which could be dually used for CVCs depending on workflow and volume. In one study, the price of the Doppler-Smart needles (which are not required for non-Doppler US guidance) was $40-70 as compared with $3-5 for the standard needles.[9] The cost of training new operators (including those whose only prior experience is with the landmark technique) requires further evaluation.

Comment

Real-time US guidance for CVC insertion, with or without Doppler assistance, improves catheter insertion success rates, reduces the number of venipuncture attempts prior to successful placement, and reduces the number of complications associated with catheter insertion. However, these benefits may not accrue until after the initial learning period for operators already experienced in the landmark techniques.[9]

There are no studies comparing the impact of CVC insertion with US guidance on overall patient outcomes (eg, mortality, length of stay). In addition, many of the complications associated with CVC insertion are minor or easily treated. The reduction in venipuncture attempts is likely associated with reductions in the pain and discomfort associated with CVC placement, though this has not been measured.

The greatest benefit of US guidance may apply to the novice or inexperienced operator and for all operators in high-risk situations. Patients with one or more risk factors, (eg, critically ill patients on positive pressure ventilation with generalized edema and coagulopathy), may reap the greatest benefit. CVC insertion training incorporating real-time ultrasound guided techniques may provide additional valuable learning benefits for new operators. This knowledge may improve the success rate of insertion of CVCs without US guidance. Simulation training has demonstrated improved identification of the desired veins with US as compared to landmark techniques.[29]

Finally, it should be noted that in addition to real-time US guidance, other approaches may reduce the risks associated with CVC insertion. PICC lines are gaining widespread acceptance and may be an acceptable substitute for CVCs for certain indications (eg, long-term IV access or parenteral nutrition).[30,31] US guidance has also been demonstrated to improve the insertion of PICCs.[32-34] Increases in the use of PICCs may help justify the purchase of ultrasound machines by individual hospitals.

For patients requiring replacement of existing CVCs, guidewire exchanges offer a way of inserting new catheters without new venipuncture attempts. A systematic review has found that guidewire exchanges are associated with fewer mechanical complications than new-site replacement, but may be associated with greater risks for catheter-related infections (Chapter 16).[35]

Alternative methods for teaching CVC insertion skills to novices (eg, first-year resident physicians and medical students) have successfully employed multidisciplinary approaches including cadaver demonstrations.[36] Future methods for teaching CVC insertion may employ computerized technologies for simulations (see also Chapter 45). Haptic, or touch-related techniques use virtual reality models to create immersive simulated environments that recreate the sensation of performing a procedure.[37,38] Through the use of this and other new technologies, novice operators may gain experience and confidence prior to clinical CVC insertion attempts and further improve patient safety.

Table 21.1. Ultrasound and Doppler ultrasound guidance of central vein catheters*

Study Setting and Population	Year Published	Intervention	Study Design, Outcomes	Relative Risk Reduction (%)†		
				Failed Catheter Insertion	Mean Insertion Attempts Required§	Compli-cations
		Ultrasound				
Tertiary care, teaching hospital ICU[13]	1990	US guidance for IJ CVC insertion without needle guide; concurrent feedback from an US technician	Level 1 Level 2	100[NS]	44	NA
Tertiary care, teaching hospital, CT surgical patients[14]	1991	US guidance (7.5 and 5.0 MHz transducers) for IJ CVC insertion without needle guide	Level 1 Level 2	100	44	83[NS]
Tertiary care, teaching hospital, cardiac patients[11]	1993	US guidance (7.5 MHz transducer) of IJ cannulation for cardiac catheterization and CVC insertion, with needle guide	Level 1 Level 2	100	48	80
Urban, teaching hospital ICU[12]	1995	US guidance (7.5 MHz transducer) for SC CVC insertion with needle guide	Level 1 Level 2	86	48	90
Urban, teaching hospital ED, during CPR[15]	1997	US guidance (7.5 MHz transducer) for femoral CVC insertion without needle guide	Level 1 Level 2	71	54	100
		Doppler Ultrasound				
Tertiary care, teaching hospital, CT/ vascular surgery patients[8]	1994	Doppler US guidance of IJ CVC insertion with probe in the needle	Level 1 Level 2	0	52	0
British hospital, cardiac surgery and ICU patients[10]	1994	Doppler US guidance of IJ CVC insertion with probe in the needle	Level 1 Level 2	-50[NS]	17[NS]	0
Tertiary care, teaching hospital ICU and OR; high-risk patients[6]	1995	Audio-guided Doppler US guidance for IJ CVC insertion with probe in the needle	Level 1 Level 2	63	18[NS]	88
French teaching hospital ICU; low-risk patients[17]	1998	Pulsed Doppler US guidance for SC CVC insertion without needle guide	Level 1 Level 2	-32[§]	0	67
Tertiary care, outpatient oncology center[9]	1998	Doppler US guidance for SC CVC insertion with probe in the needle	Level 1 Level 2	-46[§]	NA	-53[NS]

* CPR indicates cardiopulmonary resuscitation; CT, cardiothoracic; ED, emergency department; ICU, intensive care unit; IJ, internaljugular vein; NA, not available; NS, not statistically significant; OR, operating room; RCT, randomized controlled trial; SC, subclavian vein; and US, ultrasound guidance.

† The percentage relative risk reduction reflects the risks associated with CVC placement and the percentage change resulting from US guidance. Negative values indicate an increase in risks associated with US guidance.

§ Relative risk reduction of the insertion attempts to success reflects the relative reduction in the mean number of needle insertions attempted per patient until successful CVC placement resulting from US guidance.

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Chapter 22. The Retained Surgical Sponge

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Background

Although less likely to garner public notoriety, errors relating to the failure to remove surgical instruments at the end of a procedure, (ie, needles, knife blades, electrosurgical adapters and safety pins) or sponges (known as gossypiboma; *gossypium*: Latin, cotton; *boma*: Swahili, place of concealment) are no less egregious than the better known mishaps such as "wrong-site surgery" (see Subchapter 43.2).

Retained materials may cause an acute foreign body reaction with local or systemic signs that prompt investigation and reoperation. Alternatively, a fibrinous response may be elicited, and the retained instrument or sponge may become apparent some time after the original surgical procedure either serendipitously, or via fistulization into local structures.[1] The medical literature is scattered with reports of presentations of retained sponges found days, months, or even years after the original surgery.[2-5] While many cases of retained foreign body do not cause harm, some clearly do. Nevertheless, the Joint Commission on Accreditation for Healthcare Organization's (JCAHO) sentinel event policy specifically mentions that "unintentionally retained foreign body without major permanent loss of function" do not require reporting.[6] Although JCAHO's decision suggests that it considers these events less egregious than reportable sentinel events (eg, wrong patient surgery), retained foreign body events are far more common. This chapter reviews the problem and the scanty literature regarding safety practices to reduce the incidence of retained sponges and instruments.

Practice Description

Surgeons and operating room teams rely upon the practice of *sponge, sharp and instrument counts* as a means to eliminate retained surgical instruments. Counts are also a method of infection control and inventory control, and a means to prevent injury from contaminated sharps and instruments. Four separate counts have been recommended[7]: the first when the instruments are set up or the sponges unpackaged, a second before the surgical procedure begins, a third as closure begins, and the final count performed during subcuticular or skin closure.

Use of this simple preventative measure is not universal. In fact, the process by which counts are performed is not standardized and is often modified according to individual hospital policy. Even when present, counts are frequently omitted or abbreviated in emergency or transvaginal surgeries, or for vaginal deliveries.[8] An adjunctive procedure to the count, used when the count could delay care and jeopardize patients' lives or when an incorrect count is established, is an x-ray examination to detect radiopaque objects.[1,7] Since this practice is not routinely used it will not be discussed here.

Prevalence and Severity of the Target Safety Problem

A literature search revealed few data to describe population or even hospital-level information regarding the prevalence of retained surgical materials. One study from a medical malpractice insurance company reported 40 cases in a 7-year period,[9] or about 1% of all claims. Because this estimate is based on malpractice insurance claims, it is sure to be a gross underestimate of the actual incidence. A recent unstructured review cited "a prevalence ranging from 1/100 to 1/5000," and an associated mortality ranging from 11 to 35%, citing non-English language medical references.[1] Other reports are based on case series or descriptions of unusual presentations, as described above. Surgeons may not report these events for a variety of reasons, not the least of which is fear of litigation

Opportunities for Impact

Without accurate prevalence information, the true magnitude of the opportunity for impact is unclear.

Study Designs and Outcomes

Only one study provided even indirect evidence of the effectiveness of sponge and instrument counts. Kaiser et al, using a retrospective review of medical malpractice claims data from a statewide insurer in Massachusetts, reviewed 67 cases where retained sponges or surgical materials were the primary reason for the claim.[9] This study is a case series without any controls (Level 4 design, Level 2 outcomes) which reported only the outcome of retained sponges, rather than the clinical consequences of these errors.

Evidence for Effectiveness of the Practice

The Kaiser et al study reported that 55% of retained sponges were found after abdominal surgery and 16% after vaginal delivery. In cases with retained sponges, sponge counts had been falsely correct in 76% of non-vaginal surgeries; in 10% no sponge count had been performed at all. Falsely correct sponge counts were attributed to team fatigue, difficult operations, sponges "sticking together," or a poor counting system. Incorrect sponge counts that were accepted prior to closure resulted from either surgeons' dismissing the incorrect count without re-exploring the wound, or nursing staff allowing an incorrect count to be accepted. Interestingly, in 3 of 29 cases in which intraoperative x-rays were used to detect radiopaque sponges, the radiograph was falsely negative.[9]

Comment

Although literature describing the incidence of iatrogenic foreign bodies is highly limited in quantity and quality, it is unlikely that these events are as rare as other iatrogenic complications that have drawn considerable national attention. The existing system of sponge and instrument counts probably works well, but we have no evidence to describe its actual failure rate. The little existing evidence suggests that it fails due to human-related factors (ie, the count is not performed, or is ignored, and that ancillary methods such as x-rays are also fallible. Although some have advocated CT or ultrasonography as additional methods to reduce rates of these adverse events, it is possible that other technologies (eg, inventory control devices used in retail stores and libraries, possibly including bar coding (Subchapter 45.1)) may prove to be useful adjuncts. However, there are obvious logistical challenges that make such technologies too impractical at the present time. For now we are left with a paucity of data regarding the

prevalence of this error and the effectiveness of preventative measures. Use of anonymous reporting systems may reduce the fear of litigation associated with iatrogenic foreign bodies, and may allow for more accurate assessment of the incidence and causes of these events.

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Chapter 23. Pre-Anesthesia Checklists To Improve Patient Safety

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Background

No matter how rote the task or how vigilant the anesthesiologist, "slips" and other errors represent expected aspects of human performance.[1] Evaluation and subsequent improvement of standard checkout procedures promises to increase patient safety in the perioperative period by removing more of the "human factors" so often implicated in anesthesia adverse events.[2] The use of pre-flight checklists has been considered a key method in improving airline safety, largely due to the regular systematizing of complex procedures, and improvement of team dynamics through authority-neutral tasks. A checklist system has been proposed as part of routine pre-anesthesia care, with the American Society of Anesthesiologists and the US Food and Drug Administration (FDA) issuing general guidelines supporting checklists in 1986.[3] Subsequently, anesthesia professional societies in Great Britain and Europe adopted similar standards.[4]

Practice Description

In 1987, the FDA published the "Anesthesia Apparatus Checkout Recommendations" in the *Federal Register* (February, 1987). This "checkout list" provides practitioners with a standardized approach to checking anesthetic equipment prior to its use in order to ensure that the delivery system is correctly connected, adjusted, and functional. The original checklist included 24 specific processes to be performed as an initial checkout at the beginning of each day; 11 are performed between cases and after initial equipment evaluation.[5] Many clinicians regarded these protocols as too long and complex for routine use. Parties involved in revising the recommendations agreed that the average clinician should be able to check an anesthesia machine in 5 minutes or less (not possible with the 1987 recommendations). The revised checklist included only 14 major processes, 9 of which can be omitted or substantially abbreviated when the anesthesia provider uses the same equipment in successive cases.[6] The revised recommendations are available online.[7]

Prevalence and Severity of the Target Safety Problem

The earliest observational studies of mishaps within anesthesia found that equipment failure was the cause of 14% of anesthesia critical incidents.[8] Subsequent studies reduced this estimate considerably. Although equipment failure is now implicated in only 4% of anesthesia adverse events, 22% are related to failing to check equipment adequately.[2] Equipment failures can result in delivery of hypoxic gas mixtures or excessive doses of inhalational agent, or hypoventilation due to ventilator failure. These situations can be catastrophic if unrecognized, and even if recognized may result in significant morbidity (eg, delayed extubation, stroke, or myocardial infarction).[2,9]

Opportunities for Impact

The FDA checkout list is considered a template which local users are "encouraged to modify to accommodate differences in equipment and variations in local clinical practice." Estimating the frequency with which it or other checklists are used (in modified or unmodified forms) in anesthesia practice would be speculative,[5] but a survey of 4 states suggests that usage is minimal.[3] There are 41.5 million inpatient procedures each year requiring anesthesia in the US. Probably about half of these involve general anesthesia. Therefore, although the frequency of equipment failure is low, any improvement in safety from anesthesia preoperative checklists could have substantial impact.

Study Designs

Using a structured MEDLINE search, we identified 15 articles that discussed anesthesia checklists. Of these, only 2 studies came close to meeting our inclusion criteria (Chapter 3).[3,10] Because no other studies could be found, we abstracted these studies and review them here (Table 23.1).

The first investigation evaluated the ability of participating providers to detect standardized equipment faults using their own checking methods compared with the FDA checkout list.[3] Although the study involved a prospective design, it does not fit neatly into our classification system because the participants (anesthesiology residents and practitioners) served as their own controls. The second study[10] involved the revised FDA checkout list, and its design was modeled on the previous study.

Study Outcomes

The first study's outcome of interest was the detection of 4 standardized equipment faults created by the investigators (Level 2).[3] The second study used similarly designed outcomes (simulated equipment faults), but defined detection of at least 50% of these faults as the primary outcome (Level 2).[10] Neither study directly connected the use of pre-anesthesia checklists to patient outcomes, although inadequate preanesthesia equipment checks have been implicated in adverse events related to equipment failures, as discussed above.[2]

Evidence for Effectiveness of the Practice

March et al[3] found that the FDA checklist was more likely to detect faults with the nitrous oxide system (65% vs. 43%, $p<0.001$), but that the FDA checklist was no better than individual practitioners' checklists in detecting the 7 other pre-set faults. No method detected 100% of faults, but those physicians with more clinical practice and those with better knowledge of the FDA checklist were more effective at detecting equipment faults. In the study of the revised FDA checklist,[9] approximately half of the participants failed to detect at least half of the faults using both their own methods and the FDA checkout list (no statistically significant difference).

Both of these studies contain important methodologic flaws. The participants knew they were involved in a study assessing their ability to detect machine faults, and so undoubtedly approached this task with increased sensitivity. Moreover, the participants' own methods may have been quite similar to the use of the FDA checklist. Both of these problems bias these studies against finding a difference between checklist and controls. Importantly though, all methods performed poorly in both studies. Thus, even if the FDA checkout list is in fact superior

to anesthesia providers' own methods, the observed utility of this practice still is likely to be quite low.

Potential for Harm

We were unable to find literature that implicated checklists as causes of adverse events. There exists a theoretical possibility of delays due to complex checklists, but these have not been borne out in any published studies. There has also been concern raised about compulsory checklist procedures as an unnecessary duplication of work already performed by operating room technical personnel.

Costs and Implementation

The FDA checklist, or local variants thereof, is widely implemented and inexpensive. Although several authors have mentioned that checkout processes are not used in 100% of cases, this does not seem to reflect problems with checklists themselves.[4,12,13] The work of March and Crowley[3] suggests that checklists training may be critically important. However, the most important barrier to implementation is the heterogeneity of anesthesia delivery devices themselves, which makes creation of a single, effective, broadly generalizable checklist difficult if not impossible.

Comment

Given its face validity and the theoretical connection between anesthesia checklists and those used so effectively in aviation, preanesthesia checklists represent plausible safety tools. However, the reliability of modern anesthesia machines has reduced the frequency of mechanical failure to such a degree that adverse outcomes due to anesthesia machine failure are exceedingly rare. The checklists examined in the cited studies only examine the integrity of the anesthesia machine and ventilatory monitors, not cardiovascular monitors, airway equipment, intravenous apparatus, infusion pumps, or medications. Standardized checklists for these other critical components of anesthesia care do not exist in the literature. This may explain the paucity of literature exploring the use of checklists and their real effects on patient outcomes. Furthermore, the inability of anesthesiologists to detect preset faults in the cited studies may simply reflect the infrequency with which such faults are encountered in modern anesthesia practice.

The face validity of checklists and the difficulty of "probing" their value in clinical studies make additional "proof of concept" studies unlikely. Although future investigations could not ethically study the anesthesia machine checklist *per se*, they could seek to determine more effective methods for its implementation, or could develop additional checklists with a broader scope. The little evidence we have been able to uncover suggests that, like the use of voluntary guidelines elsewhere in medicine (Chapter 51), checklists are not used uniformly. This may result from a sense that these checks are low-yield, redundant, onerous, or all of the above.

The need for effective checkout procedures is likely to grow as the complexity of anesthesia equipment increases. This will increase the need to make checklists more sensitive and specific in detecting faults, while improving usability. These worthy goals may then serve as templates for other technologically dependent medical specialties, such as cardiac electrophysiology, and interventional radiology.

Table 23.1. Evaluations of the FDA "checkout list" for preoperative anesthesia equipment assessment

Study	Study Design, Outcomes	Results
March, 1991[3]: Exposure of a total of 188 anesthesiology residents and practitioners from multiple sites to a "mobile anesthesia study center" with 2 anesthesia machines pre-set to one of two different "fault sets." Each of these sets included 4 independent machine faults. Practitioners were instructed to use their own checkout methods to assess a machine with one of the "fault sets." After completion of this assessment, the machine was adjusted to display the other fault set, and the participant invited to use the FDA checkout list in the second assessment.	Mixture of Levels 2 & 3, Level 2	Participants detected an average of only 1 in 4 machine faults. A statistically significant improvement in the fault detection rate with use of the FDA checkout compared with the participants' individual methods was observed for only 1 of the 4 fault types (involving the oxygen/nitrous oxide ratio).
Manley, 1996[9]: Similar study to above, but involving only 22 participants (a mixture of anesthesiologist, nurse anesthetists, and senior nurse anesthetist students) from only one site.	As above	For both of the fault sets, approximately half of the participants detected fewer than 50% of the 4 target faults using their own individual methods. The detection rates using the revised FDA checkout list did not differ significantly (p=0.48) from these results.

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Chapter 24. The Impact Of Intraoperative Monitoring On Patient Safety

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Background

Until the 1960s, intraoperative monitoring consisted of a blood pressure cuff, electrocardiogram (ECG), stethoscope, and the vigilance of the anesthesiologist. Over the next 2 decades, the array of available monitors burgeoned, and clinical practice varied widely. In 1986, in an effort to improve patient safety, standards for intraoperative monitoring were developed and implemented by the American Society of Anesthesiologists (ASA).[1] They have been almost universally adopted by anesthesia providers in the United States and now form the standard of care in this country. The ASA standards are summarized in Figure 24.1.

Concurrently with the implementation of better monitoring, anesthesia-related mortality has fallen sharply. Proponents of monitoring claim that better monitoring is the reason for improvement in patient safety.[2-4] Others have claimed that advances in knowledge and training combined with the development of safer medications have had as much impact on patient safety as the adoption of monitoring standards.[5,6] In this chapter, we evaluate the evidence linking intraoperative monitoring to patient safety.

Practice Description

Intraoperative monitoring involves the use of mechanical devices to record and display physiologic parameters such as heart rate, blood pressure, oxygen saturation, and temperature. Standard routine monitoring is noninvasive, employing blood pressure cuff, ECG, and pulse oximetry.

Invasive monitors such as arterial and central venous catheters and transesophageal echocardiography may provide more detailed and timely physiologic information, but also pose an increased risk for iatrogenic complications. In practice these monitors are used selectively, and are not reviewed here.

Prevalence and Severity of the Target Safety Problem

Death due to anesthesia has become rare. In one large Canadian study involving 27,184 inpatients who underwent anesthesia, physician review of 115 randomly selected “major events” classified less than 20% as having any anesthetic involvement, with no deaths even partially attributed to anesthesia.[7] In the United States, the mortality due to general anesthesia has been estimated at approximately 5000 deaths per year (in the 1970s),[8] with approximately half that number estimated in the 1980s.[9] Thus, general anesthesia represents the one aspect of health care where the risk of death is low enough to rival the safety record achieved in other high-risk industries such as aviation.[10]

By contrast, morbid events (complications) related to anesthetic care are likely more prevalent and difficult to classify as preventable or unavoidable. Because certain aspects of monitoring may reduce the incidence of morbid events unrelated to anesthesia, assessing the impact of monitoring practices solely on anesthetic outcomes may be inappropriate. For example, detection of a consistent decrease in intraoperative blood pressure may signal unrecognized bleeding, allowing the anesthesiologist to alert the surgeon to this possibility and prompting appropriate management. While intraoperative hemorrhage does not represent an

anesthetic complication, intraoperative blood pressure monitoring can clearly contribute to the overall safety of the surgical patient. Thus, the scope of intraoperative morbidity targeted by anesthetic monitoring practices is much broader than the set of possible complications attributable solely to the administration of anesthesia.[7-9]

Opportunities for Impact

In the United States, there are no mandatory regulations for monitoring practices. However, virtually all anesthesiologists abide by the monitoring standards set forth by the 1986 ASA standards, last modified in 1998 (Figure 24.1). Although these standards were implemented with only speculative evidence of their benefit,[4] few clinicians doubt their merit.

Study Designs

Using a structured MEDLINE search, we identified articles presenting data related to the impact of perioperative monitoring. Many of these studies[11-17] involved Level 4 designs (eg, observational studies without a control group). For instance, several of the articles[11-13,15] reported data from the Australian Incident Monitoring Study and involved analysis of a case series of 2000 incident reports without accompanying controls. Other studies only indirectly pertained to intraoperative monitoring. One study surveyed anesthesiologists regarding their views on the appropriate alarm settings for intraoperative blood pressure monitoring.[18] Another focused on the personnel performing intraoperative monitoring—physician anesthesiologists versus certified nurse anesthetists.[19] We chose not to purse this contentious and intensely political comparison, as few studies have compared the outcomes achieved by these two groups. Moreover, our reviewer team did not include a nurse anesthetist, making any conclusions drawn more susceptible to bias. Of the 3 remaining studies, one involved a non-randomized clinical trial (Level 2), but a Level 3 outcome.[20]

The remaining 2 studies met our inclusion criteria (Chapter 3). One was a retrospective analysis of anesthesia accidents before and after the implementation of monitoring standards (Level 3),[2] and the other used a prospective, randomized, controlled trial design (Level 1) to assess the impact of pulse oximetry on postoperative complications (Level 1 outcome).[21]

Study Outcomes

The 2 studies[2,21] meeting the methodologic inclusion criterion reported morbidity and mortality (Level 1) attributable to anesthesia, ie, a major complication or death occurring in the immediate postoperative period not obviously explained by the patient's underlying condition or the operation itself.

Evidence for Effectiveness of the Practice

Through a review of cases reported to a liability insurer, Eichhorn identified 11 major intraoperative accidents solely attributable to anesthesia among over 1,000,000 cases performed at the nine Harvard hospitals from 1976-1988.[2] Eight of these accidents were judged to be preventable as they were caused by failure to ventilate or to deliver adequate oxygen to the patient. Only one of these accidents occurred after the adoption of monitoring standards in mid-1985, supporting the safety benefit of intraoperative monitoring standards, although the difference in accident frequency was not statistically significant.

In a multicenter, randomized, controlled trial of 20,802 surgical patients, Moller et al[21] studied the impact of perioperative pulse oximetry on patient outcome. Despite the large sample, the authors were unable to show a difference in in-hospital mortality or postoperative

complications. During anesthesia and in the post-anesthesia care unit (PACU), more episodes of hypoxemia and myocardial ischemia were detected in patients monitored with pulse oximetry.[21]

Potential for Harm

Routine noninvasive monitoring carries minimal (although not zero) additional risk for iatrogenic complications from the devices themselves. Current standard of practice requires that they be used in all cases of general or regional anesthesia. However the number of monitors and their concomitant alarms raises the possibility of additional harm. A study of monitor alarms in the intensive care unit (ICU) suggested that monitor alarms might actually reduce quality of care because of their high frequency and low specificity. In this study, an alarm occurred every 37 minutes, and in the majority of cases (72%) no change in management was indicated as a result.[22]

Costs and Implementation

The costs of intraoperative monitors are largely fixed in the acquisition cost of the monitoring device. Incremental patient costs for disposables are minimal.

Comment

The inability of a very large multicenter study[21] to detect a benefit in morbidity and mortality from pulse oximetry—by all accounts the most useful monitor—suggests that the magnitude of benefit may be so small that an adequate study to detect this difference may not be feasible. Along with capnography (carbon dioxide monitoring), pulse oximetry is often cited as the monitoring method most able to detect potential critical incidents early enough to prevent adverse outcomes.[2,6] This conjecture is supported by the ASA Closed Claims Study. Analyzing 1175 claims, the study concluded that the combination of pulse oximetry and capnography "could be expected" to help prevent anesthetic-related morbidity and mortality.[23]

Despite a lack of randomized trial data, the practice of noninvasive intraoperative monitoring has become standard of care. This has resulted from the ASA Monitoring Standards and physicians' faith in the practice based on its face value, along with some confirmatory evidence drawn from incident reporting systems.[11,16,17] As such, it seems likely that future research into intraoperative monitoring will be unable to study approaches that do not include standard, noninvasive monitoring. Future investigation might seek to determine which monitoring methods detect "near misses" more effectively.

Moving beyond non-invasive techniques, there is a great need to identify which specialized monitors provide a safety benefit in selected patient populations. The use of pulmonary artery catheters for monitoring critically ill patients represents a well-known example of a practice with substantial face validity but unclear impact on patient outcomes.[24,25] In addition, new, noninvasive alternatives to invasive monitors (eg, esophageal or spirometry-based cardiac output monitors) may ultimately allow us to obtain the same information at less risk to the patient.

Figure 24.1. ASA standards for basic anesthetic monitoring*

Standard 1: Qualified anesthesia personnel shall be present in the room throughout the conduct of all general anesthetics, regional anesthetics and monitored anesthesia care

Standard 2: During all anesthetics, the patient's oxygenation, ventilation, circulation, and temperature shall be continually* evaluated

Oxygenation:

- Oxygen analyzer for inspired gases
- Observation of the patient
- Pulse oximetry

Ventilation:

- Auscultation of breath sounds
- Observation of the patient
- Observation of the reservoir bag
- Capnography (Carbon dioxide monitoring)

Circulation:

- Continuous* ECG display
- Heart rate and BP recorded every 5 minutes
- Evaluation of circulation
- Auscultation of heart sounds
- Palpation of pulse
- Pulse plethysmography
- Pulse oximetry
- Intraarterial pressure tracing

Temperature:

- Monitor temperature when changes are intended, anticipated, or suspected

* The term "continuous" means prolonged without interruption; "continually" means repeated regularly and frequently. ECG indicates electrocardiography; BP, blood pressure.

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Chapter 25. Beta-blockers and Reduction of Perioperative Cardiac Events

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Background

As the most common complications of major noncardiac surgery, myocardial infarction and cardiovascular death have long been a focus of preoperative evaluations[1-4] and a target of perioperative management strategies. Until recently, methods to reduce the incidence of these complications depended upon preoperative assessments of risk combining clinical evaluation with clinical prediction rules, followed by additional tests or revascularization procedures, as appropriate.[1] The benefit of preoperative revascularization remains unclear, as no randomized prospective trial has demonstrated its benefit.[5] Indeed, concern exists that preoperative intervention might prove detrimental, as the net benefit in terms of reduced perioperative cardiac events may be offset by the risks of the revascularization strategy itself. Newer strategies, including the use of percutaneous transluminal angioplasty as the revascularization modality, may have promise.[6] Large prospective trials examining these approaches are underway.[5]

Strong evidence links myocardial ischemia with postoperative myocardial events.[7,8] One study found postoperative ischemia increased the odds of postoperative myocardial events 21-fold.[9] Based on findings from observational studies that beta-blockade blunts electrocardiographic signs of ischemia,[10-12] recent trials have examined the effects of perioperative beta-blocker administration on patient outcomes. Results of these investigations are extremely promising, and beta-blockade may represent an important new method of reducing perioperative cardiac risk. This chapter reviews the evidence from randomized controlled trials examining the effect of perioperative beta-blockade on cardiac events (ie, myocardial ischemia, angina, myocardial infarction, pulmonary edema, and cardiac death).

Practice Description

Although published studies have employed different agents, doses, and dosing schedules, the general approach in each study has been similar: administration of a therapeutic dose of beta-blocker prior to induction of anesthesia, followed by beta-blockade through the operation and in the postoperative period. In all regimens, the dose is titrated to a target heart rate, generally 70 beats per minute or lower.

Prevalence and Severity of the Target Safety Problem

Myocardial cardiac events are the most common medical complication of surgery, occurring in 2-5% of patients undergoing non-cardiac surgery[13] and as many as 30% of patients undergoing vascular surgery.[14,15] Perioperative cardiac events are associated with a mortality rate of nearly 60% per event,[14,16] prolonged hospitalization, and higher costs.[16,17] The prevalence of these events and their high mortality have made the prevention of perioperative cardiac ischemia the subject of practice guidelines[1,17] and numerous prediction rules[13,16,18] to detect patients at high risk for these complications.

Opportunities for Impact

As a relatively new therapy, few data describe the use of perioperative beta-blockade in clinical practice. However, evidence suggests it is utilized infrequently. A recent observational study in the Netherlands of patients undergoing vascular surgery showed that only 27% of these high-risk patients received beta-blockers perioperatively.[19]

Study Designs

Using a structured MEDLINE search, we identified 4 relevant randomized controlled trials of the effectiveness of perioperative beta-blockade in reducing perioperative cardiac events, including myocardial ischemia and cardiac or all-cause mortality (Table 25.1). A randomized trial by Harwood et al was excluded because both groups received beta-blockers (ie, there was no control group).[20] Although data from a study by Wallace et al[21] were derived from one of the randomized trials included in this review,[22] it reported effects of beta-blockade upon different outcomes (ie, myocardial ischemia) and was included in our review. There was sufficient evidence available to limit the review to studies of Level 1 design. Observational studies, such as those by Pasternack et al and Boersma et al,[11,19] are not included.

Study Outcomes

The studies identified included a range of clinical outcomes: 2 included assessment of myocardial ischemia[12,23] and 3 reported myocardial infarction, pulmonary edema, cardiac death, or all-cause mortality (Level 1 outcomes).[15,22,23]

Evidence for Effectiveness of the Practice

Of studies reporting the effect of beta-blockers on perioperative ischemia (Level 2 outcome), all but one found a statistically significant reduction in ischemia among treated patients. Wallace et al,[21] in a subset analysis of data from Mangano et al,[24] reported less frequent perioperative myocardial ischemia in atenolol-treated patients. Stone et al[25] suggested a similar effect of beta-blockade on Holter-monitor documented myocardial ischemia. However, the authors did not report the types of procedures included in their sample, nor did they statistically compare baseline patient characteristics, leaving their conclusions open to debate. Raby et al[12] also found a significant beneficial effect of beta-blockade using a continuous infusion of esmolol in high-risk patients undergoing vascular surgery. Although Urban et al also found a reduction in perioperative ischemia, this difference failed to reach statistical significance.[23] These findings may be explained in part by a relatively low cardiac risk in Urban's cohort, who were undergoing elective total knee replacement. The patients in many of the other studies were at higher risk of cardiac events, as demonstrated by rates of ischemia in the control groups. In studies finding a statistical difference, rates of ischemia were between 28% and 73% in controls, as compared with the 15% rate of ischemia observed in Urban's control group.

Of studies reporting cardiac events and cardiac mortality, 2 reported significant improvement in patient outcomes due to beta-blockade. In a study of male veterans undergoing major noncardiac surgery, Mangano et al[22] reported a relative reduction in all-cause mortality of nearly 55% at 2 years. This difference, which appeared within the first 8 months of follow-up, was ascribed to a marked reduction in cardiac events in the first year of therapy (67% reduction at year 1, 48% at year 2). However, patients in the beta-blocker group had less coronary disease at study entry, were on ACE-inhibitors more frequently, and were less likely to have beta-blockers discontinued perioperatively, perhaps biasing results in favor of the treatment group.[26,

[27] Accounting for these differences in multivariate models of varying stringency did not invalidate their findings.[24] Although questions remain about the generalizability of results to other patient populations, the authors favored broader use of beta-blockade in the setting of clinical trials.

Poldermans et al[15] suggested an even greater benefit of beta-blockade among high-risk patients. These investigators enrolled patients undergoing vascular surgery who had myocardial ischemia documented by dobutamine echocardiography, with an estimated rate of perioperative cardiac event of 28%. The entire patient cohort experienced a 90% reduction in cardiac death or non-fatal myocardial infarction at 30 days. Follow-up care did not include additional therapy (ie, cardiac catheterization, revascularization), raising concerns that the research algorithm did not reflect optimal clinical practice.[28, 29] However, if the true rate of events in treated patients is low (the point estimate from this small study was 3.4%), the risks associated with revascularization[30] may outweigh any benefit.

In contrast to the previous 2 studies, Urban et al[23] found no statistically significant difference in rates of in-hospital myocardial infarction. It is likely that these investigators' ability to detect a difference was limited in part by the relatively small sample size and shorter length of follow-up. Other studies of perioperative beta-blockade employed longer periods of follow-up to detect events up to 2 years following surgery.

Differences in absolute magnitude of benefit can be ascribed in part to the cardiac risks of the patients enrolled (again reflected in event rates in the control groups in each study), with the most powerful benefits seen in patients at highest risk. The greater benefit seen in Poldermans et al's study[15] may also be due to the fact that the study did not enroll patients who were receiving beta-blockers. Patients who are beta-blocker naïve may have a different response to perioperative use of bisoprolol, or the preexisting use of these agents may represent a confounding factor not completely accounted for in other studies of perioperative beta-blockade.

Beta-blockade may have additional beneficial effects for elderly patients. Patients who received beta-blockers were extubated more quickly, required less medication for pain, and were alert sooner after surgery.[31] Although the unblinded nature of this study leaves its findings open to debate, the possibility of additional benefits is tantalizing and worthy of further investigation.

Potential for Harm

Stone et al reported high rates of bradycardia (21/89 patients) in beta-blocker treated patients, "half" of whom required atropine therapy. However, the vague descriptions and more general problems with the study's design make it difficult to interpret the significance of these events in clinical practice. Adverse events related to the use of beta-blockers in other reviewed studies were infrequent (10% or less in Mangano et al[22]) and did not require therapy or result in withdrawal of the medication. Similar rates of side effects have been noted in studies examining beta-blockade in patients undergoing cardiac surgery.[20,32,33] One study examining use of propranolol in patients undergoing thoracotomy for pneumonectomy suggested that patients receiving beta-blockers had twice the rate of postoperative congestive heart failure (4/50 vs. 8/50, $p<0.01$). In addition, 16% (8/50) of patients in the treatment arm had the drug discontinued due to "bronchospasm."[34]

Finally, a recent prospective observational study has suggested that withdrawal of beta-blockade from patients immediately following surgery may result in adverse events.[35] This effect was not observed in randomized trials of beta-blockade that employed shorter treatment regimens[12,25] and should be confirmed by larger studies.

Costs and Implementation

The costs of beta-blockers are generally low, and the systems required to use them according to the protocols used in these studies are already in place. In addition, there is the potential for significant cost-savings if routine use of beta-blockers allows a safe reduction in the use of extensive preoperative cardiovascular testing.

Comment

Results from several well-designed clinical trials suggest that use of beta-blockers in the perioperative period is associated with significant reductions in patient cardiac morbidity and mortality. In the future such therapy may reduce the need for additional tests and revascularization procedures,[14] further reducing costs of care. However, several questions regarding its use remain, and should be topics of future research.

First, no clear data suggest an advantage of one particular beta-blocking agent over another. Studies to date have employed several different beta-blockers, suggesting that the efficacy of beta-blockade is class dependent if titrated to physiologically active dosages. Other (alpha-1 selective) sympatholytics also improve patient outcomes,[36] raising the possibility that combined alpha-beta antagonists (ie, labetolol) may have benefit. Second, results from Shammash et al document the hazards of discontinuation of beta-blockers immediately postoperatively,[35] and most protocols employed treatment regimens that extended longer - even up to one month following surgery. The current studies suggest beta-blockade should be continued for at least one week postoperatively. Third, effectiveness of beta-blockade in patients at high risk due to aortic stenosis or unstable or severe cardiovascular symptoms (New York Heart Association Class III-IV) is unknown, as these patients were not included in the reviewed studies. Similarly, its utility - both in terms of cardiac events and cost - in patients with very low risk of perioperative cardiac events (ie, those undergoing same-day or outpatient surgery, ophthalmic surgery, or those who have minimal cardiac risk) is unclear. Beta-blockade has not been studied in patients undergoing regional anesthesia or conscious sedation. In addition, no study to date has examined the use of beta-blockade in patients who have poor functional status and might otherwise be referred for additional non-invasive testing.[1,5,14,17]

Finally, the increasing popularity of perioperative beta-blockade, particularly catalyzed by the results of the study by Poldermans et al,[15] calls into question whether risk stratification using published guidelines or risk indices is still necessary.[28] Although beta-blockade is likely to be effective in many patients, the identification of patients at highest risk is still important, as these patients may require additional testing and therapy. A recent study of beta-blockade noted improved outcomes across a spectrum of predicted cardiac risk, but noted that cardiac events could be further reduced in high-risk patients through use of additional non-invasive testing and subsequent "usual care."[19] Thus, although beta-blockade may increase the threshold at which clinicians refer patients for additional testing, the era of risk stratification is not over.

The use of beta-blockers to reduce perioperative cardiac events and mortality represents a major advance in perioperative medicine for some patients at intermediate and high risk for cardiac events during noncardiac surgery. Wider use of this therapy should be promoted and studied, with future research focused on fine-tuning dosages and schedules and identifying populations of patients in which its use is cost-effective.

Table 25.1. Randomized controlled trials of the effectiveness of perioperative beta-blockade*

Study	Participants	Regimen	Results†	Side Effects	Comments
Mangano, 1996[22] Wallace, 1998[21]	200 patients undergoing elective noncardiac surgery	Atenolol 5-10g IV 30 min before entry into OR, after surgery, and 50-100g qd through hospital stay (up to 7 days); Target HR 55-65 bpm; doses held if HR<55 bpm or SBP<100 mmHg or defined adverse event	All-cause mortality at 2 yrs: 9% vs. 21% (p=0.019) Cardiac death at 2 yrs: 4% vs. 12% (p=0.033) Postoperative ischemia: 24% vs. 39% (p=0.03)	Intraoperative bradycardia more common with atenolol (38% vs. 15%, p=0.0002) but no difference in need for treatment No increase in third-degree heart block, hypotension, bronchospasm, or congestive heart failure	Included patients already taking beta-blockers, an excess of which (18 vs. 8%) were in the beta-blocker group NNT 9.1 (primary endpoint)
Polderman s, 1999[15]	112 patients with positive results on dobutamine echocardiography undergoing elective abdominal aortic or infrainguinal arterial reconstruction	Bisoprolol 5-10 mg po qd, begun an average of 37 days preoperatively and continued for 30 days postoperatively. Doses held if HR<50 bpm or SBP<100 mmHg	Cardiac death: 3.4% vs. 17% (p=0.02) Nonfatal MI: 0% vs. 17% (p<0.001)	No exacerbations of peripheral vascular disease	Excluded patients already on beta-blockers NNT 3.2 (cardiac death or nonfatal MI)
Raby, 1999[12]	26 patients with preoperative ischemia by Holter monitor undergoing aortic aneurysm repair, infrainguinal arterial bypass, or carotid endarterectomy	Esmolol IV for 48 hr postoperatively. Titrate to HR 20% below ischemic threshold but no less than 60 bpm	Postoperative ischemia: 33% vs. 73% (p<0.05)	No patient had beta-blocker therapy suspended because of unacceptable side effects	Clinicians prescribed alternate postoperative beta-blockers more often in control group (13% vs. 82%, p<0.05) NNT 2.5 (primary endpoint)
Stone, 1988[37]	128 untreated hypertensive patients undergoing elective surgery. Hypertension	Patients randomized to control, labetolol 100 mg po, atenolol 50 mg po, or oxprenolol 20	Myocardial ischemia: 2/89 (2%) vs. 11/39 (28%) in untreated patients	21 patients with beta- blockers had bradycardia, "half required atropine." No bradycardia in	Patients had generally similar baseline characteristics, but these were not statistically

	defined as systolic blood pressure 160-200 mmHg, diastolic 90-100 mmHg	mg po given before induction of anesthesia	(p<0.001)	control patients	compared No description of surgeries performed
Urban, 2000[23]	120 patients undergoing elective total knee arthroplasty	Esmolol IV within 1 hr after surgery, titrate to HR<80 bpm. Change to metoprolol morning of 1st postoperative day. Titrate to HR<80 bpm for next 48 hrs then continue dose until discharge	Postoperative ischemia: 6% vs. 15% (p=NS) Postoperative MI 2% vs. 6% (p=NS)	None noted	Included patients already on beta-blockers (30% in each arm)

* HR indicates heart rate; MI, myocardial infarction; NNT, number needed to treat; and NS, not statistically significant.
† Results are reported as beta-blocker group vs. control group.

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Section D. Safety Practices for Hospitalized or Institutionalized Elders

Chapter 26. Prevention of Falls in Hospitalized and Institutionalized Older People

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Introduction

A fall is defined as unintentionally coming to rest on the ground, floor, or other lower level, but not as a result of syncope or overwhelming external force. Falling is a common cause of morbidity and the leading cause of nonfatal injuries and trauma-related hospitalizations in the United States.[1] Complications include bone fractures, injury to the soft tissues, increased functional dependence, and fear of falling again, which itself can be debilitating. Each of these complications contributes to increased risk of future falls. Studies in community-dwelling older patients have identified age, gait or balance impairment, sensory or cognitive impairment, musculoskeletal diseases, environmental hazards, and many medications (such as sedative-hypnotic drugs) as risk factors.

One of the strongest predictors of future falls is having previously fallen. There are numerous other risk factors for falls in older persons, which are reviewed in detail elsewhere.[2,3] The number of risk factors is correlated with the risk of falling. A study by Tinetti and colleagues found the risk of falling increased from 19% when one risk factor was present to 78% in the presence of 4 or more risk factors.[4] Some of the factors associated with fall risk in the hospital setting, however, may differ from those in community-dwelling or institutional settings. The onset of an acute illness leading to hospitalization may increase fall risk due to immobility and deconditioning. Treatment for an acute condition, such as the addition of new medications or an altered medication regimen, may also increase fall risk.

The hospital environment itself may either be a supportive environment (eg, the presence of handrails and no-slip bathing surfaces) or may contribute to fall risk (eg, unfamiliar rooms, improper bed height). This chapter reviews general evidence regarding multicomponent falls prevention protocols, and 5 specific interventions: identification bracelets, physical restraints, bed alarms, special flooring, and hip protectors.

Prevalence and Severity of the Target Safety Problem

Falls are among the most common incidents reported in institutions,[5] although incident reports may underestimate their true occurrence.[6] The incidence of falls among hospitalized patients varies according to the risk factors and case mix of the patient population as well as the presence of falls prevention measures. Rubinstein has reported fall rates of 0.6 to 2.9 falls annually per bed in hospitalized patients and 0.6 to 3.6 falls annually per bed in long-term care institutions, based on published data.[7] About 50% of the 1.7 million nursing home residents in the United States fall at least once each year, resulting in serious injury in about 10% of residents.[7-9] The total cost of falls injuries in 1994 for adults aged 65 years and older was estimated at $20.2 billion.[10]

Hip fractures are the most feared complication of falls. Up to 20% of people sustaining a hip fracture become nonambulatory, and only 14-21% recover their ability to carry out

instrumental activities of daily living.[11] The estimated total incremental costs (the difference between costs before and after a hip fracture) of caring for an individual in the year after fracture were estimated to be between $16,300 and $18,700.[12] Estimated Medicare expenditures for hip fractures in 1991 were about $2.9 billion.[13]

Practice Description

Based on the multifactorial etiology of falls, multicomponent interventions have been developed to address patient risk factors and decrease fall rates. However, most studies have not been designed in a way to determine which components of a multicomponent intervention are most effective.

Risk Assessment

A variety of institution-based programs have been implemented to prevent falls. These programs usually begin by identifying individuals at increased risk for falling. This is accomplished by history-taking to elicit past falls history or by using more formal assessment tools.[4,14-17] Protocols used to perform falls risk assessment in hospitals or nursing homes vary by institution and often have not been validated.[18]

Community-Dwelling Elders

An overwhelming majority of the large, prospective, controlled studies have been carried out in the outpatient environment. They deserve mention because many of the interventions could be modified for a hospital-based intervention. Tinetti and colleagues[19] showed that interventions to reduce specific risk factors resulted in a 30% reduction in falls over one year in a prospective community cohort. The targeted risk factors were postural hypotension, use of any benzodiazepine or sedative-hypnotic drug, use of 4 or more prescription medications, environmental hazards, and muscular strength or range of motion impairments. Specific interventions that were part of the multicomponent program included exercise recommendations, behavioral recommendations, medication review, and environmental modifications. A systematic review of predominantly non-hospital based multi-risk factor intervention studies showed significant protection against falling (Peto OR 0.77, 95% CI: 0.64-0.91).[20] There was, however, significant heterogeneity across studies.

The large literature on community-based interventions has yielded other insights, some of which may be applicable to the acute care setting. For example, exercise-based interventions[21-25] have been studied as a means to decrease falls in older persons. Results of these trials have not been conclusive. A pre-planned meta-analysis of 7 randomized controlled trials (2 nursing home-based and 5 community-based) that included an exercise component found a 10% decrease in fall risk (adjusted incidence ratio 0.90, 95% CI: 0.81-0.99),[26] although a recent systematic review examining the effect of 4 trials of exercise alone found no protection against falling.[20] Another important insight from primarily non-hospital settings includes the association between specific medications or classes of medications and falls.[27,28] Although several studies have used pharmacist- or physician-based medication reviews as part of a multifaceted intervention, the independent effect of medication review and adjustment on fall outcomes has not been reported.

Institutionalized Elders

In a nursing home setting, a promising randomized controlled trial incorporating individualized assessment and targeting 4 falls-associated domains has been reported.[29] Intervention facilities had 19% fewer recurrent falls (95% CI: 2%-36%) compared with control

facilities and a 31% reduction in mean rate of injurious falls (13.7 vs. 19.9 falls per 100 person-years; p=0.22). Interventions in this study were made in the areas of environmental and personal safety (improvement in room lighting, flooring, footwear), wheelchair use and maintenance (assessment by an occupational therapist), psychotropic drug prescription (assessment and recommendations for change), transfer and ambulation (evaluation and recommendations for change), and facility-wide interventions (eg, in-service educational programs). No analogous study of a multi-intervention standardized protocol has been reported in hospitalized patients.

Hospitalized Elders

In the hospital, interventions have been employed as part of multiple risk factor intervention studies, but many have been poorly described and standardized. In the studies set in acute care environments,[30-45] practices include educational activities for nurse and support staff, patient orientation activities, review of prior falls, and improvement of surrounding environment. Specific environmental components included decreasing ward or room obstacles, adding supplemental lighting and grab bars in bathrooms, and lowering bedrails and bed height. Other studies have attempted to improve transfer and mobility by providing scheduled ambulatory and physical therapy activities and better footwear (eg, non-skid socks). Additionally, studies have incorporated strategies to assist cognitively impaired patients by educating family members to deal with confused patients, minimizing sedating medications, and moving confused patients closer to nursing staff. Because many of these hospital studies use small sample sizes and inadequately describe the precise number and standardization of interventions, their generalizability and reproducibility is limited. However, a recent systematic review of many of these programs concluded that a pooled effect of 25% reduction in the fall rate occurred in the studies that examined prospective interventions compared to fall risk in historical controls.[18]

Some interventions with the potential for effectiveness in isolation have been studied. Each of the following hospital- or institution-based individual interventions has been analyzed independently of a multi-component falls prevention program:

- Identification bracelets
- Physical restraints
- Bed alarms
- Special flooring
- Hip protectors

Several generally accepted interventions with high face-validity have not been independently studied, yet are commonly accepted practices. Immobility[46] is a significant risk factor for several geriatric complications, including falls, pressure ulcers, and functional decline. Minimization of bedrest is a practical, real-world intervention that has implications for prevention of a number of serious hospital-acquired complications.[47]

Comment

There are few hospital or other institution-based randomized controlled trials of standardized falls interventions, although the necessity for well-designed studies is clear. The nursing home-based intervention reported by Ray and colleagues[29] provides good evidence that a well-documented intervention can improve falls outcomes in institutionalized patients. No similarly designed trial of a multicomponent intervention in hospitalized patients was identified, although many falls prevention programs incorporate multifactorial interventions. The questions raised by multicomponent falls prevention studies include the generalizability of interventions to

diverse inpatient settings, appropriate targeting of at-risk individuals, analysis of the individual components that provide the best improvement in falls outcomes, and the transportability of interventions between institutions with variable resources for implementation. Evidence for the effectiveness of individual interventions is important, but effectiveness may change (for better or worse) when such interventions are incorporated with others as part of a falls prevention program.

Subchapter 26.1. Identification Bracelets for High-Risk Patients

Background

Some hospitals use colored bracelets to identify patients at high risk for falls. Other identification methods include signs, stickers, or tags placed above the patient's bed, at the nursing station, or on the patient's chart. In theory, these remind staff that the patient is at high risk for falls and trigger interventions that reduce the risk of falls (eg, supervision or assistance with ambulation, minimization of sedative-hypnotic medications, lowering of bed height). Identification bracelets might also impact patients' falls awareness (eg, reminding patients to call for assistance before getting out of bed).

Prevalence and Severity of the Target Safety Problem

See Introduction to Chapter 26.

Opportunities for Impact

We found no published data on the number of hospitals currently using such strategies.

Practice Description and Evidence for Effectiveness

A search of the literature identified many studies that have used identification bracelets, signs, or tags for high-risk patients.[31-33,35,40-42,44,45,48,49] Most of these involved multiple, simultaneous interventions and were designed such that estimation of the treatment effect due to the identification bracelet, signs or tags component cannot be calculated. The remaining study was a randomized, controlled trial of colored identification bracelets worn by inpatients at high risk for falls (Table 26.1.1).[50] "High-risk" was defined as history of multiple falls, an episode of incontinence, or an admitting diagnosis of stroke or ataxia. Cox proportional hazards model was used to assess the effect of identification bracelets on time-to-first-fall. The fall rate was 42% (27/65) in the intervention group and 30% (21/69) in the control group, which did not represent a statistically significant difference. After preliminary analysis of the data, the investigators and ethics committee agreed that it was not appropriate to continue for the sole purpose of obtaining statistical power, and the study was terminated.

Potential for Harm

None identified.

Costs and Implementation

Identification tags and similar interventions are associated with minimal costs.

Comment

Use of special bracelets, signs, and stickers to identify patients at high risk for falls is a relatively inexpensive and easy to implement practice. There is currently insufficient information

as to whether identification bracelets, as a isolated intervention, decrease falls. Future studies should assess the effectiveness of similar identification strategies in the context of multicomponent fall prevention programs and, if they are effective, which methods work best.

Table 26.1.1. Study of identification bracelets*

Study	Participants and Setting	Study Design, Outcomes	Results
Mayo, 1994[50]	134 high-risk patients in a rehabilitation hospital, 1990-91	Level 1, Level 1	Hazard ratio for fall with intervention: 1.3 (95% CI: 0.8-2.4)

* CI indicates confidence interval.

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Subchapter 26.2. Interventions that Decrease the Use of Physical Restraints

Background

The Health Care Financing Administration (HCFA) defines physical restraints as “any manual method or physical or mechanical device, material, or equipment attached or adjacent to the patient that the individual cannot remove easily which restricts freedom of movement or normal access to one’s body.”[1] Physical restraints have been used in nursing homes and hospitals both as a safety device and as a falls prevention tool. Because restrained patients cannot arise from a chair or transfer out of bed, they theoretically will not fall or, in the case of bedrails, will not roll out of bed. However, the use of physical restraints may lead to substantial adverse outcomes. In fact, serious injuries and even death have been reported with use of these devices.[2,3] This chapter examines interventions to reduce use of physical restraints and the concomitant effect on fall rates.

Practice Description

Studies examining the use physical restraints have considered 2 types of interventions in hospital or nursing home settings: bedrails and other mechanical restraints designed to restrict mobility. These interventions usually begin with either a physician or nurse making an assessment that a patient is at risk for falls, elopement, or other adverse outcomes. Thereafter,

use of a restraint is initiated, with periodic reassessment of the ongoing need for the device. Safety practices to reduce restraint use in nursing home patients have included nursing education strategies focusing on assessment/reassessment of the need for restraints and the use of alternatives to restraints.

Prevalence and Severity of the Target Safety Problem

See Introduction to Chapter 26.

Opportunities for Impact

Federal guidelines now discourage all but the limited, appropriate use of physical restraints and bedrails. Legislation adopted as part of the Omnibus Budget Reconciliation Act of 1987 directed nursing homes to limit physical restraints, and the Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) has adopted similar guidelines. Several statewide initiatives (eg, the Pennsylvania Restraint Reduction Initiative, begun in 1996) have been implemented under HCFA's National Restraint Reduction Initiative, resulting in notable reductions in restraint usage.[4] The Food and Drug Administration's Hospital Bed Safety Work Group has likewise actively raised awareness of the risks and benefits of bedrail use.[5] Based on an annual HCFA survey, the national restraint rate was approximately 13.5% in 1999, down from approximately 20% in 1996 when HCFA's Restraint Reduction Initiative began.[6] Nonetheless, data from selected states reveals that the rate was still as high as 26% as of 1998.[7]

Study Designs and Outcomes

Six studies were identified: 2 concerning bedrail interventions[8,9] and 4 describing mechanical restraints interventions (Table 26.2.1).[7,10-12] Most studies compare interventions with historical control or baseline rates using a before-after study design. Morbidity data on falls are reported in all studies.

Evidence for Effectiveness of the Practice

The studies reveal no statistically significant difference in falls compared with historical controls when bedrails are removed. In fact, restrained patients appear to have a modest increase in fall risk or fall injuries based on several studies. Weaknesses in study design for some of these studies preclude a final conclusion.

Potential for Harm

The potential for harm with use of bedrails is well-documented, including death from a variety of mechanisms, including death and strangulation.[13] Mechanical restraints likewise carry a risk of severe injury, strangulation, and mobility limitations that may predispose patients to other adverse outcomes (pressure ulcers, incontinence, acute confusion). Limits to patient freedom, dignity, and quality of life also contribute to the potential for harm. A potential harm of interventions to decrease restraint use is that there may be an increase in other adverse events (eg, elopement) if appropriate alternative preventive measures are not in place.

Costs and Implementation

The costs associated with interventions to reduce the use of restraints have not been described. Nonetheless, reduction in the use of physical restraints will require resources to pay for alternative interventions and rehabilitative measures and will increase labor costs.[14] Compliance with interventions to reduce bedrail rates and to decrease mechanical restraint use

has been good. In fact, given adequate alternatives to the use of these devices, hospital and nursing staffs have decreased their usage significantly. In the Neufeld study,[7] for example, restraint use fell from 41% to 4%.

Comment

There is growing evidence that physical restraints have a limited role in medical care. Restraints limit mobility, a shared risk factor for a number of adverse geriatric outcomes, and increase the risk of iatrogenic events. They certainly do not eliminate falls, and decreasing their use can be accomplished without increasing fall rates. In some instances reducing the use of restraints may actually decrease the risk of falling. Incorporating changes into physician and staff behavior may be easier if large, multicenter trials are successful in identifying safe alternatives to restraints that effectively limit falls risks for patients.

Table 26.2.1. Studies of physical restraints and fall risk*

Study	Participants and Setting	Design, Outcomes	Results
Hanger, 1999[9]	1968 hospital patients in New Zealand, 1994; formal bedrail policy and educational program to reduce bedrail use, historical controls	Level 3, Level 1	No significant difference in overall fall rate: 164.8 falls/10,000 bed days before and 191.7 falls/10,000 bed days after the intervention (p=0.18) Fewer serious falls occurred after the intervention (p=0.008)
Si, 1999[8]	246 patients in a teaching nursing home, 1993-94; interdisciplinary team assessment and removal of bedrails with provision of bedrail alternatives, historical controls	Level 3, Level 1	No significant difference in fall rates: 2/116 (1.7%) patients before and 2/130 (1.5%) patients after the intervention
Capezuti, 1996[11]	322 nursing home residents; subgroup of confused patients examined for mechanical restraint use	Level 3, Level 1	Confused patients who were restrained had increased odds of falling (OR 1.65, 95% CI: 0.69-3.98) and recurrent falls (OR 2.46, 95% CI: 1.03-5.88)
Capezuti, 1998[12]	633 nursing home residents in 3 nursing homes, 1990-1991; restraint education and consultation interventions compared with baseline rates	Level 3, Level 1	No significant increase in fall rates in the restraint-free group Decreased odds of minor injury after restraint removal, adjusted OR 0.3 (95% CI: 0.1-0.9)
Neufeld, 1999[7]	2075 nursing home beds in 16 nursing homes, 1991-1993; educational intervention to decrease mechanical restraints compared with baseline rates	Level 3, Level 1	Moderate/severe injuries decreased from 7.4% to 4.4% (p=0.0004) after educational intervention
Tinetti, 1991[10]	397 elderly patients at 12 skilled nursing facilities; observational cohort study of mechanical restraint use	Level 3, Level 1	15/275 (5%) of unrestrained patients compared to 21/122 (17%) experienced a serious fall-related injury (p<0.001) Restraint use was significantly associated with a serious fall, adjusted OR 10.2 (95% CI: 2.8-36.9)

* CI indicates confidence interval; OR, odds ratio.

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Subchapter 26.3. Bed Alarms

Background

Epidemiologic studies reveal that falls occur commonly in and around bed areas.[1,2] Decreasing the risk of falls when patients attempt to transfer into and out of bed without assistance is a potentially important target safety goal. This chapter examines the use of a bed alarm system that alerts hospital staff to patient movement out of bed as a strategy to reduce falls. General principles of alarm use in health care settings can be found in Chapter 8.

Practice Description

A sensor device is placed on the bed, under a sitting or reclining patient. When the patient changes position, it detects movement and/or absence of weight. An audible alarm is triggered at the nurses' station and, with some devices, in the patient's room. The alarm alerts nurses when patients attempt to leave the bed without assistance and may alert a patient to remain in bed if the alarm is audible in the patient's room.

Evidence for Effectiveness of the Practice

Several studies have included bed alarms as part of a multifaceted intervention.[3-6] However, the study designs do not allow calculation of the effect attributable to the bed alarm component or were not controlled. A recent, unpublished before-after study was identified in a Web search but the full report could not be obtained before completion of this chapter.[7] Tideiksaar et al randomized elderly patients at "high risk" for falls to either a group that received an alarm system (the RN+ OnCall bed monitoring system) or to a control group that did not (Table 26.3.1)[8]. The groups were similar in age and gender. No other baseline comparisons were reported. There were fewer falls in the study group but the difference failed to reach statistical significance. However, the total number of falls was low (n=17) and had there been one less fall in the alarm group or one more fall in the control group, the difference would have been statistically significant.

Potential for Harm

No harm was identified. There are theoretical electrical risks if the sensor devices are internally compromised due to bending of the sensor mats and exposure to fluids, but such events have not been reported in the literature.

Costs and Implementation

Costs of the devices vary by manufacturer, the type of bed monitoring system used, and the number of beds to be monitored. Manufacturers' charges range from several hundred to several thousand dollars for the receiving equipment. Individual sensors require replacement after pre-specified periods of use or, in some cases, can be cleaned between patients, which incurs additional hospital costs. Implementation requires adequate staffing to respond in a timely manner to the audible alarms.

Comment

At this time, there is insufficient evidence regarding the effectiveness of bed alarms in preventing falls in elderly patients to recommend the practice. Additional research sufficiently powered to identify meaningful differences, coupled with a formal economic analysis, would be useful.

Table 26.3.1. Study of bed alarms for fall prevention

Study	Participants and Setting	Study Design, Outcomes	Results (95% Confidence Interval)
Tideiksaar, 1993[8]	70 patients on a geriatric unit in a university hospital, 1992	Level 1, Level 1	Odds ratio for prevention of falls: 0.32 (0.10-1.03)

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Subchapter 26.4. Special Hospital Flooring Materials to Reduce Injuries from Patient Falls

Background

One proposed practice to prevent injury due to falls is to alter flooring material on hospital wards or in nursing homes. Carpeting, vinyl, or other biomedically-engineered materials could potentially improve falls outcomes. The use of special flooring materials has been shown to influence specific gait characteristics in hospitalized elders.[1] A recent study described the Penn State Safety Floor, which is designed to remain relatively rigid under normal walking conditions but to deform elastically to absorb impact forces during a fall.[2] The efficacy of this floor is still being tested outside the laboratory environment among nursing home residents.[3]

Practice Description

As data on the efficiency of the Penn State Safety Floor[2] are not yet available, we restrict our review to the use of *hospital-duty carpeting* compared with "usual" vinyl flooring.

Study Designs and Outcomes

We identified 2 studies of the effect of flooring type (carpet vs. "usual" vinyl flooring) on falls: a randomized controlled trial in an inpatient rehabilitation unit[4] and a retrospective study of accidents reported in a care of the elderly unit (Table 26.4.1).[5] Both studies reported Level 1 outcomes. The randomized trial measured the rate of falls. The retrospective analysis studied fall-related injury, defined as any graze, bruise, laceration, fracture or pain.

Evidence for Effectiveness of the Practice

The randomized trial by Donald et al found more falls in the group housed in rooms with carpeted flooring, although the difference barely failed to achieve statistical significance. The earlier retrospective analysis by Healey found that the rate of injury was significantly lower for patients who fell on carpet rather than vinyl flooring.[5] The severity of injuries was not reported and it was not possible to determine whether the rate of falls differed according to flooring material.

Potential for Harm

No harm was identified, although it is possible that asthmatic patients might react to increased levels of dust-mite allergens in carpeted wards.[6]

Costs and Implementation

No cost estimates for changes in flooring were reported in the literature. Implementation of this practice would require a large expenditure for facilities upgrades nationwide. Likewise, the costs associated with keeping various floor surfaces clean in the hospital or nursing home environment would also be high.

Comment

Advances in biomedical engineering could result in potentially significant redesign of the physical environment in hospitals and nursing facilities. The primary aim of specialized flooring could be either to reduce the risk of falling or to reduce the risk of an injury once a fall has occurred, or both. The two studies analyzed seem to indicate that carpeted floors may increase fall rates but decrease fall injuries; it is possible that other surfaces would yield better results. Further study of this area is warranted.

Table 26.4. Study of special flooring for falls prevention

Study	Participants and Setting	Study Design, Outcomes	Results
Donald, 2000[4]	32 patients in an elderly care rehabilitation ward in the United Kingdom in 1996	Level 2, Level 1	Rate of falls: Carpet, 10/16 (63%); vinyl, 1/16 (6%) RR 8.3 (95% CI: 0.95-73; p=0.05)
Healey, 1994[5]	Random sample of accident forms (n=213) from care of elderly unit over 4 years	Level 3, Level 1	Falls resulting in injury: Carpet, 15%; vinyl, 91% (p<0.001)

* CI indicates confidence interval; RR, relative risk.

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Subchapter 26.5. Hip Protectors to Prevent Hip Fracture

Background

Hip fractures are an important cause of morbidity and mortality, resulting in about 340,000 hospitalizations in 1996 in the United States for those aged 65 years and older.[1] Six months after hospitalization for hip fracture, 12.8% of patients require total assistance to ambulate according to a recent prospective study.[2] New dependency in physical and instrumental activities of daily living is also considerable. For those independent prior to a hip fracture, 20% of patients require assistance putting on pants, 66% require assistance in getting on or off the toilet, and 90% require assistance climbing 5 stairs after a hip fracture.[3] Mortality rates range between 18-33% within the first year post-fracture.[3] One proposed prevention measure is for a patient to wear a protective pad around the hip to absorb the impact of a fall and to reduce the risk of fracture by “shunting” energy away from the hip region.

Practice Description

External hip protectors are usually made with plastic pads or shields that are padded or constructed with foam-type materials. They fit into specially-designed pockets in undergarments or pants. They are designed to be worn during the day for people who are out of bed, walking or engaged in activities that place them at higher risk for falls. Ideally, they would be worn all the time to protect individuals from nighttime falls.

Prevalence and Severity of the Target Safety Problem

See Introduction to Chapter 26.

Opportunities for Impact

No data on the nationwide use of hip protectors in the hospital or nursing home are available. A small minority of institutions are in the process of evaluating them, and a few may have begun to use them.

Study Designs

Five relevant randomized controlled trials[4-8] were identified from a literature search and from a Cochrane systematic review.[9] The Cochrane review cites 2 additional abstracts[10,11] not included here. Four of the trials evaluate effectiveness of the devices and one study[8] examines compliance rates of wearing hip protectors as part of a pilot study. Two studies were cluster-randomized and 2 were randomized by individual patient.

Study Outcomes

Studies reported hip fractures as an outcome, although compliance with the intervention was the primary outcome in one study. Additional outcomes reported were mortality, falls, and non-hip fractures.

Evidence for Effectiveness of the Practice

External hip protectors appear to be an effective means to reduce the risk of a hip fracture in older persons aged 65 and over who fall. Table 26.5.1 lists the abstracted studies and outlines their pertinent features. The generalizability of these results to wider audiences and to lower risk populations has not been demonstrated, nor has the potential benefit for hospitalized patients been reported. Concerns with compliance could hinder their effectiveness on a population-wide level.

Potential for Harm

Discomfort from wearing the device, difficulty managing the garment while dealing with continence, and the potential for skin irritation and breakdown are causes for concern if fragile older people were to wear hip protectors. Because long-term compliance is low, it is unclear how many people would experience such problems if the devices were worn for longer periods during the day or for long-term use.

Costs and Implementation

An Australian study published in 2000 quoted a cost of A$10 per pair (approximately $5.25US).[4] The retail price quoted by one US manufacturer of a different hip protector is approximately $90 per pair. The lycra-containing undergarment used by some manufacturers to keep the hip pads in place requires special laundering and would require a tracking system similar to that used for other specialized garments or medical devices assigned to patients within a facility. Once provided, if devices can be put on and taken off by individual users, implementation is straightforward. The cost-effectiveness of the devices has not been formally reported.

Comment

One of the main philosophical concerns raised by these studies is the change in emphasis from primary prevention of the underlying cause of hip fractures (ie, falls) to an emphasis on methods of protecting patients from the deleterious consequences of falls. However, a strategy for addressing the multiple risk factor model for falls is still warranted for primary falls prevention. With this caveat in mind, there is strong evidence to support the ability of hip protectors to prevent hip fractures. This evidence, in addition to their high face validity, may encourage their rapid adoption. Further evaluation of their costs, acceptability to patients, and effectiveness in hospitalized patients (versus nursing home residents) is needed.

Table 26.5.1. Hip protectors to prevent hip fracture*

Study	Participants and Setting	Design, Outcomes	Results
Parker, 2000[9]	1752 nursing home or rest home residents in 5 countries	Level 1A, Level 1	Peto OR 0.44 (95% CI: 0.26-0.75) of hip fracture in the intervention group in cluster-randomized studies; Peto OR 0.22 (95% CI: 0.09-0.57) in patient-randomized studies
Chan, 2000[4]	71 nursing home residents in Australia, year not stated	Level 1, Level 1	RR of hip fracture in the intervention group 0.264 (95% CI: 0.073-0.959)
Ekman, 1992[5]	746 nursing home residents in Sweden, year not stated	Level 1, Level 1	RR of hip fracture in the intervention group 0.33 (95% CI: 0.11-1.00)
Kannus, 2000[6]	1801 community based elderly in Finland, 1996-1997	Level 1, Level 1	RR of hip fracture in the intervention group 0.4 (95% CI: 0.2-0.8; p=0.008)
Lauritzen, 1993[7]	665 nursing home residents in Denmark, 1991-1992	Level 1, Level 1	RR of hip fracture in the intervention group 0.44 (95% CI: 0.21-0.94)
Villar, 1998[8]	141 rest home residents in the UK, year not stated	Level 1, Level 3	30% compliance over 3 months (hip fracture outcomes not assessed)

* CI indicates confidence interval; OR, odds ratio; and RR, relative risk.

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Chapter 27. Prevention of Pressure Ulcers in Older Patients

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Background

Pressure ulcers, localized areas of tissue damage or necrosis that develop due to pressure over a bony prominence, are common causes of morbidity in older hospitalized and institutionalized persons. Other terms referring to the same phenomena are pressure sores, bedsores, and decubitus ulcers. Risk factors include immobility, friction, shear, incontinence, cognitive impairment and poor nutritional status.[1-3] Pressure ulcers are one indicator of quality of care measured by nursing homes as part of the mandatory Minimum Data Set (MDS), which is required for participation in Medicare and Medicaid. Part of the MDS evaluation includes the Resident Assessment Instrument, which serves as a guide to assess pressure ulcers and many other pertinent clinical problems.[4]

Risk assessment is an integral part of prevention efforts. The Norton scale[5] and the Braden scale[6] are widely used tools to identify at-risk patients. The Norton scale assesses five domains: activity, incontinence, mental status, mobility, and physical condition. The Braden scale assesses six domains: activity, dietary intake, friction, mobility, sensory perception, and skin moisture. Agreement between the scales is 0.73 using the kappa statistic.[7]

Different strategies have been used for primary prevention. Major clinical guidelines,[8] for pressure ulcer prevention are based primarily on published evidence, and in some areas, on professional judgment and face validity of practices. Turning and/or repositioning patients is a practice with high face validity, but there are no well-designed controlled trials that examine its effect in the absence of other interventions. Other practices include regular skin inspection and assessment, use of appropriate pressure-relief surfaces, improved mobility, adequate nutritional intake, and documentation of the skin examination. Additionally, the use of general educational interventions for hospital staff is supported by before-after study designs.[9, 10] Several reports suggest the value of using topical applications applied to intact skin in an attempt to prevent ulcers.[5, 11, 12] This chapter focuses on the use of pressure-relieving strategies that can be incorporated into hospital or nursing home practice and are based on evidence from controlled clinical trials.

Practice Description

The preventive practices that have received the most research attention are the use of specific beds or mattresses. Many studies have compared a specific mattress with either another high-technology mattress or with a “standard” hospital mattress. A standard mattress, which is not uniformly defined in the literature, may be described as a hospital-issue, usually foam-based mattress found in a typical hospital room. The lack of consensus as to what constitutes a standard hospital mattress presents an interpretative challenge to investigators and administrators hoping to extrapolate results of a published trial to another locale.

In 1991 Krasner reported that there were over 115 different pressure-relieving support surfaces on the market.[13] Sheepskin and other inexpensive pads (eg, “egg-crate” mattresses) are common pressure-reducing devices. Other static devices include pressure-relieving pads (eg,

fabricated from elastic polymers) such as those used to cover operating room tables. Constant, low-pressure supports maintain uniform pressure throughout. Examples include higher-grade foam, and gel-, air-, or water-filled supports. In contrast, dynamic or alternating air devices have a built-in pump that continually redistributes air pressure. Low air-loss beds, as their name implies, permit small amounts of air to escape through a network of pores, whereas high air-loss (or air-fluidized) beds purposefully pump air through ceramic-type beads. Finally, kinetic turning beds, which allow continual rotation, are used more commonly in critically ill patients.

Prevalence and Severity of the Target Safety Problem

In 1990 a large, prospective epidemiologic study reported the one-year incidence for pressure ulcer development in nursing homes to be 13.2%,[14] with prevalence reports ranging from 7% to 23% in a systematic review.[15] Risk-adjusted rates of new pressure ulcers have been reported to decrease by 25% from 1991 to 1996, based on a recent study using data from the Minimum Data Set.[16] In hospitalized patients, prevalence ranges from about 3% to 11%.[17] Meehan reported that the prevalence of pressure ulcers was 11.1% in 177 hospitals surveyed in 1993 and that 54% of the pressure ulcers occurred in patients 70 to 89 years old.[18] Eckman estimated that almost 1.7 million hospitalized patients had pressure ulcers.[19] Approimately 60% of pressure ulcers develop in these acute care settings. The National Health and Nutrition Examination Survey found that less than 20% of pressure ulcers arise in non-institutional environments.[20]

Pressure ulcers result in both increased length of hospital stay and hospital costs[21] and increased nursing care time, as demonstrated by a study of long-term care patients.[22] Cellulitis, osteomyelitis, and sepsis are morbid complications of untreated pressure ulcers. Increased mortality has also been associated with pressure ulcers.[17]

Opportunities for Impact

The passage of the Omnibus Budget Reconciliation Act of 1987 and subsequent implementation regulations provided a written mandate for hospitalized and institutionalized patients to receive regular assessment, preventive measures, and treatment of pressure ulcers. There are no specific data on the current utilization of preventive measures by hospitals. The pressure ulcer protocols often vary from institution to institution.

Study Designs

We identified a recent systematic review of pressure-relieving devices[23] that evaluated 37 randomized controlled trials (RCTs), 31 of which were focused on pressure ulcer prevention (Table 27.1). Seven trials compared standard foam mattresses with various “low-technology” supports. These low-technology supports were defined as beds with constant low-pressure supports, including bead-, water-, or gel-filled supports; static air-filled supports; or foam or Silicore-filled supports. Seven of the trials compared constant low-pressure devices with alternating pressure devices. Six studies limited enrollment to orthopedic patients, 5 to patients in intensive care units, and 3 to patients undergoing operations (ie, the study evaluated different operating table surfaces). We identified no further RCTs of pressure ulcer prevention published after the systematic review identified above.

Study Outcomes

All studies reported pressure ulcer development in both intervention and control groups. Pressure ulcer grading systems were used in most trials. Typically, a 4-level grading system was

employed, ranging from Grade 1 (discolored skin) to Grade 4 (full-thickness skin lesions with bone involvement).

Evidence for Effectiveness of the Practice

Many specialized beds appear to be effective in reducing the development of pressure ulcers when compared with standard mattresses. For example, in 4 studies[24-27] cited by the systematic review[23] that compared standard hospital foam mattresses to enhanced foam alternatives, a summary relative risk of 0.29 (95% CI: 0.19-0.43) was calculated, favoring the intervention group. Between-group comparisons of the previously defined low-technology constant low-pressure devices did not yield clear conclusions. Similarly, in 7 RCTs the comparison of alternating pressure devices with a variety of constant low-pressure devices (a water mattress, foam pad, static air mattress, and foam overlays) showed no significant difference in pressure ulcer development (summary RR 0.84, 95% CI: 0.57-1.23).[23] However, a study of alternating pressure supports compared with standard foam mattresses did demonstrate lower pressure ulcer development in the intervention group (RR 0.32; 95% CI 0.14-0.74).[28] Comparing pressure-reducing devices among themselves (versus against a standard mattress) yields no significant differences in the prevention of pressure ulcers. These trials have been summarized in a recent review.[29]

In addition, 2 published trials evaluating different operating table-like surfaces suggest reduction in pressure ulcer development with enhanced surfaces.[30, 31] In a well-designed RCT of 446 patients, Nixon and colleagues[31] showed that a dry gel-polymer pad placed on an operating table decreased the incidence of new pressure ulcers by almost half—11% for intervention patients vs. 20% for control patients placed on a standard operating table mattress (RR 0.46, 95% CI: 0.26-0.82).

Several caveats temper the interpretation of studies of specialized pressure-relieving surfaces. In general the studies had poor methodologic design, as the systematic review points out.[23] The trials were mostly small, true baseline comparability was hard to confirm, standardization of protocols was often unclear, and assessments were frequently unblinded. Patient selection across trials was not consistent, and differences in pressure ulcer risk at enrollment were difficult to compare across studies.

Potential for Harm

None reported.

Costs and Implementation

The costs of treating a pressure ulcer are estimated to range from $4000 to $40,000 for newly developed ulcers.[32] Indeed, both hospital costs and length of stay are significantly higher for patients who develop pressure ulcers during hospitalization, as noted earlier.[21] In the nursing home in particular, failure to prevent this adverse outcome carries increasing liability—the median settlement for pressure ulcer-related disputes was $250,000 between the years 1977 and 1987.[33] The cost of specialized beds and mattresses to prevent pressure ulcer development can be high, ranging from $40 to $85 per day for low air-loss beds.[34] Specialized beds and intensive nursing interventions all carry clear resource implications. Inman and colleagues[35] have demonstrated the cost-effectiveness of an air suspension bed compared to a standard intensive care unit bed. Yet cost-effectiveness studies of the many different pressure-relieving devices have not been formally completed.

In terms of the feasibility of implementing these specific devices and following guidelines for high-risk patients, both cost and time considerations must be examined.[36] Other considerations relate to the design and functionality of a particular bed or mattress—for example the ability of nursing staff to move and transfer patients placed on deeper or bulkier beds. Finally, difficulty in accurately assessing changes in the incidence and prevalence of pressure ulcers resulting from the institution of preventive measures is another barrier to documenting progress.[37]

Comment

Overall there is adequate evidence that specially designed surfaces effectively prevent the development of pressure ulcers in high-risk patients, but the definition of high risk varies across studies. The variety of pressure-relieving devices makes it difficult to recommend one over another because there are few direct comparisons among the many different types of surfaces. Of note, the treatment of established pressure ulcers is a separate topic, and the type of pressure-relieving surface that is effective in treatment may not prove best for prevention. Appropriate patient selection criteria need further development and refinement because the cost of many prevention interventions is high. The necessity for larger RCTs to assess both clinical and cost-effectiveness of these specially designed mattresses is clear. Better descriptions of what constitutes a "standard" bed or mattress, and improved reporting of baseline comparability between experimental and control groups are also necessary to adequately interpret existing studies. To better track progress in prevention, standardized strategies should be developed so that accurate prevalence estimates can be documented.

Table 27.1. Studies of pressure ulcer prevention*

Participants and Setting	Study Design, Outcomes	Relative Risk of Pressure Ulcer
Systematic review of 31 RCTs from the US, UK and elsewhere assessing pressure relieving interventions for prevention of pressure ulcers[23]	Level 1A, Level 1	Enhanced alternative foam mattresses vs. standard hospital mattresses: RR 0.29 (95% CI: 0.19-0.43) Alternating pressure vs. constant low pressure devices: RR 0.84 (95% CI: 0.57-1.23)

* CI indicates confidence interval; RCT, randomized controlled trial; and RR, relative risk.

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Chapter 28. Prevention of Delirium in Older Hospitalized Patients

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Background

Delirium, or acute confusional state, is a common complication among hospitalized older patients. Delirium is characterized by a sudden onset and fluctuating course, inattention, altered level of consciousness, disorganized thought and speech, disorientation, and often behavioral disturbance. As with other common geriatric syndromes, the etiology of delirium is multifactorial. Previous research has identified a broad range of predisposing and precipitating factors.[1-4] These include older age, cognitive or sensory impairments, dehydration, specific medication usage (eg, psychoactive drugs), concurrent medical illness, and sleep deprivation. The multifactorial nature of delirium suggests that intervention strategies targeting multiple known risk factors might be effective in preventing its occurrence in hospitalized older patients. In this chapter, we review multicomponent prevention programs that can be applied to a general hospitalized patient population, not restricted to one admitting diagnosis (in keeping with the crosscutting patient safety focus of the Report; Chapter 1). For example, a study comparing the effect of postoperative analgesia using intravenous versus epidural infusions after bilateral knee replacement surgery was not included.[5]

Practice Description

A number of individual interventions have been used in efforts to prevent delirium. Some could be considered part of general nursing practice, whereas others involve medical assessments by physicians or consultants. General strategies to prevent delirium include use of patient reorientation techniques (such as verbal reassurance, re-introduction of team members, review of the daily hospital routine and patient schedule), environmental modifications (visible clocks and calendars), and scheduled patient mobility. The number and complexity of these interventions can vary, with individual nursing discretion usually determining how and when these interventions are implemented. Patient education,[6] nursing staff education,[7] and family involvement[8] are also useful. Approaches for primary prevention that incorporate physician consultants or geriatric consultative teams[9-11] are reviewed elsewhere in this Report (see Chapters 29 and 30).

Formal prevention programs target defined risk factors by implementing multiple practices according to standardized protocols. For example, a recently reported, multicomponent strategy focused on 6 risk factors and successfully developed intervention protocols to address each of them.[12] Patients with cognitive impairment received daily orientation interventions and 3-times daily cognitive stimulation activities. To target sleep impairment, patients received non-pharmacologic sleeping aids (eg, back massage and relaxation tapes), while hospital staff engaged in noise-reduction strategies such as setting beepers to vibrate and using silent pill crushers. Immobility was addressed with a 3-times daily exercise protocol adapted for use with bed-bound and ambulatory patients. Sensory impairments were addressed by providing devices such as auditory amplifiers, visual aids, and larger size push-button phones. Patients with

evidence of dehydration received standardized repletion interventions. A geriatric nurse specialist and staff assisted by trained volunteers carried out all the interventions.

Prevalence and Severity of the Target Safety Problem

The target safety problem is the primary prevention of delirium, rather than the treatment[13] of existing delirium. In the United States, delirium affects an estimated 2.3 million hospitalized elders annually, accounting for 17.5 million inpatient days, and leading to more than $4 billion in Medicare costs (1994 dollars).[12] Studies have found that delirium in hospitalized patients contributes to longer lengths of stay,[14] increased mortality,[15-17] and increased rates of institutional placement.[18, 19] New cases of delirium occur in approximately 15% to 60% of hospitalized older patients, depending on the number of risk factors present at admission.[4,15,18,20,21] Moreover, because many cases of delirium go unrecognized during hospitalization and because symptoms may persist for months after discharge,[22] these may be conservative estimates. Safety practices to reduce delirium may thus have substantial impact on the health and well-being of older patients in hospitals. These practices may also impact nursing home residents and other institutionalized patients, but our practice review did not identify any studies carried out among these patient populations.

Opportunities for Impact

It is difficult to estimate the extent of existing practices aimed at decreasing delirium. A comprehensive model, the Hospital Elder Life Program,[23] which incorporates the delirium interventions reviewed in one study in this chapter,[12] is presently in the initial dissemination phase at 6 replication sites, with 16 hospitals on a waiting list. Present evidence suggests that few facilities currently have intervention programs designed for the primary prevention of delirium. The opportunity for impact in nursing homes and other long-term care facilities is great, but thus far studies have not targeted these settings.

Study Designs

Cole[24] conducted a structured search of the medical literature and identified 10 intervention trials to prevent delirium in hospitalized patients. Of these, we excluded one study of much younger patients (mean age, 49 years)[25] and one study that incorporated interventions not applicable to most hospitalized elders (eg, early surgery, prevention and treatment of peri-operative blood pressure falls).[26] Three used psychiatric consultations[27-29] which did not fit our criteria for risk factor intervention (see Chapter 29 for similar studies). Table 28.1 lists the remaining 5 studies[6, 8, 30-32] and a later study,[12] which is the largest controlled trial to date.

Study Outcomes

All of the studies in Table 28.1 reported delirium or confusion symptoms as an outcome measure. Each study, however, used a different instrument to identify delirium: DSM-III,[33] the Confusion Assessment Method,[34] the Short Portable Mental Status Questionnaire,[35] or a scoring system based on delirium symptoms.

Evidence for Effectiveness of the Practice

The earliest studies, by Owens[6] and Chatham,[8] focused on the effects of patient and family education, respectively. Delirium symptoms modestly improved but achieved statistical significance in only 5 of the 11 symptom categories reported in the latter study. Both studies were limited by small numbers of patients, non-standardized interventions, and minimal data on

baseline co-morbidities of the enrolled patients. The study by Williams and colleagues,[32] which targeted a population at high risk for delirium (older patients with hip fracture), also demonstrated a statistically significant reduction in delirium symptoms by targeting environmental nursing interventions and patient education. Two subsequent studies did not show a reduction in delirium. The low incidence of delirium (only 3 cases in 30 intervention patients) in the study by Nagley et al[30] created inadequate power to detect a significant effect with only 60 total patients. Although a high percentage of patients experienced delirium in the study by Wanich et al,[31] 79% of cases were diagnosed at the time of admission (prevalent rather than incident cases) and therefore could not have been prevented by the intervention. Both of these studies may also have suffered from contamination bias. The greatest benefit in delirium prevention, a 40% risk reduction, occurred in the study by Inouye et al,[12] a carefully designed and implemented hospital program targeting 6 well-recognized risk factors for delirium, in which adherence to each intervention protocol was tracked. The intervention reduced the number and severity of patients' risk factors and was successful in preventing patients' first delirium episode.

Potential for Harm

None noted.

Costs of Implementation

The only recent estimate of cost per case of delirium prevented was $6341 in a delirium prevention trial,[12] which is less than the cost associated with prevention of other hospital complications such as falls. A further analysis of the same patients reveals that the multicomponent strategy is cost-effective for those at intermediate risk of delirium, but not for those at highest risk.[36]

Comment

The literature for delirium prevention studies is small, and the methodologic quality of many studies is poor. However, one high quality study[12] has demonstrated that multicomponent interventions can prevent incident delirium in hospitalized patients. The interventions have high face validity and are both feasible and transportable across institutions and hospital units, suggesting that implementation in different practice settings would be practical. Implementing a multicomponent intervention on a hospital-wide basis throughout the United States would require significant commitment from hospital staff. Programs such as the Hospital Elder Life Program[23] can be readily integrated into hospital practice and have been successful in preventing both cognitive and functional decline using targeted, practical interventions. Others of these practices could be incorporated by either support staff or trained volunteers, which may save resources and underscore the fact that many common sense interventions do not require a larger professional staff. Future studies should focus on refining the most effective multifactorial programs, determining the optimal combination of interventions, defining appropriate target populations based on delirium risk, demonstrating effectiveness across multiple clinical sites, and disseminating the most cost-effective practices.

Table 28.1. Six studies of delirium prevention*

Study	Study Setting	Interventions	Study Design Outcomes	Results†
Chatham, 1978[8]	20 surgical patients in a university affiliated hospital, 1977	• Family education • Patient education	Level 2, Level 1	Delirium symptoms rate: intervention resulted in improvement in 5 of 11 areas—orientation, appropriateness, confusion, delusions, and sleep ($p<0.05$ for each)
Inouye, 1999[12]	852 patients in a university hospital, 1995-1998	Targeted 6 risk factors: • Cognitive impairment • Immobility • Visual impairment • Hearing impairment • Dehydration • Sleep deprivation	Level 2, Level 1	Delirium rate: intervention 9.9%, control 15.0% (matched OR 0.60, 95% CI: 0.39-0.92); Episodes of delirium: intervention 62, control 90 ($p=0.03$); Total days with delirium: intervention 105, control 161 ($p=0.02$)
Nagley, 1986[30]	60 patients at a university affiliated hospital	16 interventions, including: • Orientation strategies • Providing sensory aides • Ambulation • Hydration measures • Nursing interaction	Level 2, Level 1	No significant difference in mental status scores between groups ($p>0.05$)
Owens, 1982[6]	64 surgical patients in a university hospital	• Patient education	Level 2, Level 1	Delirium symptoms rate: intervention 59%, control 78% ($p>0.05$)
Wanich, 1992[31]	235 patients in a university hospital, 1986-1987	• Nursing education • Caregiver education • Orientation strategies • Mobilization • Environmental modifications • Medication evaluation	Level 2, Level 1	Delirium rate: intervention 19%, control 22% ($p=0.61$)
Williams, 1985[32]	227 orthopedic patients in 4 hospitals	• Patient education • Orientation strategies • Providing sensory aides	Level 2, Level 1	Delirium symptoms rate: intervention 43.9%, control 51.5% ($p<0.05$)

* CI indicates confidence interval; OR, odds ratio.

† Delirium rate is the percentage of patients with one or more episodes of delirium.

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Chapter 29. Multidisciplinary Geriatric Consultation Services

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Background

Multidisciplinary geriatric consultation teams provide comprehensive assessment of physical, emotional, and functional status in older persons and make recommendations regarding prevention and management of common geriatric syndromes, functional impairments, and other problems. Teams vary in composition but usually include a geriatrician, nurse, social worker and other health professionals such as rehabilitative therapists, psychologists, and dieticians. Their expertise may improve the safety of hospitalized elders (or nursing home residents) by reducing hospital-acquired complications such as falls, delirium, functional decline, and "preventable" deaths. Consultation teams and inpatient geriatric evaluation and management (GEM) units share this multidisciplinary approach but differ in who controls the implementation of recommendations. A patient's primary physician decides whether to implement a consultation team's recommendations, whereas geriatric teams have direct control over implementation in GEM units. As this difference may impact effectiveness, GEM units are reviewed separately (Chapter 30). Multidisciplinary consultation services are available to elders living in the community, however this chapter reviews the evidence for geriatric consultation improving the safety of hospitalized patients or nursing home residents.

Practice Description

The structure of consultation teams, the types of evaluations they routinely perform, and the recommendations they make vary from institution to institution. A review of published studies reveals some common features. A team has at least one physician, a nurse practitioner or similarly professionally-trained provider, rehabilitative experts, and usually a social worker. Assessments typically include measures of mobility and functional status, mental status examinations, psychological screening, evaluation of common geriatric problems (eg, risk for falls, incontinence, and polypharmacy), and plans for rehabilitation and/or appropriate placement at the time of discharge. The team notes its recommendations in the hospital chart, communicates them to the physician directing care for the patient, and provides follow-up until the patient is discharged.

Prevalence and Severity of the Target Safety Problem

Patients aged 65 years and older account for almost half of inpatient hospitalization days.[1] In 1996, they comprised 13% of the population yet accounted for 38% of the approximately 31 million discharges from non-government, acute care hospitals.[2] The actual target population is smaller because, although all hospitalized elders are at risk for complications, some patients are unlikely to benefit from multidisciplinary geriatric consultation. Strategies to target geriatric services to those patients most likely to benefit have been reviewed in the literature.[3] The characteristics associated with potential benefit include advanced age (eg, over 75 years old), specific geriatric conditions (eg, falls or confusion), functional impairments

(eg, limitations in bathing, feeding, or transferring), and psychosocial impairments (depression or living alone).

As a patient safety practice, consultations may decrease the occurrence of iatrogenic complications such as functional decline related to hospitalization, delirium, and falls. Functional decline occurs in 25 to 60% of older persons after entering acute care, due to the interaction of a patient's existing co-morbidities with the hospital environment.[4] It results in worsened cognitive status and physical functioning due to the stressors of hospitalization (bedrest and immobility, medical procedures and pharmacotherapy, and the hospital environment) in older patients. For information on the prevalence and severity of falls and delirium, see Chapters 26 and 28, respectively.

Mortality is another important clinical outcome that may be affected. The number of deaths that might be prevented by implementation of this practice is unknown, although the most common medical diagnoses of patients enrolled in these consultation studies (cardiac, pulmonary, and gastrointestinal disorders) reflect the prevalent admitting medical diagnoses for all older patients. The in-hospital, all-cause mortality in the reviewed studies (approximately 5 to 15%) provides a context against which one can consider the potential for improvement if these practices influence mortality.

Opportunities for Impact

The number of hospitals with multidisciplinary geriatric consultation services is not reported in the literature. However, data from the American Hospital Association[5] indicate that fewer than half of hospitals offer comprehensive geriatric assessment.* Researchers in the field believe that even in those hospitals with consultation services, only a minority of the patients most likely to benefit are being referred. Thus, if the practice is effective, there is substantial opportunity for improvement by increasing its utilization in this vulnerable patient population.

Study Designs

A structured literature search identified 14 controlled trials: 12 randomized,[6-17] 1 alternate-allocation,[18] and 1 prospective cohort study[19] (see Table 29.1). Four of the 14 articles report different outcome measures from the same clinical trial.[6-9] One study focuses on nursing home residents;[14] all other studies were of hospitalized patients. Three of the studies were performed in Canada and one in the United Kingdom.[16-19] Two trials were limited to elderly patients with hip fractures.[15, 17] In the study by Fretwell et al, patients were admitted to a medical ward designated for seniors and staffed with specially trained nurses.[13] Because the team still functioned in a consultative role and could not implement its own recommendations, the study is included here rather in the chapter on GEM units (Chapter 30).

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* Of the 4953 acute medical/surgical hospitals in the American Hospital Association (AHA) database, 4398 (89%) responded to the AHA 1999 Annual Survey. Of responding hospitals, 1823 (41%) indicated availability of "geriatric services," which was defined as providing one or more of the following: comprehensive geriatric assessment, adult day care, Alzheimer's diagnostic-assessment services, geriatric acute care units, and/or geriatric clinics. A conservative, upper-limit estimate assuming all 555 non-responding hospitals have "geriatric services" would be 48%. As the survey does not ask the availability of each type of geriatric service, the percentage of hospitals offering inpatient comprehensive geriatric assessment based on the AHA Survey data can only be described as "less than 48%" (how much less is unknown).

Study Outcomes

Ten studies reported functional status outcomes, measured by the Katz[20] or Lawton[21] index of activities of daily living, or the Barthel Index.[22] Marcantonio et al[15] measured the occurrence and severity of delirium defined according to the Confusion Assessment Method criteria.[23] Ray and colleagues reported the proportion of recurrent fallers and the rate of injurious falls in nursing home patients during one year.[14] Becker et al measured 6 classes of hospital-acquired complications: medication-related, procedures, infections, trauma or injury (eg, falls and pressure sores), psychiatric, and other (eg, urinary retention, fecal impaction).[7] Eight trials reported all-cause mortality in-hospital, at 6 months, or at one year.[8,10-13,16,18,19] A recent meta-analysis[24] incorporated unpublished mortality data from several other studies[6,17] reviewed here. Other clinically relevant outcomes were changes in pharmacotherapy prescribed, length of hospital stay, and discharge location.

Evidence for Effectiveness of the Practice

Two non-blinded trials showed a statistically significant improvement in patients' functional ability.[17,18] Kennie et al targeted a population at high risk for functional decline during hospitalization: elderly women with hip fractures.[17] In the study by Hogan et al,[18] the difference was significant at one year but not at 3 or 6 months, suggesting that the intervention group's post-discharge follow-up by a geriatric team may have accounted for the difference rather than prevention of iatrogenic functional decline in-hospital. The study by Thomas and colleagues[12] showed a trend towards improved functional status. No other study reported improved functional outcomes.

The trial by Becker et al[7] showed no significant difference in the incidence of hospital-acquired complications between intervention and control groups. Two studies that targeted specific high-risk populations did show benefit.[14,15] In the study by Marcantonio et al, a multidisciplinary consultation including assessment and targeted recommendations per a structured protocol in 10 domains (including pain treatment, bowel/bladder function, nutrition, pain treatment, mobility, and environmental stimuli) resulted in a significant decrease in perioperative delirium in patients with hip fracture.[15] Ray et al enrolled nursing home residents 65+ years of age who had fallen in the previous year and had a possible problem in at least one of 4 safety domains: environmental safety, wheelchair use, psychotropic drug use, or mobility.[14] Patients who received care from the consultation team, including structured assessments and specific recommendations in these safety domains, experienced a significant reduction in the rate of recurrent falls (43.8% intervention group vs. 54.1% control group, p=0.03).[14]

The reported randomized clinical trials yielded mixed results for the outcome of all-cause mortality, with most studies demonstrating no benefit. The study by Thomas[12] reported a statistically significant improvement in mortality at 6 months, but Gayton et al[19] reported only a trend toward improvement at 6 months. Neither of Hogan's studies found in-hospital mortality benefits. One study[16] showed improved mortality at 4 months and one[18] at 6 months but these benefits were not sustained at one year. Hospital-acquired complications would be expected to reduce in-hospital or short-term mortality, so the survival benefit observed many months after hospitalization in these studies suggests that other carry-over effects (eg, improved medication regimens) or better post-discharge care may be influencing these results. According to a meta-analysis[24] the summary odds ratio for 6-month mortality in 8 of the studies cited[6,10,12,13,16-19] was 0.77 (95% CI: 0.62-0.96), but the effect on 12-month mortality was not statistically significant. The authors tested for heterogeneity of outcomes before pooling results of the trials (p=0.07). Of

note, the large trial (n=2353) by Reuben et al[11] was not eligible for inclusion in the meta-analysis because it was published later. Because it was larger than all other studies combined, its effect on the pooled estimate of 6-month mortality would be to reduce any statistically significant differences between intervention and study groups, since no survival advantage was reported at up to one year in the study (p=0.89 for survival curve).

Potential for Harm

No harm attributable to the geriatric consultation was reported in the trials.

Costs and Implementation

Implementation of the multidisciplinary team entails logistic planning to determine the number and type of consultative team members, and human resource coordination regarding time allocation and staffing. Few studies included data on costs of the practice, such as hospital costs incurred by assembly of the consultation team. Fretwell and colleagues,[13] however, have reported hospital charges in their study of 436 patients in a university-affiliated hospital. The percentage of patients exceeding DRG reimbursement for hospitalization was similar in both intervention and control groups, 69.7% and 71.2%, respectively. Winograd[25] reported that the cost of screening about 1200 patients to identify suitable candidates for consultation (using predefined criteria discussed in the paper) could be accomplished by employing a trained employee working one-quarter time, at a cost (in 1998 dollars) of about $7000 over the course of one year.

Comment

Inpatient geriatric consultation may have an impact on care for the hospitalized older patient, but the potential improvement in patient-safety outcomes is unclear. All-cause mortality differences may be due to differences in patient selection, and the data for improvement in functional outcomes suggests that certain patients may experience greater benefit than others. Appropriate targeting of services to patients at high risk for adverse outcomes such as falls and delirium seems to result in benefit. Consequently, multidisciplinary geriatric consultation and other efforts directed towards preventing iatrogenic functional decline, the most common complication of older hospitalized patients, deserve careful attention.

Identified problems in the reviewed studies include inadequate targeting of individuals who would most benefit from the intervention, potential between-group cross-contamination, and differences in local expertise in carrying out recommended interventions. Lack of effectiveness in some studies may reflect poor compliance with team suggestions or inadequate staffing to implement a consultant's recommendations, regardless of desire to comply. Lack of control over the direct management of the patient could also represent a serious shortcoming that limits effectiveness of this practice.

Multidisciplinary geriatric consultative teams, in contrast to specialized geriatric evaluation and management (GEM) units, provide expertise in geriatric care throughout a hospital, but in a consultative role. In comparing this strategy with GEM units or Acute Care for Elders (ACE) units, several differences should be noted. Multidisciplinary teams are less expensive to organize and can be implemented within a shorter period of time. Since older patients reside throughout an institution, there is also greater opportunity to reach a larger number of patients when the consultation team is not single-unit based. There is no bed limit, and the capacity of the team to provide interventions is therefore limited by their available time rather than the number of beds in any one unit. The resources required to assemble an

experienced geriatric team in a hospital that has no pre-existing geriatric expertise remains an important consideration. In addition, costs associated with enhancing and monitoring adherence with recommendations should be included when designing an effective program. Physical redesign of the unit environments to accommodate special needs (eg, special flooring, bed layout, reorienting devices) is likewise not part of this practice. Specially trained geriatric nurses are also not available equally throughout the hospital, in contrast to designated geriatric inpatient units, which have nurses focused exclusively on care of the older patient.

Notwithstanding these considerations, the practice of multidisciplinary geriatric consultation services has high face validity. More research is needed to evaluate which patients might receive maximal benefit for the associated resource commitment. Other areas for further research include examining the problems most appropriate for geriatric assessment and consultation in the hospital, developing strategies to improve adherence to and execution of recommendations, and identifying the components of a successful and cost-effective consultation team.

Table 29.1. Studies of multidisciplinary geriatric consultation services

Study	Setting and Participants	Study Design, Outcomes	Results
Allen, 1998[6] Becker, 1987[7] Saltz, 1988[8] McVey, 1989[9]	185 patients at a VA hospital, 1983-1984	Level 1, Level 1	No significant differences in hospital-acquired complications (overall 38% for both groups) No statistically significant improvement in functional status (activities of daily living) No statistically significant differences in rehospitalization or placement Compliance with recommendations: 71.7% overall (from 47-95% for selected interventions)
Fretwell, 1990[13]	436 patients at a university-affiliated hospital, 1985-1987	Level 1, Level 1	No significant difference in mortality at discharge No significant differences in length of stay, physical or cognitive function, or hospital charges
Gayton, 1982[19]	222 patients at a Canadian university-affiliated hospital, 1982-1984	Level 2, Level 1	No significant mortality difference up to 6 months follow-up, but trend favoring intervention group No significant differences in functional status, length of stay, or mental status between study groups
Hogan, 1987[16]	113 patients at a Canadian tertiary care hospital, 1984	Level 1, Level 1	Mortality at 4 months lower in the intervention group ($p<0.05$), but not at 12 months Fewer medications on discharge ($p<0.05$) and improved mental status ($p<0.01$) in the intervention group
Hogan, 1990[18]	132 patients at a Canadian hospital, 1985	Level 1, Level 1	Decreased 6-month mortality in the intervention group ($p<0.01$) No significant difference in outcomes at discharge Improved functional ability at one year but not at 3 or 6 months in the intervention group
Kennie, 1988[17]	144 orthopedic patients at a U.K. district hospital, year not stated	Level 1, Level 1	Intervention patients more functionally independent ($p=0.005$) at discharge and were discharged to home at higher rates ($p=0.03$)

Marcantonio, 2001[15]	126 orthopedic patients at an academic medical center, year not stated	Level 1, Level 1	Occurrence of delirium: 32% vs. 50% in control group (p=0.04) Adherence to recommendations: 77%
Ray, 1997[14]	482 residents in 14 nursing homes, 1993-1995	Level 1, Level 1	Lower rate of recurrent falls: 19% vs. 54% in control group (p=0.03) Trend toward lower mean rate of injurious falls
Reuben, 1995[11]	2353 patients at 4 HMO-run hospitals, 1991-1994	Level 1, Level 1	No statistically significant differences in mortality at up to one-year follow-up No significant change in functional status at 3 or 12 months
Thomas, 1993[12]	120 patients at a community hospital, year not stated	Level 1, Level 1	Reduced 6-month mortality: 6% vs. 21% controls (p=0.01) Trend toward improved functional status in the intervention group Hospital readmission in 6-months significantly lower in the intervention group
Winograd, 1993[10]	197 men at a VA hospital, 1985-1989	Level 1, Level 1	No significant mortality differences between groups No significant change in physical function, length of stay, or placement between groups Compliance with all recommendations: 67%

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Chapter 30. Geriatric Evaluation and Management Units for Hospitalized Patients

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Background

Inpatient care of elders with multiple co-morbidities requires close attention to the special needs and geriatric syndromes that arise in this vulnerable population.[1,2] One strategy to address the risks of hospitalization is to provide care by a multidisciplinary team in a dedicated geriatric unit, principally *Geriatric Evaluation and Management (GEM) Units*. This model of care, in many ways similar to coordinated stroke units,[3] may improve mortality and other clinically relevant outcomes compared with outcomes achieved on a general medical ward. An alternative strategy, reviewed elsewhere in this Report, is the comprehensive geriatric consultation service, analogous to a typical medical consultation team (see Chapter 29).

In a GEM unit, a multidisciplinary team provides comprehensive geriatric assessment, detailed treatment plans, and attention to the rehabilitative needs of older patients. A typical team is composed of a geriatrician, clinical nurse specialist, social worker, and specialists from such fields as occupational and physical therapy, nutrition, pharmacy, audiology, and psychology. GEM units are typically separate hospital wards that have been redesigned to facilitate care of the geriatric patient. Multidisciplinary team rounds and patient-centered team conferences are hallmarks of care on these units, which, in contrast to geriatric consultation services, have direct control over the implementation of team recommendations.

Practice Description

In all the studies reviewed in this chapter, the GEM unit team included a physician experienced in geriatric medicine, skilled geriatric nurses and rehabilitation specialists. (The latter may not have been on site but were accessible). The teams completed multidimensional geriatric assessments, conducted interdisciplinary team rounds, and provided comprehensive discharge planning. Units were physically separate wards that were designed to facilitate geriatric care. *Acute Care of Elders (ACE) Units*[4] incorporate the GEM unit design with additional enhancements and admit patients with acute illnesses. ACE units often provide improved flooring and lighting, reorienting devices, and other environmental improvements such as common rooms for patient use. For example, in the ACE unit studied by Landefeld and colleagues[5] the GEM unit concept was enhanced by the use of more nurse-initiated protocols and a greater number of environmental and design modifications.

Both styles of unit emphasize the early assessment of risk factors for iatrogenic complications and the prevention of functional decline.[4,6] Studies of both are included in this chapter.

Prevalence and Severity of the Target Safety Problem

One-third of hospitalized patients are aged 65 years and older. In 1996, although comprising only 13% of the US population they accounted for 38% of the approximately 31 million discharges from non-government, acute care hospitals.[7] Since all hospitalized older patients are potentially at risk, the target population is quite large. Appropriate selection of patients who are at risk for hospital-related complications and who are likely to receive benefit from this practice, however, would decrease this number.[8]

The target safety problems are preventable deaths and hospital-related functional decline in older persons. The number of deaths that could be prevented if the practice were to be widely implemented is unknown. On the other hand, since hospital-related functional decline occurs in 25 to 60% of older hospitalized patients, there is substantial opportunity to improve clinical outcomes.[9] Other clinical problems explicitly studied in controlled trials include cognitive status and nursing home placement.

Opportunities for Impact

Data from the American Hospital Association (AHA)[10] indicate that fewer than half of hospitals providing care for the elderly have geriatric acute care units or offer comprehensive geriatric assessment. (see footnote in Chapter 29). Researchers in the field believe the number is increasing. The Department of Veterans Affairs reports that in 1997 there were 110 active GEM units, although some concentrate solely on outpatient assessment.[11] A recent national survey[12] identified at least 15 active ACE units, with average daily censuses ranging from 5 to 25 patients. Depending on the screening and targeting criteria used to identify eligible patients, the potential for impact could be quite large and raises the question of the physical and manpower capacity of these units to meet the apparent demand.

Study Designs

A structured literature search identified a systematic review[13] that included 6 studies (4 randomized controlled trials,[14-17] one retrospective cohort study with historical controls,[18] and one published abstract of a randomized controlled trial[19]). We also identified 2 randomized controlled trials of ACE units[5,20] that were published later (see Table 30.1). All of the cited studies were single center in design. Five of the studies[5,14,16,17,20] provided sufficient data to evaluate the baseline level of function of enrolled patients.

Study Outcomes

All-cause mortality was reported in each study. For this outcome, most patients were followed 6 or more months after hospitalization. Other clinically important outcomes measured in some studies were functional status,[5,14,16,17,20] cognitive status,[14,16,17] length of stay,[5,14-16,18,20] and discharge rates to institutional settings.[5,14-20]

Evidence for Effectiveness of the Practice

In some studies mortality during hospitalization, at 3 months, or at 6 months was reduced in the intervention group but the differences failed to achieve statistical significance. A meta-analysis[13] of 6 studies[14-19] found the summary odds ratio for 6-month mortality was 0.65 (95% CI: 0.46-0.91), using both published and unpublished data from the included trials. Tests for heterogeneity across studies were reported with $p<0.10$ for the pooled analyses.

Cognitive function, as measured by the Kahn-Goldfarb Mental Status Questionnaire,[21] showed no statistical improvement over the course of one study,[17] nor did 2 other studies[14,16] demonstrate improvement, using the Mini-Mental State Examination[22] to assess mental status. Two trials of ACE units examined functional status, using the basic activities of daily living (ADL).[23] Landefeld et al[5] reported statistically significant improvements, while Counsell et al[20] found benefit in a composite outcome of ADL improvement and nursing home placement, but not in discharge ADL levels alone. Two other studies also demonstrated statistically improved functional status in the six months after randomization[14] and at 12 months follow-up.[17]

In individual studies, GEM units were associated with a higher likelihood of home residence, rather than in an institutional setting (skilled nursing facility or nursing home).[5,14, 17] The meta-analysis by Stuck et al calculated a combined odds ratio that revealed a statistically significant increase in patients discharged from GEM units who were living at home at 6 months (summary odds ratio 1.80, 95% CI: 1.28-2.53) and 12 months (summary odds ratio 1.68, 95% CI: 1.17-2.41) thereafter.[13] ACE unit trials in a community hospital[20] and a university hospital[5] were also both successful in decreasing patient placement in institutional settings and would likely have strengthened the summary estimate if included. Extrapolating their study findings to the US population, Rubenstein and colleagues[17] estimated that approximately 200,000 nursing home admissions per year could be avoided using their geriatric evaluation unit approach. Winograd noted that this multidisciplinary practice would potentially be more effective if target populations were better identified and enrolled using specific criteria.[8]

Potential for Harm

No data suggest that GEM units were associated with harm.

Costs and Implementation

Implementation of the practice requires construction or redesign of hospital ward(s) to create a suitable environment, training or recruiting experienced staff, establishing selection criteria to determine patient eligibility, and implementing a continuous evaluation process to assess clinical and non-clinical outcomes.

A working group has recommended including costs as an important outcome measure in future studies of GEM units.[24] Applegate and colleagues reported in a later analysis[25] of their randomized controlled trial[14] that the increased costs associated with their intervention study were not balanced by savings in subsequent health care spending, but if charges were adjusted for days spent at home (versus in long-term care) the charges were similar. Lower direct costs were demonstrated by one intervention study,[17] particularly after adjusting for differences in survival (mean institutional-care costs per year survived, $22,597 for intervention patients vs. $27,826 for control-group patients). The study by Landefeld et al[5] reported mean hospital charges of $10,289 for intervention patients compared with $12,412 for control patients, with similar median charges (p=0.3). Additional costs of about $75,000 attributable to staffing and physical redesign of the unit resulted in a cost of about $230 per patient in the intervention group. Counsell et al,[20] in a recent large randomized trial of an ACE intervention, reported no difference in hospital costs for patients in the intervention group compared with the usual care group ($5640 vs. $5754, respectively; p=0.68). Included in the costs was $28 per hospital day per intervention patient, representing costs of the geriatric nurse specialist, unit medical director, and unit renovations ($300,000).

Comment

Reasonable evidence supports the use of GEM units, despite varying findings across individual studies with respect to their effectiveness at preventing outcomes such as mortality. Nonetheless, mortality appears to be improved after pooling results of smaller trials. There is good evidence that this model of care decreases nursing home placements, which in itself is a noteworthy finding. Furthermore, the intervention costs may not be significantly higher in these specialized units. The generalizability of the practice requires further examination, and the need for multicenter studies, as advocated by a previous consensus group,[26] has thus far not been undertaken.

Limitations of this practice compared with multidisciplinary geriatric consultation teams (Chapter 29) include limited bed availability in most units, decreased transferability of geriatric practices throughout a hospital, and a larger resource commitment compared with a hospital-wide consultation team. The advantages of the GEM and ACE unit model are direct control over implementation of clinical recommendations, the presence of dedicated geriatric nursing and rehabilitative staff associated with the unit, and the beneficial effects of a ward designed to address older patients' needs. In sum, the practice of a dedicated GEM or ACE unit carries much promise.

Table 30.1. Randomized Controlled Trials of Geriatric Evaluation and Management Units*

Study	Study Setting	Study Design	All-Cause Mortality and Other Outcomes†
Stuck, 1993[13]	6 studies (published 1983-1991) in the US, UK, Australia, and Canada, involving 1090 patients (meta-analysis of Refs. 14-19)	Level 1A	6-month mortality: summary odds ratio 0.65 (95% CI: 0.46-0.91); 12-month mortality: summary odds ratio 0.77 (95% CI: 0.56-1.06)
Applegate, 1990[14]	155 patients in a university-affiliated community hospital, 1985-1987	Level 1	6-month mortality: 10% vs. 21% (p=NS); After 6 months: greatest difference p=0.08 by log-rank test; Improvement in ADLs: 3 of 8 ADLs better in intervention group (p<0.05)
Counsell, 2000[20]	1531 patients in a community hospital, 1994-1997	Level 1	Inpatient mortality: 3% vs. 4% (p=0.30); Length of stay: no significant difference; Long-term placement or decline in ADLs At discharge: 34% vs. 40% (p=0.027); At 12 months: percentages not reported (p=0.022)
Gilchrist, 1998[15]	222 women on an orthopedic-geriatric service in the UK, 1984-1986	Level 1	Inpatient mortality: 4% vs. 10% (p=0.06); 6-month mortality: 14% vs. 18% (p>0.1)
Harris, 1991[16]	267 patients in an Australian hospital, 1985-1986	Level 1	Inpatient mortality: estimated from Figure 1 in paper, 8% vs. 6% (p=NS); 12-month mortality: 23% vs. 29% (p=NS)
Landefeld, 1995[5]	651 patients in a university-affiliated hospital, 1990-1992	Level 1	Inpatient mortality: 7% in both groups (p=NS); 3-month mortality: 14% vs. 13% (p=NS); Improvement in ADLs at discharge: 34% vs. 24% (p=0.009); Discharged to nursing home: 14% vs. 22% (p=0.01)
Powell, 1990[19]	203 patients in two Canadian teaching hospitals, year not stated	Level 1	Mortality: lower in intervention group; timing not stated (p not stated); Transferred to long-term care: fewer in intervention group (p not stated)

Rubenstein, 1984[17]	123 patients in a VA hospital, 1980-1982	Level 1	Inpatient mortality: 14.3% vs. 15.0% (p=NS); 12-month mortality: 23.8% vs. 48.3% (p<0.005) 12-month improvement in basic functional status: 48.4% vs. 25.4% (p<0.01) 12-month improvement in mental status: 35.6% vs. 22.4% (p=NS)
Teasdale, 1983[18]	124 patients in a VA hospital, 1981-1982	Level 3	Inpatient mortality: 12% vs. 14% (p=NS); 6-month mortality: 28% vs. 35% (p=NS)

* ADL indicates activities of daily living; NS, not statistically significant.
† Comparisons are reported as intervention group vs. control group.

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Section E. General Clinical Topics

Chapter 31. Prevention of Venous Thromboembolism

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Background

Venous thromboembolism (VTE) refers to occlusion within the venous system. It includes deep vein thrombosis (DVT), typically of the lower extremities, and embolism to the pulmonary vasculature. Distal DVT is occlusion confined to the deep calf veins, while thrombosis at or above the popliteal vein is considered proximal DVT. A distal DVT becomes clinically important if it extends proximally, where the chance of pulmonary embolization (PE) is clinically significant.

In hospitalized patients, VTE occurs with relatively high frequency. A patient's risk of VTE varies depending on multiple factors including age, medical condition, type of surgery, duration of immobilization, and the presence of an underlying hypercoagulable state such as malignancy. Measures to prevent VTE have been widely studied for many reasons, including VTE's high incidence, its associated mortality and morbidity, its cost of treatment, and its treatment-related complications.

VTE is often clinically silent. As a result, studies evaluating the efficacy of preventive measures generally screen patients who are asymptomatic. As widespread screening is not recommended in general practice, the incidence of VTE in most studies appears higher than that encountered in clinical practice. The importance of clinically undetected VTE is not fully understood.

Practice Description

Both mechanical and pharmacologic interventions have been evaluated for prevention of VTE (Table 31.1). Mechanical devices include graduated elastic stockings (ES) and intermittent pneumatic compression (IPC); pharmacologic measures include low dose unfractionated heparin (LDUH), low molecular weight heparin (LMWH), warfarin, and aspirin .

Prevalence and Severity of the Target Safety Problems

There are over 23 million surgeries performed each year in the United States.[1] The frequency of DVT and PE varies by type of procedure and specific patient risk factors, as set forth below. In general, without prophylaxis DVT occurs after approximately 20% of all major surgical procedures and PE in 1-2%. Over 50% of major orthopedic procedures are complicated by DVT and up to 30% by PE if prophylactic treatment is not instituted.[2]

In addition, of the more than 31 million patients admitted each year for medical conditions, up to 16% of patients will develop DVT in the absence of prophylaxis.[1,2]

Opportunities for Impact

Despite the frequency with which VTE occurs in hospitalized patients, and the well-established efficacy and safety of preventative measures, prophylaxis is often underused or used inappropriately. One survey of general surgeons found that 14% did not use VTE prophylaxis.[3] Another survey of orthopedic surgeons found that only 55% placed all hip fracture patients on VTE prophylaxis, and 12% never used prophylaxis.[4] When performing total hip replacement (THR) and total knee replacement (TKR), 81-84% of surgeons placed all patients on prophylaxis, and 3-5% used no prophylaxis. Taken together, these data imply that VTE prophylaxis is used in 92% of THR patients, 89% of TKR patients, and 73% of hip fracture repairs. For spinal procedures, 21-38% of surgeons used prophylaxis with all patients, while 46-64% did not use prophylaxis with any patients, an overall rate of prophylaxis of 25-44%.[4] A more recent chart review of Medicare patients over age 65 undergoing major abdominothoracic surgery from 20 Oklahoma hospitals found that only 38% of patients were given VTE prophylaxis.[5] Of patients considered at very high risk for VTE, the same percentage received some form of prophylaxis, but only 66% of those received appropriate preventive measures.[5]

Another chart review of high-risk patients at 10 acute care US hospitals found that some type of VTE prophylaxis was used in 94% of orthopedic patients and 75% of abdominal surgery patients.[6] However, the 1995 American College of Chest Physician grade A recommendations[7] (those therapies supported by the most rigorously designed studies) were followed in only 84% of THRs, 76% of TKRs, 45% of hip fracture repairs, and 50% of abdominal surgery patients. Compliance with grade A recommendations was no better in the 3 hospitals that had critical pathways, pocket guides, or a policy for VTE prophylaxis.[6]

Inadequate VTE prophylaxis among medical patients may be even more prevalent. In one study, only 33% of patients admitted to a medical intensive care unit received VTE prophylaxis. Eighty-seven percent of these patients had one risk factor, and over 50% had multiple risks for VTE.[8] Another study found that of patients who developed VTE during admission or within 30 days of discharge, 48% had not received prophylaxis during hospitalization. Most of these were medical patients.[9]

Study Designs and Outcomes

There are a large number of randomized control trials (RCTs) and high quality meta-analyses that examine the efficacy of VTE prophylaxis. Most studies considered surgical rather than medical patients. Several differences in study design may account for heterogeneity among these studies, including differences in patients or procedures, the intervention (type, duration, or dose of prophylaxis), the method used to diagnosis VTE, the outcome measured (distal or proximal DVT, fatal or nonfatal PE), and whether the endpoint was a clinical event or one found by routine screening.

The "gold standard" for diagnosis of DVT is contrast venography, which is generally used in studies screening high-risk patients. Venography may detect a significant number of clots that are not clinically important, and is often technically limited.[10] Other common screening methods are fibrinogen leg scanning (fibrinogen uptake test, FUT) and duplex ultrasonography, both of which have low sensitivity for calf vein thrombosis.[11,12] Meta-analysis of studies using the FUT in orthopedic patients showed a sensitivity of 55% for calf vein thrombosis and 45% for all DVT, with a specificity of 92%.[11] For detection of calf vein thrombosis, duplex ultrasonography had a sensitivity and specificity of 39% and 98% in symptomatic hospitalized patients, and of 13% and 92% in patients undergoing arthroplasty.[12] In studies of general surgery

patients, the incidence of DVT was 25% when diagnosis was made by FUT, and 19% when confirmed by venogram.[2] However, in trials of VTE prophylaxis using elastic stockings in neurosurgical patients, the study using FUT found a DVT rate of 9%, while 3 others using venography found the rate of DVT to be 28%.[2]

In many studies, all patients are screened for DVT, although several studies only tested for DVT if clinical signs or symptoms occurred. Clearly, in the latter a number of DVT are missed; however, the clinical importance of these asymptomatic clots is unknown.

The gold standard for diagnosis of pulmonary embolus is pulmonary angiography. However, reliable evidence confirms that combining clinical probability with results of ventilation-perfusion scanning is an accurate and less invasive method of making this diagnosis.[13] Most studies report the incidence of symptomatic or fatal PE. Studies rarely screen for PE in asymptomatic patients. Silent pulmonary embolism may occur in up to 50% of patients with proximal DVT, however, the clinical importance of these emboli is unclear.[14]

Evidence for Effectiveness of the Practice

Studies of VTE prophylaxis are best grouped by the population at risk (Table 31.2). The sections that follow describe the prevalence of thromboembolism in patients in each category and discuss the efficacy of various prophylactic strategies.

General Surgery

For general surgery patients not receiving VTE prophylaxis, the incidence of DVT confirmed by venogram is 19%. Proximal DVT occurs in 7% of patients, PE in 1.6%, and fatal PE in 0.9%.[2]

In general surgery patients, the risk of VTE is highest in those undergoing major surgery who are over the age of 40 and have an underlying hypercoagulable state, prior VTE, or cancer. (Patients with spinal cord injury, trauma, and those undergoing hip or knee arthroplasty or hip fracture surgery also fall in this risk group and are discussed separately below). Incidence rates for patients in this "very high" risk group are as follows: calf DVT, up to 80%; proximal DVT, 20%; PE, 10%; and up to 5% may suffer a fatal PE if no prophylaxis is provided.[2] The risk of VTE is lowest in those surgical patients who are young, otherwise healthy, and whose surgeries are "minor." Such patients have incident rates as follows: calf DVT, 2%; proximal DVT, 0.4%, PE , 0.2%; and fatal PE , 0.002%.

Numerous studies show that both LDUH and LMWH reduce the risk of proximal DVT, PE, and fatal PE in patients undergoing general surgery. Pooled results from 46 randomized trials show that prophylaxis of general surgical patients with LDUH compared with placebo reduced the risk of DVT (diagnosed by FUT or FUT confirmed with venography) by 68%, (from 25% [95% CI: 24-27%] to 8% [95% CI: 7-8%]).[2] LMWH has comparable efficacy to LDUH for prevention of VTE, and may be more effective for preventing proximal DVT and PE.[2,15,16] Pooled results (though heterogeneity was present) from 26 studies showed that high dose LMWH (>3400 anti-Xa units) does not reduce DVT more than low dose LMWH does ($\leq$3400 anti-Xa units), but it does increase wound hematomas.[16] Both IPC and ES significantly reduce overall incidence of DVT, but have not been shown to diminish the incidence of proximal DVT or PE in general surgical patients.[17-20]

Orthopedic Patients

All studies included in the evaluation of prophylaxis for orthopedic patients used venography to diagnose DVT.

Total Hip Replacement

Within 7-14 days after total hip replacement (THR), patients not receiving prophylaxis have an incidence of total and proximal DVT of 54% and 25%, respectively. Asymptomatic PE may occur in 5-15%, symptomatic PE in 1-2%, and fatal PE in 0.1-0.4%.[2,21] In patients undergoing THR, many RCTs have shown that both mechanical and pharmacologic measures are highly effective in the prevention of VTE.

A meta-analysis of 52 RCTs showed that patients receiving prophylaxis with LMWH, LDUH, warfarin, aspirin or IPC had fewer total DVTs (proximal plus distal).[21] IPC and ES reduce distal DVT but do not significantly reduce proximal DVT in these patients.[2,17] Compared with placebo, prophylaxis with warfarin or LMWH resulted in the greatest reduction in proximal DVT: a reduction of 70-80% with either method (risk of proximal DVT with warfarin 5-6%, RR 6.3% [95% CI: 4.7-8.4%]; with LMWH 6–8%, RR 7.7% [95% CI: 5.7-10.3%]).[2,21] Both LMWH and warfarin resulted in significantly fewer proximal DVTs compared with LDUH or IPC ($p<0.006$ for each comparison).[21] Pooled data from 5 trials that directly compared LMWH with warfarin showed rates of proximal DVT of 3.4% and 4.8%, respectively.[2]

Following THR, symptomatic PE occurs significantly less frequently with warfarin (0.16%, 95% CI: 0.002-0.59) and LMWH (0.36%, 95% CI: 0.22-0.57) than with placebo (1.51%, 95% CI: 0.81-2.57). IPC, LDUH and aspirin do not reduce the risk of symptomatic PE more than placebo. Fatal PE did not occur in any control patients in these trials, and occurred in only 0.04-0.16% of those receiving prophylaxis with LMWH or warfarin.[21]

Recombinant hirudin, not approved in the United States for VTE prophylaxis, was found more effective than LDUH or LMWH in reducing VTE in 3 trials of patients undergoing THR. Bleeding did not increase.[2]

Hip Fracture Repair

Surgery for hip fracture carries a risk of DVT comparable to THR, however, the incidence of PE is higher, with fatal PE occurring in 4-12% of patients.[2] As with hip replacement surgery, LMWH and warfarin are the most effective agents for VTE prophylaxis for patients undergoing hip fracture repair.[2] In a trial of over 13,000 hip fracture patients, aspirin significantly reduced the risk of VTE, but with an absolute reduction of only 0.5% and a greater increase in adverse events, particularly major bleeds.[22] LDUH has been less well studied.

Total Knee Replacement

Compared to THR, knee replacement surgery carries a higher overall risk of DVT, but lower risk of proximal DVT, with a prevalence of approximately 64% and 15%, respectively. Total DVT and PE occur with the following frequencies in patients receiving prophylaxis: aspirin, 53% and 12%; warfarin, 45% and 8%; and IPC, 17% and 6%. DVT occurs in 29% of those treated with LMWH.[23] While IPC reduces total DVT compared to aspirin and warfarin, it does not significantly reduce proximal DVT.[2,23]

LMWH is the most effective method to prevent proximal DVT in patients undergoing TKR. Data from 13 trials with 1740 patients show a 63% decreased risk of proximal DVT with LMWH compared with placebo, 6% (95% CI: 5%-7%) vs. 15% (95% CI: 10%-23%).[2] Pooled

data show that aspirin (6 studies, 443 patients), warfarin (9 studies, 1294 patients), and LDUH (2 studies, 172 patients) do not significantly reduce proximal DVT following TKR.[2] Patients given warfarin prophylaxis who were routinely screened with venography had an 8–12% risk of proximal DVT. However, one study that followed patients for 3 months following TKR found that patients who received warfarin had a rate of *symptomatic* VTE of only 0.8%.[24]

The incidence of PE is low in TKR patients. Studies in which PE was diagnosed by lung scan or angiography showed the rate of symptomatic and asymptomatic PE in patients treated with aspirin to be 1.3% and 11.7%, respectively, with warfarin 0.4% and 8.2%, and with IPC 0.5% and 6.3%. Symptomatic PE occurred in none of 177 patients receiving LMWH. No studies of LMWH used routine lung scanning.[23]

Initiation of Therapy

Meta-analysis of patients undergoing THR found that LMWH initiated preoperatively resulted in a lower risk of VTE than LMWH started postoperatively (10% vs. 15%, p=0.02).[25] Major bleeding occurred less frequently in the group receiving preoperative LMWH (0.9% vs. 3.5%, p=0.01).

Duration of Therapy

The appropriate duration of VTE prophylaxis following orthopedic surgery is not clearly established. However, it is clear that the increased risk of DVT persists post-discharge. In the largest randomized trial of post-discharge LMWH, 533 patients received either 35 days of dalteparin or 6 days of warfarin followed by placebo. Patients treated with extended LMWH had significantly fewer total and proximal DVTs from day 6 to day 35 (for all DVT, dalteparin 4.8% vs. placebo 10.5%, p=0.03; for proximal DVT, dalteparin 1% vs. placebo 4.8%, p=0.02), as well as from day 1 to day 35 (dalteparin 2.6% vs. warfarin/placebo 9.2%, p=0.002). Seventy five percent of these DVTs were asymptomatic. Symptomatic thrombi occurred in approximately 1-2%. No patient had symptomatic, objectively documented pulmonary embolism.[26] Pooled data from this study and 5 others that compared in-hospital LMWH followed by LMWH or placebo found that prolonged LMWH resulted in a 66% reduction in total DVT (14% vs. 27%) and a 66% reduction in proximal DVT (4% vs. 12%) by 35 days.[2]

Neurosurgery

Patients undergoing neurosurgical procedures carry a risk of developing DVT of approximately 22%, and a risk of proximal DVT of 5%.[2] The risk of DVT is increased in patients undergoing intracranial surgery compared to spinal surgery. Among patients undergoing intracranial surgery, those with malignant tumors have a higher risk of DVT than those with benign tumors. Increasing age and increasing duration of neurosurgery further increase the risk of VTE. Meta-analysis of randomized studies comparing LMWH to placebo (one study) or LMWH plus ES to ES alone (2 studies) in neurosurgical patients found that LMWH was associated with a 38% reduction in total DVT (18% vs. 28%, p<0.001). Results in the two studies evaluating proximal DVT found a 50% reduction with LMWH compared with placebo (6% vs. 12%, p=0.008). There was no increase in major bleeding. All studies used venography to assess DVT.[27] The one randomized trial using LDUH (5000 U every 8 hours) found an 82% reduction in all DVT (6% vs. 34%, p=0.005). In this trial, DVT was diagnosed with FUT.[28] Two meta-analyses evaluating IPC for VTE prophylaxis showed a 66% reduction in all DVT compared with untreated controls (7% vs. 18-22%, p<0.001).[2,17] Compared with placebo, IPC also significantly reduced proximal DVTs in neurosurgical patients (6% vs. 17%, p<0.001).[17]

Trauma

Trauma patients, especially those with orthopedic injuries, are at very high risk for VTE. DVT occurs in over 50% of these patients, proximal DVT in approximately 20%, and fatal PE in up to 2%.[2] Few randomized trials have studied VTE prophylaxis in trauma patients. Meta-analysis shows that VTE prophylaxis, either with LDUH (4 randomized trials, OR 0.97, 95% CI: 0.35-2.6 for LDUH vs. control) or ES (3 randomized trials, OR 0.77, 95% CI: 0.27-2.2), did not reduce DVT in trauma patients compared with placebo.[29] Heterogeneity was present for all comparisons due to differences in methods used to diagnose DVT and differences in trauma populations. Pooled data from 4 studies (2 randomized and 2 nonrandomized) of LDUH versus mechanical prophylaxis found no difference in risk of DVT (OR 1.16, 95% CI: 0.5-2.7).[29] One randomized trial comparing LDUH with LMWH in trauma patients screened with venography found that DVT was reduced by 30% with enoxaparin (31% vs. 44%, p=0.01).[30] Of the 265 patients randomized, only one patient (in the LMWH group) suffered a PE.

Acute Spinal Cord Injury

The risk of DVT (diagnosed by FUT or impedance plethysmography) in patients with acute spinal cord injury ranges from 40-90%.[2] The only trial using screening venography in patients with acute spinal cord injury who were not receiving prophylaxis found DVT in 81% and proximal DVT in 35%.[31]

Prophylaxis in acute spinal cord injury has not been well studied. In the only study evaluating use of IPC, proximal DVT occurred in 40% of patients with IPC alone, and in 25% of patients with IPC combined with aspirin and dipyridamole.[32] One randomized trial with 35 patients found that LMWH (tinzaparin 3500U daily) compared to LDUH (5000U three times a day) reduced DVT from 16% to 0%, a reduction that did not reach statistical significance.[33] However, a later prospective cohort study diagnosed DVT in 13% of 48 patients prophylactically treated with LMWH.[34] In both studies, screening for DVT was done with ultrasound or ultrasound plus impedance plethysmography, with confirmation by venography. Of 15 acute spinal cord injury patients from a randomized trial of major trauma patients, DVT was detected in 67% of those given LDUH and 50% with LMWH. Proximal DVT occurred in 13% receiving LDUH and none prophylaxed with LMWH.[30]

Medical Patients

VTE prevention in hospitalized medical patients has not been studied as extensively as in surgical patients. DVT occurs in 24% of patients with myocardial infarction, and is reduced by 71% with LDUH compared with placebo with no increase in bleeding (4 studies with 165 patients).[2] However, most patients with acute myocardial infarction receive full anticoagulation for treatment of the acute coronary syndrome.

After ischemic stroke, 55% of untreated patients develop DVT. Prophylaxis with either LDUH or LMWH given for 10-14 days reduces DVT by 56%, from 55% (95% CI: 49%-60%) to 24% (95% CI: 20%-29%). Two studies directly comparing LDUH (5000 U three times daily) to LMWH (enoxaparin 40 mg once daily), using venography for diagnosis, found greater reduction in DVT with LMWH.[2]

Among hospitalized patients with other medical conditions, the rate of DVT is approximately 16%.[2] A meta-analysis of studies of hospitalized patients with conditions other than myocardial infarction or ischemic stroke given VTE prophylaxis with unfractionated or low molecular weight heparin showed a 56% reduction in DVT (RR 0.44, 95% CI: 0.29-0.64) and a 52% reduction in PE (RR 0.48, 95% CI: 0.34-0.68). No significant difference was found between LMWH and LDUH in incidence of DVT, PE, or mortality; however, major hemorrhage was lower with LMWH than with LDUH (RR 0.48, 95% CI: 0.23-1.00).[35]

Another randomized trial comparing enoxaparin with placebo in 866 medical patients found a 63% reduction in overall VTE risk with enoxaparin (40 mg) compared with placebo in the first 14 days (5.5% vs. 15%, RR 0.37, 95% CI 0.22-0.63). Proximal DVT was reduced by 65% (1.7% vs. 4.9%, RR 0.40, 95% CI 0.23-0.69). Significant reductions in total and proximal DVT persisted at 110 days. VTE was not reduced in the group receiving 20 mg of enoxaparin. The most common medical conditions were acute infectious disease, acute respiratory failure, New York Heart Association Class III or IV congestive heart failure.[36]

The risk of VTE is higher in patients with malignant disease, especially those with adenocarcinoma or brain tumors. Factors associated with increased VTE in cancer patients include chemotherapy, surgery, and indwelling central venous catheters. Breast cancer patients treated with tamoxifen also have higher rates of VTE. In patients with indwelling central venous catheters who received low dose warfarin (1 mg per day), upper extremity DVT was reduced by 75% (9.5% vs. 37.5%).[37]

In summary, for general surgery patients who are at moderate risk or greater for VTE, LDUH and LMWH are the most effective methods for prophylaxis. IPC also provides effective DVT prevention, but in very high risk patients should only be used in conjunction with heparin. For orthopedic procedures, LMWH and warfarin are the most effective preventive measures. Neurosurgical patients should receive LMWH or LDUH, while in acute spinal cord injury or trauma, LMWH provides the largest reduction in VTE. For stroke or medical patients, LMWH and LDUH show the greatest benefit for VTE prevention (see Table 31.2).

Summary of Prophylaxis Recommendations

For general surgery patients at moderate to high risk, LDUH and LMWH have comparable effectiveness for prevention of VTE, with similar bleeding risks. LDUH is generally more cost-effective. For high risk patients, IPC has not been consistently shown to prevent proximal DVT (See Table 31.3).

For major orthopedic procedures (THR, TKR, hip fracture repair), prophylaxis with LMWH or warfarin results in the greatest benefit, with a small increase in bleeds compared with

no prophylaxis, but no difference between the two agents. Warfarin may be more cost-effective, but necessitates monitoring and dose adjustment. This should be considered in choosing between the two agents.

IPC, LMWH, and LDUH are all acceptable methods of prophylaxis for neurosurgical patients. Each effectively reduces proximal DVT with no increase in major bleeding. There are no data on cost-effectiveness of prophylaxis for these patients.

Data for prophylaxis of trauma patients does not show conclusive VTE reduction with any agent. However, the risk of VTE among these patients is high and prophylaxis should be considered, especially for those with orthopedic injuries. LMWH is a safe method of prophylaxis and has not been shown to increase major bleeds in blunt trauma patients. However if a patient is at high risk for major bleeding, IPC should be considered.

For medical patients, LDUH and LMWH are both effective for reducing VTE. LDUH may result in slightly more bleeding, but is more cost-effective. Patients at high risk for bleeding should be given prophylaxis with ES or IPC.

Potential for Harm

There is no documented risk associated with mechanical devices, although there is a potential risk that patients' legs will be examined less frequently. The major risk of pharmacologic prophylaxis is bleeding. Bleeding is typically considered major when the hemoglobin decreases by at least 2 g/dL, when red blood cell transfusion is necessary, when intracranial or retroperitoneal bleeding occurs, or when bleeding requires surgical intervention. Another consequence of heparin therapy may be thrombocytopenia.

For general surgery, there is no difference in the risk of major bleeding between LMWH and LDUH, although fewer minor bleeds may occur with LMWH (RR 0.64, 95% CI 0.58-0.70).[15] However, when evaluated according to dose of LMWH, compared with LDUH, low-dose LMWH (<3400 anti-Xa units) resulted in a significant decrease in wound hematomas, while high-dose LMWH carries a significant increase.[16]

Bleeding related to VTE prophylaxis is uncommon after orthopedic surgery. The greatest risk of bleeding occurs with LDUH (3.4% vs. 0.56% with placebo, RR 3.46, $p<0.0001$).[21] The risk of bleeding with LMWH is significantly greater than with placebo, but the absolute risk increase (ARI) is small (for TKR, 2.8% vs. 0.9%, ARI 1.7%; for THR, 1.2% vs. 0.9%, ARI 0.3%).[21] With warfarin, bleeding occurs in 0.5% of patients following THR.[2] Studies comparing LMWH to warfarin for THR found no difference in major bleeding.[21,26]

Among neurosurgical patients treated with LMWH, there was a two-fold increase in all bleeding compared with controls (6% vs. 3%, $p=0.02$), however, there was no significant difference in major bleeds.[27] Similar results were found in a study using LDUH.[28]

Blunt trauma patients who received enoxaparin 30mg q12h started within 24 hours of hospitalization had no bleeding events attributed to this treatment. This included patients with closed head injury, grade III liver injury, and grade IV splenic injury.[38]

Prophylaxis of medical patients with enoxaparin 40 mg/d did not increase the risk of bleeding compared to placebo. Of 711 patients treated with LMWH, there were no cases of severe thrombocytopenia (platelet count less than 50,000 per cubic millimeter).[36] Compared with LDUH, prophylaxis with LMWH results in fewer major bleeds (RR 0.48, 95% CI: 0.23-1.00).[35]

Costs and Implementation

A Swedish study evaluating general surgery patients at moderate risk for VTE and hip surgery patients found LDUH and LMWH were more cost-effective than no prophylaxis, and

LMWH was more cost-effective than LDUH.[39] An economic evaluation using decision analysis compared LDUH and LMWH for patients undergoing colorectal surgery. There was no difference in risk of VTE between groups. Per 1000 patients treated, prophylaxis with enoxaparin compared with LDUH resulted in 12 excess major bleeds and an additional cost of $145,667.[40] This supports LDUH as a more cost-effective measure for patients undergoing general surgery.

Meta-analysis of studies of the cost-effectiveness of VTE prophylaxis for patients undergoing hip arthroplasty found that with a 2.6 to 1 price ratio between LMWH and LDUH, use of LMWH would save the health care system approximately $50,000 per 1000 patients treated.[41] For VTE prophylaxis after TKR, LMWH was more cost-effective than warfarin, saving $2401 per 100 patients ($9197 vs. $11,598 per 100 patients).[42] This study was done in Canada, where LMWH is less costly than in the United States. Another meta-analysis of THR patients found that LDUH would decrease the cost of care related to DVT by $200 per patient. Compared with warfarin, LMWH would be more effective in preventing DVT (expected DVT rate 420/10,000 with warfarin and 250/10,000 with LMWH), and death from VTE (110/10,000 with warfarin and 70/10,000 with LMWH). However, preventing one death with LMWH use instead of warfarin would cost approximately $12,000.[43]

In medical patients, LDUH given 3 times daily was found to be more cost-effective than LMWH, with a savings per 1000 patients of $10,753 compared with enoxaparin 40 mg/d, and $15,000 compared with enoxaparin 20 mg/d.[44] The higher cost associated with enoxaparin 20 mg/d results from the higher incidence of complications with this regimen. This supports use of LDUH as the preferred method of prophylaxis for medical patients at the present time, though this is an area of active investigation. No studies were found evaluating the cost of DVT prophylaxis in neurosurgery patients.

Comment

As noted earlier, despite the clear evidence of effectiveness, DVT prophylaxis is underused. The reasons for this underuse have not been completely elucidated, nor have the optimal strategies for improving prophylaxis been fully identified. Various strategies have been tried in an effort to improve physician utilization of appropriate VTE prophylaxis. One hospital studied the impact of educational programs promoting guidelines for prophylaxis. It found that presentations to staff, distributions of cards with the hospital's guidelines, and posters increased prophylaxis of surgical patients from 59% to 70%, and to 77% for high-risk patients (see also Chapters 51 and 54).[45]

In another study, a computer-based clinical decision support system (CDSS) (see Chapter 53) providing information pertaining to VTE prophylaxis was used in an orthopedic surgery department of a teaching hospital. The investigators monitored the impact of CDSS use in 1971 patients undergoing orthopedic surgery. Compliance with guidelines was 83% during control periods and 95% during intervention periods. Inappropriate practice decisions occurred almost 4 times more frequently during control versus intervention periods.[46]

A third study evaluating methods to improve VTE prophylaxis among intensive care unit patients found that staff education improved use of appropriate prophylaxis from 38% to 62%. When required computerized order sets were added to education, appropriate prophylaxis increased to 97%.[47]

These studies suggest that either a knowledge gap or lack of awareness may exist among practitioners. For institutions or groups attempting to improve appropriate use of measures to prevent VTE, guidelines made available via computerized support systems or order sets provide

the most effective means of implementing appropriate VTE prophylaxis, especially when these systems are linked to effective educational programs.

Table 31.1. Mechanical and pharmacologic preventative measures for VTE

Practice	Type	Description	Comment
Graduated Elastic Stockings (ES)	Mechanical	Fitted hose that extend above the knee	Fitted hose are more efficacious than non-fitted
Intermittent pneumatic compression (IPC)	Mechanical	Devices fitted over lower extremities that sequentially inflate and deflate	
Aspirin	Pharmacologic	Usually 325 mg/d	
Warfarin	Pharmacologic	5-10 mg started the day of or after surgery; adjust to achieve an INR of 2-3	Monitoring of INR needed
Low-dose unfractionated heparin (LDUH)	Pharmacologic	Generally 5000 U subcutaneous bid or tid, though some studies have adjusted dose to maintain PTT at high end of normal	Contraindicated if active bleeding or history of thrombocytopenia; no need to follow coagulation studies (unless adjusted dose is used)
Low Molecular Weight Heparin (LMWH)	Pharmacologic	Dose depends on type of surgery and VTE risk*	No need to monitor coagulation studies

* LMWH dosing: Enoxaparin 20 mg SC daily (moderate risk surgery) or 40 mg SC daily (can go up to 30 mg SC q12h for high risk general surgery, major trauma or acute spinal cord injury); dalteparin 2500–5000 U SC daily; nadroparin 2500 U SC daily; tinzaparin 3500-4500 U SC daily (may be dosed 75U/kg/d for orthopedic surgery).

Table 31.2. Summary of DVT risk and prophylactic methods providing significant risk reduction*

Surgery/ Condition	Risk of all DVT in untreated patients	Type of Prophylaxis	Risk Reduction with Prophylaxis	Number of Studies
General Surgery[2]	25%	ES	44%	3
		LDUH	68%	47
		LMWH	76%	21
		IPC	88%	2
THR[2]	54%	LMWH	70%	30
		warfarin	59%	13
TKR[2,23]	64%	LMWH	52%	13
		IPC	73%	6
Neuro-surgery[27,28]	28%	LMWH	38%	3
		LDUH	72%	1†
Trauma[2,30]	30-60%	LMWH	30% (compared to LDUH)	1
Acute Spinal Cord Injury[2]	80%	Not established		
Ischemic stroke[2]	55%	LDUH	56%	5
		LMWH	58%	3
		Danaparoid	82%	4
Medical conditions[2]	16%	LMWH	76%	2†
			39%	2
		LDUH	61%	3†

* DVT indicates deep venous thrombosis; ES, graduated elastic stockings; IPC, intermittent pneumatic compression; LDUH, low-dose unfractionated heparin; LMWH, low molecular weight heparin; THR, total hip replacement; and TKR, total knee replacement.

† DVT diagnosed by fibrinogen uptake test (FUT)

Table 31.3. Recommended VTE prophylaxis for surgical procedures and medical conditions*

Surgery/Condition	Recommended Prophylaxis	Comments
General Surgery – low-risk: minor procedures, <40 years old, no additional risks	None	Early ambulation
General Surgery – moderate risk: minor procedure but with risk factor, nonmajor surgery age 40-60 with no risks, or major surgery <40 years with no risks	LDUH, LMWH, ES, or IPC	
General Surgery – high risk: nonmajor surgery over age 60 or over age 40 with risks.	LDUH, LMWH	
General Surgery – very high risk: major surgery over age 40 plus prior VTE, cancer or hypercoagulable state	LDUH or LMWH combined with ES or IPC	May consider postdischarge LMWH or perioperative warfarin
Elective Hip Replacement	LMWH or warfarin	May combine with ES or IPC; start LMWH 12 hours before surgery, 12-24 hours after surgery, or 4-6 hours after surgery at half the dose for initial dose. Start warfarin preoperatively or immediately after surgery, target INR 2.0-3.0.
Elective Knee Replacement	LMWH or warfarin	
Hip Fracture Surgery	LMWH or warfarin	
Neurosurgery	IPC, LDUH or LMWH	Start LMWH post-surgery
Trauma	LMWH with ES or IPC	If high risk of bleeding, may use ES and/or IPC alone.
Acute Spinal Cord Injury	LMWH	Continue LMWH during rehabilitation or convert to warfarin (target INR 2.5)
Ischemic Stroke	LDUH, LMWH, or danaparoid	If contraindication to anticoagulant, use ES or IPC.
Medical Conditions	LDUH or LWMH	

* Adapted with permission from Geerts WH, Heit JA, Clagett GP, Pineo GF, Colwell CW, Anderson FA, et al. Prevention of venous thromboembolism. Table: Regimens to prevent VTE, pp. 156S-158S. *Chest* 2001. Sixth ACCP Consensus Conference on Antithrombotic Therapy.[2] ES indicates graduated elastic stockings; INR, international normalized ratio; IPC, intermittent pneumatic compression; LDUH, low-dose unfractionated heparin; LMWH, low molecular weight heparin; and VTE, venous thromboembolism.

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Chapter 32. Prevention of Contrast-Induced Nephropathy

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Background

Radiocontrast-induced nephropathy (RCIN) represents an increasingly common cause of treatment-related renal failure[1-3] and increases mortality independent of other risk factors.[4] Major risk factors for RCIN include chronic renal insufficiency,[2,3,5] diabetes mellitus[2,3,5] (especially when accompanied by renal insufficiency[1]), any condition associated with decreased effective circulating volume,[6] and use of large doses of contrast media.[2,3,5,6]

For at-risk patients, clinicians must use their judgment to determine if imaging modalities that do not involve contrast media are an acceptable alternative to contrast studies. In many cases, however, such alternatives do not exist. Moreover, RCIN occurs in patients without obvious risk factors. Thus, strategies for reducing the incidence of RCIN include not just risk factor identification, but modification of these risk factors, choice of contrast media less likely to cause RCIN, and administration of therapeutic agents that further reduce the risk of RCIN.

Practice Description

The specific practices reviewed in this chapter are:

- *Use of high versus low osmolar iodinated contrast media to prevent RCIN.*[7]
- *Use of a standard intravenous or oral hydration protocol for patients with risk factors for RCIN.*[8-10] Typical intravenous protocols evaluated consist of normal saline administered at 75 mL/hr beginning at 12 hours before and ending 12 hours after the procedure. Oral protocols require ingestion of 1000 mL of water during the 10 hours prior to the procedure, followed by intravenous normal saline at 300 mL/h for 30-60 minutes and continued for a total of 6 hours after the procedure.
- *Use of a standard hydration protocol supplemented by pretreatment with theophylline*[11-15] (various doses and schedules)
- *Use of a standard hydration protocol supplemented by pretreatment with N-acetylcysteine*[16] (600 mg bid one day before and day of procedure)

Single studies evaluating atrial natriuretic peptide, prostaglandin E1[17] and captopril[18] were not reviewed, as the data are too preliminary, despite findings that suggest a reduction in the risk of RCIN. Although the evidence supporting the use of N-acetylcysteine largely comes from a single study as well, we do review this practice because the study was large, published in a prominent journal, and has received considerable attention among clinicians.[16]

The use of calcium channel blockers in preventing RCIN was not evaluated, as the existing literature predominantly indicates the practice is ineffective.[19-23]

Prevalence and Severity of the Target Safety Problem

While definitions of RCIN vary, most study definitions include a 25% increase in serum creatinine (SCr) and/or at least a 0.5 mg/dL increase in SCr within 48 hours of contrast administration. Using this definition, one large community-based study of 1826 patients undergoing invasive cardiac procedures reported a rate of RCIN of 14.5%.[2] A controlled prospective study of the onset of RCIN after contrast-enhanced brain CT found an incidence of 2.1% in low-risk patients without diabetes mellitus or chronic renal insufficiency versus 1.3% in a similar control group that did not receive any contrast (p=NS).[24] In comparison, patients in a prospective controlled study undertaken to determine the risk of nephrotoxicity from contrast radiography in patients with diabetes and renal insufficiency (SCr >1.7mg/dL) found a 9% incidence of RCIN.[1]

The cumulative effect of multiple risk factors increasing the risk of RCIN was demonstrated in one uncontrolled study that evaluated the effect of 5 factors (contrast volume >200 mL, albumin <3.5 g/L, diabetes, serum sodium <135 mmol/l, SCr>1.5 mg/dL).[3] When all risk factors were present the risk of RCIN was 100%, compared with just 1.2% when none were present. While most patients with RCIN suffer little morbidity and recover to near baseline renal function within 7-10 days (and thus we characterize it as a Level 2 outcome), rare patients require temporary dialysis. Two studies suggested that the development of RCIN may lead to longer lengths of stay[8,11] and one large retrospective study showed that hospitalized patients who develop RCIN had a mortality rate of 34% compared with 7% in control subjects, even after controlling for underlying co-morbidities.[4] The development of RCIN appeared to increase the risk of death from non-renal causes such as sepsis, bleeding, respiratory failure and delirium.

Opportunities for Impact

Few studies have rigorously evaluated current practice patterns among radiologists or cardiologists with respect to evaluation of a patient's threshold creatinine prior to ordering contrast procedures. One survey study of academic and private practice radiology departments found that only about 20% of practices routinely obtain serum creatinine levels before contrast administration.[25] Interestingly, when patients were known to have a high-risk condition like diabetes, approximately 60% of the same practices would require a serum creatinine before contrast administration. Therefore, many high-risk patients are not identified prior to undergoing contrast radiography studies. In addition, no studies have evaluated the frequency with which physicians recommend pre-hydration for patients prior to contrast studies. Overall, physicians and institutions do not follow a consistent practice in screening patients for risk factors for RCIN prior to the use of contrast radiography. If rigorous evidence identifies patients at risk for RCIN, and effective, standardized preventative measures are developed and implemented, there is substantial opportunity to reduce morbidity.

Study Designs

The literature on strategies for preventing RCIN includes: one meta-analysis evaluating the nephrotoxicity of high versus low-osmolality iodinated contrast media,[7] one randomized controlled study of pre-treatment with acetylcysteine[16] for high-risk patients, one randomized controlled trial of pre-treatment with prostaglandin E1[17] for high-risk patients, and 5 randomized controlled trials assessing the impact of theophylline[11-15] in preventing RCIN. Unfortunately, each of the studies of theophylline employed different routes and dosages (and, in fact, one of

the studies used aminophylline, rather than theophylline). Table 32.1 summarizes the salient features of these studies.

One randomized trial compared inpatient versus outpatient hydration regimens,[26] but we found no randomized controlled trial that evaluated pre-hydration versus no hydration. Thus, support for the standard use of pre-hydration to prevent RCIN is extrapolated from randomized controlled studies of saline versus saline *plus* additional pre-treatment agents like mannitol, furosemide and dopamine[8-10] and smaller observational studies[6,27,28] evaluating the benefits of pre-hydration.

Study Outcomes

Studies evaluated Level 2 outcomes, primarily by measuring changes in serum creatinine, creatinine clearance or glomerular filtration, and assessing the frequency of developing acute renal failure after radiocontrast infusions. Most studies defined RCIN as a 25% increase in creatinine and/or at least a 0.5 mg/dL increase in serum creatinine within 48 hours of contrast administration.

Evidence for Effectiveness of the Practice

All of these studies (Table 32.1) evaluated the effects of various prophylactic measures to reduce the incidence of RCIN. Use of low-osmolar contrast media was supported by one large meta-analysis [7] that compared low versus high osmolar contrast media. Low osmolar contrast media was found to be less nephrotoxic than high osmolar contrast media, with an odds ratio for RCIN of 0.61. Among patients with baseline renal insufficiency (SCr >1.4 mg/dL) the odds ratio of developing RCIN was 0.5 if low osmolar instead of high osmolar contrast media was used.

As previously noted, no randomized controlled trials have evaluated the efficacy of pre-hydration versus no pre-hydration. Data from 3 randomized controlled trials[8-10] using pre-hydration versus other pre-treatments *and* pre-hydration revealed that pre-hydration alone was equivalent to pre-hydration and low dose dopamine or mannitol,[8] and, in one study, superior to pre-hydration and furosemide.[10] The incidence of RCIN in patients with SCr >1.6 mg/dL or creatinine clearance <60 mg/min treated with pre-hydration alone undergoing cardiac catheterization was 11%; excluding the patients with SCr >3 mg/dL, the incidence was only 4%.[8] One retrospective, observational study of high-risk patients undergoing cardiac catheterization supports the benefit of pre-hydration (>500 mL of 0.9% NS in the pre-catheterization period, p• 0.01) in reducing RCIN.[6] In addition, 2 observational studies without controls[27,28] showed that pre-hydration in high-risk patients was associated with low rates of RCIN, although one of these studies[27] used a stricter definition for RCIN (increase in BUN by 50% or 20 mg/dL, and/or increase in SCr of 1 mg/dL within 24 hours).

A recent study of the oral antioxidant acetylcysteine in combination with pre-hydration in high-risk patients with renal insufficiency showed significant protective effect against RCIN versus pre-hydration plus placebo.[16] This protective effect appeared to be even more significant among patients with more advanced renal dysfunction and SCr >2.5 mg/dL. The overall relative risk reduction of 90% observed in this study is so large that it raises the possibility of some sort of bias or other explanation for the observed results. Additional studies of this practice would be valuable, despite the safety and low cost of N-acetylcysteine.

Studies employing theophylline are more controversial. Three randomized control trials showed a significant protective effect of various dosages and administration routes of theophylline among low-risk patients with relatively normal baseline renal function.[12-14] All 3 studies showed theophylline to be protective against a decrease in glomerular filtration rate

(GFR) or creatinine clearance (CrCl) after contrast administration. On the other hand, 2 studies conducted in high-risk patients with renal dysfunction showed no effect for theophylline in reducing RCIN.[11, 15] Thus, insufficient evidence supports the use of theophylline as prophylaxis against RCIN in high-risk patients.

Potential for Harm

The impact of a system to identify high-risk patients prior to contrast radiography and implement aggressive prophylactic measures to reduce the incidence of RCIN has not been studied. While most patients will not experience any harm from contrast, the potential for "harm" due to delayed or cancelled investigations may be greater than the harm prevented by screening for risk factors, aggressive hydration, or use of particular pre-treatment regimens.

Costs and Implementation

At least 4 studies have evaluated the cost-effectiveness of low-osmolality versus high-osmolality contrast media.[29-32] In all 4 studies, the selective use of low-osmolar contrast media was more cost-effective than its universal use because of the overall small benefits were outweighed by the considerable increased institutional costs. Alternatively, a standardized system to identify high-risk patients and implement the simple prophylactic treatment of pre-hydration would diminish the frequency of the target problem. It would require collaboration between the patients' own physician and the personnel performing the particular contrast study (radiology department, radiologist, diagnostic/interventional cardiologist). This type of intervention could be implemented as part of a hospital-based pathway (see Chapter 52) targeted at reducing radiocontrast-induced nephropathy.

There are no cost-effectiveness or feasibility studies that evaluate protocols for aggressive identification of high-risk patients undergoing contrast radiography and utilization of standardized hydration protocols to reduce RCIN. Two studies suggest most patients with normal renal function (SCr <1.7 mg/dL) can be easily identified by simple questionnaire, resulting in significant cost savings from a reduction in the number of routine serum creatinine levels obtained prior to imaging.[33,34] The cost-effectiveness of using pharmacologic pre-treatment with N-acetylcysteine or theophylline has not been studied.

Comment

In summary, patients with multiple risk factors for RCIN who need radiography with contrast media should receive pre-hydration and low osmolar iodinated contrast. Overall, there appears to be indirect evidence that RCIN can be attenuated by pre-hydrating high-risk patients. Clearly, the use of low osmolar contrast media is associated with less RCIN, but its high cost militates against routine use in all patients. We believe that it should continue to be reserved for the patient with multiple risk factors for RCIN. While newer pre-treatment regimens like N-acetylcysteine, prostaglandin E1, and captopril look very promising in preventing RCIN, these results need to be replicated in further studies. Finally, many institutions would benefit from a hospital-based pathway that identifies patients with multiple risk factors for RCIN prior to contrast radiography. Guidelines (Chapter 51) for appropriate pre-hydration and the timely use of low osmolar contrast media to reduce the development of RCIN would be beneficial.

Table 32.1. Studies of strategies for preventing radiocontrast-induced nephropathy (RCIN)*

Study Setting	Study Design, Outcomes	Results
Low osmolar contrast media		
Meta-analysis of the relative nephrotoxicity of high (HOCM) vs. low (LOCM) osmolar iodinated contrast media[7]	Level 1A, Level 2	LOCM less nephrotoxic than HOCM; pooled p=0.02 Odds of ARF with LOCM 0.61 times that of HOCM (95% CI: 0.48-0.77). Patients with RF at baseline, odds of ARF were 0.5 (CI: 0.36-0.68).
Pre-hydration plus diuresis		
Patients with SCr >1.8mg/dL randomized to IVF, IVF + furosemide, IVF + furosemide + low dose IV dopamine +/- mannitol (if post-cardiac catheterization, PCWP <20 mmHg)[9]	Level 1, Level 2	No differences in rates of renal failure between groups. Rates of RCIN 21.6% if UOP >150 mL/h, 45.9% if UOP <150 mL/h.
Patients with SCr >1.6mg/dL or CrCl <60mL/min randomized to IVF, IVF + mannitol or furosemide pre-cardiac catheterization[8]	Level 1, Level 2	No statistically significant difference in RCIN, among the three groups. After exclusion of patients with SCr >3 mg/dL, RCIN in patients with IVF alone 4%, IVF + mannitol 24% (p=0.02), IVF + furosemide 25% (p=0.02). LOS increased by 4 days in RCIN group.
Patients with SCr >1.7 or CrCl <60mL/min randomized to IVF + furosemide vs. discretion of treating physician during contrast radiography[10]	Level 1, Level 2	SCr increased by 0.42 mg/dL +/- 0.20 treatment group vs. 0.023 mg/dL +/- 0.073 (p<0.01) controls. Significant weight loss in treatment group vs. controls (p<0.03)
Observational study of "high risk" patients with SCr >1.9 mg/dL who underwent cardiac cath[6]	Level 3, Level 2	Statistically significant risk factors for RCIN: volume of contrast used (168+/- 11 vs. 122+/16 mL, p=0.001) and use of prehydration (>500mL 0.9% normal saline in preceding 24 hrs, p<0.01)

Table 32.1. Studies of strategies for preventing radiocontrast-induced nephropathy (cont.)*

Study Setting	Study Design, Outcomes	Results
N-Acetylcysteine		
Patients with SCr >1.2 mg/dL or CrCl <50 mL/min randomized to pre-hydration (IVF) with oral acetylcysteine or placebo prior to contrast CT[16]	Level 1, Level 2	RCIN developed in 2% treatment group vs. 21% control group (p=0.01). Among patients with SCr >2.5 mg/dL, RCIN 0% treatment vs. 42% controls (p=0.02)
Theophylline		
Patients randomized to theophylline (165mg IV x 1) vs. placebo prior to contrast radiography.[12]	Level 1, Level 2	GFR reduced 85.4 +/- 3.8 mL/min controls vs. 107 +/-3.6 mL/min treatment group (p• 0.001).
Patients randomized to theophylline (2.8 mg/kg orally q12 x 2 days) vs. placebo prior to contrast radiography with LOCM or HOCM.[13]	Level 1, Level 2	CrCl after LOCM decreased by ~18% at 24 hrs in control (p<0.05) vs. no significant change over 48 hrs in treatment group. CrCl after HOCM decreased by ~40% at 24 hrs and remained low at 48 hrs in controls (p<0.01) vs. ~24% at 24/48 hrs in the treatment groups (p<0.05). CrCl after HOCM significantly lower in control vs. treatment group (p<0.01).
Patients randomized to pre-hydration + theophylline (5mg/kd IV) or placebo prior to contrast CT or DSA.[14]	Level 1, Level 2	GFR decreased at 4 hrs and 2 days in placebo (88 +/- 40 to 75 +/- 20 mL/min, 89+/- 41 mL/min to 66+/- 32 mL/min, p<0.01) with no significant change in CrCl in the treatment group.
Patients with SCr $\geq$1.5mg/dL randomized to pre-hydration vs. pre-hydration with low dose dopamine or aminophylline prior to cardiac catheterization.[11]	Level 1, Level 2	Overall incidence of RCIN was 38%. No significant differences were noted among the groups. LOS was longer in patients with RCIN (7.1 days vs. 3.1 days, p=0.02).
Patients randomized to pre-hydration + theophylline (270 mg q am/540 mg q pm 2d before, 3d after) or placebo prior to contrast CT or DSA.[15]	Level 1, Level 2	No significant differences in SCr or CrCl between groups (RCIN 3.4% controls, 5.7% in treatment, p=NS).

* ARF indicates acute renal failure; CI, confidence interval; CrCl, creatinine clearance; CT, computed tomography scan; DSA, digital subtraction angiography; GFR, glomerular filtration rate; IVF, intravenous fluids; LOS, length of stay; NS, not statistically significant; PCWP, pulmonary capillary wedge pressure; SCr, serum creatinine; and UOP, urine output.

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Chapter 33. Nutritional Support

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Background

There is a consensus that nutritional support should be routinely provided to intensive care unit (ICU) patients.[1] Hospitalized patients with malnutrition (macronutrient and/or micronutrient deficiency) suffer from increased infectious morbidity, prolonged hospital stays, and increased mortality.[2] Moreover, even those hospitalized medical and surgical patients without antecedent malnutrition are typically subjected to stress, infection and impaired organ function, resulting in a hypercatabolic state. Often these patients are unable to meet their caloric needs, as they are either too sick or physically unable to ingest food. Although strong evidence demonstrates that providing nutritional support for such patients results in improved clinical outcomes, the optimal method of delivery, timing of administration, and specific formulation requires further research.

Practice Description

There are several ways to provide nutritional support to patients in the ICU. Enteral nutrition (EN) can be administered via transoral, transnasal, or percutaneous transgastric routes, or by surgical jejunostomy. Total parental nutrition (TPN) is generally used when the enteral route is either inaccessible or its use is contraindicated. It is also used as a supplement to enteral feeding if adequate nutrition is not possible via the enteral route alone.

The total caloric requirement of critically ill patients can be estimated or directly measured. Calorimetry, although accurate, is not practical in the clinical setting as it is costly, time consuming, and requires technical skill. It is also unclear that exactly matching energy input with energy expenditures improves patient outcomes. Therefore, a pragmatic approach is to attempt administration of 25 kilocalories per kilogram ideal body weight per day for most patients.[3] The total caloric daily requirement should be administered in a fluid volume consistent with the patient's needs (usually 1mL/kcal). Protein sources should comprise 15-20% of the total daily calorie requirement. The generally accepted amount of protein is between 1.2 and 1.5 g/kg per day, except in severe losses such as burns. Glucose should comprise 30-70% of the total calories and fats 15-30%.[1]

Prevalence and Severity of the Target Safety Problem

Malnutrition in hospitalized patients often goes unrecognized.[4,5] Early studies reported a prevalence of malnutrition in 30-50% of hospitalized patients.[6] A later study revealed that up to 40% of patients were malnourished at the time of their admission.[7] The majority of these patients continued to be nutritionally depleted throughout their hospital course. These patients are also at a greater risk for the development of severe malnutrition than those patients whose nutritional status was adequate at the time of admission.

Unfortunately, there is no single, readily available measure of malnutrition that is both sensitive and specific in critically ill patients.[1] Most studies have used body mass index (BMI=weight (kg)/height (m)) and/or anthropometry (measuring skin fold thickness) to assess patients' nutritional status.[7] BMI alone is not a sensitive indicator of protein-energy malnutrition as it does not distinguish between depletion of fat or muscle.[4] In a large number of studies,

malnutrition has been defined as a BMI ≤20 kg/m and a triceps skin fold thickness (TSF) or mid-arm muscle circumference (MAMC) <15th percentile.[7] Patients with a BMI of ≤18 and ≤16 kg/m with anthropometric measurements below the 5th percentile were considered to have moderate and severe malnutrition respectively.[7] Weight loss exceeding 10% of ideal body weight (IBW) also suggests malnutrition.[1]

Opportunities for Impact

Providing nutritional support has the potential to significantly reduce several clinically relevant endpoints (eg, infectious complications, hospital stay, mortality). However, even when malnutrition is recognized, adequate nutrition is often not delivered. Prescription of optimal enteral nutrition to meet energy requirements ranged from 76% to 100% in a prospective survey of 5 ICUs in the United Kingdom.[8] Another study of enteral nutrition among patients receiving no oral nutrition in medical and coronary care units at 2 US university-based hospitals, documented that physicians ordered only 65.6% of daily goal requirements and only 78.1% of this was actually delivered.[9] A recent prospective study of both enteral and parenteral nutrition in a French university-affiliated ICU found that physicians prescribed only 78% of the mean caloric amount needed by patients, and only 71% of this was effectively delivered.[10] Efforts targeted at increasing physician awareness of the problem and early delivery of appropriate nutrition may improve patient outcomes.

Study Design

The field of nutritional support can be divided into several basic areas of investigation. First, research has evaluated whether nutritional support is of benefit to malnourished critically ill patients. Second, studies have compared the impact of EN versus TPN on patient outcomes. Further investigations have looked at the timing of administering nutritional support. Lastly, recent research has focused on the type of EN, specifically considering whether immune-enhancing formulas (immunonutrition) improve outcomes.

At least 26 randomized controlled trials (RCTs) have compared the use of TPN to standard care (usual oral diet plus intravenous dextrose), and one meta-analysis reviewed these studies.[11] A different meta-analysis specifically reviewed the use of TPN in surgical patients.[12] A systematic review with meta-analysis (duplicated in the other publications[11,12]) included evaluation of 6 randomized trials in surgical patients that compared the benefits of early enteral nutrition with standard care.[2] Numerous randomized controlled trials have compared EN to TPN. Three RCTs of surgical patients evaluated the merits of early enteral feeding postoperatively. A few studies have compared EN delivered into the stomach versus into the small bowel (jejunum). Several randomized controlled trials have studied the effects of using immunonutrition and we found 2 meta-analyses of immune-enhancing enteral supplementation in critically ill patients after trauma, sepsis or major surgery.

Study Outcomes

The majority of studies reported Level 1 outcomes including infectious complications and mortality. Some measured hospital length of stay (Level 3) as well. Several studies evaluating immunonutrition reported its effects on surrogate outcomes such as wound healing. Studies evaluating immediate enteral nutrition in burn patients have also used surrogate markers. Animal studies have assessed the effects of immunonutrition on gastrointestinal physiology as well as wound strength.

Evidence for Effectiveness of the Practice

Nutritional supplementation in hospitalized patients may reduce mortality and is associated with weight gain (see Table 33.1).[13] However, there are no randomized controlled trials comparing supplemental nutrition to starvation in critically ill patients. Research does show that patients not receiving any nutritional support for more than 2 weeks postoperatively have a much higher complication and mortality rate than patients receiving TPN or some short-term glucose administration.[14] A large body of research in the past 2 decades has focused on determining the ideal type and method of delivery of nutritional support.

A meta-analysis comparing supplemental TPN to standard care (oral diet as tolerated and intravenous dextrose) found no effect on mortality (relative risk (RR) 1.03, 95% CI: 0.81-1.31).[11] There was a trend toward a lower complication rate among those receiving TPN (RR 0.84, 95% CI: 0.64-1.09), but this is due mainly to benefit among malnourished patients.[11] There are no data from randomized controlled trials to support the use of supplemental TPN among patients with an intact gastrointestinal tract ("If the gut works, use it").

Several studies have evaluated the use of supplemental EN in surgical patients. These studies often used surrogate outcomes, but one randomized double-blind trial of early EN versus standard diet as tolerated following surgery found fewer total complications (26.7% vs. 63.3%, $p=0.009$), fewer infectious complications (6.7% vs. 46.7%, $p<0.001$) and a trend towards a reduction in hospital length of stay (8 vs. 11.5 days, $p=0.08$) with early EN.[15] Based on this evidence, early EN is recommended in critically ill surgical patients. There is no specific research evaluating the benefits of supplemental EN in critically ill medical patients, but results from research in surgical patients appear to be applicable.[2] In animal studies, EN promotes gut motility, reduces bacterial translocation, prevents mucosal atrophy and stimulates the secretion of IgA that helps to reduce infectious complications.[3] There is also evidence that EN improves nutritional outcomes and results in greater wound healing.[2] A review of 5 trials studying postoperative EN found no significant reduction in morbidity or mortality.[6] However, a recent study of patients with non-traumatic intestinal perforation and peritonitis found there to be a total of 8 septic complications in the early EN group versus 22 in the control group ($p<0.05$).[16]

Multiple studies comparing use of EN to TPN in critically ill medical and surgical patients demonstrate that EN is safe, less expensive, and results in similar or better outcomes.[2] Among patients with acute severe pancreatitis, those fed enterally had fewer total complications (44% vs. 75%, $p<0.05$) and fewer septic complications (25% vs. 50%, $p<0.01$).[17] In numerous studies of surgical patients, EN also appears to be more effective than TPN. A study of patients undergoing total laryngectomy revealed no difference in mortality or infectious complications. However, the patients who received TPN had a longer length of stay (34 days vs. 11 days, $p<0.05$).[18] In another study of patients with abdominal trauma, those fed enterally had significantly fewer septic complications (15.7% vs. 40%, $p<0.02$).[19] A meta-analysis combining data from 8 prospective randomized trials found that 18% of patients receiving EN developed infectious complications compared with 35% in the TPN group ($p=0.01$).[20] Of note, EN may not be preferred to TPN in head-injured patients.[2] In a study of patients with head trauma there appeared to be no significant difference in relation to infectious outcomes and mortality between EN and TPN. However, patients fed enterally had a trend toward a higher incidence of aspiration pneumonia (32% vs. 13%, $p=0.11$), though no difference in overall infections and mortality.[21]

The effects of preoperative TPN have been evaluated in 13 prospective randomized controlled trials of patients undergoing surgical resection of a gastrointestinal tumor. Combining the data from these studies reveals a modest reduction in surgical complications (approximately

10%) in those patients receiving TPN.[6] This benefit appears to be due entirely to significant reduction in surgical morbidity among patients who are severely malnourished.[22] Therefore, preoperative TPN may be of benefit in severely malnourished patients undergoing major gastrointestinal surgery, but EN should be used instead, if possible. The use of postoperative TPN has been evaluated in 8 prospective randomized trials of patients undergoing gastrointestinal surgery. Patients in the combined TPN group experienced an increased rate of complications (27.3% vs. 16.0%; $p<0.05$). Thus, routine use of postoperative TPN in this setting is not recommended.[6]

Since enteral administration is the preferred method of nutritional support, additional research has focused on the utility of early administration of EN to severely ill surgical patients. In animal studies early EN is associated with greater wound strength after abdominal surgery.[23] In burn patients immediate EN was associated with a decrease in catecholamines and glucagons, and improved nitrogen balance compared to delayed EN.[24] A prospective randomized controlled study evaluated the effect of immediate jejunal feeds in patients with major abdominal trauma. The overall complication rate was similar in both groups, but 9 patients in the control group developed postoperative infections versus 3 in the EN group ($p<0.025$).[25] Although other studies do not show a change in outcomes, based upon this data it is reasonable to begin EN as soon as possible in surgical patients. More research is needed to evaluate the necessity of administering EN into the jejunum.[2]

Recently, intense study has focused on use of immunomodulating enteral formulations (containing arginine, glutamine, omega-3 fatty acids, and nucleotides). In animal and human studies, specific immunonutrients have had favorable effects such as promotion of T-cell blastogenesis, enhancement of cellular immunity and increased concentration of trienoic eicosanoids.[2] The largest (n=390) prospective, double-blinded RCT comparing enteral immunonutrition (IMPACT™, Novartis Nutrition, Bern, Switzerland) to isocaloric, isonitrogenous control enteral feed revealed no significant difference in hospital mortality rate in the intention-to-treat analysis (48% vs. 44%, $p=0.36$).[26] This study, conducted in a 13-bed adult general ICU in a London teaching hospital, resulted in randomization of patients with higher Acute Physiologic and Chronic Health Evaluation (APACHE) II scores ($p=0.07$, ie, they were "sicker") to the immunonutrition group, with this possibly accounting for the slightly higher mortality rate. Subgroup analyses of patients who received some enteral nutrition (n=369) and therapeutic levels of enteral feeding (>2.5 L within 72 hours of ICU admission, n=101) also showed non-significant higher mortality rates in the group receiving IMPACT. However, the subgroup analyses also showed significant reductions in days of mechanical ventilation, length of ICU stay, and overall hospital length of stay (LOS) in the group receiving immunonutrition compared to the control group (see Table 33.1). Of note, the reductions in length of stay may be attributable to the higher mortality rates in the group receiving immunonutrition, as more patients died sooner in the immunonutrition group than the control group (ie, LOS reduced by early death).[27]

A meta-analysis of 12 randomized controlled trials (including the aforementioned study) comparing use of one of two commercially available enteral feeding preparations (IMPACT™ or Immun-Aid™, McGaw, Irvine, CA) to standard enteral nutrition did not find any effect on mortality (RR 1.05, 95% CI: 0.78-1.41).[28] However, patients receiving enteral immunonutrition had significant reductions in infection rate (RR 0.67, 95% CI: 0.50-0.89), ventilator days (reduced 2.6 days, 95% CI: 0.1-5.1) and hospital length of stay (reduced 2.9 days, 95% CI: 1.4-4.4).[28] The benefits were most pronounced in surgical patients. Another meta-analysis of 11 prospective RCTs (not including the aforementioned RCT) also found reductions in the odds of

developing major infectious complications (odss ratio 0.47, 95% CI: 0.32-0.70), and hospital length of stay (reduced 2.5 days, 95% CI: 1.0-4.0).[29] Though there was no "significant" difference in mortality between patients receiving immune-enhanced versus standard nutritional support, there was a trend toward increased mortality (odds ratio 1.77, 95% CI: 1.00-3.12).[29]

Potential for Harm

TPN has been associated with an increase in septic complications. Patients may also be placed at increased risk from attempts to obtain central venous access. While EN decreases the overall rate of infectious complications when compared to TPN, it may place patients, especially those with head injuries, at greater risk of aspiration pneumonia. Use of a promotility agent, such as metoclopramide, has reduced this risk in one study.[30]

Costs and Implementation

TPN is itself expensive. Moreover, hospital costs can climb dramatically if patients who receive TPN suffer infectious complications that prolong their hospital stay. Obtaining central venous access also increases the costs of administration. Nutritional support teams (NSTs) can help ensure that patients are receiving adequate nutrition while at the same time reducing the rate of line complications.[28] However, the use of NSTs is expensive and has not been subject to a cost analysis.[28] The economics of early postoperative enteral nutrition was studied in a recent nonrandomized, prospective, clinical trial of patients undergoing bowel resections. There was a reduction in variable cost of $1531 per success in the treatment group (p=0.02) and $4450 total cost savings per success in the treatment group (p=0.04).[31] Immunonutrition is significantly more expensive than standard enteral formulas but in 2 prospective randomized controlled trials of patients undergoing upper gastrointestinal surgery it has been shown to be cost-effective. In one study, the cost per patient for nutrition and complications in the control group was $1633 compared to $783 in the immunonutrition group.[32] In another study the cost per patient for nutrition and complications in the control group was $1107 compared with $755 in the treatment group.[33]

Comment

The literature on appropriate nutritional support for critically ill patients is complex to analyze. A wide variety of treatment modalities have been evaluated in a fairly heterogeneous patient population, making interpretation of the various studies difficult.

Nonetheless, there are several general recommendations that can be made. First, malnutrition leads to poor outcomes and should be avoided or treated if present. Patients who have prolonged starvation for more than 2 weeks are at a significantly increased risk for complications. EN in these patients decreases this risk, and should be administered to all critically ill medical and surgical patients who can tolerate it. There are no data to support the use of TPN in critically ill patients who have a functional gastrointestinal tract. However, TPN may be of benefit preoperatively when given electively to severely malnourished patients undergoing gastrointestinal resection. Postoperative administration of TPN worsens outcomes. There is no evidence to suggest that postoperative enteral nutrition is superior to advancing a patient's oral diet, as tolerated, if they are capable of eating, but research into early administration of EN via the jejunum is ongoing.

Use of immune-enhanced EN appears to significantly reduce infectious complications, number of days of mechanical ventilation, and overall hospital length of stay, though it does not appear to affect overall mortality (and may increase it). Of note, study groups with increased

mortality rates may also have a diminished incidence of infectious complications and decreased length of stay artifactually due to patients dying early in the study. One expert interpreted the published research as strongly suggesting that immune-enhancing formulas should be used in critically ill patients, especially surgical patients, despite their high cost.[34] Nonetheless, a large multicenter RCT is needed to resolve with certainty whether or not use of these expensive formulas is safe and improves outcomes in critically ill patients before formally recommending their widespread use.[29]

Table 33.1. Studies evaluating nutritional support*

Study	Study Design, Outcomes	Results (95% Confidence Interval)
Routine protein energy supplementation in adults; systematic review[13]	Level 1A, Level 1	Reduced mortality: OR 0.66 (0.48 to 0.91) Increased body weight gain (%): Oral Sip Feeds: 2.39 (1.80 to 2.96) Oral natural feeds: 5.36 (1.73 to 8.99) Nasogastric feeding: 4.04 (3.15 to 4.94) Percutaneous or enteral feeding, enterostomy: -1.38 (-2.35 to -0.41)
TPN in critically ill patients; meta-analysis[11]	Level 1A, Level 1	No effect on mortality: RR 1.03 (0.81 to 1.31) Complication rate: RR 0.84 (0.64 to 1.09) Complication rate (malnourished subgroup): RR 0.52 (0.30 to 0.91)
TPN in surgical patients; meta-analysis[12]	Level 1A, Level 1	No effect on mortality: RR 0.97 (0.76 to 1.24) No effect on mortality (malnourished subgroup): RR 1.13 (0.75 to 1.71) Major complication rate (malnourished subgroup): RR 0.52 (0.30 to 0.91)
Immunonutrition in critically ill patients; systematic review and meta-analysis[28]	Level 1A, Level 1	No effect on mortality: RR 1.05 (0.78 to 1.41) Reduction in infection rate: RR 0.67 (0.50 to 0.89) Reduction in days of mechanical ventilation: 2.6 days (0.1 to 5.1) Reduction in hospital LOS: 2.9 days (1.4 to 4.4)
Immunonutrition in patients with critical illness and cancer; meta-analysis[29]	Level 1A, Level 1	Trend toward increased mortality: OR 1.77 (1.00 to 3.12) Reduction in infectious complications: OR 0.47 (0.32 to 0.70) No reduction in pneumonia risk: OR 0.91 (0.53 to 1.56) Reduction in hospital LOS: 2.5 days (4.0 to 1.0)
EN vs. TPN in seriously ill hospitalized patients; systematic review and meta-analysis[2]	Level 1A, Level 1	Reduction in septic complications: EN 18% vs. TPN 35% (p=0.01) Reduction in infectious complications: EN 16% vs. TPN 35% (p=0.01)
Enteral immunonutrition in the critically ill; double-blind randomized controlled trial[26]	Level 1, Level 1	<u>Overall analysis</u> (immunonutrition vs. control formula) Mortality: 48% vs. 44% (p=0.36) Total days of mechanical ventilation (median): 4 vs. 4 days (p=NS) Hospital LOS (median): 12 vs. 13 days (p=NS) <u>Early enteral feeding subgroup</u> Total days of mechanical ventilation (median): 6 vs. 10.5 days (p=0.007) Hospital LOS (median): 15.5 vs. 20 days (p=0.03)

* LOS indicates length of stay; NS, not statistically significant; OR, odds ratio; and RR, relative risk.

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Chapter 34. Prevention of Clinically Significant Gastrointestinal Bleeding in Intensive Care Unit Patients

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Background

Stress-related gastric ulceration was first described in the early 1970s,[1] and has since received extensive study. Appreciation of the physiologic changes that promote stress-related gastritis[2-4] and general improvements in the care of critically ill patients have likely played a role in reducing the frequency of this complication.[3] Nonetheless, the use of specific pharmacologic agents for the prevention of stress-related gastrointestinal (GI) bleeding is increasingly promoted as standard therapy in the ICU setting.[5-8] Despite the common use of these agents, controversy about the evidence supporting this practice remains.[5,9] Because specific pharmacologic prophylaxis for stress ulceration may increase the risk of other complications (eg, nosocomial pneumonia[10]) and is associated with significant costs,[11] recent efforts have focused on delineating an appropriate definition of clinically important GI bleeding and identifying patients who derive a clear benefit from pharmacologic prevention of this complication.

Practice Description

This chapter reviews evidence supporting the use of pharmacologic therapies for stress ulcer and GI bleeding prophylaxis in the ICU setting. We considered the use of histamine-2 receptor blocking agents (H_2-receptor antagonists) and sucralfate, a mucosal protecting agent. Although the efficacy of aluminum- and magnesium-based antacids has been demonstrated, their use is limited by dosing frequency and side effects.[12] Proton-pump inhibitors (PPIs) and enteral nutrition have also shown benefit in small studies, but there are yet no large randomized evaluations.[6,12,13]

Prevalence and Severity of the Target Safety Problem

The risk of stress ulceration and subsequent GI bleeding depends on a patient's underlying illness, its severity, and related comorbidities. Using liberal criteria for assessment of bleeding, early reports estimated the incidence of GI bleeding due to stress ulceration in ICU patients to be as high as 5-25%.[14,15] However, more recent prospective studies, using stricter definitions of clinically significant GI bleeding and following large cohorts of patients, have revealed more modest estimates of 0.1% in low-risk ICU patients and 2.8% in ventilated patients.[2,13,16]

Opportunities for Impact

A recent, prospectively collected database of over 7000 patients admitted to surgical and medical intensive care units at a tertiary care center (1988-95) revealed that 59.9% of patients received pharmacologic prophylaxis with ranitidine or sucralfate for stress ulceration.[16] Another study assessed the annual change in stress ulcer prophylaxis in nearly 3000 patients admitted to a medical intensive care unit at a tertiary care hospital from 1993 to 1996. It found a significant decrease in rates of prophylaxis, with a 71% rate in 1993 progressively decreasing to a 21% rate in 1996, likely reflecting emerging evidence regarding high and low-risk populations in the

literature during that time.[17] Identifying appropriate patients for stress ulcer prophylaxis and avoiding its use in other cases both offer potential opportunities for improving patient safety in the ICU.

Study Designs

Although multiple meta-analyses have reviewed the prophylaxis of GI bleeding in critically ill patients, many were performed more than a decade ago.[18-20] Since then, results of additional randomized trials have been published. More recent, well-designed search strategies, strict quality-scoring of literature, and rigorous adherence to criteria defining clinically significant GI bleeding have improved the breadth and quality of literature captured, likely making older systematic reviews less relevant. Because of these changes in quality measures as well as overlap of information and trials from older reviews contained within more recent ones, only those meta-analyses published within the last 5 years (and large randomized controlled trials not included in these reviews) are included here.

A 1996 meta-analysis found 269 studies through a broad search of multiple databases and extensive efforts to find unpublished trials.[5] Sixty-three of these met inclusion criteria. The analysis evaluated multiple types of prophylaxis for GI bleeding, including antacids, H_2-antagonists, and sucralfate. The study authors compared each type of prophylaxis to placebo and to each other when literature was available. The same study group then followed-up unanswered questions from their meta-analysis with a large randomized controlled trial (RCT) of 1200 patients, comparing ranitidine to sucralfate without a placebo group.[21]

A more recent meta-analysis abstracted evidence from the literature to compare ranitidine (instead of all H_2-antagonists) versus placebo, and sucralfate versus placebo for GI bleed prophylaxis in the ICU.[9] The search methods were less rigorous and the target population narrower than the 1996 meta-analysis, but the authors claimed to assess a more clinically relevant population and outcome.

Results from 2 prospective cohort studies that evaluated risk factors for occurrence of clinically important GI bleeding also provide key recommendations regarding clinical practice.[2,13]

Study Outcomes

Both meta-analyses and the large RCT reported outcomes of clinically important GI bleeding and nosocomial pneumonia (Level 1). The 1996 meta-analysis and randomized trial also evaluated overt GI bleeding and mortality. Cohort studies (Level 2) present results of multivariate regression analyses, identifying the salient risk factors for clinically important GI bleeding in the ICU patient.

Evidence for Effectiveness of the Practice

Table 34.1 summarizes the outcomes for the 2 meta-analyses and large RCT. The disparity in results of the meta-analyses is partly due to differing article selection criteria. While the 1996 analysis evaluated all H_2-antagonists, the 2000 study excluded trials evaluating cimetidine because of its virtual replacement (attributable to its undesirable side effect profile) by ranitidine in current clinical practice.[5,9] Excluding studies with cimetidine substantially reduced the number of studies available for review. Additionally, the 1996 study evaluated comparisons of therapies to each other as well as to placebo, while the 2000 study only considered trials of effectiveness with a placebo control as relevant.

The 2000 meta-analysis found no statistically significant reduction in clinically important GI bleeding when comparing H_2-antagonist agents with placebo, or sucralfate to placebo.[9] However, the 1996 study revealed a significant difference between ranitidine and placebo for clinically important GI bleeding.[5] It was unable to demonstrate such a difference between ranitidine and sucralfate. The results of these 2 reviews reveal discrepant findings, in large part due to exclusion of cimetidine in the 2000 study. However, that study also included at least one moderate-sized trial that used remarkably strict criteria for defining clinically important GI bleeding. This factor likely contributed an element of bias towards the null result in that meta-analysis.

Furthermore, the large RCT (1998) comparing ranitidine to sucralfate, without a placebo comparison group, revealed a statistically significant difference in the rate of clinically important upper GI bleeding, favoring H_2-antagonists.[21] In this RCT the number needed to treat (NNT) with ranitidine compared to placebo to prevent one clinically important GI bleed compared to placebo was 47. However, no reduction in mortality or length of ICU stay was found. Interpretation of the results of the RCT are complicated by: 1) wide confidence intervals surrounding the relative risk estimate; 2) very small numbers of patients with clinically important GI bleeding (ranitidine group: 10/596; sucralfate group: 23/604), only 42% of whom had endoscopic confirmation of the source of bleed; 3) a large number of patients (70%) receiving concomitant enteral nutrition, believed to reduce the risk of GI bleeding (see Chapter 33); and 4) unreported incidence of coagulopathy or duration of prophylaxis prior to GI bleeding.[22]

The 2 large cohort studies found respiratory failure (odds ratio 15.6, $p<0.001$), coagulopathy (odds ratio 4.3, $p<0.001$), and renal insufficiency (relative risk 1.16, $p=0.023$) to be independent risk factors for predicting clinically important GI bleeding in ICU patients.[2,13] Enteral nutrition had a protective effect on GI bleed outcome (relative risk 0.30, $p=0.004$). Even though previous studies found a high incidence of overt GI bleeding among head trauma patients, this was not supported by the most recent cohort study cited above, which evaluated ventilated head trauma patients.[13,23]

Potential for Harm

Table 34.2 summarizes the harm evaluated in the 2 recent meta-analyses and large RCT. All 3 studies showed either a trend toward reduction or statistically significant reduction of nosocomial pneumonia in sucralfate groups compared with ranitidine groups.[5,9,21] The number needed to harm (NNH) to cause one nosocomial pneumonia with ranitidine compared with sucralfate was calculated as 21 to 34 (see also Subchapter 17.4). However, this effect was not statistically significant in the RCT. No study demonstrated a harmful effect for ranitidine compared to placebo.

Costs and Implementation

One cost-effectiveness analysis extracted relevant literature from MEDLINE between 1985 and 1995, representing 15 controlled clinical trials (Level 1).[19] Assumptions made in the analysis included equal efficacy for the H_2-antagonist cimetidine and sucralfate, a baseline risk of bleeding of 6%, and a 50% risk-reduction due to prophylaxis. The average cost per bleeding episode averted was $1144 for sucralfate, but 6.5 times greater for cimetidine. However, low-risk patients amassed a cost per bleeding episode averted of $103,725 compared to a cost of $279 for very high-risk patients. Cost per bleeding episode averted increased significantly if the risk of nosocomial pneumonia was included in the analysis.

The large RCT reported no difference in the duration of ICU stay for the group treated with ranitidine compared with the group treated with sucralfate (9 days for each group).[21] However, no placebo group was used.

Comment

Overall, the evidence available in the literature does not conclusively demonstrate that the benefits of GI prophylaxis outweigh its risks for every patient admitted to the intensive care unit. As refinements have been made in defining *clinically* important and significant episodes of GI bleeding, the population that may reap benefit from prophylaxis has narrowed substantially. In turn, a reduction in the use of prophylactic agents has followed. Most recent estimates reveal a negligible incidence of clinically important stress-related GI bleeding in low-risk ICU patients (approximately 0.1%) and a small incidence (less than 3%) in higher-risk patients. Improvements in overall ICU care and use of enteral nutrition may be contributing to this decrease in incidence.

Although a statistical benefit of H_2-antagonists compared with placebo or with sucralfate has been shown in some studies, the overall *clinical* benefit of these agents has been disputed. Some research shows a greater absolute number of nosocomial pneumonia cases related to therapy with H_2-antagonists than the benefit from reduction in GI bleeding, causing the NNH to be potentially smaller than the NNT (see Subchapter 17.4). Furthermore, the overall cost-to-benefit ratio of prophylaxis increases dramatically in lower-risk patients, as shown in the analysis noted above that accounted for increases in nosocomial pneumonia.[21] Thus, the clear benefit of administering H_2-antagonists to prevent GI bleeding among many patients in an ICU remains to be shown. This is partly due to variations in the definition of clinically significant bleeding and pneumonia. Additional large trials are necessary to identify the patients who truly derive net benefit from this practice, as published evidence does not yet support this practice for many patients currently receiving the therapy.

At the present time, clinicians may consider use of prophylactic agents, an H_2-antagonist or sucralfate, to prevent clinically important GI bleeding in very high-risk patients admitted to the ICU. Such patients may include those with respiratory failure, coagulopathy, renal failure, and/or burns (the latter group has been excluded from most studies because its risk is believed to be so great). However, the risk of pneumonia may influence clinicians to use prophylactic agents only in patients with multiple risk factors for GI bleeding, and simply provide enteral nutrition to others at less risk. The use of PPIs requires further study before any recommendation can be made regarding them. Further research should focus on identifying subgroups of patients who do derive net benefit from ranitidine or other acid-reducing agents.

Table 34.1. Studies evaluating effectiveness of pharmacologic prophylaxis of ICU patients to prevent clinically significant GI bleeding*

EFFECTIVENESS			
Study	**Study Design, Outcomes**	**Comparison Groups**	**Effect Size (95% CI)**
Cook, 1996[5]	Level 1A, Level 1	H_2-antagonist vs. placebo	OR 0.44 (0.22-0.88)
		Sucralfate vs. placebo	OR 1.49 (0.42-5.27)
		H_2-antagonist vs. sucralfate	OR 1.28 (0.27-6.11)
Messori, 2000[9]	Level 1A, Level 1	Ranitidine vs. placebo	OR 0.72 (0.30-1.70)
Cook, 1998[21]	Level 1, Level 1	Ranitidine vs. sucralfate	RR 0.44 (0.21-0.92) NNT 47

* CI indicates confidence interval; NNT, number needed to treat (for benefit); OR, odds ratio; and RR, relative risk.

Table 34.2. Studies evaluating harm (nosocomial pneumonia) due to pharmacologic prophylaxis of ICU patients to prevent GI bleeding*

HARM			
Study	**Study Design, Outcomes Measured**	**Comparison Groups**	**Effect Size (95% CI)**
Cook, 1996[5]	Level 1A, Level 1	Sucralfate vs. H_2-antagonist	OR 0.78 (0.60-1.01)
Messori, 2000[9]	Level 1A, Level 1	Ranitidine vs. sucralfate	OR 1.35 (1.07-1.70) NNH 21
Cook, 1998[21]	Level 1, Level 1	Ranitidine vs. sucralfate	RR 1.18 (0.92-1.51) NNH 34

* CI indicates confidence interval; NNH, number needed to harm; OR, odds ratio; and RR, relative risk.

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Chapter 35. Reducing Errors in the Interpretation of Plain Radiographs and Computed Tomography Scans

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Background

Misinterpretation of radiographic studies is a common source of medical error in both the inpatient and outpatient arenas.[1,2] Of particular concern is the significant number of misinterpretations of plain radiographs and cranial computed tomography (CT) scans in emergency departments (ED) or urgent care settings by non-radiologists.[3-6] The prevalence of this patient safety issue may result from the large volume of patients receiving these radiologic tests, which are often done outside normal working hours when radiologists are not available to provide an initial interpretation. This chapter focuses on practices to reduce non-radiologists' higher rates of misinterpretation of these commonly ordered studies.

Intuitively, it would seems that institutions could minimize the number of such mistakes by routinely having studies interpreted by the most accurate and experienced physicians, usually radiologists. The American College of Radiology (ACR) recommends that all imaging procedures culminate in a written, expert opinion from a radiologist or another licensed physician specifically trained in diagnostic radiology.[7,8] However, due to the associated costs, fewer than 20% of hospitals have full-time on-site coverage by a board-certified radiologist.[9] Instead, radiologists are generally available for 8 to 12 hours a day and may not provide an interpretation until the following morning, particularly when studies are performed after normal working hours.[9] For many routine examinations, it may be possible to delay interpretation without harm to patients. If results are needed urgently and a radiologist is unavailable, other physicians (eg, emergency physicians, hospitalists, neurologists) must take responsibility for the initial interpretation.

Patient safety may be enhanced by improving the diagnostic accuracy of these physicians or by implementing other systems to prevent initial misinterpretations from adversely affecting patient care. Several strategies reviewed here that may be effective in reducing these errors include educational courses to improve the diagnostic accuracy of non-radiologists, on-site coverage by radiology residents, and mandatory subsequent reinterpretation of studies by radiologists.

Another approach that deserves mention is to have the initial readings made by off-site radiologists or other specialists using a *teleradiology link*. Teleradiology has been effective in facilitating emergent neurosurgical consultation prior to the interhospital transfer of patients with head injury.[10-12] Teleradiology also allows rural physicians to obtain remote consults for selected patients,[13-16] which in one report led to treatment changes in 26% of cases.[17] Despite teleradiology's impact in these two specific settings, few studies have tested its accuracy and utility in more general circumstances.[18] Teleradiology of course requires the use of digitized rather than film-based radiographs. In two mixed case series, discrepancies of interpretation between digitized and original radiographs occurred in approximately 10% of cases,[13,14] with significant discrepancies in 1.5-5%.[19,20] For more subtle findings the sensitivity of on-screen images may be as low as 49%,[21] leading several investigators to conclude that teleradiology is

inferior to film interpretation for difficult cases.[21-23] At present, it appears that image quality is the major reason behind the variable performance of teleradiology. Although the ACR has established detailed standards for equipment and image resolution,[24] radiology practices often utilize less expensive alternatives for viewing images, including personal computers.[23,25,26] The variation in practice, rapid evolution of technology, and lack of large prospective trials make it difficult to examine teleradiology from the standpoint of patient safety. Therefore, this chapter will not discuss teleradiology in detail; reviews can be found elsewhere.[27-30]

Interventions to improve the technical quality of imaging studies, such as ensuring proper patient positioning and film exposure, are certainly important but are also outside the scope of this chapter. Finally, although radiologists make mistakes in interpreting films,[31-37] this chapter focuses on practices to reduce the higher rate of misinterpretations made by non-radiologists.

Practice Descriptions

Training Courses

Training courses for non-radiologists are presumably common, but we could locate only 2 descriptions in the literature.[38,39] Both courses concerned interpretation of cranial CT scans, were conducted by radiologists, and targeted ED residents and faculty physicians. The training lasted 1-2 hours and consisted of a review of neuroanatomy and a small library of CT scans. Two continuous quality improvement initiatives were also recently described, in which radiologists provided regular feedback to ED physicians about their radiograph interpretations.[40,41]

Initial Interpretations by Radiology Residents

Initial interpretation of ED films by radiology residents follows no standardized practice. Their hours of coverage and the degree to which they interact with ED physicians vary widely.[42] It is also unclear to what extent emergency physicians rely on the resident interpretations when they are available.

Review of All Studies by Radiologists

Reinterpretation of all studies by a radiologist is already commonly used. When a radiologist finds that a study was initially misinterpreted, the medical error has already occurred. In this case, the safety practice concerns how the radiologist communicates the corrected interpretation to providers in order to minimize the risk of harm to patients. The method of communication varies among health care facilities and includes placing the interpretation in the patient's medical record, sending a report to the referring physician, or contacting the physician or patient directly for more urgent concerns (see also Subchapter 42.4).[7]

Prevalence and Severity of the Target Safety Problem

Many investigators have focused on the prevalence of <u>all</u> ED readings that are discordant with radiologists' subsequent interpretations (with the radiologists' interpretation assumed to be the "gold standard"). Against this standard, ED physicians and residents misinterpret 1-16% of plain radiographs[43-51] and approximately 35% of cranial CT scans.[52] However, many discordant readings involve subtle or incidental findings that are not clinically significant (ie, they do not affect patient management or outcome). From the standpoint of patient safety, it is the rate of clinically significant misinterpretations and related errors in management that are of concern.

Most ED studies show that important errors in interpretation occur in 1-3% of plain radiographs.[40,43,46-51] However, one pediatric study calculated a 6.8% rate of significant

radiograph misinterpretation.[53] The most common error is failure to recognize an extremity fracture.[43,46,51,54] Lufkin and colleagues examined the readings of 16,410 consecutive radiographs and the effect of emergency physicians' confidence on the accuracy of their interpretations.[55] When ED physicians were confident in their interpretation, the rate of discordant readings was 1.2%. More importantly, the rate of clinically significant errors was only 0.1%.

Rates of misinterpretation are even higher for CT scans. In one study, ED residents and attending physicians overlooked new infarcts, mass lesions, and cerebral edema, as well as parenchymal, subarachnoid, and subdural hemorrhages.[52] The rate of clinically important errors was 20-25%, with failure to recognize a cerebral infarction the most common.[52] It is unclear how many patients had adverse outcomes as a result, but the authors estimated that less than 1% of patients were managed inappropriately by ED staff.[52] Other studies confirm that the radiographic accuracy of non-radiologists in detecting a major cerebral infarction is poor, with misinterpretation rates of 30-40%.[56-59] This may directly impact patient outcomes since management of suspected stroke, specifically determining eligibility for thrombolytic therapy, requires an immediate and accurate interpretation of the CT. In addition, intraobserver and interobserver reliability are fair to poor, with kappa (κ) values ranging from 0.41-0.20.[57,59]

Radiology residents have better accuracy in interpretation of cranial CT scans, though not as high as that of certified radiologists. As part of a departmental quality control program, Lal and colleagues found the rate of significant misinterpretations by radiology residents was 0.9%.[60] Roszler et al reported moderate or major errors in 2.1% of resident interpretations of post-traumatic head CT scans.[61] Wysoki and colleagues[62] found that major discrepancies between the interpretations of residents and staff radiologists occurred in 1.7% of neuroradiologic studies and that the rate was significantly higher when CT scans were abnormal rather than normal (12.2% vs. 1.5%). Residents missed 9% of intracranial hemorrhages and 17% of cranial or facial fractures.

Opportunities for Impact

The accepted standard of care, supported by the ACR, calls for routine review of all radiologic studies by a radiologist or other qualified physician in a timely fashion.[8] Given the available data on staffing patterns,[9] we estimate that on-site radiologists are available to interpret radiographs about half the time. Radiologists generally read any remaining studies the following day. In academic centers, the percentage of films initially interpreted by residents may range from 20% to 100%, and the availability of on-call residents is highly variable.[42] It is also unclear what proportion of academic and community hospitals provides radiographic training courses for non-radiologists.

Study Designs

Few studies specifically focus on methods to reduce clinically significant misinterpretations of radiographs and CT scans. No randomized trials have evaluated the effectiveness of the 3 patient safety practices identified above. Table 35.1 shows 4 prospective before-after studies (Level 2 design) of educational interventions and quality improvement initiatives.[38-41] Evidence for the other 2 strategies (initial interpretations by radiology residents and review of all studies by radiologists) is limited to descriptive studies reporting rates of discordant interpretations for various groups of physicians (see above).

Study Outcomes

Most studies reported the rate of clinically significant misinterpretations (Level 2 outcome).[38,40,41,53,55,63] However, the definition of "clinically significant" was subjective and varied among reports. One trial reported only the percentage of correct CT interpretations (Level 3), without describing the significance of specific errors.[39]

Evidence for Effectiveness of the Practices

Levitt and colleagues[38] found a significant improvement in cranial CT scan interpretations by ED physicians after a one-hour training course. However, there were several limitations of this study. The intervention was not tested before implementation, raising concerns regarding its reliability and reproducibility. Previously published research at the same institution showed a 38.7% misinterpretation rate of cranial CT scans by ED physicians.[39] Because physicians were aware of these results, they may have engaged in their own efforts that led to improvement in CT scan interpretation. The improvement might also be explained by significant changes in case-mix, which was not measured. A multicenter study by Perron et al[39] showed that a reproducible educational course significantly improved residents' ability to interpret CT scans. However, the study is limited by possible selection bias (participation in the course was voluntary; post-test data were obtained in only 61 of 83 subjects). Although subjects in the study by Perron were retested after a 3-month washout period, neither course has been shown to result in sustained improvement. Quality improvement programs such as those described by Espinosa and Preston[40,41] successfully reduced the rate of misinterpreted radiographs and number of callbacks, respectively. Through ongoing feedback and review of misinterpreted radiographs, Espinosa and colleagues lowered the rate of important errors from 3% to 0.3%, a relative risk reduction of 90%. The initiative described by Preston led to a 42.9% relative reduction in callbacks to the ED, although the absolute magnitude was less impressive (0.3% absolute risk reduction).

We found no studies that compared the readings of ED physicians with those of radiology residents in a real-world environment. Only one investigation compared their diagnostic skill in an experimental situation.[18] Eng and colleagues exposed 4 groups of physicians (ED attendings, ED residents, radiology attendings, and radiology residents) to a series of 120 radiographs and calculated their receiver operating characteristic (ROC) curves. The radiographs were selected for their difficulty, and ED physicians had previously misinterpreted many of them. The area under the ROC curve was 0.15 higher for radiology faculty than for ED attendings (95% CI: 0.10-0.20) and 0.07 higher for all faculty than all residents (95% CI: 0.02-0.12). Compared with ED faculty, radiology residents had an additional area under the ROC curve of 0.08 (95% CI: 0.02-0.14).

Potential for Harm

There is a potential for both radiologists[51] and non-radiologists[64] to overread films (ie, falsely identify non-existent findings), which may result in unnecessary diagnostic testing or treatment. Since the vast majority of this literature considers the radiologist's reading to be the gold standard, the proportion of discrepancies in interpretation that are due to false-positive readings by radiologists is unclear.

Costs and Implementation

Only one study reported the costs of false-positive readings by ED physicians, which averaged $85 per false-positive radiograph.[64] Given the paucity of research, it is not possible to estimate the costs of implementing universal review of emergency films by an on-site radiologist. Finally, no studies have measured the costs of misreads to the patient and health care system (eg, transportation, return visits, repeat or unnecessary studies, unnecessary medications) which could potentially offset staffing costs. The marginal costs of after-hours staffing alone may be prohibitive, especially for low-volume sites. No information is available to estimate the cost of establishing a high-quality teleradiology program, or of educational programs for ED physicians or trainees.

Comment

The rates of misinterpreted radiographs and CT scans are high in many studies. Of particular concern is the 20-25% rate of clinically significant errors in reading cranial CT scans, even among experienced emergency physicians and neurologists. Although plain films are correctly interpreted more than 90% of the time, even "low" error rates of 1% or less are important given the sheer number of films.

The relative roles of ED physicians, radiology residents, certified radiologists, and other physicians will depend on their accuracy and their cost. The literature is notable for the relative dearth of studies of interventions to reduce radiologic misinterpretation by non-radiologists, even though dozens of studies have documented the problem. Where radiographs must be interpreted by non-radiologists, there is limited evidence that brief educational interventions and continuous quality improvement programs improve diagnostic accuracy. (Chapter 54 reviews general issues surrounding changing practice behavior through education.) It is possible that radiologists' routine review of plain radiographs may not be cost-effective when the non-radiologist clinician has a high level of confidence in the initial interpretation, but this has not been rigorously established. Coverage by radiology residents may add back-up accuracy to the reading of an ED attending, but Eng's study was biased toward a difficult set of radiographs that had previously been misinterpreted by emergency physicians.[18] The added value of a radiology resident's interpretation may be much lower in actual practice.

One avenue of research that could yield effective safety practices is human resource management. Essentially, staffing could be optimized such that specific tests could be triaged to the individual with the highest diagnostic accuracy. This kind of intervention would require assessment of both potential coverage gaps and the skill mix of the available labor force. A formal protocol might be developed and tested to identify coverage vulnerabilities and develop realistic coverage options based on measured performance of the available personnel at a particular site. While the value of this strategy is entirely speculative, it draws on general management science and could be explored more explicitly in health care.

Table 35.1. Educational interventions for non-radiologists*

Study	Study Setting	Intervention	Study Design, Outcomes	Results†
Levitt, 1997[38]	14 ED physicians at a level 2 trauma center in California	One-hour course on cranial CT interpretation	Level 2, Level 2	Clinically significant misinterpretations decreased from 23.6% to 4.0% (ARR 19.6%, RRR 83%)
Espinosa, 2000[41]	ED physicians at an academic hospital in New Jersey, 1993-99	Training on plain radiograph interpretation and ongoing feedback from radiologists about their errors	Level 2, Level 2	Clinically significant false negative interpretations: from 3% to 0.3% (ARR 2.7%, RRR 90%)
Preston, 1998[40]	ED physicians and radiologists at a 150-bed community hospital in Louisiana, 1990-95	Continuous quality improvement initiative with regular review of film discrepancies	Level 2, Level 2	Patient callbacks to ED for clinically significant misinterpretation: from 0.7% to 0.4% (ARR 0.3%, RRR 42.9%)
Perron, 1998[39]	83 ED residents at 5 academic centers in the southeast US, 1997-98	Two-hour course on neuroanatomy and cranial CT interpretation	Level 2, Level 3	Correct interpretation of a series of 12 CT scans: baseline 60%; 3 months after the course, 78% ($p<0.001$ for difference)

* ARR indicates absolute risk reduction; ED, emergency deparment; and RRR, relative risk reduction.
† Results reported as change from baseline to after intervention.

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Chapter 36. Pneumococcal Vaccination Prior to Hospital Discharge

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Background

Streptococcus pneumoniae (pneumococcus) is a leading cause of serious community-acquired infections, especially pneumonia, the sixth leading cause of death in the United States.[1] It causes over 50,000 cases of bacteremia and at least 500,000 cases of pneumonia annually in the United States.[1-3] Although pneumococcus is an important pathogen in meningitis, bronchitis, and otitis media, these disease processes will not be discussed in this report.

The epidemiologic rationale for targeting pneumococcal vaccination among hospitalized patients derives from research showing that two-thirds of patients hospitalized with serious pneumococcal infections had been hospitalized at least once in the previous 3-5 years.[4-6] One retrospective study showed that about 60% of persons 65 years of age and older hospitalized with pneumonia had been discharged from a hospital at least once in the prior 4 years.[4] A prospective cohort study of patients aged ≥65 discharged from the hospital showed that the 5-year probability for readmission with pneumonia was over 7%.[4] Hospitalization, therefore, is a marker for patients at increased risk of developing subsequent pneumococcal infection. Despite the scope of the problem and the appeals for action from multiple specialty societies and national health care organizations, the vaccine is underutilized in the inpatient setting.[5-7] This underutilization has been attributed to uncertain effectiveness of the vaccine and ineffective methods of vaccine delivery during hospitalization.

Hospital-based vaccination for patients at high risk of contracting pneumococcal infections is part of the action plan for adult immunizations developed by the Federal Centers for Disease Control and Prevention (CDC) and the Health Care Financing Administration (HCFA).[6] It is also endorsed by the CDC's Advisory Committee on Immunization Practices (ACIP)[5, 6] and the National Vaccine Advisory Committee. In addition, most national guidelines for the management of patients hospitalized with community-acquired pneumonia recommend vaccination against pneumococcus at time of discharge.[1,8]

Practice Description

Currently, pneumococcal vaccines contain 23 capsular polysaccharide antigens of *S. pneumoniae* (23-valent vaccines). Over 88% of the serotypes that cause invasive disease in the United States, as well as 88% of serotypes accounting for penicillin-resistant isolates, are included in the 23-valent vaccine.[2,9] Newer conjugate vaccines designed primarily to enhance the immune response in children are not covered in this review.

The practice of hospital-based pneumococcal vaccination is recommended for patients at increased risk for pneumococcal infection or increased risk of experiencing severe disease. Patients ≥65 years of age, or patients with certain chronic illnesses, including chronic cardiovascular disease, chronic pulmonary disease, diabetes, alcoholism, chronic liver disease, and functional or anatomic asplenia, are deemed high-risk.[3] It is also recommended that all immunocompromised patients (due to HIV infection, leukemia, lymphoma, long term steroid use, or organ transplantation, among other causes) and any patient admitted with a diagnosis of community-acquired pneumonia be vaccinated.[1,3,8] Vaccination could occur at any time during the hospitalization, but is often recommended at discharge.

Prevalence and Severity of the Target Safety Problem

The goal of pneumococcal vaccination in hospitalized patients is to reduce the morbidity and mortality associated with pneumococcal infection, namely pneumococcal bacteremia and pneumococcal pneumonia. The CDC estimates the annual incidence of pneumococcal bacteremia at 15-30 cases per 100,000 population and 50-83 cases per 100,000 in persons aged ≥65.[3] A recent study of the epidemiology of invasive *S. pneumoniae* (ie, associated with bacteremia) in the United States found an overall incidence of 23.2 cases per 100,000, corresponding to 62,840 cases annually.[2] The incidence among adults aged 65 and older was 59.7 per 100,000. The overall fatality rate was 10%, but patients aged 18-64 with an ACIP indication for vaccination had a fatality rate of 12.1%. Patients ≥65 years of age accounted for 51.4% of all deaths. These figures result in national estimates of over 6000 deaths in 1998 attributed to invasive pneumococcal disease.[2]

The precise incidence of pneumococcal pneumonia is harder to estimate due to the poor sensitivity and specificity of diagnostic tests for this disease. At least 25-35% of all pneumonias are linked to *S. pneumoniae,* resulting in a minimum of 500,000 cases of pneumococcal pneumonia annually. Bacteremia complicates pneumococcal pneumonia in 10-25% of cases.[3] The mortality rate for all patients hospitalized with community-acquired pneumonia is estimated at between 10-15%.[1]

Opportunities for Impact

Despite recommendations to routinely vaccinate eligible hospitalized patients, pneumococcal vaccine is underutilized. The high potential impact of vaccination is borne out by recent epidemiologic evidence. Based on 1998 projections, 76% of invasive pneumococcal disease and 87% of deaths occur in patients who are eligible for pneumococcal vaccine.[2] In addition, 88% of penicillin-resistant isolates during the same time period were of serotypes included in the 23-valent vaccine.[9]

The vaccine is currently recommended for over 30 million persons aged ≥ 65 and over 23 million persons <65 who are at high risk.[3] In 1997 only 45% of persons 65 and over reported ever receiving the vaccine.[7] A 12-State study of Medicare patients hospitalized with pneumonia showed that the opportunity to provide the vaccine was missed in over 80% of patients, and only 0.4% of hospitalized elderly patients were vaccinated prior to discharge.[5] More recent data from 1999 found a hospital vaccination rate in elderly patients screened, and not already vaccinated, of less than 9%.[6] In this same study, vaccination rates were higher for patients with a discharge diagnosis of pneumonia (23.6%), but still far below the Public Health Service goal of 60%. Few data are available on rates of vaccination in patients <65 years of age who are otherwise at risk for pneumococcal infection.

In this chapter we considered two independent, but linked sets of studies: those evaluating the effectiveness of pneumococcal vaccination and those assessing strategies to increase vaccination rates in hospitalized patients. These two areas are reviewed separately below.

36.1. Vaccine Effectiveness

Study Designs and Outcomes

Three meta-analyses (published in 1994,[10] 1999,[11] and 2000[12]) have analyzed the effectiveness of pneumococcal vaccination in adults. The first study by Fine et al[10] included 9

randomized controlled trials (RCTs) of vaccines (valences ranging from 6 to 17) in adults with and without risk factors for pneumococcal infection. Results were pooled and analyzed for effects in various subgroups with careful attention to study heterogeneity (rate differences (RD) were reported when significant heterogeneity existed).[10]

The second study[11] included 13 randomized and quasi-randomized studies of vaccines with valences ≥2. Consequently, this study [11] included 2 quasi-randomized studies with vaccine valences <6 that were excluded by Fine, but included a study by Austrian et al[13] that was only partially included in the Fine meta-analysis. Results of this second meta-analysis were reported as pooled odds ratios; when significant heterogeneity existed, ranges were presented instead of pooled results.[11]

The most recent meta-analysis identified 12 reports of 13 randomized controlled trials.[12] The authors excluded 3 prior trial reports[14-16] based on a predetermined decision to exclude quasi-randomized trials. Of these 3 quasi-randomized studies, the 2 older studies[14, 15] (26,000 patients) reported efficacy for the vaccine, while the more recent study (27,000 Finnish patients over aged 65) found no efficacy for pneumococcal vaccination.[16] The 13 trials included 3 reports[17-19] published after 1996 that were not included in either of the prior meta-analyses.

Despite the volume of RCTs that have been published, controversy still exists as to vaccine effectiveness in certain patient populations (high-risk, elderly), as wells as to the vaccine's effectiveness in reducing certain outcomes (pneumonia generally, and pneumococcal pneumonia). Consequently, we reviewed the 1997 summary report and recommendations of the Advisory Committee on Immunization Practices, which synthesizes multiple case-control and cohort studies of vaccine effectiveness in high-risk patients.[3] As an additional means to evaluate effectiveness, researchers from the CDC reported results of an indirect cohort analysis using a national database of pneumococcal bacteremia that compared distribution of pneumococcal serotypes causing infection in vaccinated and unvaccinated patients.[20]

The 3 meta-analyses reported Level 1 outcomes, including systemic pneumococcal infection and pneumococcal pneumonia. Two of these studies report infection rates with vaccine-type and non-vaccine-type organisms,[10,11] and 2 of the 3 meta-analyses additionally report on all-cause pneumonia, bronchitis and mortality.[10,12] All studies analyze data separately for elderly patients and high-risk patients, but the study by Hutchison et al[11] differs from the other two with respect to this part of the analysis. In this study,[11] vaccine efficacy in elderly and high-risk patients is assessed with logistic regression analysis after pooled odds ratios were determined, in contrast to the 2 other groups who report pooled odds ratios[10] and relative risk[12] separately for elderly, high-risk patients. The definition of pneumococcal pneumonia varied in many studies included in the pooled results, and in subsequent studies looking at the 23-valent vaccine.

The indirect cohort analysis by Butler et al[20] reported presumptive measures of effectiveness based on differing rates of isolation for certain serotypes of pneumococcus in vaccinated and unvaccinated patients (Level 2 outcome).

Evidence for Effectiveness of the Practice

The meta-analyses by Fine et al[10] and Hutchison et al[11] showed a protective effect of vaccination for systemic pneumococcal disease (66% effective overall, 83% effective against vaccine-types[10] in the former; 73% effective overall, 83% effective against vaccine-types in the latter[11]). Fine et al[10] found the vaccine 53% effective for presumptive pneumococcal pneumonia, but analysis for heterogeneity showed that the rate difference was not statistically significant. The summary odds ratios for all other outcomes did not achieve statistical significance, either

overall or in high-risk patients (ie, patients age • 55 years, patients with one or more chronic medical problems, and immunocompromised patients). Results for pneumococcal infection-related outcomes did achieve significance in low-risk patients.[10]

Hutchison et al found effectiveness against pneumococcal pneumonia ranging from 31% to 76% (results were significant in 3 trials), but study heterogeneity prevented a pooled estimate.[11] Regression analysis suggested similar benefits for systemic pneumococcal infection in elderly patients, but were inconclusive for systemic infection in chronically ill patients. For elderly patients, the authors estimated a number needed to treat (NNT) of 2520 to prevent a single case of pneumococcal bacteremia per year.[11]

The most recent meta-analysis[12] reported that in 3 comparisons involving approximately 21,100 immunocompetent subjects, pneumococcal vaccination was associated with significant reductions in the incidence of all-cause pneumonia (relative risk 0.56, 95% CI: 0.47-0.66), pneumococcal pneumonia (relative risk 0.16, 95% CI: 0.11-0.23), pneumonia deaths (relative risk 0.70, 95% CI: 0.50-0.96) and bacteremia (relative risk 0.18, 95% CI: 0.09-0.34). However, in 10 comparisons involving over 24,000 subjects who were elderly or likely to have impaired immune systems, the authors found no benefit to pneumococcal vaccination in terms of any clinical outcome of interest.[12] While the relative risk for pneumococcal bacteremia in elderly or high-risk patients showed a trend towards benefit, the results were not statistically significant (relative risk 0.53, 95% CI: 0.14-1.94).

One additional publication[21] has appeared since the search period covered by this most recent meta-analysis.[12] This publication represents a 6-month preliminary report from a prospective comparison between 2 large cohorts (>100,000 subjects each) of Swedish patients age • 65 years. Patients in one group received pneumococcal vaccine, influenza vaccine, or both. The other cohort consisted of all patients from the same region and age group who chose not to receive either of the vaccines. Among all vaccinated patients (results are pooled for pneumococcal and influenza vaccines), hospital admission for pneumonia (including all-cause pneumonia, pneumococcal pneumonia and invasive pneumococcal pneumonia) was significantly reduced, and overall mortality was reduced by 57% (95% CI: 55-60%). This study design has significant potential for bias, in that people who elect to participate in clinical studies tend to have better outcomes independent of the treatments they receive.[22-25] Nonetheless, it seems unlikely that the results observed in this study, including a 57% reduction in all-cause mortality over a 6-month period, could be attributable solely to a selection effect tied to patients' decision to participate in the study.

36.2. Vaccine Delivery Methods

Study Designs and Outcomes

Multiple studies have evaluated the effectiveness of various methods of increasing rates of vaccination among eligible patients in both the inpatient and outpatient settings. We focused our review on interventions relating to inpatient settings (ie, hospitals and nursing homes). Two systematic reviews published in 1994 and 1999 evaluate multiple strategies.[26, 27] The first review identified 3 studies in hospitalized patients and one in institutionalized patients.[26] The second review includes studies identified in the first, and comments on several additional studies.[27] Both reviews grade the included studies and report pooled estimates of effectiveness. The 2 reviews use slightly different definitions of the types of interventions, but are internally consistent with respect to the most effective strategy, namely *standing orders*.

All studies of the effectiveness of vaccine delivery methods reported vaccination rates. The results of several heterogeneous studies were pooled. There are few RCTs included in the summary estimates, and most interventions were studied with a before-after analysis of vaccination rates. Where possible, we report pooled estimates for given methods of improving vaccine delivery, and then comment on individual studies with the most promise for improving vaccination rates. No study of delivery methods looked at clinical outcomes.

Evidence for Effectiveness of the Practice

The systematic reviews of vaccine delivery methods with provider reminders in the inpatient setting were associated with absolute increases in vaccination rates that ranged from 7.5%-17% (Table 36.2.1).[26,27] One subsequent before-after study of chart reminders in hospitalized patients showed that vaccination rates in eligible patients increased from 0% to 28.8%.[28] The most impressive effects were seen for system-related changes, which increased vaccination rates by 45-51%. The most effective system-related change was the implementation of standing orders, which produced increases of 69-81% over usual care.[27] Studies of pneumonia clinical pathways (Chapter 52) have shown no effect on pneumococcal vaccination rates despite improvements in other pathway processes.[7]

Potential for Harm (from pneumococcal vaccination)

Three of the studies analyzed by Fine et al[10] reported data on adverse effects. Erythema ranged from 30.6-35.1% in the vaccine group compared with 1.7-3.5% in the control group. Fever developed in 2.0% of vaccinated patients compared with 1.2% of controls. No fatal or life-threatening adverse events occurred. Moore et al[12] report that in one study, in addition to increased rates of fever, vaccine recipients were more likely to experience a swollen or sore arm. There is the theoretical concern that patients vaccinated in the hospital may have an increased chance of being inappropriately revaccinated if they are unaware of their prior vaccination status (due to illness, etc.) or are being cared for by a physician other than their primary care doctor. A recent study compared the safety of the vaccine in patients receiving a first vaccination and patients receiving re-vaccination 5 years after their prior dose. There was an increase in self-limited local reactions with re-vaccination (RR 3.3, 95% CI: 2.1-5.1), but no serious adverse reactions were reported.[29] Few data address rates of adverse reactions in hospitalized patients vaccinated at discharge who receive re-vaccination earlier than 5 years after their prior dose.

Finally, the recent study in Ugandan HIV-infected adults showed trends toward increased rates of invasive pneumococcal disease, all pneumococcal events, and a statistically significant increase in all-cause pneumonia (hazard ratio 1.89, 95% CI: 1.1-3.2) among vaccine recipients.[19] This study calls into question the utility of giving pneumococcal vaccine to HIV-infected individuals.

Costs and Implementation

The cost-effectiveness of hospital-based pneumococcal vaccination is difficult to determine in light of the debate over how effective the vaccine is in reducing pneumococcal outcomes in at-risk populations. A cost-effectiveness analysis of vaccination for all elderly patients in the United States recently demonstrated a wide range of possible outcomes that depended on assumptions of vaccine effectiveness and duration of protection.[30] Base-case estimates showed that vaccination was cost saving at $8.27, and gained 1.21 quality-adjusted days of life per person vaccinated. Factoring in the future medical costs of survivors, vaccinating all patients ≥ 65 years of age would cost $9600 per quality-adjusted life year under the most

optimistic assumptions about vaccine effectiveness, and $51,661 per quality-adjusted life-year under worst-case assumptions.[30] A recent systematic review of pneumococcal vaccine cost-effectiveness by authors from the Cochrane Vaccines Field concluded that there is too much variability in assessments of cost-effectiveness (largely attributed to uncertainty over vaccine effectiveness) to reach any firm conclusions.[31] The authors called for a moratorium on all economic modeling until completion of a Cochrane review of pneumococcal vaccine effectiveness.

Comment

Pneumococcal vaccine is effective in reducing invasive disease in low-risk patients. It appears effective in reducing invasive disease in the elderly and high-risk patients based on results of one meta-analysis, multiple case-control studies, and a CDC serotype prevalence study. Importantly however, 2 meta-analyses failed to demonstrate a significant benefit of the vaccine for any outcomes in elderly or other high-risk patients. The vaccine appears efficacious in non-bacteremic disease (pneumococcal pneumonia) in low-risk patients, and one meta-analysis suggests a protective effect against pneumococcal pneumonia in the elderly,[11] but the others do not.[10,12] No study has demonstrated reductions in mortality. Thus, in the population most likely to be targeted by hospital-based immunization programs (elderly, high-risk) vaccine efficacy remains inconclusive. If it is assumed to be effective in reducing the incidence of the most serious outcome in this population (pneumococcal bacteremia), best estimates suggest a very large NNT (>2500).

Increasing antibiotic resistance, the aging of the US population and the major burden of pneumococcal disease among adults and elderly patients make increasing vaccination rates an obvious goal if, in fact, the vaccine is effective. The evidence supports system changes (in particular, the use of standing orders) as the best method of increasing vaccine rates in eligible, hospitalized patients. Though such rates can be increased, available data regarding vaccine efficacy raise doubts about the overall utility of both local and national initiatives aimed at increasing the rates of pneumococcal vaccination at hospital discharge. Early enthusiasm explains the large number of national pneumococcal vaccine initiatives, however available data on effectiveness provide only modest support for these initiatives.

Table 36.1. 1. Pneumococcal vaccine efficacy*

Study Description	Study Design, Outcomes	Results (95% Confidence Interval)
Meta-analysis of 9 RCTs. Vaccine valences 6-17, included international studies, high- and low-risk patients.[10]	Level 1A, Level 1	Definitive pneumococcal pneumonia: OR 0.34 (0.24-0.48), RD 4/1000 (0-7) Definitive pneumococcal pneumonia, vaccine types: OR 0.17 (0.09-0.33), RD 8/1000 (1-16) Presumptive pneumococcal pneumonia: OR 0.47 (0.35-0.63), RD 13/1000 (-21 to 47) All cause pneumonia: OR 0.90 (0.77-1.04) Mortality: OR 1.02 (0.90-1.14) Stratified results show no benefit in any outcome for high-risk patients.
Meta-analysis of 13 RCTs and "quasi-randomized" trials. Vaccine valences 2-17, includes international trials, high and low-risk patients.[11]	Level 1A, Level 1	Systemic infection, vaccine type: OR 0.17 (0.09-0.31) Systemic infection all types: OR 0.27 (0.13-0.49) All cause pneumococcal pneumonia: OR range 0.24-0.69, results significant in 3 studies Pneumococcal pneumonia, vaccine types: OR range 0.08-0.85, 8 of 9 studies showed reduced risk, results significant in 6 studies. Stratified results show benefit in elderly, mixed results in chronically ill.
Meta-analysis of 13 RCTs including three recent trials published after the last meta-analysis.[12]	Level 1A, Level 1	All pneumonias: Healthy (H), RR 0.56 (0.47-0.66), NNT 29 (24-36); Elderly, High Risk (E) RR 1.08 (0.92-1.27) Pneumococcal pneumonias: H, RR 0.16 (0.11-0.23), NNT 38 (33-45); E, RR 0.88 (0.72-1.07) Pneumococcal bacteremia: H, RR 0.18 (0.09-0.34), NNT 32 (26-44); E, (3 trials and only 927 pts), RR 0.53 (0.14-1.94) Pneumonia-related death: H, RR 0.70 (0.50-0.96), NNT 213 (114-1660); E, RR 0.93 (0.72-1.20)
Six-month preliminary results report from prospective comparison between cohort of 100,242 Swedish patients age • 65 years who received pneumovax, influenza vaccine, or both, and patients from the same region and age group who chose not to participate in the study.[21]	Level 2, Level 1	Results pool all vaccinated patients. Hospital admission for all cause pneumonia reduced by 29% (24-34), for pneumococcal pneumonia 36% (3-58), invasive pneumococcal pneumonia 52% (1-77). Overall mortaliy reduced by 57% (55-60)

* OR indicates odds ratio; RD, risk difference; and RR, relative risk.

Table 36.2. 1. Vaccine delivery

Study Description	Study Design, Outcomes	Results
Systematic review of studies from 1980-1997 of methods to increase vaccination rates. Multiple vaccines (eg, pneumococcal, influenza, hepatitis) delivered in multiple inpatient and ambulatory settings were reviewed, but this summary focuses on pneumococcal vaccine in hospitalized patients	Level 2A-3A Vaccination rates (Level 2)	Provider reminders increased vaccination rates by 17% (pooled absolute increases for all vaccines in all settings, with a range of 1-67%). Standing orders achieved a 51% mean absolute increase in vaccination rates (range 30-81%) for all vaccine types; pneumococcal vaccination in particular the increases ranged from 69% to 81% (in hospital setting and long-term care facility).
Systematic review of studies from 1979-1992. Multiple vaccine types in multiple settings.	Level 2A-3A Vaccination rates (Level 2)	Provider-oriented interventions resulted in a 7.5% increase in vaccination coverage (3.4-11.6%) System-oriented interventions resulted in a 45.5% increase in vaccination coverage (95% CI: 37.2-53.7%).

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Chapter 37. Pain Management

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Approximately 23 million people undergo surgery each year in the United States.[1] Despite pharmacologic interventions, at least 40-50% of postoperative patients report inadequate pain relief.[2] In addition, the practice of withholding analgesics due to fear of masking symptomatology and delaying diagnosis is still widespread in many emergency rooms and acute care settings. The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) and the Agency for Health Care Policy and Research (AHCPR) have established guidelines for the appropriate assessment and management of pain in general and postoperatively. Yet efforts to educate clinicians as to appropriate pain management, particularly in emergency departments (ED) and following surgery, have lagged behind the available evidence.

We have taken the point of view that untreated pain represents a patient safety problem. This chapter reviews pain management techniques and interventions in 4 domains: use of analgesics in patients with acute abdominal pain, the use of acute pain services, prophylactic antiemetics during patient-controlled analgesia therapy, and non-pharmacologic interventions for postoperative pain.

Subchapter 37.1. Use of Analgesics in the Acute Abdomen

Background

The use of analgesics in patients with acute abdominal pain has traditionally been condemned. The 1987 edition of Cope's *Early Diagnosis of the Acute Abdomen* states "though it may appear crude, it is really prudent to withhold morphine until a reasonable diagnosis has been made and a plan of action formulated."[1] The most recent edition of Cope's *Early Diagnosis of the Acute Abdomen* (1996) begins to question this long-accepted dogma, but still states that analgesia medication should be given only after a "responsible surgeon" takes a thorough history and performs a thorough physical examination.[3] As patients with acute abdominal pain are rarely evaluated by a surgeon within the first few hours of presentation, it seems inappropriate and inhumane to withhold pain medication if this practice is not supported by evidence.

Practice Description

Prescribing analgesics to patients with acute abdominal pain is infrequently done. When prescribed, dosages and routes vary, from intramuscular to intravenous morphine in 5 to 10 mg increments, or 0.1 mg/kg of body weight. Although JCAHO and AHCPR have established guidelines for the appropriate assessment and management of pain in general and postoperatively, neither addresses pain management in patients with acute abdomens. Therefore, the traditional practice of withholding analgesia in this setting has not been seriously challenged.

Prevalence and Severity of the Target Safety Problem

According to the National Center of Health Statistics, there were 100,385,000 total visits to US emergency departments in 1998. The most frequent principal reason for visits was stomach or abdominal pain (5.9 million).[4] Despite studies suggesting that the early administration of pain medication is safe and does not interfere with, and may actually facilitate, the ability to make a correct diagnosis, recent surveys of emergency room physicians and

surgeons indicate that the majority withhold analgesics in patients presenting with an acute abdomen. Wolfe et al[2] surveyed 443 emergency medicine physicians and found that although 85% believe that the conservative administration of pain medication did not change important physical findings, 76% choose not to give an opiate analgesic until after the examination by a surgeon. Graber et al[5] surveyed 131 practicing surgeons in Iowa and found 67% agreed that pain medications interfere with diagnostic accuracy, and 82% cited their concerns about diagnostic accuracy when deciding to withhold pain medication.

Opportunities for Impact

Limited data suggest that the number of patients with acute abdominal pain who actually receive pain relief before surgical evaluation is small. Therefore, by educating providers in appropriate pain management for these patients, the potential impact in emergency departments across the country is large.

Study Designs

Five prospective randomized controlled trials (Level 1) were evaluated. Four of the 5 used a double-blind design. In each study, patients were randomly assigned to receive opiate analgesia or placebo, and evaluated pre- and post-intervention for pain using variations of visual analog scales (Table 37.1.1).

Study Outcomes

All 5 studies evaluated the effects of analgesia on pain relief (Level 1), and diagnoses and treatment decisions (Level 2) in patients with acute abdominal pain. Two studies evaluated the effects of analgesia on physical examination findings and one evaluated the effects of analgesia on the diagnostic performance of ultrasonography in patients with acute abdominal pain (Level 3).

Evidence for Effectiveness of the Practice

All 5 studies showed that provision of analgesia decreased pain more than it decreased localization of tenderness. None of the 5 studies indicate that the practice of providing early analgesia is harmful. Specifically, no study found compromises in diagnosis or treatment of the acute abdomen after increasing the use of analgesia.

Potential for Harm

The traditional belief that analgesic use in patients with acute abdominal pain may mask signs and symptoms, delay diagnosis, and lead to increased morbidity and mortality was not supported in these studies. All 5 studies analyzed diagnostic or management errors that occurred in each group.

Attard et al[6] found no difference in localization of physical signs, and no difference in the surgeon's diagnostic confidence or management decision (to operate or to observe) between the 2 groups (opioids vs. placebo). The decision to operate or to observe was incorrect in 2 patients in the opioid group (4%) and in 9 patients in the placebo group (18%). The surgeon's initial diagnosis one hour after the injection was incorrect in all of these patients. These same 2 patients in the opioid group were incorrectly diagnosed as having non-specific abdominal pain when first assessed, but the diagnosis was subsequently changed and both patients had an inflamed appendix removed within 24 hours of admission. Neither appendix was perforated. There were no deaths or side effects from the injection for either group.

LoVecchio et al[7] documented changes in localization of physical examination findings and differences in diagnosis between patients receiving opioid analgesia and placebo. The use of opioids was associated with some change in tenderness and localization in half the patients but led to no delays in care or eventual morbidity. The emergency department diagnosis differed from the final discharge diagnosis in 4 of the 49 total patients. One such patient had received placebo and 3 had received high-dose morphine (no significant difference). There was no delay in outcome or time to treatment in any patient.

Zoltie[8] demonstrated that 17/134 (12%) of those receiving opioids had altered physical signs. Of the 50 patients (out of 288 in the total opiate and placebo groups) whose signs changed during the evaluation, the most common change (n=32) was alteration in bowel sounds. The remaining 18 had altered sites of tenderness, in most cases a migration of a large region to a smaller, more precise area. In no case was the diagnosis altered by a change in physical signs. To the contrary, the correct diagnosis was facilitated in several cases, particularly in the 18 cases where the site of pain changed.

Vermeulen et al[9] also found that the use of opioids did not change the appropriateness of the surgeons' decision making. Among female patients, the decision to operate was appropriate more often in the opioid group, but the difference between this group and the placebo group was not statistically significant. In male patients and overall, opiate analgesia did not influence the appropriateness of the decision. The appropriateness to discharge patients without surgery was 100% in both groups. No patient who had left the hospital after 24 hours of observation without surgery was readmitted or operated on at another local hospital. The study also assessed the impact of analgesia on the accuracy of abdominal sonography. For diagnosis of appendicitis, ultrasound had lower sensitivity (71.1%) and higher specificity (65.2%) in the opioid group than in the placebo group, 80.6% and 53.8%, respectively.

Similarly, Pace et al[10] found 3 diagnostic or management errors in each group (out of 35 morphine and 36 control patients). The use of opioids did not alter the physicians' ability to evaluate accurately and treat patients appropriately.

Costs and Implementation

The costs associated with implementing appropriate analgesic practice for patients with acute abdominal pain are limited to physician education programs and the cost of the analgesia and associated monitoring. There were no cost outcomes reported in any of the 5 studies.

Comment

From the available evidence, we conclude that appropriate use of analgesics in patients with acute abdominal pain effectively decreases pain and does not interfere with diagnosis or treatment. Recent surveys suggest many physicians believe conservative administration of pain medication does not interfere with diagnosis and treatment of patients with acute abdominal pain. Despite this recognition, the gap between understanding and practice remains large, and abdominal pain is often undertreated.

Table 37.1.1. Randomized controlled trials of analgesia in patients with acute abdominal pain*

Study	Study Participants; Intervention	Outcomes	Results†
Zoltie, 1986[8]	268 adults with acute abdominal pain admitted to a hospital in the UK; sublingual buprenorphine vs. placebo	Level 1	Pain better after 1 hour: 64/134 vs. 59/122 (p=NS). Only 6/32 (19%) patients who received no tablet reported pain was better after 1 hour Change in physical signs after 1 hour: 22/134 (16%) vs. 24/122 (20%); when site of tenderness changed, it usually was resolution of a large region to a smaller, precise area In no case was the diagnosis altered by a change in physical signs
Attard, 1992[6]	100 selected adults admitted with clinically significant abdominal pain; intramuscular papaveretum vs. placebo	Level 1	Pain score: 3.1 vs. 8.3 (p<0.0001) Tenderness score: 5.1 vs. 8.3 (p<0.0001) Diagnostic or management errors: 2/50 vs. 9/50 (p=0.05)
Pace, 1996[10]	75 patients with acute abdominal pain at a US military emergency department; morphine	Level 1	Improvement in pain‡: 3.9±2.8 vs. 0.8±1.5 (p<0.01) Accuracy of provisional diagnosis: no difference between groups Diagnostic or management errors: 3/35 vs. 3/26 (p=NS)
LoVecchio, 1997[7]	49 adults with acute abdominal pain and peritoneal signs ("acute abdomen") admitted to the emergency department of a tertiary care hospital in NY; intravenous morphine vs. placebo	Level 1	Pain after 15 minutes: subjective and objective improvement with morphine (p<0.005) but not with placebo (p• 0.05) Significant change in physical exam with regard to tenderness and localization: 16/32 vs. 1/16 (p<0.005)§ Initial and final diagnosis differed in 4 patients (morphine 3, placebo 1) but there was no delay in outcome or time to treatment (by retrospective chart review)
Vermeulen, 1999[9]	340 adults with pain in the right lower part of the abdomen at a university hospital emergency department; intravenous morphine vs. placebo	Level 1	Pain after approx. 45 minutes: significantly reduced with placebo and, to a greater extent, with morphine (p<0.001) Ultrasound had lower sensitivity (71.1% vs. 80.6%, p<0.05) and higher specificity (65.2% vs. 53.8%, p<0.05) in patients who received morphine. The negative predictive value of US was significantly lower in female patients who received morphine rather than placebo. Other changes in predictive value did not achieve statistical significance. Opiate analgesia did not significantly influence the appropriateness of the decision to operate

* NS indicates not statistically significant.
† Results are reported as intervention group vs. control group.
‡ Pain was measured on visual analog scale; larger values represented greater pain relief.
§ Change in tenderness from 2 or more quadrants to one and the loss of rebound tenderness or vice versa were considered significant

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Subchapter 37.2. Acute Pain Services

Background

The concept of an acute pain service (APS) was first reported in 1988. Its genesis was the recognition of the problems wrought by inadequate postoperative pain management and appreciation that acute pain may prolong recovery or precipitate complications. Over the past 15 years, in the United States and worldwide, hospitals have created multidisciplinary acute pain services, with specially trained staff and resources geared toward providing up-to-date techniques and education. The APS creates a framework in which postoperative pain can be managed more effectively, hopefully leading to less discomfort and fewer postoperative complications.

Practice Description

An APS attempts to bridge the gap between physicians, nurses and patients to coordinate pain management. The roles of the APS are 1) educating patients, 2) educating nurses and physicians, 3) selecting appropriate analgesic techniques for different situations, 4) preparing guidelines for different analgesic regimens, 5) helping to manage acute pain problems, and 6) performing quality control activities.

Most acute pain services in the United States are anesthesiology-based. The comprehensive pain management teams usually consist of staff anesthesiologists, resident

anesthesiologists, specially trained nurses, pharmacists and physiotherapists. Some services are nurse-based rather than anesthesia-based.

Prevalence and Severity of the Target Safety Problem

Approximately 50% of patients undergoing surgery do not receive adequate pain relief.[1] Failure to appropriately treat pain stems from lack of knowledge and skills on the part of health care providers and those responsible for health care system management, and insufficient patient education. The "safety" problem targeted by the practice of implementing an APS is postoperative pain and morbidity.

Opportunities for Impact

Approximately 34-44% of hospitals in Europe[2,3] and most major institutions in the United States[4] have organized APSs. In general, few smaller hospitals have an APS. Therefore, there are many opportunities to institute acute pain services in hospitals.

Study Designs

Six articles were reviewed for this chapter. All are observational studies; one with a control, 5 without controls. All 6 studies looked at the intervention of an acute pain service in patients undergoing surgery (Table 37.2.1).

Study Outcomes

Three of the 6 studies assessed postoperative pain (Level 1). Two of the 6 studies assessed adverse effects and safety (Level 2) and one assessed knowledge and attitudes, perceived adequacy of patients' pain relief and the effect on staff workload and relationships.

Evidence for Effectiveness of the Practice

All 3 studies that assessed postoperative pain scores found improvements. Bardiau et al[2] showed that differences in pain score were most pronounced (around 50%) in patients undergoing vascular, maxillofacial, gynecologic, oral and urologic surgeries. Gould et al[5] showed a reduction in median visual analog scores for pain during relaxation, movement and deep inspiration. Tighe et al[6] showed a significant improvement in patient perception of pain relief after introduction of an APS.

Schug and Torrie[7] found no complications resulting in sustained morbidity or mortality when anesthesiology-based APS provided postoperative pain relief. Potentially severe complications (without sequelae) occurred in 0.53% of patients. In one study by Tsui et al,[8] 1.8% of patients developed respiratory complications (bradypnea, hypercapnia, oxygen desaturation), 1.2% developed hypotension, and 28.8% and 15.1%, respectively, developed nausea and vomiting. None suffered long-term sequelae.

Although the postoperative setting is a logical place for acute pain services, they may also be useful in patients who experience pain as part of a disease process. Although used more for managing chronic conditions such as cancer and low back pain, acute pain services are also gaining popularity in treating hospitalized patients with pain due to a medical condition. There are no rigorous trials of APSs as they are used for medical patients.

Potential for Harm

Fragmentation of care (ie, lack of continuity between the anesthesiologist performing preoperative evaluation and anesthesiologist providing postoperative pain control, or

fragmentation of care among multiple physicians) and decreased attention by the physician-of-record may result in problems from the intervention. However, no studies have examined these concerns.

Costs and Implementation

Although none of the studies directly examined costs of implementing an acute pain service, one study estimated that an APS might be cost-effective.[6] Some data suggest that a nurse-based APS may be more cost-effective than an anesthesiologist-based APS, although there are no formal analyses of this supposition.[9]

Principal obstacles to implementing such acute pain services include financial constraints, the challenges of educating newly qualified doctors regarding pain management, and the complexity of published guidelines.[9]

Comment

Studies of APSs are mostly observational, measuring postoperative pain, adverse outcomes and staff knowledge and attitudes regarding its implementation. Although these studies indicate that acute pain services can improve postoperative pain without endangering patient safety, no formal recommendation can be made in the absence of high quality, systematic reviews of the benefits, costs and feasibility of implementing these services.

Table 37.2.1. Studies of acute pain services in postoperative pain management*

Study Setting	Study Design, Outcomes	Results
1304 patients in the pre-APS inception phase and 671 patients after its implementation undergoing various surgeries in a university teaching hospital[2]	Level 3, Level 1	Significant reduction of all pain indicators after APS inception ($p<0.0001$); major improvement (>50%) in patients undergoing vascular, maxillofacial, gynecologic, urologic and oral surgeries
2035 patients undergoing various surgical operations at a university hospital[5]	Level 3, Level 1	Reduction in mean pain from 45 (95% CI: 34-53) to 16 (95% CI: 10-20) after APS
1518 patients undergoing various surgeries at a district general hospital[6]	Level 3, Level 1	Significant reduction of pain ($p<0.0001$) after APS
2509 patients under APS care at a tertiary referral teaching hospital; 1759 received systemic analgesia, 590 epidural; 160 other techniques[8]	Level 3, Level 2	Side effects were unusual (1.8% respiratory, 1.2% hypotension, 28.8% nausea, 15.1% vomiting)
3016 patients treated by an APS for postoperative pain[7]	Level 3, Level 2	0.53% potentially severe adverse reactions and no severe complications
48 staff members (36 nurses, 12 house officers) working in two surgical units[10]	Level 3, Level 3	Two-thirds of staff thought APS decreased their workload; perception of patient pain relief significantly better in APS unit

* APS indicates acute pain service; CI, confidence interval.

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Subchapter 37.3. Prophylactic Antiemetics During Patient-controlled Analgesia Therapy

Background

Nausea and vomiting are common side effects of patient-controlled analgesia (PCA) with opioids. When severe, nausea and vomiting may limit a patient's tolerance of PCA. Giving antiemetics prophylactically has been suggested as a way to prevent PCA-associated nausea and vomiting.

Practice Description

No study has definitively determined the best prophylactic antiemetic in patient-controlled analgesia. Prophylactic treatments that have been used include droperidol, 5-HT_3 receptor antagonists (ondansetron, tropisetron), clonidine, promethazine, hyoscine, propofol and metoclopramide. Prophylactic antiemetics have been given both at the induction of anesthesia and at the end of surgery. A relatively new approach to minimizing nausea and vomiting associated with PCA involves the addition of an antiemetic to PCA, so that the patient receives both analgesic and antiemetic with each PCA demand dose.

Prevalence and Severity of the Target Safety Problem

The incidence of postoperative nausea and vomiting has varied widely (from 8 to 92%) among studies.[1] There is no evidence that the incidence of nausea and vomiting with PCA is any different than that with intramuscular opioids. In patients receiving PCA, 57-90% report nausea and 27-40% report vomiting. There appears to be no clear advantage to using one opioid over any others in PCA in terms of postoperative emesis.

Opportunities for Impact

The degree to which prophylactic antiemetics are used in routine practice with PCA is unknown.

Study Designs

Tramer and Walder[2] conducted a systematic search for randomized trials (MEDLINE, Embase, Cochrane library, reference lists, hand-searching, no language restriction) that compared prophylactic antiemetics with placebo or no treatment in patients receiving postoperative PCA with opioids. Their review identified 14 placebo-controlled trials with different regimens of droperidol, ondansetron, hyoscine transdermal therapeutic system, tropisetron, metoclopramide, propofol and promethazine. One PCA delivered tramadol; all others delivered morphine.

Both relative risk and number needed to treat were calculated. To estimate the frequency of drug-related adverse effects, the relative risk and the number needed to harm were calculated.

Study Outcomes

The main end point for efficacy was prevention of emetic events (Level 1). The incidence of emetic events with active treatments (experimental event rate) and with placebo or no treatment (control event rate) was extracted. Nausea, vomiting, and "any emetic event" (nausea, vomiting, or nausea and vomiting) were extracted from each trial. Data on drug-related adverse effects (Level 2) were extracted as well.

Evidence for Effectiveness of the Practice

Without antiemetic drugs, the incidence of nausea averaged 43% (range 22-80%), vomiting 55% (45-71%), and any emetic event 67% (54-87%). At 24 hours postoperatively, the cumulative incidence of nausea and vomiting in patients not receiving any antiemetic treatment added to their PCA-morphine was approximately 50%.

The best-studied antiemetic was droperidol. It was added to morphine-PCA in 6 placebo-controlled trials involving 642 patients. Droperidol 0.017-0.17 mg/mg of morphine (0.5-11 mg/d droperidol) was significantly more effective ($p=0.04$) in preventing nausea than placebo, without evidence of dose-responsiveness. Compared with placebo, the number needed to treat with droperidol to prevent nausea was 2.7 (95% CI: 1.8-5.2) and to prevent vomiting was 3.2 (95% CI: 2.3-4.8).

The second most frequently reported drugs were 5-HT_3 receptor antagonists (ondansetron, tropisetron). Their effect on vomiting was satisfactory, with numbers needed to treat of approximately 5 compared with placebo. There was no evidence of any antinausea effect.

Promising results were shown with some of the other interventions (clonidine, promethazine). However, the limited numbers of patients studied did not generate sufficient evidence to make a recommendation.

Potential for Harm

With placebo, the absolute risk of minor adverse events (sedation, drowsiness and dizziness or anxiety, restlessness and agitation) was 0-20%. In those trials that reported adverse events with droperidol, doses of the antiemetic ranged from 1.2 mg to cumulative doses of 7.4 mg. There were no obvious differences in the incidence of minor adverse effects compared with placebo with droperidol doses $\leq$4 mg. In all droperidol trials, 2 adverse effect-related study withdrawals were documented. No extrapyramidal symptoms were documented in any trial.

Costs and Implementation

Costs of prophylactic antiemetics during patient-controlled analgesia have not been evaluated. However, 1-4 doses of droperidol per day (0.25-0.5 mL q 4 h) costs $2.83-$11.32 while 1-3 doses of ondansetron per day costs $22.50-$67.50. Implementing prophylactic antiemetics during PCA seems neither difficult nor time-consuming.

Comment

Postoperative nausea and vomiting is a common event and patients may refuse to continue PCA because of these side effects. Prophylactic droperidol appears to decrease such side effects. Of 100 patients who have droperidol added to their PCA pump with morphine, 30 who would have vomited or been nauseated had they not received droperidol will not suffer these effects.

The results of this systematic review should be confirmed, as a pooled effect size estimated by meta-analysis must be considered provisional. Additional randomized, placebo-controlled trials assessing droperidol's prophylactic efficacy in the morphine-PCA setting can establish its optimal use in this clinical setting.

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Subchapter 37.4. Non-pharmacologic Interventions for Postoperative Plan

Background

Over the past decade, increased attention has been paid to non-pharmacologic interventions in conjunction with pharmacologic interventions to treat postoperative pain. The Agency for Health Care Policy and Research's (AHCPR) 1992 Clinical Practice Guideline on Acute Pain Management recommends that preoperative preparation includes educating patients concerning pain control. The Guidelines specifically state that management of postoperative pain may include cognitive-behavioral interventions, such as relaxation, distraction, and imagery.[1] Nonetheless, non-pharmacologic interventions can only be considered beneficial if postoperative pain is effectively decreased.

Practice Description

Non-pharmacologic interventions typically fall into 3 categories: health care information, skills teaching and psychosocial support.[2] Health care information includes information on preparation for surgery, timing of procedures, functions and roles of health care providers, self-care responsibilities, and pain/discomfort information. Skills teaching includes coughing, breathing and bed exercises, hypnosis, cognitive reappraisal and relaxation exercises. Relaxation strategies include such techniques as the modified Jacobson method, Flaherty and Fitzpatrick jaw relaxation, relaxation tapes, tapes with structured breathing, muscle relaxation and pleasant imagery, and cognitive relaxation. Psychosocial support includes identifying and alleviating concerns, providing reassurance, problem solving with the patient, encouraging questions and increasing frequency of support.

Prevalence and Severity of the Target Safety Problem

The safety problem targeted by the practice of non-pharmacologic interventions is postoperative pain. At least 40-50% of postoperative patients report inadequate pain relief, despite pharmacologic interventions.[3] Postoperative pain can have deleterious psychological and physiologic consequences that contribute to patient discomfort and longer recovery periods, and may compromise outcomes.[1] It also consumes greater health care resources.

Opportunities for Impact

Non-pharmacologic interventions are increasingly used in management of postoperative pain, although the exact proportion of patients receiving such interventions is unknown.

Study Designs

We identified 7 meta-analyses of studies evaluating the effectiveness of non-pharmacologic interventions on postoperative pain. Two of these meta-analyses evaluated various non-pharmacologic interventions for the management of acute pain. Devine[2] conducted a meta-analysis of 191 studies looking at psychoeducational care (including all 3 intervention categories above) for adult surgical patients. Sindhu[3] conducted a meta-analysis including 49 randomized controlled trials looking at non-pharmacologic nursing interventions (preoperative education/information, relaxation, music, imagery, biofeedback, multidisciplinary approaches and others) for the management of acute pain. AHCPR[1] conducted a systematic search of non-drug intervention studies on postoperative pain management. One hundred forty studies were included and formal meta-analysis of 3 was performed. The American Society of Anesthesiologists Task Force on Pain Management, Acute Pain Section[4] performed a systematic search for acute pain management in the perioperative setting. Two hundred thirty-three articles were used in the formal meta-analysis; the number of articles regarding education of patients was not reported. Good[5] performed a systematic search of trials evaluating the effects of relaxation and music on postoperative pain. Suls and Wan[6] performed a systematic search of trials evaluating the effects of sensory and procedural information on coping with stressful medical procedures and pain. Seers and Carroll[7] performed a systematic review of various relaxation techniques for postoperative pain relief. Table 37.4.1 lists the 7 articles and briefly describes their salient features.

Study Outcomes

All studies reported postoperative pain (Level 1) as a primary outcome measure. Other outcomes, such as recovery time, psychological distress, and opioid intake were reported in some cases (Level 1).

Evidence for Effectiveness of the Practice

The extensive literature covered by the meta-analyses suggested beneficial effects of psychoeducational care, education and instruction of patients, music and relaxation techniques (Table 39.5.1). The 2 meta-analyses that examined opioid intake failed to show an effect of non-pharmacologic interventions in reducing postoperative opioid consumption.

Potential for Harm

One study[7] reported no adverse events in any of the trials for any of the treatment or control groups. Otherwise, adverse consequences of non-pharmacologic interventions on postoperative pain management were not addressed.

Costs and Implementation

Direct information on costs of non-pharmacologic interventions was not reported in these 7 studies. Devine and Cook[8] found that the beneficial impact on length of stay and medical complications rendered non-pharmacologic interventions cost-beneficial. Another review[2] hypothesized that costs could potentially be decreased by non-pharmacologic interventions, since the length of hospital stay was shortened by an average of 1.5 days (11.5%).

The most obvious direct cost of psychoeducational care is the increased staff time to provide these services. Based on average treatment duration of 42 minutes, a comprehensive version of the intervention would probably not take more than 1 hour per patient.[8] Less obvious direct costs might result from staff time to plan the protocol for psychoeducational care and/or to develop patient education materials, in-service programs or staff meetings to teach or review the protocol, printing or purchasing patient education materials, transporting patients to group teaching sessions, and staff time to document the level of care provided.

Comment

Effective treatment of postoperative pain continues to be a challenge. In addition to analgesia, non-pharmacologic interventions may provide some benefit in reducing postoperative pain. Clinicians have a wide range of options to consider when developing a comprehensive version of non-pharmacologic care appropriate for their patients. As such interventions are low risk and appeal to many patients, they should be explored in practice and further research.

Table 37.4.1. Studies of non-pharmacologic interventions for postoperative pain

Study setting; Practice Examined	Study Design, Outcomes	Results*
Adult surgical patients (# not stated), 92% in American hospitals (45% teaching, 43% general hospitals); health care information, skills teaching, psychosocial support[2]	Level 1-3 A, Level 1	79-84% of studies found beneficial effects; Average effect size values were 0.43 for recovery, 0.38 for pain, 0.36 for psychological distress; Length of stay decreased 11.5%
Not reported; transcutaneous nerve stimulation, education/instruction, relaxation[1]	Level 1-3 A, Level 1	Simple/complex relaxation techniques, education/ instruction effective in reducing mild-moderate pain
Not reported; education and participation of patients and families in pain control[4]	Level 1-3 A, Level 1	Education improves pain control, reduces adverse outcomes
Adult pts who have undergone torso surgery (# not stated); relaxation techniques, music[5]	Level 1-3 A, Level 1	Total pain decreased in 10 of 13 studies; Sensory pain† reduction was reported in 6 of 12 studies; Affective pain‡ decreased in 10 of 13 studies; Unidimensional pain decreased in 4 of 7 studies; Observed pain decreased in 4 of 4 studies
Not reported; sensory and procedural information (explanations of what will be happening and how patients can expect to feel) [6]	Level 1-3 A, Level 1	Combination of procedural and sensory preparation significantly better than control on all measures; effect sizes with combination larger than with either type of information alone
362 patients undergoing fractured hip repair, removal of malignant skin lesions, major elective abdominal surgery, elective cholecystectomy, abdominal hysterectomy, femoral angiography; jaw relaxation, imagery, music, breathing, relaxation tapes[7]	Level 1-3 A, Level 1	3 of 7 studies showed significant decrease in pain sensation/pain distress in those who had relaxation; 1 out of 5 trials showed significant improvement in psychological outcomes; less anxiety in relaxation group
3387 adult patients; education, relaxation, music, imagery, biofeedback, multidisciplinary approach[3]	Level 1-3 A, Level 1	Effect sizes ranged from 2.25 to 1.78; strong heterogeneity

* Effect size is the standardized difference between the control and experimental groups regarding the measure of interest in each study. Positive values indicate benefit with the intervention.

† Sensory pain refers to ability to discriminate where pain is occurring and respond appropriately.

‡ Affective pain is the sensation of pain as something unpleasant and to be avoided.

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Section F. Organization, Structure, and Culture

Chapter 38. "Closed" Intensive Care Units and Other Models of Care for Critically Ill Patients

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Background

Patients in the intensive care unit (ICU) require complex care relating to a broad range of acute illnesses and pre-existing conditions. The innate complexity of the ICU makes organizational structuring of care an attractive quality measure and a target for performance improvement strategies. In other words, organizational features relating to medical and nursing leadership, communication and collaboration among providers, and approaches to problem-solving[1] may capture the quality of ICU care more comprehensively than do practices related to specific processes of care.[2]

Most features of ICU organization do not exert a demonstrable impact on clinical outcomes such as morbidity and mortality.[3] While hard clinical outcomes may not represent the most appropriate measure of success for many organizational features, the role of "intensivists" (specialists in critical care medicine) in managing ICU patients has shown a beneficial impact on patient outcomes in a number of studies. For this reason, the Leapfrog Group, representing Fortune 500 corporations and other large health care purchasers, has identified staffing ICUs with intensivists as one of three recommended hospital safety initiatives for its 2000 purchasing principles (see also Chapter 55).[4]

In this chapter, we review the benefits of full-time intensivists and the impact of "closed ICUs" (defined below) on patient outcomes. Much of this literature makes no distinction between improved outcomes in general and decreased harm in particular. However, given the high mortality[5] and complication rates[6-8] observed in ICUs, it seems reasonable to consider global interventions such as organizational changes as patient safety practices.

Practice Description

The following practice definitions are synthesized from studies reviewed for this chapter. For all of these models, the term "intensivist" refers to a physician with primary training in medicine, surgery, anesthesiology or pediatrics followed by 2-3 years of critical care medicine (CCM) training.

Open ICU model—An ICU in which patients are admitted under the care of an internist, family physician, surgeon or other primary attending of record, with intensivists available providing expertise via elective consultation. Intensivists may play a *de facto* primary role in the management of some patients, but only within the discretion of the attending-of-record.

Intensivist Co-management—An open ICU model in which all patients receive mandatory consultation from an intensivist. The internist, family physician, or surgeon remains a co-attending-of-record with intensivists collaborating in the management of all ICU patients.

Closed ICU model—An ICU in which patients admitted to the ICU are transferred to the care of an intensivist assigned to the ICU on a full-time basis. Generally, patients are accepted to the ICU only after approval/evaluation by the intensivist. For periods typically ranging from one week to one month at a time, the intensivist's clinical duties predominantly consist of caring for patients in the ICU, with no concurrent outpatient responsibilities.

Mixed ICU models—In practice, the above models overlap to a considerable extent. Thus, some studies avoid attempting to characterize ICUs in terms of these models and focus instead on the level of involvement of intensivists in patient care regardless of the organizational model. This involvement may consist of daily ICU rounds by an intensivist (thus including "closed model ICUs" and "intensivist comanagement"), ICU directorship by an intensivist (possibly including examples of all 3 models above), or simply the presence of a full-time intensivist in the ICU (also including examples of all 3 models.)

Intensivist models—ICU management may include all of these models. These models are contrasted with the open ICU model, in which an intensivist generally does not participate in the direct care of a significant proportion of the ICU patients.

Prevalence and Severity of the Target Safety Problem

ICUs comprise approximately 10% of acute care hospital beds.[9] The number of annual ICU admissions in the United State is estimated to be 4.4 million patients.[10] Due to an aging population and the increasing acuity of illness of hospitalized patients, both the total number of ICU patients and their proportional share of hospital admissions overall are expected to grow.[11]

ICU patients have, on average, mortality rates between 12 and 17%.[25] Overall, approximately 500,000 ICU patients die annually in the United States. A recent review estimated that this mortality could be reduced by 15 to 60% using an intensivist model of ICU management.[12]

Young and Birkmeyer have provided estimates of the relative reduction in annual ICU mortalities resulting from conversion of all urban ICUs to an intensivist model of management model.[10] Using conservative estimates for current ICU mortality rates of 12%, and estimating that 85% of urban ICUs are not currently intensivist-managed, the authors calculated that approximately 360,000 patients die annually in urban ICUs without intensivists. A conservative projection of a 15% relative reduction in mortality resulting from intensivist-managed ICUs yields a predicted annual saving of nearly 54,000 lives.

By only measuring ICU mortality rates, this analysis may underestimate the importance of intensivist-managed ICUs. In addition to mortality, other quality of care outcome measures that might be improved by intensivists include rates of ICU complications, inappropriate ICU utilization, patient suffering, appropriate end-of-life palliative care, and futile care.

Opportunities for Impact

Currently, a minority of ICUs in the United States utilizes the intensivist model of ICU management.[13] Intensivists are even less frequently found in non-teaching and rural hospitals. The potential impact of the intensivist model is far-reaching.

Study Designs

Among 14 studies abstracted for this chapter, 2 were systematic reviews and 12 were original studies. One systematic review is an abstract that has not yet appeared in journal form and does not provide cited references.[12] The other systematic review evaluated 8 references, all of which are included in this chapter.[10] An additional 4 studies absent from the systematic review are included here. These 4 studies include 2 abstracts that were published after the 1999 systematic review,[14,15] and 2 studies of pediatric ICUs with intensivists.[16,17]

Among the original studies, 6 incorporated historical controls and 5 used a cross-sectional approach. One study[18] had both historical and cross-sectional components. The original studies include 4 studies of adult medical ICUs, 6 studies of adult surgical ICUs and 2 studies of

pediatric multidisciplinary ICUs. Intensivist models used by the studies cited for this review include 4 closed ICUs, 4 mixed ICUs, 3 ICUs with intensivist comanagement and one open ICU.

Several studies were excluded, including abstracts with insufficient data,[19-25] unclear distinctions in patient management between control groups and intervention (intensivist managed) groups,[26,27] intensivist models that may have important roles in future practice (eg, telemedicine consultation with remote management) but are not yet widely available[28,29] and considerably older studies.[30]

Study Outcomes

Required outcomes of interest in studies chosen for this chapter were ICU mortality, overall in-hospital mortality, or both. Some studies also included morbidity outcomes, adverse events and resource utilization (eg, length of ICU and hospital stay), levels of patient acuity or severity of illness (ICU utilization) and levels of high-intensity intervention usage. Studies addressing the impact of intensivist ICU management on resource utilization without mortality or outcome data were excluded. There are no data regarding the impact of intensivists.

Evidence for Effectiveness of the Practice

As shown in Table 38.1, most of the studies report a decrease in unadjusted in-hospital mortality and/or ICU mortality, although this decrease did not reach statistical significance in 3 of the 14 studies.[16,18,31] One study found a statistically insignificant increase in the unadjusted mortality rates associated with the intensivist model ICU.[32] This study also found that the ratio of expected-to-actual mortality was reduced in the intensivist-model ICUs. This finding was associated with a higher severity of illness scores in the intensivist-model ICU population. A similar finding of significantly improved outcomes after adjusting for severity of illness and comparing expected-to-actual mortality rates was demonstrated in one pediatric study.[16] Overall, the relative risk reduction for ICU mortality ranges from 29% to 58%. The relative risk reduction for overall hospital mortality is 23% to 50%. These results are consistent with those of a previous systematic review that found a 15% to 65% reduction in mortality rates in intensivist-managed ICUs.[10]

Data concerning long-term survival (6 and 12 months) for patients cared for in ICUs with and without intensivist management is not available. Differences in outcomes between closed ICUs, mixed ICU models and co-managed ICUs are difficult to assess. Studies that have addressed conversion from an open to a closed model did not utilize full-time intensivists in the open model study phases.[18,32-34] Therefore it is not clear to what extent improved patient outcomes resulted only from changes in intensivists' direct patient care and supervision.

The observational studies evaluating these practices suffer from 2 major limitations. Half of the studies retrospectively compared post-implementation outcomes with those during an historical control period. Because none of these studies included a similar comparison for a control unit that remained open in both time periods, we lack information on secular trends in ICU outcomes during the time periods evaluated. The other major limitation associated with comparing mortality rates for ICU patients relates to differences in ICU admission and discharge criteria under different organizational models. Under the intensivist model, patients are generally accepted to the ICU only after approval/evaluation by the intensivist. Thus, conversion to an intensivist model ICU may bring about changes in the ICU patient population that are incompletely captured by risk-adjustment models and confound comparisons of mortality rates. Moreover, these changes in ICU admitting practice may exert contradictory effects. For example, an intensivist model ICU may result in fewer ICU admissions for patients with dismal

prognoses, and less futile care for patients already in the ICU. On the other hand, intensivist-managed ICUs with stricter admission and discharge criteria may result in a greater overall acuity of illness for the ICU patients and therefore higher mortality rates.

Potential for Harm

The potential for harm resulting from intensivist management is unclear. Concerns raised in the literature about intensivist-managed ICUs include the loss of continuity of care by primary care physicians, insufficient patient-specific knowledge by the intensivist,[35] reduced use of necessary sub-specialist consultations, and inadequate CCM training of residents who formerly managed their own ICU patients.

Perhaps more worrisome is the impact that adoption of this practice would have on physician staffing and workforce requirements. Without a substantial increase in the numbers of physicians trained in CCM, projected increases in the ICU patient population over the next 30 years will result in a significant shortfall in the intensivist workforce.[11]

Costs and Implementation

These studies did not address the incremental costs associated with implementation of full-time intensivists. Several studies have analyzed resource utilization and length of stay associated with intensivist-managed ICUs.[13,16,18,19,29,31,32,36] The results of these studies are variable with respect to costs. Some demonstrate a decrease in ICU expenses. Others found increased costs, likely due to the increased use of expensive technologies. Still others show little overall cost differential. The cost-effectiveness and cost-benefit of an intensivist-model ICU requires further study.

Comment

Outcomes research in critical care is particularly challenging for several reasons. It typically relies on observational outcomes studies, and must account for the diversity and complexity of variables measured and controlled for, such as patient-based, disease-based, provider-based and therapy-based variables. Despite these challenges and limitations, the literature fairly clearly shows that intensivists favorably impact ICU patient outcomes. What remains unclear is which intensivist model to recommend—intensivist consultation versus intensivist co-management versus closed ICUs. Also, we do not know the degree to which the choice among these models depends on intensivist background – ie, medicine, anesthesiology or surgery. Finally, because the mechanism of the benefit of intensivist models is unknown, the degree to which this benefit can be captured by other changes in practice (eg, adoption of certain evidence-based processes of ICU care) remains unclear.

The major incentive for clarifying these issues concerns the implications for staffing ICUs in the future. While the evidence supports the beneficial role of full-time intensivists, the current number of trainees is insufficient to keep pace with the expected increase in the number of ICU patients.[11] Until we are able to sufficiently increase the size and number of CCM training programs for physician specialists, complementary solutions for meeting critical care management demands should be considered. These might include incorporating physician-extenders such as nurse practitioners and physician assistants with specialized critical care training, increased participation by hospitalists in care of ICU patients,[37] regionalization of critical care services,[38] or providing innovative methods to extend intensivists' expertise to remote sites through telemedicine consultations.[28] The latter practice seems particularly promising—a recent time series cohort study found an approximately 33% decrease in severity-

adjusted hospital mortality and a nearly 50% decrease in ICU complications when a technology-enabled remote ICU management program was instituted in a community-based ICU.[28]

Table 38.1. Intensivist management in the care of critically ill patients*

Study Setting	Study Year	ICU Type	Study Design, Outcomes	Intensivist Intervention	Mortality Relative Risk Reduction (%)	
					ICU	Hospital
Closed ICU Model						
Tertiary care, urban, teaching hospital; patients with septic shock; historical control[33]	1982-1984	MICU	Level 3, Level 1	Closed	NA	23
Teaching hospitals (n=2); two study designs using historical and concurrent controls[18]	1992-1993	MICU	Level 3, Level 1	Closed	NA	Retrospective: 19 (p=NS) Prospective: 26 (p=NS)
Tertiary care, urban, teaching hospital; historical control[32]	1993-1994	MICU	Level 3, Level 1	Closed	NA	-38 (p=NS)† 0/E 13‡
Tertiary care, urban, teaching hospital; historical control[34]	1995-1996	SICU	Level 3, Level 1	Closed	58	50§
Mixed ICU models						
ICUs (n=16) with different characteristics; cross-sectional[16]	1989-1992	Pediatric MICU SICU	Level 3, Level 1	Mixed	RRR 25¶ OR 1.5**	NA
ICUs (n=39) with different characteristics; cross-sectional. Patients with abdominal aortic surgery[38]	1994-1996	SICU	Level 3, Level 1	Mixed	NA	OR 3.0§§
ICUs (n=31) with different characteristics; cross-sectional. Patients with esophageal resection[14]	1994-1998	SICU	Level 3, Level 1	Mixed	NA	RRR 73¶ OR 3.5**
ICUs (n=39) with different characteristics; cross-sectional. Patients with hepatic resection[15]	1994-1998	SICU	Level 3, Level 1	Mixed	NA	RRR 81¶ OR 3.8**
Community teaching hospital; historical control[40]	1992-1994	MICU	Level 3, Level 1	Open	29	28
Co-managed ICUs						
Tertiary care ICU in a teaching children's hospital[16]	1983-1984	Pediatric MICU SICU	Level 3, Level 3	Co-manage	48 (p=NS)	NA
Tertiary care, Canadian teaching hospital; historical control[39]	1984-1986	SICU	Level 3, Level 1	Co-manage	52	31
Tertiary care, urban, teaching hospital; cross-sectional comparison (concurrent control)[31]	1994-1995	SICU	Level 3, Level 1	Co-manage	NA	32 (p=NS)

* ICU indicates intensive care unit; MICU, medicalintensive care unit; Mixed, mixed intensivist model (including daily ICU rounds by an intensivist, the presence of a full-time intensivist, open units with comanagement and closed units with mandatory consultations or only intensivist management); NA, not available as outcome (was not evaluated); NS, not stastically significant; and SICU, surgical intensive care unit.

† Negative value indicates an increase in relative risk of mortality.

‡ O/E is observed to expected mortality ratio based risk adjustment

§ Hospital mortality measured 30-days after discharge

¶ RRR is the unadjusted mortality relative risk reduction
** OR is the adjusted odds ratio of increased mortality associated without an intensivist model.

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Chapter 39. Nurse Staffing, Models of Care Delivery, and Interventions

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Background

Unlike the work of physicians, the work of registered nurses (RNs) in hospitals is rarely organized around disease-specific populations. Rather, patients are generally grouped by age and/or intensity of nursing care (eg, pediatrics or intensive care). Adult patients who require the least amount of nursing care (the largest proportion of hospitalized patients), may be separated into medical or surgical units but may also be combined on one unit. Because the work of RNs and other nurses is organized differently than the work of physicians, this chapter explores the literature related to nursing structure and process variables that may affect outcomes that relate to patient safety.

Investigations of patient outcomes in relationship to nurses and their professional responsibilities in hospitals commonly involve *structural measures* of care[1-4] including numbers of nurses, number of nurse hours, percentage or ratios of nurses to patients, organization of nursing care delivery or organizational culture, nurse workload, nurse stress, or qualification of nurses. Less commonly, studies involve *intervention or process measures* of care including studies based on the science of nursing and others using nurses as the intervention.[1-5] The use of structural variables rather than process measures to study the impact of nursing activities reflects the greater availability of data relating to the former (often obtainable from administrative sources) compared with the latter (typically requiring chart review of direct observation). A number of structural measures have received considerable attention, specifically measures of staffing levels in the face of major cost cutting and other changes in health care over the past 15-20 years. In 1996, the Institute of Medicine[6] reported that there were insufficient data to draw conclusions about the relationship between nurse staffing and inpatient outcomes. However later studies have revisited this issue, allowing us to review the literature relating patient outcomes to various measures of nurse staffing levels, such as full time equivalents (FTEs), skill mix (proportion of RN hours to total hours), or RN hours per patient day.

This chapter does not address patient outcomes as they relate to various "patient classification systems" (PCSs), although the prevalence of the use of such systems deserves mention. PCSs predict nursing care requirements at the individual patient level in order to determine unit staffing, project budgets, define an objective measure for costing out nursing services, and to maintain quality standards.[8] Although PCSs are used for multiple purposes, they are an inadequate tool for determining unit staffing on a daily or shift basis.[9-11] In addition, there are numerous patient classification systems[12-14] and most are specific to one hospital or one nursing unit. The validity and reliability of PCSs are inconsistent and the systems cannot be compared with each other.[8-10,15-28] Thus, rather than reviewing studies that analyze various PCS scores to patient outcomes, we review studies addressing the question of whether or not "safe thresholds" exist for levels of nursing care.

Practice Description

The availability of nurses, the organization of nursing care, and the types of nursing interventions vary by institution. Structuring nurse staffing (eg, availability of nurses, organizational models of nursing care) and care interventions to meet "safe thresholds" could be considered a patient safety practice. However, no studies have evaluated thresholds explicitly. This chapter reviews the precursor evidence from observational studies about the strength of the relationship between nursing variables and patient outcomes, so that possible safe thresholds may be inferred. We assess evidence that relates patient outcomes to:

1) *specific numbers, proportions, or ratios of nurses to patients (nurse staffing);* Nurse availability variables generally characterize the number of hours nurses spend with patients. Typically, the time is not measured for each patient, but rather averages are measured based on the census of nurses to patients at a particular point in time. There are several common ways of accounting for this nurse staffing and no standardized way to measure it (Table 39.1).

2) *specific organization of nursing care delivery, nursing models of care, or organizational culture;* Organization of nursing care variables (Table 39.2) may also include various nursing care delivery models, nursing unit or hospital culture, or governance structures. An issue of governance that has been studied by Aiken[29] and others[30] includes how much autonomy a nurse has to make practice decisions, how much control she has over practice decisions, how much collaboration occurs between physicians and nurse in the organization, and communication patterns; and

3) *specific nursing interventions*; Although nursing interventions are frequently studied in outpatient setting,[31,32-39] perhaps because these venues provide nurses more flexibility to make independent decisions,[40-42] studies in the inpatient setting have included measures of *education, training,* or *retraining of nurses, providing audit data* to nurses, and capturing nurse *assessment* of patient outcomes.

The varieties of intevention studies require some comment. Education interventions are popular in nursing research because they involve less risk than interventions that directly involve patients and are more readily approved by hospitals and physicians.[43-51] Unfortunately, some investigators have made the assumption (which led to the failure to measure clinical outcomes) that increasing nursing knowledge or changing a practice, such as handwashing, automatically improves outcomes.[52,46,48,53]

Because a large part of a nurse's job is assessment, investigators have used various nursing assessments as interventions, such as fall risk assessment, pressure ulcer risk assessment, or identification of patients at high risk for malnutrition,[55-60] to reduce adverse events. In multidisciplinary protocols, the nursing activity is often assessment, rather than a nursing process or procedure.[49]

Other process-oriented interventions that lack sufficiently rigorous data to evaluate here, include *specialty nurses*,[61,62-65] and *interventions based on nursing science* in the realm of nurse decision making in acute care hospitals (eg, mouth care to reduce mucositis, nonpharmacutical

interventions to reduce pain, nausea and vomiting, increase sleep, and improve wound healing).[31,66-73]

Prevalence and Severity of the Target Safety Problem

The target safety problems are patient adverse events such as mortality and morbidity. The challenge is to create an optimum practice environment so that nurses can ideally reduce safety problems.

Commonly studied adverse hospital events such as falls (Chapter 26), medication errors (Part III, Section A), and pressure ulcers (Chapter 27), are often used as outcome indicators for nursing practice.[83-90] Less commonly studied are issues related to improving basic symptom management (eg, symptoms related to poor sleep, nutrition, or physical activity, or anxiety, pain, distress and discomfort caused by symptoms, or distress caused by diagnostic tests). In the last decade there has been increasing public and legislative pressure to improve hospital environments and address some of the heretofore ignored issues.[91-93]

Opportunities for Impact

Unfortunately, there is no definitive evidence as to specific thresholds for RN or total nursing staff hours per patient day, or nursing skill mix for various patient populations or nursing unit types. The lack of empirical evidence has been problematic for politicians, the public and the nursing community. Because decisions about nurse staffing do not have a scientific basis and are instead based on economics and anecdotes, nurse executives and managers are frequently at odds with staff nurses; especially those represented by labor unions, over staffing. Nurse executives are charged with providing safe patient care at a responsible cost. The need to constrain budgets by reducing nursing hours is in conflict with the needs of the unions and, some allege, in conflict with the needs of patients.

Based in part on some limited data, New York and Massachusetts have passed legislation requiring formulae to be developed that ensure safe patient care.[95,96] New Jersey has regulations which state that licensed nurses shall provide at least 65% of the direct care hours and requires an acuity system for patient classification.[97] California Assembly Bill 394 directs the California Department of Health Services to establish nurse-to-patient staffing ratios for acute care hospitals by January 1, 2002. Sixteen states other than California have nurse staffing legislation on the calendar but have not implemented ratios.[94]

Staffing and ratios are items for collective bargaining and contract negotiations in some areas.[98-104] Registering complains about “unsafe staffing” may be the nurses’ only recourse unless there is a negotiated agreement between the union and the hospital.

Current utilization of practices using nursing interventions to make an impact on adverse hospital events is most likely limited due to uncertainty about effectiveness of specific interventions. Resources necessary for conducting systematic studies of nursing care provided in hospitals and then implementing the practices found to be helpful are scarce.[105-109]

Study Designs

Searches of MEDLINE from 1990, CINHAL from 1966, documents published by the American Nurses Association, and the Cochrane Collaboration Library identified no randomized clinical trials or non-randomized controlled trials analyzing nurse staffing and adverse events. The study designs for nurse availability (Table 39.3) and organization of care (Table 39.4) are

Level 2 or 3 designs. Mitchell et al[111] references several randomized trials in her review article. However, the articles mentioned used advanced practice nurses such as clinical nurse specialists, or home care visits as the intervention.[62,112,113] The study by Jorgensen et al[114] was set in a hospital but the comparison was between a specialty stroke unit and a regular care unit. The difference was between the different organization of stroke treatment, not nurse skill mix. The studies abstracted are observational studies that are case control, cohort, before-after, or health services research using data from large public databases.

The study designs for nurse interventions (Table 39.5) vary from Level 1 to 3. Five studies use education of nurses as the intervention, and an additional 3 studies cover enhancements to education efforts (ie, providing data to nurses about adverse events in their units).

Study Outcomes

The studies of structural measures reported Level 1 or 2 outcomes, along with various other outcomes such as length of stay, patient satisfaction or nurse satisfaction. Most of the studies corrected for potential confounders and most adjusted outcomes based on patient acuity. The process measure studies vary between Level 2 and 3 outcomes. The studies also often included Level 4 outcomes, such as nurse knowledge, but these did not meet inclusion criteria. Most of the studies used adverse events such as falls, nosocomial infection, pain, phlebitis, medication errors or pressure ulcers as outcomes.

Evidence for Effectiveness of the Practice

Nurse Staffing

Table 39.4 summarizes the findings of studies exploring measures of nurse availability. When measured at the hospital level, there is mixed evidence that nurse staffing is related to 30-day mortality.[30,83,115-118] There is scarce but positive evidence that leaner nurse staffing is associated with unplanned hospital readmission and failure to rescue.[117,119-121] There is strong evidence that leaner nurse staffing is associated with increased length of stay, nosocomial infection (urinary tract infection, postoperative infection, and pneumonia), and pressure ulcers.[122-125]

Results are conflicting as to whether richer nurse staffing has a positive effect on patient outcomes. Although 5[30,89,118,120,129] of the 16 studies in Table 39.3 reported no association between richer nurse staffing and positive patient outcomes, the other 11 that report an association tend to be more recent, with larger samples and more sophisticated methods for accounting for confounders. These studies had various types and acuities of patients and, taken together, provide substantial evidence that richer nurse staffing is associated with better patient outcomes. Although the optimum range for acute care hospital nursing staffing is most likely within these ranges, none of the studies specifically identify the ratios or hours of care that produce the best outcomes for different groups of patients or different nursing units.

Models of Nursing Care Delivery

The 7 studies in Table 39.4 provide mixed evidence about the relationship between organization of nursing care and patient outcomes. Aiken et al[29] found that hospitals with "magnet" characteristics have lower mortality in one study, but not in another,[115] and Shortell et

al[30] also does not find an association in ICUs. Seago[79] found a reduction in medication errors after a change to patient-focused care and Grillo-Peck et al[130] found a reduction in falls after a change to a RN-UAP (unlicensed assistive personnel) partner model was introduced. The 2 review articles[111,131] reported mixed results about whether nursing models, nurse surveillance or work environment is associated with patient outcomes. Thus, the evidence is insufficient to direct practice.

Nursing Interventions

Table 39.5 provides details about studies using nurse interventions. The first 3 studies provide support for the idea that added education of nurses reduces infection and thrombophlebitis. The subsequent 2 studies, however, found no difference in bloodstream infection or medication error before and after added education. The overall evidence indicates that using education as the sole intervention does not always change patient outcomes. Educational interventions were related to changes in nurse practices and, in some studies, also related to decreasing adverse events.[44,47,54] However adding another intervention such as providing feedback data or benchmarking results, was more likely to be associated with improved patient outcomes,[55-57] including decreased infection rates, pressure ulcer rates, and fall rates.[55-57]

Potential for Harm

The potential for harm of patients associated with structural interventions such as too few nurses has been documented.[83-85,124,125] Studies involving process interventions such as using education of nurses, providing data to nurses, and interventions based on nursing science, seem to have a low probability of harm, but that is as yet unknown.

Costs and Implementation

Few of the abstracted studies mentioned cost, although several measured length of stay as an outcome variable. Pratt et al[63] found no difference in quality of care measures using a 100% RN skill mix and an 80% RN skill mix in 2 wards in one hospital in the United Kingdom. The cost was less with the 80% skill mix but the nurses who worked with less experienced staff reported an increase in workload and increase in stress. California is faced with impending legislated minimum nurse staffing ratios in the acute care hospitals. Based on early studies,[149] at least 40% of California hospitals may see a negative financial effect because of the need to increase staffing. Additionally, based on a number of predictions,[150,151] there is now, and there will continue to be, a significant shortage of registered nurses in the US. Thus, implementing any increase in RN staffing may be very difficult.

One investigator who provided data to nurses as the intervention related to urinary catheter infection reported an estimated cost savings of $403,000.[55] Another investigator who also provided data to nurses related to nosocomial pressure ulcer rates estimated implementation costs but not cost saving.[57] The investigator who studied adding an IV team (specialty nurses) reported a savings of $53,000/saved life and $14,000/bloodstream infection. Using clean rather than sterile dressings on open postoperative wounds saved $9.59/dressing with no change in rate of wound healing. Based on these studies, it is likely that some nursing interventions can save costs.

Comment

The studies evaluated in this review include only medical, surgical and ICU nursing units. Other data from more specialized units, the outpatient setting, and those pertaining to subsets of patients tend to mirror the findings of the evidence evaluation, and are cited in this section alongside those abstracted and presented in the evidence tables.

The relationship of hospital environment to patient outcomes is still being debated. However, evidence using *hospital-level* data indicates increasing the percentage of RNs in the skill mix, increasing RN FTEs or hours per patient day or average daily census is associated with decreased risk-adjusted mortality.[116,131,152,153] Other studies, also aggregating data to the hospital level, found that increasing RN hours per patient day is associated with decreased nosocomial infection rates,[121,154] decreased urinary tract infections, thrombosis and pulmonary complications in surgical patients,[124] decreased pressure ulcers, pneumonia, postoperative infection and urinary tract infection.[122,125] Hunt[117] found that decreasing ratios were related to increasing readmission rates but were not related to mortality rates.

The cost of primary data collection has limited the number of studies using data aggregated to the individual *nursing unit*. There is some evidence that decreased nurse-to-patient ratios in the ICU was associated with an increase in blood stream infections associated with central venous catheter,[126] while an increase in agency nurses was related to other negative patient outcomes.[156] A study in the NICU setting found understaffing and overcrowding of patients led to an outbreak of Enterobactor cloacae.[155] In 42 ICUs Shortell et al. found that low nurse turnover was related to shorter length of stay[30]; in 65 units an increase in nurse absenteeism was related to an increase in urinary tract infection and other patient infections but not to other adverse events.[157] Amaravadi et al[158] found that night nurse-to-patient ratio in ICUs in 9 hospitals for a select group of patients who had undergone esophagectomy was not associated with mortality but was associated with a 39% increase in length of stay and higher pneumonia rates, reintubation rates, and septicimia rates. As noted previously, Blegan et al found that as the percentage of RNs per total staff (skill mix) increased there was a decrease in medication errors, decubitus ulcers, and patient complaints up to a skill mix of 85-87% RNs.[83,84]

In several studies, increasing skill mix was associated with decreasing falls, length of stay, postoperative complications, nosocomial pneumonia, pressure ulcer rates, urinary tract infection, and postoperative infection.[122-125,130] Several studies with varying sample sizes have found skill mix to be unrelated to mortality.[111,118,159,160] Others have found skill mix to be unrelated to treatment problems, postoperative complications, unexpected death rates, or unstable condition at discharge[129] and found no relationship between skill mix or nursing hours per patient day and medication errors, falls, patient injuries, and treatment errors.[161] In an early study of primary (all RN) and team (skill mix) nursing care delivery models, there was no relationship between percent of RNs and quality of care as measured by nurse report[162] and in 23 hospitals in the Netherlands, there was no relationship between RN-to-patient ratio and incidence of falls. 89

Although mixed, the overall evidence seems to indicate that proportion of RN hours per total hours and richer RN-to-patient ratios likely do not affect 30-day mortality, may be

associated with in-hospital mortality, and are probably associated with adverse events such as postoperative complications, nosocomial infection, medication errors, falls, and decubitus ulcers.

Based on recent work, nurse staffing was examined in "best practices" hospitals. This included hospitals recognized by the American Nurses Association's Magnet Hospital program, those commended by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), those listed in *USA Today's* Top 100 Hospitals, those listed in *US News and World Report's* set of high-quality hospitals, those noted for having better than expected mortality for heart attacks and newborn readmission rates by the Pacific Business Group on Health (PBGH), and those recognized by the Bay Area Consumer Checkbook for high quality. There is significant variation in nurse staffing among these best practices hospitals. The staffing data for best practices hospitals do not consistently demonstrate that hospitals rated highly for quality of patient care have uniformly richer staffing than do other hospitals.[74] Because units within hospitals vary widely in nurse staffing and outcomes, results from data aggregated to the hospital level are difficult to interpret.

At present the literature is insufficient to make a reasoned judgment about organization of the work environment of nurses. Further work is needed in the area of nurse interventions. If there truly is to be an emphasis on reducing adverse events in hospitals and creating hospital environments that promote health and healing, resources for research related to nurses and nursing interventions must be found.

Table 39.1. Measures of nurse staffing

Nurse Staffing Measure	Definition
Nurse to patient ratio	Number of patients cared for by one nurse typically specified by job category (RN, Licensed Vocational or Practical Nurse-LVN or LPN); this varies by shift and nursing unit; some researchers use this term to mean nurse hours per inpatient day
Total nursing staff or hours per patient day	All staff or all hours of care including RN, LVN, aides counted per patient day (a patient day is the number of days any one patient stays in the hospital, ie, one patient staying 10 days would be 10 patient days)
RN or LVN FTEs per patient day	RN or LVN full time equivalents per patient day (an FTE is 2080 hours per year and can be composed of multiple part-time or one full-time individual)
Nursing skill (or staff) mix	The proportion or percentage of hours of care provided by one category of caregiver divided by the total hours of care (A 60% RN skill mix indicates that RNs provide 60% of the total hours of care)

Table 39.2. Models of nursing care delivery

Nursing Care Delivery Models	Definition
Patient Focused Care	A model popularized in the 1990s that used RNs as care managers and unlicensed assistive personnel (UAP) in expanded roles such as drawing blood, performing EKGs, and performing certain assessment activities
Primary or Total Nursing Care	A model that generally uses an all-RN staff to provide all direct care and allows the RN to care for the same patient throughout the patient's stay; UAPs are not used and unlicensed staff do not provide patient care
Team or Functional Nursing Care	A model using the RN as a team leader and LVNs/UAPs to perform activities such as bathing, feeding, and other duties common to nurse aides and orderlies; it can also divide the work by function such as "medication nurse" or "treatment nurse"
Magnet Hospital Environment/Shared governance	Characterized as "good places for nurses to work" and includes a high degree of RN autonomy, MD-RN collaboration, and RN control of practice; allows for shared decision making by RNs and managers

Table 39.3 Structural measures: availability of nurses and patient outcomes (First 11 studies showed positive associations; final 5 studies detected no significant effect)

Study Setting	Study Design, Outcomes	Availability of Nurses	Effect Size (coefficient, mean differences, OR)
1. Data were collected form 1,205 consecutively admitted patients in 40 units in 20 acute care hospitals and on 820 nurses in the US[115]	Level 3, Level 1&3	0.8 mean nurse/ patient day with a range of 0.5-1.5 nurses/patient day	This measure was significantly associated with 30-day mortality (OR .46, 95% CI: 0.22-0.98). An additional nurse per patient day reduces the odds of dying by one-half.
2. All patients who developed a central venous catheter bloodstream infection during an infection outbreak period (January 1992 through September 1993) and randomly selected controls. Cohort study: all SICU patients during the study period (January 1991 through September 1993)[126]	Level 3, Level 1	1.2 patient/nurse and 20 nursing hours per patient day (HPPD) 1.5 patient/nurse and 16 nursing HPPD 2 patient/nurse and 12 nursing HPPD	There was a significant relationship between nurse to patient ratios and nursing hours and central venous catheter bloodstream infection in the SICU. For 1.2 patients/nurse and 20 HPPD the adjusted odds ratio was 3.95 (95% CI: 1.07-14.54), 1.5 patients/nurse and 16 nursing HPPD, 15.6 (95% CI: 1.15-211.4), and for 2 patients/nurse and 12 HPPD, 61.5 (95% CI:1.23-3074).
3. 39 nursing units in 11 hospitals for 10 quarters of data between July, 1993 and December, 1995 in the US [84]	Level 3, Level 1&2	Proportion of direct care RN hours; total direct care hours; Up to 87.5% RN skill mix	With patient acuity controlled, direct care RN proportion of hours was inversely associated with medication errors (-0.525 $p<0.05$), decubiti (-0.485 $p<0.05$), and complaints (-0.312, $p<0.10$). Total direct care hours was positively associated with decubiti (0.571, $p<0.10$), complaints (0.471, $p<0.10$), and mortality (0.491, $p<0.05$). A curvilinear relationship was found so that as RN proportion increased, rates of all adverse events decreased up to a proportion of 88% RNs. Above that level, as RN proportion increased, the adverse outcomes increased.

4. 42 inpatient units in one 880-bed hospital in the US [83]	Level 3, Level 1&2	8.63 mean total hours of care; 69% RN skill mix; up to 85% skill mix	With patient acuity controlled, direct care RN proportion of hours was inversely associated with medication errors/doses (-0.576, $p<0.05$) and falls (-0.456, $p<0.05$). Total direct care hours was positively associated with medication errors/doses (0.497, $p<0.05$). A curvilinear relationship was found so that as RN proportion increased, medication error rates decreased up to a proportion of 85% RNs. Above that level, as RN proportion increased, the medication error increased
5. Data from hospital cost disclosure reports and patient discharge abstracts from acute care hospitals in California and New York for fiscal years 1992 and 1994[125]	Level 3, Level 1&2	7.56-8.43 mean total hours of care/nursing intensity weight (NIW); 67.7% to 70.5% RN skill mix	Total hours/NIW was inversely associated with pressure ulcer rates (-15.59, $p<0.01$). RN hours in California, but not New York, was inversely associated with pneumonia (-0.39, $p<0.01$) Nonsignificant association with postoperative infection rates.
6. Data from hospital cost disclosure reports, patient discharge abstracts and Medicare data from acute care hospitals in Arizona, California, Florida, Massachusetts, New York, and Virginia for 1996[123]	Level 3, Level 1&2	5.76 mean licensed hours of care/ 83.3% RN skill mix	Skill mix was inversely associated with pneumonia (-0.20, $p<0.01$), postoperative infection (-0.38, $p<0.01$), pressure ulcers (-0.47, $p<0.01$), and urinary tract infections (-0.61, $p<0.01$).
7. Data from hospital cost disclosure reports, patient discharge abstracts from acute care hospitals in California, Massachusetts, and New York for 1992 and 1994[122]	Level 3, Level 1&2	7.67-8.43 mean total hours of care; 67.7-70.5% skill mix	RN hours were inversely associated with pneumonia (-0.39, $p<0.01$), pressure ulcer rates (-1.23, $p<0.01$), and postoperative infection (-0.47, $p<0.01$) but not significant for urinary tract infections.

8. Data from HCFA Medicare Hospital Mortality Information 1986 and the American Hospital Association 1986 annual survey of hospitals[116]	Level 3, Level 1	0.9 mean RN/ADC (average daily census); 60% skill mix	Controlling for hospital characteristics, number of RNs/ADC was not significantly related to adjusted 30-day mortality rate but proportion of RNs/all nursing staff was significantly related to adjusted 30-day mortality rate (adjusted difference between lower and upper fourth of hospitals -2.5, 95% CI: -4.0 to -0.9)
9. Data from the American Hospital Association 1986 annual survey of hospitals and medical record reviews from July 1987 to June 1988 in 6 large PPOs[128]	Level 3, Level 3	52.2 (Texas)-67.6% (California) skill mix	Controlling for hospital characteristics, number of RNs/ADC was not significantly related to problem rate but proportion of RNs/all nursing staff was significantly related to lower problem rates (California lower rates 3.58, upper rates 2.30 $p<0.0001$)
10. Data from the American Hospital Association Annual Survey of Hospitals for 1993 and the Nationwide Inpatient Sample from the Agency for Health Care Policy and Research for 1993 (HCUP-3)[124]	Level 3, Level 1	67.8% mean skill mix	Proportion of RN FTEs/all nursing FTEs was inversely related to thrombosis after major surgery (beta -33.22, 95% CI: -57.76 to -8.687), urinary tract infection after surgery (beta -636.96, 95% CI: -852.78 to -421.15), pneumonia after major surgery (beta -159.41, 95% CI: -252.67 to -66.16), and pulmonary compromise after major surgery (beta -59.69, 95% CI: -117.62 to 1.76).

11. Data were collected form March 1 to June 7, 1986 and included 497 patients[127]	Level 3, Level 2	Adequate staffing	The adequately staffed unit had fewer complications than the inadequately staffed unit.
12. 390 patients admitted within 1 week after stroke onset in 9 acute care hospitals in The Netherlands. Surviving patients were interviewed 6 months post-stroke and asked about falls. Fall and other patient data were collected from medical records. Ward characteristics were provided by senior nurses. There is complete data on 349 patients[89]	Level 3, Level 2	0.04 mean difference in nurse to patient ratios	There was no statistical difference in falls between case and control groups in number of nurses or nurse ratios on any shift. Days (mean difference -0.06, CI: -0.51 to 0.39); Evening (mean difference -0.24, 95% CI: -0.97 to 0.50); Nights (mean difference 1.24, 95% CI: 0.28 to 2.20); All shifts (mean difference 0.04, 95% CI, -0.33 to 0.40).
13. 17,440 patients across 42 ICUs in the US[30]	Level 3, Level 1-3	Mean .66 patient/nurse with a range of 0.31-1.31	Neither nurse to patient ratio nor caregiver interaction was found to be significantly associated with risk-adjusted mortality.
14. Data were collected from April, 1994-March, 1995 from 23 trusts (groups of hospitals) in Scotland[117]	Level 3, Level 1	Mean RN FTE was 1.21 per patient	There was no association between RN FTE per occupied hospital bed and mortality
15. Data were collected form the American Hospital Association Annual Survey of Hospitals in 1989-1991, the observed and predicted 30-day post-admission mortality for patients with a primary diagnosis of COPD from the HCFA Hospital Information Reports from 1989-1991 and the Medicare Case Mix Index[118]	Level 3, Level 1	RN FTE/100 adjusted admissions	There was no association between RN FTE/100 adjusted admissions and 30-day post-admission mortality for patients with a primary diagnosis of COPD
16. Data from staffing and accounting records of 60 community hospitals across the US in 1985, hospital and nursing unit surveys, 1981 case mix indexes from the Federal Register, and the Health Area Resources File[129]	Level 3, Level 3	52% RN skill mix; 33% LPN mean nursing HPPD was 4.93	None of the staffing variables of interest were associated with medication errors, patient injuries, IV administration errors, or treatment errors.

Table 39.4 Structural variables: nursing organization models and patient outcomes

Study Setting	Study Design, Outcomes	Organization of Care/Models	Effect Size (coefficient, mean differences, OR)
Data were collected from 39 "magnet" hospitals, which are hospitals designated as good places for nurses to work, and 195 nonmagnet matched hospitals[29]	Level 3, Level 1	Magnet hospitals	Magnet hospitals had a 4.6% lower adjusted Medicare mortality rates (p=0.026, 95% CI: 0.9-9.4 fewer deaths per 1,000)
Data were collected form 1,205 consecutively admitted patients in 40 units in 20 acute care hospitals and on 820 nurses in the US[115]	Level 3, Level 1&2	Magnet hospitals (nurse control over practice variable)	Nurse control over practice was not significantly associated with any clinical outcomes, but was significantly associated with patient satisfaction (coefficient 0.56 (95% CI: 0.16-97)
17,440 patients across 42 ICUs in the US[30]	Level 3, Level 1-3	Magnet hospitals (nurse unit culture captured in caregiver interaction variable)	Caregiver interaction was not significantly associated with clinical outcomes, but was significantly associated with lower risk-adjusted length of stay (-0.16, $p<0.05$) and lower nurse turnover (-0.21, $p<0.05$)
Data were collected at 3 points in time; 6 month before the intervention, 6 months, and 12 months after the introduction of the new model and included the time between October 1996 to December 1997[79]	Level 3, Level 2	Patient Focused Care	There was a significant reduction in medication errors between the pre-model change (0.97%) and the post-model change (0.78%, p=0.016) and no difference in the other measures
Data were collected 6 months before and 6 months after the introduction of the new model and included the time between January-June, 1992 and January-June, 1993[130]	Level 3, Level 2	RN-UAP Partnership similar to Patient Focused Care	There was a significant reduction in falls (4.7732, $p< 0.05$) and no difference in the other measures between the pre- and post-measures.
Review article: Pierce, 1997[131]	Level 3A, Level 1&2	Nursing Environment	There are mixed results in studies about whether the predictor variables related to nurses and nursing are related to the outcomes of interest or whether the conceptual models being used are incomplete.

Review article: MEDLINE from 1966-1996, CINAHL from 1982-1996, Expanded Academic Index from 1989-1996, search by author for investigators known to be working in the field, manual searches of the bibliographies of review articles and monographs (Mitchell)[111]	Level 3A, Level 1&2	Nursing Environment	Mixed results in studies about whether nursing surveillance, quality of working environment, and quality of interaction with other professionals predict hospitals with lower mortality. With more sophisticated risk adjustment, evidence suggests that mortality and complications are related more to patient variables and adverse events may be more closely related to organizational characteristics.

Table 39.5 Process measures: nurse intervention and patient outcomes

Study Setting	Study Design, Outcomes	Intervention	Effect Size (coefficient, mean differences, OR)
Data were collected from 60 hospitalized patients on 1 surgical service in a university hospital in Turkey between September 1996 and September 1997 [44]	Level 2, Level 2&3	Added education to intervention group	Positive colonization of catheter hub was 68.6% in the control group and 25% in the intervention group (chi square=5.75, $p<0.05$); mean positive nurse practice scores in control group was 45.7 and 66.5 after education ($p<0.05$)
2 surgical and 2 medical wards in one hospital in Sweden were randomly assigned to either a control or experimental group. 18 nurses on the experimental wards and 18 nurse on the control wards; 90 patients on the experimental wards and 39 patients on the control wards; 112 Peripheral IVs on the experimental wards and 60 PIVs on the control wards[47]	Level 1, Level 2&3	Added education to intervention group	50% of the PIV lines in the control group had thrombophlebitis/complications compared with 21% in intervention ($p<0.001$); positive association observed for nurse practices related to care of PIV lines was 12% in the control group and 72% in the experimental group; there was complete nursing documentation in 10% of the control group and 66% of the experimental group.
One hospital in Spain; all nosocomial infection data between March 1982 and December 1990[54]	Level 3, Level 1	Added education to intervention group	Additional training was associated with a significant 3.63% decrease ($p<0.01$) in nosocomial infection rates**.**
One university hospital in Washington, DC; all adult patients with bloodstream Infections between July 1984 and February 1994 (n=432)[45]	Level 3, Level 2	Added education	No significant difference in total BSI rates or central line BSI rates before, during or after the program.
One general hospital in Illinois; all omitted and wrong dose medication errors between October 1992 and March 1993[43]	Level 3, Level 2	Added education	No difference in wrong dose IV medication errors for 12 months after training; there was a decrease in omitted dose IV mediation errors for 12 months after training ($p<0.01$).

All urinary catheter-patient-days between January 1995 and September 1996 in 1 VA hospital[55]	Level 3, Level 2	Provided infection rate data to nurses	Pre-intervention there were 32/1000 catheter-patient days (95% CI: 22.9-43.7); for the 5 quarters post intervention, there was a significant decrease ($p<0.01$) in the average infection rate (17.4/1000 catheter-patient-days (95% CI: 14.6-20.6)) compared to pre-intervention
Stanford University Hospital; all pressure ulcers and nosocomial pressure ulcers during 1992 through 1996[57]	Level 3, Level 2	Provided nosocomial pressure rate data to nurses plus added education	After Intervention #1, total pressure ulcer rate went from 20% to 21%; nosocomial pressure ulcer rates went from 19% to 21%. After Intervention #2 total pressure ulcer rates stayed at 21% but nosocomial pressure ulcer rates went from 21% to 13%. One-year later, total pressure ulcer rates were 10.9% and nosocomial pressure rates were 8.1%.
8. Stanford University Hospital 52 bed medical surgical unit; all falls between 1995 through 1996[56]	Level 3, Level 2	Provided fall rate data to nurses and added education	Pre-intervention the fall rate ranged from 4.2 to 3.7 fall per thousand patient days (FPTPD); after Intervention #1 the fall rate was 5.2 FPTPD; after Intervention #2 the fall rate ranged from 5.1 to 3.7 FPTPD.

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Chapter 40. Promoting a Culture of Safety

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Background

In a number of high hazard organizations, where the risk of error involves dire consequences, leaders manage for safe, reliable performance. As a result, the term *High Reliability Organization* has been coined to describe organizations with exemplary track records of safety: aviation, chemical manufacturing, shipping, nuclear power production, and the military.[1-10] This concept is rooted in the analyses of errors that reveal organizational failures, along with technical failures (related to system performance) and human limitations (related to human behavior).[11]

Theories about antecedents to accidents abound but major schools of thought include Reason's belief that a number of latent factors embedded in organizational systems can align and result in accidents,[12-14] and Rasmussen's approach to categorizing the different sources of error that interact with latent factors to produce accidents.[15-17] Another school of thought, developed by Charles Perrow and first publicized shortly after the Three Mile Island nuclear accident, *Normal Accident Theory*,[18,19] emphasizes the ever-present possibility of accidents in organizations that exhibit complexity and "tight coupling" of processes and the inevitability of accidents. *Normal Accident Theory* stands somewhat in opposition to *High Reliability Theory*, which holds that accidents can be prevented through organizational design and management. Scott Sagan's analysis of the nuclear weapons industry, addressing the question of why there has never been an 'accidental' nuclear war, represents a fascinating investigation of a test case for these two schools of thought.[20] Despite the obvious apparent confirmation of the *High Reliability Theory* perspective (ie, such an accident has thankfully never occurred), Sagan uncovers a surprising amount of evidence that also seems to confirm the *Normal Accident* perspective.*****

Regardless of the underlying theory, health care is vulnerable to error. The application of safety promotion theories utilized to positive effect in other high hazard organizations are being considered for health care, where "accidents" tend to occur one person at a time instead of in sweeping disasters.[25]

Attention to organizational issues of structure, strategy and culture may be a promising direction for medicine. Although organizational elements are intertwined and must be aligned for optimum performance[26] this chapter focuses on the culture component, especially "safety cultures." Following a description of the prevailing models of culture and safety, we review approaches that both medical and non-medical industries have used to promote a culture of safety. On the medical side, the discussion is limited to the Veterans Health Administration's comprehensive safety initiative.[27] On the non-medical side, specific methods other high

* Invited commentaries on Diane Vaughn's in-depth analysis of the Challenger crash[21] also provide an interesting comparison between the *Normal Accidents* [22] and *High Reliability Theory* [23,24] perspectives and indicates that they are more complementary than contradictory.

reliability industries have applied to promote a safety culture,[4] including a behavior-based industry approach, are reported.[28]

Organizational Culture

Helmreich defines culture as "a complex framework of national, organizational, and professional attitudes and values within which groups and individuals function."[29] Corporate culture is often referred to as the glue that holds an organization together, and is therefore assumed to be a contributor to organizational performance by socializing workers in a way that increases commitment to the goals of the entity.[4,30,31] As such, it embodies the philosophy of senior leaders, which is translated into, and affects the behaviors of employees.[32] Although some schools of thought focus on the role of leaders of an organization (board members and executives), others note that middle management likely plays a substantial role as well, conveying the culture to front-line workers in any organization, as evidenced by studies of the effective use of total quality management.[33] The power of culture often goes unrecognized, since employees may assume that the dominant paradigm is simply "the way we do things here."[29]

Safety Culture

While an exact definition of a safety culture does not exist, a recurring theme in the literature is that organizations with effective safety cultures share a constant commitment to safety as a top-level priority, which permeates the entire organization. More concretely, noted components include: 1) acknowledgment of the high risk, error-prone nature of an organization's activities, 2) blame-free environment where individuals are able to report errors or close calls without punishment, 3) expectation of collaboration across ranks to seek solutions to vulnerabilities, and 4) willingness on the part of the organization to direct resources to address safety concerns.[3,4,29,34-36] Based on extensive field work in multiple organizations, Roberts et al have observed several common, cultural values in reliability enhancing organizations: "interpersonal responsibility; person centeredness; [co-workers] helpful and supportive of one another; friendly, open sensitive personal relations; creativity; achieving goals, strong feelings of credibility; strong feelings of interpersonal trust; and resiliency."[4]

Culture Surveys

The aspect of organizational safety culture that may be visible or measurable is sometimes referred to as the safety "climate," which includes management systems, safety systems, and individual attitudes and perceptions.[32] Health care organizations are now adapting safety culture and climate surveys from other industries to benchmark and identify potential deficiencies in their unique safety culture. Kaiser Permanente, the oldest and largest not-for-profit health maintenance organization in the United States, has administered an executive attitudes and beliefs survey to identify perceptions of patient safety for the purposes of planning and measurement (written communication, February 2001, Suzanne Graham). The VA Palo Alto Patient Safety Center of Inquiry and Stanford University's Center for Health Policy/Center for Primary Care and Outcomes Research are conducting a patient safety culture survey that builds on past work by Gaba and collaborators. The survey includes items on production pressures and safety consequences, and draws from several other sources (personal communication, June, 2001, Sara Singer). Spath provides a checklist of elements that health care managers can use to identify which cultural elements should be addressed in order to improve safety[37] (Table 40.1). Previous work in assessing organizational culture effects on total quality management,[38] and

organizational culture in high reliability organizations[39] may also be pertinent to efforts to measure culture and its consequences for patient safety.

Industries Outside Medicine

Promoting a culture of safety has historically been a priority for the chemical, electrical, food processing, petroleum, plastic, and transportation industries. Since the 1930s, safety managers within various industries have recognized that most occupational injuries have a strong behavioral component, typically rooted in the safety culture.[28] In these settings, behavior analysis has been used as an approach to solving safety problems. Behavioral analyses typically involve assessing upstream and downstream behaviors associated with the problem, with further analysis as to which behaviors may be modifiable. Once relevant behaviors are identified, a behavior change intervention is implemented, and behavioral changes are measured. Interventions are customized, and draw upon techniques of behavior science, organizational development, safety science, and quality. Researchers have shown associations between behavior-based safety programs and reduced rates of accidents.

In an extensive field study of three organizations (nuclear aircraft carriers, a nuclear power plant, and the Federal agency responsible for air traffic control) whose operations have the potential for widespread harm, Roberts et al proposed several management processes that "cradle" a culture of perfection.[4] One process requires distributing decision making, while having mechanisms that allow decisions to migrate up and down the chain of command as circumstances develop. The mechanism for localizing decision making is often extensive training, while the approach to moving decisions to higher levels is based on management by exception when acceptable operation is in question. Finally, these researchers suggest that both top-level managers and local operators develop a deep understanding of their organizations, and use this "big picture" perspective to provide intuitive judgments when situations arise.

Practice Description

Veterans Health Administration Approach

The Veterans Health Administration (VHA) has implemented a multifaceted safety initiative, which was designed to build a culture of safety and address system failures.[27] The approach consists of 4 major elements: 1) partnering with other safety-related organizations and affiliates to demonstrate a public commitment by leadership, 2) establishing centers to direct safety efforts, 3) improving reporting systems, and 4) providing incentives to health care team members and division leaders. These tactics are detailed below. In addition, several specific initiatives were implemented to address problems, such as bar coding of medications (Subchapter 43.1) and use of computerized medical records.

To demonstrate a public commitment to the importance of patient safety, the VHA leadership founded the *National Patient Safety Partnership*, along with several major health-related organizations (the American Association of Medical Colleges, the American Hospital Association, the American Medical Association, the American Nurses Association, and the Institute for Healthcare Improvement). In addition, key senior management officials sounded the safety message in congressional testimony.

The second part of the VHA's approach involved establishing centers dedicated to the promotion of patient safety. The first of these was the *National Center for Patient Safety*, which directs patient safety efforts for the VHA at a national level. The Director of the Center oversees patient safety efforts for the entire VHA health system and is a recognized authority.

Subsequently, four Patient Safety Centers for Inquiry were funded, which are primarily responsible for safety-related research and development. Specifically, the centers are responsible for identifying problems in the patient care process, implementing corrective measures, and studying effects. Currently, one of these centers is studying safety cultures in health care organizations. Finally, the *VHA's Virtual Learning Center* contributes to the safety initiative by allowing VHA facilities to share lessons learned. Additional information, such as training, educational programs, alerts, and advisories are planned.

The third major component of the VHA's initiative involves *incentives* aimed at improving safety. There are two types of incentives offered: 1) the "carrot," which is a monetary award of up to $5000 for individuals and teams that develop approaches to improve safety issues; and 2) the "stick," which is a performance expectation imposed on leaders to improve patient safety. Leaders of the VHA's 22 regional networks must demonstrate involvement in safety-promoting activities, or be subject to consequences, including possible termination of employment. The primary objective of this incentive is to align regional and national leaders' goals.

Last, the VHA has implemented a two-pronged system for capturing adverse events. The first of these systems, the *Patient Safety Event Registry*, mandates reporting of adverse events and “close calls” occurring within the system. Before implementing the Patient Safety Event Registry, regional review of event cases was sporadic. After implementation, event data is systematically shared both regionally and nationally. The second of the systems, the *voluntary reporter identity system*, was developed in conjunction with the National Aeronautics and Space Administration, and allows for anonymous event reporting. It is intended that the use of both reporting systems will together provide a more comprehensive picture of safety management than would be possible with one system alone.

Behavior-Based Safety Programs

Outside of medicine, the objective of behavior-based safety interventions is to reduce incidents by managing at-risk behaviors of the organization and work teams. An approach described by Krause and colleagues consisted of safety assessments, steering committee formation, development of checklists of well-specified critical behaviors related to safety, observer training regarding the critical behaviors, observation and feedback.[28] These steps, somewhat analogous to aspects of crew resource management training approaches (see Chapter 44), most likely reflect an active safety culture. The Krause study assessed the effectiveness of behavioral safety initiatives in reducing accidents in 229 facilities in various industries, including chemical, electrical, food, plastic, petroleum, transportation, service, and paper manufacturers.[28] The study used an interrupted time series design with the participating industrial sites. Event rates after implementation of the behavioral program were compared with the Occupational Safety and Health Administration (OSHA) recordable illness/injury rates. Of the 229 participating sites, 73 provided necessary data (others were excluded either because they failed to provide OSHA illness/injury rates or results of the behavioral initiative). Compared with baseline, the behavioral initiative resulted in an average 26% improvement in targeted safety behaviors during the first year, which rose to 69% by the fifth year.

Prevalence and Severity of the Target Safety Problem

There is no known information about the prevalence of medical error emanating from cultural/organizational problems in health care. Culture is known to contribute to the occurrence of errors and accidents. Its contribution relative to other causal factors is unknown, but likely to

vary, depending on the type of accident and work environment.[3,7,29] The aviation industry attributes its successful safety record in part to analysis of near miss and accident reports (see Chapter 4).[40-43] These types of analyses are only possible if the culture supports reporting of errors. Culture changes may, in fact, have their greatest impact on "underground" (unreported) errors, which are extremely difficult to quantify.

Opportunities for Impact

Although no data from ongoing surveys has yet emerged to permit us to accurately quantify safety culture penetration, we nonetheless speculate based on anecdotal evidence that health care organizations have plenty of room for improvement. A number of observers have noted large-scale obstacles to promotion of safety culture within health care: a pervasive *culture of blame* that impedes acknowledgment of error, and *professional "silos"* that offer unique challenges to changing any universal aspect of health care, including culture.[44-46]

Even before the Institute of Medicine's pivotal *To Err is Human* report was delivered to the public, promoting a safety culture within health care had received widespread attention. The Institute for Healthcare Improvement's Web site features a report "Reducing Medical Errors and Improving Patient Safety: Success Stories from the Front Lines of Medicine."[47] It includes articles about the transformation of culture at the prestigious Dana-Farber Cancer Institute after a highly publicized chemotherapy overdose in 1994, which resulted in the death of a patient. Another article in the same series highlighted the major steps, including cultural change, as noted above, taken by leaders of the nation's largest health care provider—the Veterans Affairs Healthcare System—after fatal medical errors were reported by the media.[47]

Comment

Measuring the impact of culture on safety-related outcomes is challenging. Culture is a complex and abstract construct that must be inferred from behaviors, and analysis often relies on self-reported data.[29] Research continues to develop a working model of safety culture that permits measurement of several connected concepts: individuals' perceptions and attitudes about safety, individuals' observable safety behaviors, and an organization's safety management system as evidenced by its policies and management styles.[35] The relative impact of each of these measures on outcomes is another layer of ongoing research.

Although some data support the effectiveness of the entire VHA initiative in improving safety, there are no direct data supporting the effect of promoting a culture of safety. The use of incentives to reward safety-promoting behavior and publicly demonstrating a commitment to safety are approaches that could be applied in both large and small health care settings. The VHA's reporting system will likely be watched, and potentially adapted by large providers who have inconsistent and/or insufficient reporting of safety problems at local, regional, and national levels.

The evidence presented by Krause provides compelling support for the effectiveness of behavior-based safety programs in a wide range of industrial settings. Although this exact approach has not been evaluated in health care environments, its emphasis on promoting safety culture seems applicable to patient care environments.

As noted in *To Err is Human*, researchers who have studied organizations with a strong safety culture believe that it is "the most critical underlying feature of their accomplishments."[48] Although the nature of the evidence is based on field studies and other methods not typical of medical evidence, it is considered compelling by a number of experts from organizational and other social sciences. At this point, promoting a culture of safety remains surprisingly

unexplored in health care settings, where the risks of error are high. Further research in this area is warranted, though the threshold for evidence may need a different yardstick than is typically applied in medicine (Chapter 2).

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Table 40.1. Checklist of elements that contribute to a patient-safe environment

- ❑ All people acknowledge that top management provides essential patient safety improvement leadership.
- ❑ The organization has clearly defined patient safety polices.
- ❑ All people can explain the organization's patient safety policies.
- ❑ All people are involved in developing patient safety goals, and everyone can explain desired results and measures.
- ❑ All people are actively involved in identifying and resolving patient safety concerns.
- ❑ All people can explain how their personal performance affects patient safety.
- ❑ All people believe they have the necessary authority and resources to meet their responsibilities for patient safety
- ❑ Patient safety performance for all people is measured against goal, clearly displayed, and rewarded.
- ❑ A comprehensive review of patient safety is conducted annually, and there is a process in place that drives continuous improvement.
- ❑ Regular workplace hazard analyses are conducted to identify patient safety improvement opportunities. The results are used to make changes in patient care activities.
- ❑ All people are empowered to correct patient safety hazards as they are identified.
- ❑ A comprehensive system exists for gathering information on patient safety hazards. The system is positive, rewarding, and effective, and people use it.
- ❑ All people are fully aware of patient incident trends, causes, and means of prevention.
- ❑ All injury-producing patient incidents and significant "near misses" are investigated for root cause, with effective preventive actions taken.
- ❑ All people who operate patient care equipment are trained to recognize maintenance needs and perform or request timely maintenance.
- ❑ All people know immediately how to respond to an emergency because of effective planning, training, and drills.
- ❑ Facilities are fully equipped for emergencies; all necessary systems and equipment are in place and regularly tested; and all people know how to use equipment and communicate during emergencies.
- ❑ Ergonomics experts are provided when needed and are involved in patient safety assessment and training.

- ❑ All supervisors/managers assist in patient safety workplace analyses, ensure physical protections, reinforce training, enforce discipline, and can explain how to provide safe patient care.

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Section G. Systems Issues and Human Factors

Chapter 41. Human Factors and Medical Devices

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Introduction

Human factors engineering (HFE), also known as *usability engineering* or *ergonomics*, is the study of how humans interact with machines and complex systems.[1] Through the merging of cognitive psychology, engineering and other disciplines, human factors researchers have detailed numerous principles concerning device and software program designs that allow for optimal usage.[2] When these principles are violated, improper use of a machine is more likely to result.[3,4] Specific examples have been detailed during observations of user errors with electronic infusion devices.[5]

Medical device misuse is an important cause of medical error,[6,7] and therefore, incorporating human factors methodology into the design of medical devices has assumed an important role in ensuring patient safety.[2,8] This chapter first describes the use of HFE principles as a safety practice in the design of medical devices and their evaluation both prior to and after institutional purchase. Next, medical device alarms and the contribution of HFE to alarm improvements will be evaluated. Finally, the chapter reviews the use of preoperative checklist procedures to reduce anesthesia device failures (see also Chapter 23).

Subchapter 41.1. The Use of Human Factors in Reducing Device-related Medical Errors

Background

Human factors engineering is a powerful component in the design of usable, safe medical devices.[8] HFE principles can be incorporated as safety practices that occur at various points during device development and usage. Industry can use HFE principles at multiple times in the design and developmental cycle of medical devices and software packages.[3] Health care institutions can consider results of HFE evaluations when deciding which products to purchase. Finally, HFE principles can also be incorporated into the ongoing evaluation of devices that have already been purchased and are in use. While these practices have high face validity, there has been little formal study of their effectiveness in reducing medical error. They are presented here because they may hold promise if scrutinized rigorously, and to familiarize readers with their potential to reduce medical error.

Design and Developmental Phase

Data collected by the United States Food and Drug Administration (FDA) in the late 1980s demonstrated that almost half of all medical device recalls resulted from design flaws.[9] In 1990, Congress passed the Safe Medical Devices Act, giving the FDA the ability to mandate good manufacturing practices (GMP). These GMP involve design controls for manufacturers that help ensure the use of HFE within medical device design.[9] As described in the Good

Manufacturing Practice Regulation, Design Control subsection (Title 21-Section 820.30), these include the use of iterative design and testing during the developmental phase. The Act requires that designs be "appropriate and address the intended use of the device, including the needs of the user and patient."[10] Multiple human factors techniques, such as user studies, prototype tests, and task/function analysis, are utilized in the development and design process.

Manufacturers are required not only to use human factors principles to repeatedly test the product in all phases of design, but also to validate the ultimate device design. Validation entails testing the device, either in an actual clinical situation or a simulation, and documenting that the device conforms to the individual user's needs. Thus, manufacturers are required to apply HFE methods through the multiple phases of device design and development cycles.[10]

Human factors engineering practices for medical device design and evaluation have been well described. In 1993 the Association for the Advancement of Medical Instrumentation and the American National Standards Institute established guidelines for the incorporation of HFE principles into medical device design.[11] This comprehensive document helped direct attention to the problem of poor medical device design and helped establish the design standards necessary to ensure safe medical equipment and thus should stand as the safety benchmark for industry.

Only limited data are available concerning the application of HFE principles to medical device design, and most are not published. Nonetheless, the application of human factors principles during a device's design phase has been demonstrated to reduce user error. Patient controlled analgesia (PCA) pumps are a case in point of how HFE principles in product design reduce user error. User errors associated with poor interface design have been described with PCA pumps.[12,13] Lin and colleagues investigated whether applying human factors engineering principles to the design of the user interface of a PCA pump could result in fewer dosage errors as well as less time spent programming the device.[14] Information on device usage was obtained through cognitive task analysis. This involved observing and interviewing nurses operating PCA pumps both in the laboratory setting and in the field. Utilizing this feedback, as well as other human factors design principles, a "new" PCA pump interface was designed. Twelve recovery room nurses were required to complete specific tasks with both the standard PCA user interface and the newly designed interface. There were 29 programming errors on the traditional interface and 13 on the redesigned interface (an error reduction of 55%, $p<0.01$). Furthermore, users were able to program in the necessary orders in 18% less time.[13]

Another example involves the design of an ultrasound machine. In this study, Aucella and colleagues[15] interviewed sonographers, videotaped the ultrasound device being used, and performed usability testing through simulation to collect information regarding the operator-machine interface of the ultrasound machine. After their extensive investigations they implemented over 100 design changes to the console and control panel. Although errors with the machine were not measured, comments collected by the authors from the beta operators of the newly designed device suggested that the resulting machine was much easier to use.

There are enormous numbers of medical devices and software being designed and developed. Thus the FDA has initiated several regulatory mechanisms to ensure compliance with these guidelines. Some of the mechanisms include site inspections of manufacturers, review and approval of medical devices before marketing, and review of medical device incident reports.[16] Despite the tremendous amount of effort put forth by the FDA to ensure compliance with the Good Manufacturing Practices Regulation, individual institutions should critically analyze whether a device they intend to purchase meets HFE principles for user-centered design.

Device Evaluation Prior to Purchase

Adhering to HFE principles during initial design stages of a medical device is essential. However, human factors analysis should also be incorporated into the institutional decision to acquire a new medical device or software program.[3] Device purchasers should strongly consider institution-specific human factors testing. Usability testing at the institutional level establishes built-in redundancies to capture any design problems missed by manufacturers. Furthermore, the users and environments at individual institutions will differ, possibly in important ways, from the users and environments in which the device or program was initially designed and tested. It is important for an institution to be aware of who the intended users of the device or software will be, as well as where and when they plan to use the device. The information for such evaluations may be obtained from vendors, from an in-house analysis, or from independent organizations.

Vendors must be able to prove to the FDA that the user will be able to operate the medical device in the way in which it was intended.[10] As companies are required to collect human factors analysis data, it is important that institutions wishing to purchase a new medical device or software receive and carefully review this information. Gosbee provides a list of questions to ask a vendor before a purchase, which include: "How long does it take to learn to operate the system? How long does it take to complete typical set-up tasks? What are the types and frequency of errors that could happen, and the systems to thwart them?"[3]

It is also important to consider the environment in which a device will be used. Idiosyncratic features of the environment, such as excessive noise or poor lighting, and differences in user skill or acuity due to fatigue or otherwise, may affect safety and the device's in-house usability.

Some institutions have developed in-house usability labs, in order to rigorously test any device before purchasing. The Mayo Clinic uses simulations to test the usability of medical software before purchasing.[17] By carefully measuring user performance with the software they are able to uncover latent errors in the design. The usability lab is also able to measure the time necessary to learn to use the new software. This important information can help predict the device's or software's influence on workflow as well as its predilection for operator misuse.

Even without sophisticated usability laboratories, an institution can use basic human factors techniques to evaluate a product before purchase.[3] Powerful techniques such as cognitive walk-through can be easily utilized at any institution. This involves observing the end-users of a product interact with the product. As they attempt to use the device, they are instructed to "think out loud." Careful observation of the user's actions and comments can identify potential design flaws that might make it difficult to utilize the device or software.

Independent organizations are another potential source of information on device safety. Unfortunately, most independent sources do not make clear to what degree HFE principles were used in product evaluations, although they do provide some assessment of safety. One such organization is ECRI (formerly the Emergency Care Research Institute), a nonprofit international health services research agency. Another is the Institute of Safe Medical Practices (ISMP). Both release newsletters and publications regarding product safety. By searching these and similar databases, institutions can gather additional information concerning product safety prior to purchasing a device. ERCI also publishes articles specifically geared to the institutions that might wish to purchase a medical device or software.

Regardless of the level of pre-procurement testing, some unsafe designs will not be detected until after the product is in use.[3] Therefore, it is important for institutions to continuously evaluate these products to ensure safety.

Ongoing Device Evaluation

Devices and software at greatest risk for user error should be systematically evaluated. This is particularly important in areas where multiple devices are used with different interfaces, such as the operating room or the intensive care units.[3] Furthermore, areas where multiple medications are stored together should be scrutinized for potential latent errors within device or software user interfaces prior to user errors occurring.

Resources are available that can help direct an institution's search. Through publications from the FDA, ECRI, ISMP and similar organizations, medical device problems identified at other institutions can be targeted. Thus an important safety practice may be using this published information to search for latent errors within already purchased medical devices and applying this information toward a directed product evaluation at the local institution.

Another potential safety practice is to educate practitioners about HFE principles to increase awareness of medical device user error.[3] Several groups, including the American Nurses' Credentialing Center and the American Society of Health-Systems Pharmacists, recommend incorporating HFE training within health care curricula as a means to reduce error.[18]

To create a culture of safety within medicine, practitioners must couple the ability to identify potential design weaknesses with a change in the prevailing culture of silence surrounding medical errors. Educational programs directed at health care providers in training should address both of these important concerns. Curricula for teaching medical student and medical residents HFE principles have been described[18] and will likely be adopted at other institutions. Casarett and Helms caution that an unintended result of error curriculum[19] may be that residents become too willing to attribute an error to system causes. Their concern is that the resident will ignore any possible individual contribution to the adverse medical event and not learn from analyses of the event. This concern has been discounted by Gosbee, stating that any error-in-medicine curriculum should aim to "teach residents to see when errors are due to inadequate skills and knowledge versus when they are due to inherent cognitive limitations and biases."[18]

Subchapter 41.2. Refining the Performance of Medical Device Alarms

Background

Numerous aspects of patient care compete for providers' attention and can reduce their vigilance in monitoring medical devices. Alarms can alert providers to urgent situations that might have been missed due to other distractions and have become a necessary part of patient monitoring. In a study looking at critical incidents within a neonatal intensive care unit, 10% were detected through alarms.[20]

However, fundamental flaws in the design of current alarm systems likely decrease their impact.[21] There are reports documenting some alarm failings in the medical literature,[22] but few data address interventions to improve alarm system effectiveness. For an alarm to be effective it requires that a medical problem trigger the alarm, that personnel identify the source and reason for the alarm, and that the medical problem be corrected prior to patient injury. This section reviews 2 aspects of alarm safety: (1) the use of HFE principles in the redesign of medical alarms to improve identification of the source and reason for alarm, and (2) practices in both device design and programming that may improve safety by decreasing false positive alarms.

Identification of Alarm Source and Reason

The recognition accuracy of alarms within the operating room is quite low. When presented with alarm sounds and asked to identify the source, anesthesiologists, operating room technicians, and operating room nurses correctly identify the device producing the alarm only 33 to 53.8% of the time.[23-25] Furthermore, experiments suggest that humans have difficulty reliably recognizing more than 6 alarms at one time.[26] The sheer number of different medical devices with alarms can make it difficult to discern one alarm from another and studies within the human factors literature have documented the inability of medical providers to discern between high priority and low priority alarms.[27] While this is a known problem in operating rooms and intensive care units, how well alarms are recognized in other settings has not been described.

Some effort has been made to improve alarm systems through redesign.[28] One non-medical study examined ways to improve the recognition of auditory alarms by comparing abstract alarm sounds with specially designed alarms using speech and auditory icons.[29] Other studies within the human factors literature have revealed certain acoustical properties that are more likely to result in a higher sense of perceived urgency by the operator.

In a series of experiments, Edworthy required subjects to rank the level of urgency associated with different alarms.[30] The acoustical properties of the alarms were altered for the different subjects. Level of urgency was then correlated with a specific alarm sound. After ranking a set of acoustic parameters based on perceived urgency, the experimenters predicted what urgency ranking the alarm would receive and played the alarms for a new set of subjects. The correlation between the subjects' urgency rating and the investigators' predicted ratings was 93% ($p<0.0001$). Acoustical properties such as fundamental frequency, harmonic series, and delayed harmonics all affected the users perceived urgency.

Another study looked at the redesign of an alarm to improve detectability within the operating room.[31] An alarm that was spectrally rich, frequency-modulated, and contained small amounts of interpolated silence was detectable with at least 93% accuracy over background operating room noise. However, both of these alarm experiments have only been done in laboratory settings. In addition, Burt and colleagues found that when subjects were required to urgently perform a task, the prior acoustically manipulated perception of urgency was ignored in order to attend to the situational urgency of the task.[32] Furthermore, with both alarms and clinical tasks competing for an operator's attention, the newly designed alarm might not be as discernible. It has continued to be a challenge to create the best auditory alarm sound to indicate an emergency.

Visual Interfaces for Alarms

Alarms can also be visual. Some research has been done to improve hemodynamic monitoring device displays. Responses to abnormal values are delayed when workload for the anesthesiologist is high,[33] prompting interest in improving current visual displays. Furthermore, the clinical decision process often rests on the practitioner's interpretation of a patient's hemodynamic parameters. Thus, it is important that this information be presented in a way that assists with decision making and minimizes errors of interpretation.

Two observational studies have compared different visual displays of data to traditional visual monitors.[34,35] Each evaluated errors in performing a designated task as well as response time to completion. One measured how quickly subjects recognized a change in a parameter[34] and the other measured how long it took for anesthesiologist to manipulate a set of abnormal parameters to a stable set.[34,35] Both studies used computerized simulations of anesthesiology

cases, with subjects serving as their own controls. In one study, subjects were required to identify when changes in physiologic parameters occurred using different visual formats.[34] Response time and accuracy to the simulated cases was compared among a histogram, polygon, and numerical display. Subject responses were more accurate with the histogram and polygon displays ($p=0.01$).

In the other study, 20 anesthesiologists with an average working experience of 5 years were required to perform specific tasks on an anesthesia simulator[35] (see Chapter 45). The tasks consisted of returning a set of abnormal hemodynamic parameters to normal using intravenous medications. A specific time for the completion was determined and this time was compared among 3 different visual interfaces. Trial time was significantly shorter with the traditional display ($p<0.01$), yet there were fewer failed trials using the other monitor displays (26% with the profilogram display, 11% with the ecological display, and 42% with the traditional display). The slower time with the non-traditional displays could have resulted from the subject's lack of experience with such screens. Nevertheless, the newer interfaces produced fewer failed attempts at arriving at the appropriate hemodynamic parameters on the simulator, suggesting that these displays might improve the clinical decision process.

None of the studies comparing traditional auditory alarms and visual monitor displays reported any adverse event associated with the newer technology. However these studies are limited by the artificial nature of the experiments.[29,34,35] Anesthesiologists have many tasks to perform during anesthesia, often amidst great distraction. Attending to monitors is only one aspect of their workload. Because these laboratory experiments do not include all of the different "real world" problems and diversions that an anesthesiologist might face, it is difficult to generalize them to the workplace. Also, because this experimental task might be taken out of the context of caring for a patient in the operating room, the subject might simply focus on the completion of the experimental task and not consider other tasks that the anesthesiologist would be required to perform in a real situation.

Decreasing the Frequency of Alarms

Poorly designed device alarms can create not only problems with alarm recognition but also frequent false positive alarms. Two observational studies found that from 72 to 75% of alarms during routine general anesthesia did not require corrective action.[36,37] Another study showed that only 3% of all auditory alarms during routine anesthesia monitoring represented a patient risk.[38] Providers frequently must interrupt clinical tasks to silence these false positive alarms. More concerning is the fact that when alarms are unreliable, they tend to be ignored.[21,39] This "cry-wolf" effect is a significant detriment to the optimal performance of alarm systems and may result in dire consequences when "true alarms" are ignored.

False alarms can be managed in two ways. Devices can be designed so that they identify and eliminate false alarms before triggering or users can manipulate alarm parameters to reduce false alarms. User manipulation can range from adjusting alarm thresholds[40] to even turning the alarms off.[22] There are no data describing how often operators reset alarm parameters to reduce false positive rates.

Some research has focused on the identification of alarm parameters that improve or optimize alarm accuracy (ie, to improve the ratio of true positives to false positives—the "signal-to-noise" ratio). For example, Rheineck-Leyssius and Kalkman studied how altering an alarm parameter on a pulse oximeter would affect the incidence of hypoxemia.[40] Consecutive patients admitted to the recovery room of a regional hospital in the Netherlands after general or regional anesthesia were randomized to either a lower limit of SpO_2 90% or SpO_2 85%. The 2 groups were comparable at baseline. The outcomes measured were hypoxemia, defined by a pulse oximeter reading less than or equal to 90% or 85%. The authors were also required to judge if they believed a signal to be artifact versus a true positive. The authors were blinded as to which group the subject was randomized to during artifact assessment and data analysis. The relative risk of having a hypoxic episode ($Sp0_2 \leq 85\%$) in the group with the lower alarm limit set at 85% (as compared with those with the lower alarm limit set at 90%) was 3.10 (95% CI: 1.32-7.28, $p<0.001$). One weakness of this study was the lack of a bedside observer to verify the validity of the measurement, so that it is unclear to what degree measurement bias could have affected the results. The pulse oximeter was considered the "gold standard" for measuring hypoxia and thus false positives were calculated based on alarm artifact rates (outliers, loss of signal). Keeping the lower alarm limit for a pulse oximeter at 90% did reduce the number of patients with hypoxemia, however it also increased the false positive rate (33% versus 28%). A higher false positive rate on an alarm could make it more likely that an operator might disregard the alarm. The majority of alarms were transient and lasting less than 20 seconds. The authors also noted a 60% reduction in the number of triggered alarms in the $Sp0_2$ 90% group by introducing a "theoretical delay" of 15 seconds between crossing the alarm threshold and actually triggering the alarm. Other investigators have documented a 26% reduction in mean alarm rate by increasing the alarm delay from 5 to 10 seconds.[41]

Overall, only modest evidence supports the practice of not lowering pulse oximeter lower alarms limit settings below 90%. This intervention could reduce hypoxemic events with little added cost. However, there would be an increased number of false positive alarms, which might affect attendance to the device. Fortunately, newer technological advances in oximetry appear to reduce false positives rates and may make this less of a problem. In a study in the Netherlands, a conventional pulse oximeter was compared with a "third generation" pulse oximeter equipped with a signal processing technique designed to reduce false positives.[42] This "smart" pulse oximeter applied signal quality tests, differentially amplified the input signal, and applied

motion-detection testing to the identified pulse. The "smart" pulse-oximeter only triggered one false positive (an alarm that did not coincide with hypoxia) and had a relative risk of 0.09 (95% CI: 0.02-0.48) for generating a false positive alarm when compared with conventional pulse oximetry with a 21-second delay.

Comment

Observational studies have suggested that current alarm systems could be improved, but future laboratory studies are needed to determine which properties of alarm systems are most effective to alert operators. These tests must be followed by field studies and ultimately with trials looking at actual patient outcomes to determine the best designs. Information concerning the cost and feasibility of implementing these changes should also be gathered.

False positive alarms remain a significant problem. Few data exist on the incidence of resetting alarm parameters or at what parameter values alarm accuracy is optimized. Advances in alarm technology aimed at reducing false positives appear a promising alternative to resetting parameters.

Subchapter 41.3. Equipment Checklists in Anesthesia

Events related to medical equipment can be divided into two categories, user-error and equipment failure.[43] Health device inspection and preventive maintenance by biomedical or clinical engineering departments have high face validity as an important patient safety practice in reducing equipment failure.

There are many calls in the engineering literature to standardize equipment maintenance.[44-46,46] Standardization of protocols is believed to help make the processes more efficient and reduce errors.[47] However, it has been difficult to standardize equipment maintenance practices due to a lack of the appropriate units on which to base measurement.[46] Some authorities have suggested outcomes based on engineering endpoints such as reliability and accuracy.[48] Others have tried to validate a set of maintenance outcome units based on cost or quality metrics.[44,45,49] Some engineers have suggested the incorporation of clinical endpoints into medical equipment assessment.[48,50] Notwithstanding differing views as to measurement of endpoints, experts uniformly believe that standardization of engineering endpoints is vital to ensure adequately inspected and maintained equipment.[46] No studies to date have developed a widely used standardized protocol for equipment maintenance for clinical engineering departments, largely because the lack of standardization of endpoints renders assessing the relative value of any particular maintenance protocol impossible.[44-46,48,50] Nonetheless, equipment failure does result in a small fraction of clinical events and thus is an important safety intervention. Hopefully, future studies will help delineate the most effective practices for equipment maintenance processes.

Use of checklists is another practice that helps ensure equipment readiness, particularly for equipment that is needed in critical situations and/or where equipment failure may have dire consequences. For example, a nurse at the beginning of each shift may use a checklist to ensure the readiness of a hospital ward's resuscitation cart ("crash cart") should it be needed (eg, the defibrillator is plugged-in and charged, the back-up suction pump works, medication is not past its expiration date). Similarly, a perfusion technologist can use a checklist to ensure cardiac bypass circuit and back-up equipment are ready before surgery. Published studies on the effectiveness of equipment checklists largely relate to the use of preoperative checklists to prevent anesthesia equipment failures since, to date, studies on the effectiveness of equipment

checklists in medicine have been limited to this area.[51-53,54] These studies are reviewed in Chapter 23.

Final Comment to Chapter 41

Human factors testing is yielding important data regarding safe and effective medical device and alarm designs that take into account the users' cognitive limitations. Machines can be designed and redesigned that enhance patient safety, rather than compromise it.

Currently, there are no widely accepted standards for equipment maintenance intervals and protocols. Maintenance endpoints that incorporate clinical events as one component of the endpoint have been suggested. Until a reliable and validated engineering endpoint metric is widely recognized it will remain difficult to investigate the most effective maintenance practices.

Other than the pioneering work in anesthesiology, HFE has been underutilized in medicine. Hopefully, in the near future, more attention will be focused on integrating human factors engineering within all aspects of medical training and practice, which will help create a culture of safety.

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Chapter 42. Information Transfer

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Introduction

Patient safety can be compromised by discontinuities in care. Studies suggest that discontinuity results from poor information transfer[1] and faulty communication,[2] which in turn may cause avoidable adverse events.[3]

Improving information transfer and communications among health care providers is an important patient safety practice and has been strongly recommended as a means to improve patient care.[1,3-7] This chapter evaluates safety practices involving improvements of provider-to-provider information transfer. Practices for evaluation include transfer of information between inpatient and outpatient pharmacies (Subchapter 42.1), sign-out systems for medical housestaff (Subchapter 42.2), automatically generated electronic discharge summaries (Subchapter 42.3), and systems to improve patient notification of abnormal results (Subchapter 42.4).

Subchapter 42.1. Information Transfer Between Inpatient and Outpatient Pharmacies

Background

Accurate and timely information transfer between community and acute care pharmacies is an important safety practice. Patients admitted to the hospital could benefit from the hospital's pharmacy obtaining better information concerning their medication allergies as well as prior therapeutic failures.[8] Furthermore, when patients transition from acute care to outpatient care, changes in medications that occurred during hospitalization may cause confusion for both patients and providers. In one study surveying patients one week after hospital discharge, patients' knowledge of their drug indications were worse for medications introduced during their hospitalization than for those taken prior to hospitalization (OR 0.69, 95% CI: 0.53-0.89).[9]

Confusion and incomplete information may increase the risk of under- or overmedication, harmful drug interactions, and other problems. Existing literature suggests that pharmacist interventions may reduce potential adverse drug events and have a modest impact on patient morbidity and mortality.[10,11] However, these studies have used independent reviewers to judge the impact of the intervention and have not specifically measured adverse drug events or patient outcomes. Clinical pharmacists' consultations prior to discharge might also improve patient medication compliance (see Chapter 7).[12]

Uncontrolled studies report that information-exchange programs between hospital and community pharmacies are perceived as beneficial and may have a positive impact on patient outcomes.[13] Although not the primary outcome measured in their small (n=127) observational study, Dvorak et al did note that using a pharmacy-to-pharmacy referral form was effective in preventing 2 medication errors. Thus, practices that improve information transfer between hospital and community pharmacies may improve patient safety.

Of the many potential methods for improving information transfer between hospitals and outpatient pharmacies, controlled trials have been reported in the literature for only 2: pharmaceutical care plans cards[14] and patient information facsimiles between pharmacies.[8] Although direct electronic communication of pharmacy data may be superior to these methods,

no controlled studies are currently available regarding this practice and therefore it is not reviewed within this chapter.

Practice Description

In a study by Smith and colleagues, patients received a card prior to discharge listing their pharmaceutical care plan, which included medication doses, indications, schedules, side effects, information as to the importance of drug compliance, and how to obtain medication refills.[14] Patients were instructed to give the card to their community pharmacist. In another study, the intervention consisted of pharmacy-to-pharmacy facsimile transmission at the time of admission and discharge from the hospital.[8] In this study, when a patient was admitted to the hospital their community pharmacy transmitted patient demographic information, historical information concerning allergies and adverse drug reactions, current medications, refill history, pharmacist's monitoring notes, communications with patient and physician, and a detailed medication history to the admitting hospital. After discharge the hospital pharmacy transmitted to the community pharmacy a list of any potential medication problems identified by the hospital pharmacist on admission, the patient's daily monitoring log, the pharmacist's discharge summary, and a discharge medication table. The medical records department of the hospital also transmitted the patient's discharge summary and laboratory test results to the community pharmacy.

Prevalence and Severity of the Target Safety Problem

Medication problems can arise because patients are frequently discharged from the acute care hospital on medications different from their ambulatory regimen.[15] Elderly patients in particular are at risk after discharge.[16] In one study, hospital providers changed 53% of the drugs prescribed by the primary care providers.[15]

The extent to which these medication changes and lack of communication result in recently discharged patients failing to receive medications or appropriate monitoring for their drug therapy is unclear. In one study of elderly patients, 32% of medications prescribed at discharge were not being taken 2 days after discharge.[17] Another study found that 51% of patients recently discharged from acute care hospitals had deviated from their prescribed regimen.[18] Of those that had deviated from the prescribed drug regimen, 70% did not understand the medication regimen. In a Scottish study, recently discharged, elderly patients were issued a 5-day supply of their medication on discharge and visited in their homes after these 5 days had elapsed.[16] Twenty-seven percent of the patients had not received a new prescription ordered on discharge. Of the patients with new prescriptions issued, 19% received inaccurately labeled medications. Medications were considered mis-labeled when non-specific container labels, such as "take as directed" replaced the more specific labels given on discharge. Some authors have suggested that improving communication about medications prior to and just after hospital discharge might reduce these medication errors.[18,19]

Poor communication is not the only problem.[16] Patient factors influence whether a medication is ultimately picked up and taken as directed. Deviations from prescribed drug regimens are multifactorial and improving pharmacy-to-pharmacy communication is only one aspect of the overall problem.

Opportunities for Impact

Data from primary care providers reveal that 96% of the respondents would like information concerning hospital drug changes.[20] Ninety-four percent of community pharmacists

surveyed also wished to be provided with information concerning hospital drug changes.[20] We were unable to identify data regarding what percentage of hospital pharmacies routinely transfer information on patients' medication regimens when they are admitted to and discharged from acute care.

Study Design and Outcomes

Two controlled studies were identified in the literature (Table 42.1.1). Both were randomized trials but neither was blinded. In Smith et al, patients received a written pharmacy care plan at discharge. Home visits were made 7 to 10 days later to assess compliance and discrepancies in the medication that patients were taking versus those ordered at discharge (Level 2).[14] In the study by Kuehl et al,[8] patients were randomly assigned to either usual care or to a bi-directional exchange of pharmacy information by facsimile between the ambulatory pharmacy and the admitting hospital, upon admission and discharge (Level 1). The outcomes were pharmacist interventions, such as changing medication doses or making allergy recommendations (Level 2).[8]

Evidence for Effectiveness of the Practice

Smith et al's small study (n=53) of a pharmacy care plan card found that in both groups patients were taking different medications than those ordered at discharge. The authors found that compliance with post-discharge medications was significantly better in the group that had received the information card ($p<0.01$). Unintentional changes to the medication were found in 14/28 (50%) of the study patients and 17/25 (68%) of the control patients during the follow-up visits (Pearson's chi-square $p=0.18$)

In the study by Kuehl et al, significantly more experimental group patients than control group patients had at least one in-hospital pharmacist intervention documented (47% vs. 14%, $p<0.001$). The mean number of in-hospital pharmacist interventions per patient was also significantly higher in the experimental group (1.0 vs. 0.2, $p<0.0001$). The types of interventions made by hospital pharmacists included addition of a medication the patient was taking as an outpatient that was not originally ordered on admission, dosage changes, and changes related to drug allergy. Interventions by ambulatory care pharmacists were also more frequent in experimental group patients compared with control group patients. Community pharmacists who received hospital pharmacy records performed interventions on one or more patients 42% of the time, while no interventions were performed in the control group ($p=0.001$). Specific community pharmacist interventions included monitoring of therapy (13/57), taking actions related to drug allergy problems (13/57), requesting documentation of an indication for a particular medication (9/57), and making a dosage change (8/57).

Although the data abstractor was blinded with regard to study group, the nature of the intervention did not permit blinding of participating pharmacists (ie, they received faxed information for some patients but not others). Also, the pharmacists were not explicitly blinded to the study's objectives. It is unclear how this knowledge might have affected the results. It could have resulted in more careful scrutiny of any potential drug problem (bias away from the null) or less scrutiny of these orders (bias towards the null). Kuehl et al note that although the results suggest discriminatory documentation did not play a major role, the possibility cannot be ruled out.

Another potential limitation of this study was the completeness of follow-up. Of the eligible patients from ambulatory care pharmacies, only 50% returned to their pharmacy during the study period. There were no comparisons presented between the ambulatory pharmacy visit

group and the loss to follow-up group. This large loss to follow-up could have significantly altered their findings.

Potential for Harm

None of the studies evaluating different hospital-community pharmacy communication processes detailed any adverse events. However, the degree of added workload and effects on current workflow must be taken into account.

Costs and Implementation

The 2 reviewed interventions for improving hospital to community pharmacy information transfer seemed simple and relatively inexpensive.[8,8,13,14,14] Although no formal cost analysis was performed, Dvorak et al described their method (use of a pharmacy-to-pharmacy referral form) as being "labor-intensive." No records were kept of the time necessary to provide the referrals but the authors estimated the time commitment per patient to be 30 minutes.[13] It is also important to note that complete information transfers occurred for 75% of the subjects in Kuehl's study, indicating that there is still room for improving the process. With improvements in information transfer technology, automated transfer of information from hospital to community pharmacy could have important patient safety benefits without excessively increasing providers' workloads.

Comment

Providing patients with data forms to convey transfer of information between hospital and ambulatory pharmacies has potential for reducing discontinuities resulting from inadequate medication information. Few studies have evaluated the effect of these interventions on patient outcomes, although any improvement in the transfer of this information would likely be well received by ambulatory providers. Future studies are necessary to determine if and how improved pharmacy-to-pharmacy communications reduce preventable adverse drug events and improve patient outcomes. Identifying the most effective and least disruptive forms of inter-pharmacy communication remains an area for further investigation.

Table 42.1.1. Practices to improve transfer of medication information

Study	Study Setting	Intervention	Study Design, Outcomes	Results
Smith, 1997[14]	53 patients (>65 yrs old) discharged to home who were likely to experience difficulties with their medications	Copies of medication doses, indications, side effects, importance of compliance and refill information given to patients at discharge	Level 1, Level 2	Patients taking medication not prescribed at discharge: information card 75%, control 96% ($p<0.01$)
Kuehl, 1998[8]	156 patients admitted to small mid-western community hospital	Pharmacy-to-pharmacy facsimile transmission o medication regimen at time of admission and discharge from hospital	Level 1, Level 2	Patients with • 1 pharmacist interventions in hospital: faxed-summary 47%, control 14% ($p<0.001$) Patients with • 1 pharmacist interventions in community: faxed summary 42%, control 0% ($p<0.05$)

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Subchapter 42.2. Sign-Out Systems for Cross-Coverage

Background

As physicians go off duty, they provide information to a "cross-covering" physician who will care for patients in the interim. The process of information transfer, known as "sign-out," is often informal and unstructured. Various methods are used, including handwritten lists, PC-based word processing or spreadsheet programs, and personal digital assistants (PDAs), but little literature has assessed their effectiveness in assuring continuity of care for patients and preventing medical errors. Although notes in the medical record often contain all the information needed to care for patients, cross-covering physicians make many decisions without the benefit of the patients' charts.[1] Jelley found lack of consistency in the content of weekend sign-out lists in a community-based internal medicine inpatient program.[1] Lee and colleagues found that medical interns recorded information elements such as patient age, DNR status, and medications more often when a standardized sign-out card was used.[2] In this section, we review evidence of a computerized sign-out system to reduce medical errors during cross-coverage.

Practice Description

The proposed safety practice is a structured sign-out process in which patient information is provided for various standardized data fields. The computerized sign-out program described by Peterson and colleagues consisted of a summary of the patient's medical status, a problem list, recent laboratory data, resuscitation status, allergies, and a "to do" list.[3] This information was accessible from any computer within the hospital and was accessed and maintained on a daily basis by housestaff physicians.

Prevalence and Severity of the Target Safety Problem

Discontinuities in provider care during hospitalization have been associated with an increased risk of adverse events. The Petersen et al study found the odds ratio for a preventable

adverse medical event occurring during cross-coverage as opposed to regular provider coverage to be 6.1 (95% CI: 1.4-26.7).[4] In the surgical domain, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) publication on wrong-site surgeries noted a number of cases involving last minute personnel changes.[5] It is possible that these rapid substitutions in the operating room with inadequate communication may have contributed to these adverse events.

Opportunities for Impact

The number of hospitals using either a computerized or paper-based sign-out process is unknown, but computerized sign-outs are probably unusual. One study found that 26% of adverse events in a single institution occurred during cross-coverage.[4] These data suggest that a standardized sign-out procedure could have a significant impact on improving patient safety.

Study Design and Outcomes

We identified one study evaluating the effect of a standardized sign-out system on the occurrence of adverse events (Table 42.2.1). In this study, adverse medical events detected by self-report were compared before and after implementation of a computerized sign-out system (Level 3).[3] This study involved internal medicine housestaff and any management of a patient performed by an intern from a different team or a night-float resident was considered cross-coverage. During chart review, the investigators recorded whether the physician at the time of the event was the patient's regular physician or a cross-covering physician. Adverse medical events, defined as "an injury due to medical therapy that prolonged hospital stay or disability at discharge"[3] were the primary outcomes (Level 2).

Evidence for Effectiveness of the Practice

There were significantly fewer adverse events during the intervention period compared with the baseline period (2.38% vs. 3.94%, $p<0.0002$). There was also a trend toward fewer preventable adverse events with the intervention (1.23% vs. 1.72%, $p<0.1$) but no significant difference in the rate of preventable events during cross-coverage (0.38% vs. 0.24%, $p>0.10$). Using a logistic regression model including factors for Acute Physiology and Chronic Health Evaluations (APACHE) II scores and alcohol use (the 2 variables significantly associated with adverse events during the intervention period), the authors calculated the odds ratio for a patient to experience an adverse medical event during cross-coverage in the baseline period to be 5.2 (95% CI: 1.5-18.2).

After implementation, the odds ratio for a cross-coverage adverse event was no longer statistically significant (OR 1.5, 95% CI: 0.2-9.0).[3] The authors noted that housestaff used the sign-out information not only for cross-coverage but for their primary patients as well, which may have contributed to the overall decrease in adverse events. Secular trends may also have played a role in this reduction.

Another limitation of this study was that it relied on self-report to capture adverse medical events. The investigators performed a review of a random sample of 250 charts and detected only 8 unreported, preventable adverse medical events. If extrapolated to the entire sample (3747), this represents 120 missed adverse events. These adverse events could have influenced the results either toward or away form the null hypothesis, depending on their distribution among regular and cross-covering physicians.

Potential for Harm

The study reported no adverse events as a result of the sign-out system. As with other sign-out systems, particularly those that are computerized or Web-enabled, the issues of data security and protection of confidentiality must be addressed.[6]

Costs and Implementation

Implementation of a computerized sign-out system like that described by Peterson et al would require information systems that allow extraction and aggregation of patient specific data (eg, laboratory and pharmacy) and financial support for programming. These resources may not be present at some institutions. Although housestaff responded favorably to the computerized system, physicians at other institutions or in other specialties may not be as willing to use this system.

Comment

One study has shown that an inpatient's risk of preventable adverse events was less after implementation of a computerized sign-out process. The method appears appropriately suited for hospitals with cross-coverage arrangements similar to those described by Peterson et al, specifically in-house coverage by resident trainees. It will be important to know if similar systems are as effective and well received at other institutions, including those without trainees. Such systems would be difficult to implement in hospitals with limited information systems or where physicians outside the hospital provide coverage through paging systems. Although a computerized system has the advantage of being accessible from any location in the hospital and may be able to automatically import important information, events attributable to faulty communication during cross-coverage could also be amenable to other strategies for standardizing the process (eg, sign-out cards, Web-based programs, PDAs). No evidence is available concerning the relative effectiveness of other standardized sign-out methods. Future research should address what data fields are most helpful to physicians providing cross-coverage in preventing adverse events and how different methods of standardized sign-out compare in effectiveness (eg, handwritten cards vs. PDAs).

Table 42.2.1. Computerized sign-out program

Study Setting	Study Design, Outcome	Results (95% Confidence Intervals)
8767 patients admitted to the medical service of a tertiary care teaching hospital in Boston[3]	Level 3, Level 2	Odds ratio (OR) of preventable adverse events occurring during cross-coverage compared with care under regular physician: baseline, OR 5.2 (1.5-18.2) with intervention, OR 1.5 (0.2-9.0)

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Subchapter 42.3. Discharge Summaries and Follow-up

Background

Discharge summaries are important tools for communicating pertinent patient information regarding hospitalizations to outpatient care providers. Yet their relatively unstructured, narrative format often invites inaccuracies.[1] In addition, there can be significant delays transmitting discharge summaries to patients' health care providers.[2,3]

Prior studies have investigated processes to improve discharge summaries, such as standardizing their format[4-6] and instituting physician education programs.[7] This chapter focuses on the use of structured, database-generated discharge summaries to improve the quality of the information content communicated after patient discharge, as well as to reduce the time required for this information transfer.[8]

Practice description

During the hospital course, physicians provide information corresponding to specific sections of the computerized discharge summary either on data collection forms which are manually entered into a database[8] or directly into a computer system. When the patient is discharged the database generates a structured discharge summary that can be sent to the patient's outpatient providers.

Prevalence and Severity of the Target Safety Problem

In one study examining the effectiveness of inpatient follow-up care, 9.7% of discharged patients experienced worsening of symptoms or functional capacity as a result of an inadequately managed discharge process.[2] Hospital discharge summaries are an important means of communication between hospital and community physicians, but have several problems. First, community physicians do not always receive summaries for recently discharged patients. In one study only 34% of patients had a discharge summary sent to their outpatient care provider.[2] Although no analysis was undertaken to determine if receiving a discharge summary had an effect on patients' follow-up, another study demonstrated that patients may be less likely to be readmitted to the hospital if their primary care provider receives a discharge summary.[9]

As mentioned above (Subchapter 42.1), patients frequently have their medication regimen changed while admitted.[10] The majority of ambulatory providers would like to have information regarding these medication changes.[11] Improvement in information transfer from acute care to ambulatory care might reduce medication discrepancies; however, patient compliance will also heavily influence these factors.

Opportunities for Impact

We found no data describing how many hospitals currently use database-driven discharge summaries.

Study Design and Outcomes

Several studies were identified that evaluated electronically generated discharge summaries, but these were limited by a lack of randomization or limited outcomes reporting.[12-14] One randomized controlled trial was identified that compared traditional dictated discharge summaries to summaries generated from a database (Table 42.3.1).[8] The primary outcome was the proportion of admissions with a discharge summary completed by 4 weeks after discharge (Level 3).[8] Overall quality of the discharge summaries was also assessed (Level 3) but patient level outcomes were not.

Evidence for Effectiveness of the Practice

Patients randomized to the database group were significantly more likely to have a discharge summary generated within 4 weeks of discharge than were patients randomized to the dictation group (113/142 vs. 86/151, $p<0.001$). Even with the database method, 20% of patients did not have a completed discharge summary by 4 weeks. Of the patients with a discharge summary generated within 4 weeks of discharge, 94.7% of the database-generated summaries were produced within one week, while only 80.2% of the dictated discharge summaries were completed in this timeframe ($p<0.001$). Physician ratings of the quality and timeliness of the discharge summaries were available for 210 of 302 (69.5%) summaries. The quality and timeliness of the 2 summaries were judged to be similar overall, but differed when stratified by provider specialty. Database-generated summaries were thought to be more timely by family physicians ($p=0.04$) and of lower quality by consultant physicians ($p=0.02$).

Potential for Harm

No adverse events were mentioned as a result of the database-generated discharge summary study.

Costs and Implementation

The direct and indirect costs of implementing and maintaining a system for database-generated discharge summaries have not been formally evaluated in the literature. Results of a mail survey of housestaff in the van Walraven study[8] suggest their intervention did not adversely affect the workflow of housestaff physicians. Housestaff significantly preferred ($p<0.001$) the database system and found it less burdensome ($p=0.002$). With the advent of electronic medical record systems, data can be automatically abstracted from various fields and collated into a discharge summary, eliminating the costs associated with abstraction form distribution, collection, and data entry. This is already a practice at some institutions.[12,15]

Comment

With the documented inefficiencies, inaccuracies and incompleteness of discharge summary information, interventions that improve the hospital discharge communication process without increasing provider workload could have a significant impact. A database method can significantly decrease the time for completion of discharge summaries. The amount of work required to generate the database discharge summaries could potentially be reduced in the future through electronic record-keeping. Further studies are required to determine how to best transfer discharge summary information to outpatient providers. A feasibility study has assessed the utility of faxing discharge summaries to community providers.[3] This remains an active area for study, recognizing that the optimal strategy to reduce discontinuities in care after hospital discharge will depend on the methods for generating discharge summaries, the accuracy and usefulness of their content, and the timeliness and method of their delivery to patients' providers.

Table 42.3.1. Improvements in discharge summary communications

Study	Study Setting	Study Design, Outcome	Results
van Walraven, 1999[33]	293 patients admitted to the General Medicine Service of a tertiary care teaching hospital in Ottawa	Level 1 Level 3	Discharge summary completed within 4 weeks: database group, 79.6% dictation group, 57% ($p<0.001$)

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Subchapter 42.4. Notifying Patients of Abnormal Results

Background

One of the most distressing safety issues of the clinical encounter is the failure to follow-up on diagnostic tests, particularly when a patient is not notified of an abnormal result. The complexities of this problem are legion. Contact methods—whether by phone, mail, fax or e-mail, and whether sent by the lab, clinic or individual clinician—vary widely in their reliability (with most being imperfect). In some instances patients are told that if they do not hear back regarding their test results it signifies normal results. Of course, not hearing may mean that the test was lost or that the contact method was faulty. Other issues arise when the content of the notification is not clear, either as to result or the recommended follow-up for re-testing or treatment options.

This chapter evaluates safety practices aimed at improving patient notification of abnormal results. Adequate medical and/or surgical care during follow-up is essential to reducing patient morbidity and mortality, but practices to address this are beyond the scope of patient safety as defined in this Report. We have chosen the example of Pap smear results, although many of the issues should be transferable to other laboratory (eg, PSA level) and radiologic (eg, mammogram) results.

Practice Description

Our search revealed only one study evaluating patient notification practices.[1] In this study, the patient's mailing address was included on the Pap smear request form. Two weeks after the patient's primary care provider received the results, the laboratory directly notified the patient by mail. The notification was by form letter advising the patient of her results and providing advice on the recommended follow-up step: discuss results with the doctor, return in two years time, or make an appointment to see the doctor without delay.

Prevalence and Severity of the Target Safety Problem

Few data exist concerning physician follow-up and patient notification of abnormal results. In a survey of attending physicians and residents practicing at a large urban teaching hospital and 21 suburban primary care practices, virtually all respondents believed it was moderately or extremely important to notify patients of abnormal results, yet 36% of physicians did not always do so.[2] Among the most common reasons reported by physicians were forgetfulness and inability to reach patients. One large cross-sectional study examined physician documentation of notification to patients of abnormal mammograms, Pap smears, and cholesterol tests. The results demonstrated that certain patient characteristics such as race, language, and education may be associated with a failure to transmit abnormal results to patients.[3]

An estimated 4600 American women died of cervical cancer in 2000.[4] There are no data regarding to what extent delays in notification result in worse patient outcomes, including mortality. One study evaluating processes to reduce non-adherence rates with the follow-up of abnormal Pap smears noted that many women (the exact number was not presented) reported that they were never notified of their abnormal Pap smear result initially.[5]

Tracking systems for abnormal Pap smear results have been briefly mentioned in the context of studies evaluating interventions to improve overall follow-up, not patient notification.[5,6] However, the effectiveness of these tracking systems was not specifically evaluated so they are not reviewed here.

Opportunities for Impact

Compliance rates with follow-up medical care after abnormal Pap smears typically ranges from 50% to 70%.[5,7-9] It is unclear how often losses to follow-up resulted from failure to notify. There are no data indicating how many practice groups directly mail abnormal Pap smear results to patients. Even with successful patient notification practices, a corresponding reduction in morbidity and mortality may not occur because of the other barriers to adequate follow-up described in the literature.[5,10]

Study Design and Outcomes

The study reviewed for this chapter was a randomized control design (Level 1).[1] (Table 42.4.1). Providers were randomized into 2 groups. In the intervention group, the pre-cervical smear questionnaire form had been redesigned to allow the patient to request that results be mailed directly to her. The physicians in the intervention group determined which patients would be offered direct notification. Patients of physicians in the control group were notified of results using whatever protocol the provider typically used. The authors did not elaborate on the methods used to notify patients in the control group.

The primary outcome was adherence with follow-up visits (Level 2), which was defined by searching the laboratory records for evidence of a follow-up Pap smear one year after notification. If a cervical smear result was not located through the laboratory database search then the patient's provider was contacted.[1]

Evidence for Effectiveness of the Practice

Significantly fewer women with cervical intraepithelial neoplasia (CIN) on Pap smear who were randomized to the intervention group were lost to follow-up (0/52 vs. 9/39 in the control group, $p<0.001$). In the group of women with atypia, 13% (15/116) were lost to follow-up in the intervention group and 10% (10/104) were lost to follow-up in the control (p=NS).

A limitation of this study was that providers decided who in the intervention group actually received the intervention after randomization. Only 41% of patients in the intervention group were actually mailed their results. However, analysis was performed with an intention-to-treat design.

Potential for Harm

Although the patients in this study were not interviewed, other reports reveal that psychological distress is common after notification of an abnormal Pap smear.[11] Thus a potential harm of this practice, or any practice to directly notify a patient of an abnormal result, could be anxiety and distress that might be mitigated if a health practitioner were to deliver the information.

Costs and Implementation

Buy-in of health care providers is an important aspect of practice implementation and may be affected by the concern for potential harm and the specifics of the notification process. In the Del Mar study, 23% of providers were unhappy with the wording of the letter.[1] Direct patient notification systems require accuracy and reliability of the administrative database. One study trying to improve adherence to follow-up after an abnormal Pap smear result was only able to make telephone contact with 42% of the eligible patients.[5] They found that 16%-20% of their telephone and address data were inaccurate.

Although patient tracking systems are not evaluated in this chapter because of the lack of published literature, in one study clinical personnel stated that they were reluctant to perform the tracking function of the intervention, and even discontinued the Pap smear log once the study was completed.[12]

Comment

Failure to notify patients of abnormal results is a little-studied but major problem involving both patient safety and health care quality. One study evaluated direct mailings of abnormal results to patients and found improved follow-up in one subset of patients. More data are required before recommending implementation of this practice.

We were unable to find any studies evaluating specific interventions aimed at providers that resulted in increased notification to patients of abnormal results. Interventions that target providers through computerized reminders linked with patient tracking systems might have an impact on improving patient notification of abnormal results. This area is an important source of future investigation.

Table 42.4.1. Randomized controlled trial of direct notification of abnormal Pap smear results*

Study	Study Setting	Outcomes	Results (95% Confidence Interval)†
Del Mar, 1995[1]	311 women with abnormal Pap smears from 42 general practices in Australia	Level 2	Patients with CIN lost to follow-up: Direct mail notification: 0 (0-0.07) Control: 0.23 (0.11-0.39) Patients with atypia lost to follow-up Direct mail notification: 0.10 Control: 0.13 (p=NS)

* CIN indicates cervical intraepithelial neoplasia; NS, not statistically significant.
† Proportion of patients lost to follow-up reported in intervention group vs. control group.

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Final Comment to Chapter 42

Faulty information transfer causes discontinuities of care that may result in adverse events. However, interventions to improve information transfer have received relatively little attention in the medical literature. Unfortunately, numerous barriers impede the appropriate transfer of information between institutions and between patient and provider. Future technologies that allow for more seamless transfer of information may mitigate these gaps in patient care. Further evaluation is critical.

Chapter 43. Prevention of Misidentifications

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Subchapter 43.1. Bar Coding

Background

Machine-readable automatic identification (ID) systems, including bar codes, magnetic stripes, optical character recognition and radiofrequency labeling, have improved productivity and quality in diverse industries. Bar codes represent the oldest and most common of these machine-readable ID systems,[1,2] and are widely used in industrial manufacturing, shipping and inventory tracking operations. Prior to bar coding, these processes would have involved keystroke entry of identification numbers, producing approximately one error in every 300 entered characters. In contrast, bar coding produces misidentification errors at rates ranging from one character in 15,000 to one character in 36 trillion.[3]

The use of bar coding in health care was first described over 30 years ago in clinical laboratories and blood banks.[1,4] In 1984, Rappoport identified 3 areas for the use of automatic ID technology in lab medicine: patient identification, document identification, and specimen identification.[1] However, in a 1987 survey by the American Hospital Association, the use of bar codes was most widespread in materials management departments, rather than in clinical application.[5] Other areas in which hospitals employed bar codes at that time included the clinical laboratory, pharmacy, radiology, medical records and asset management. Despite the Health Industry Bar Code Council's call for standardization in the mid-1980s, the implementation of bar code technology has been stymied by lack of industry standards and failed cooperation among all stakeholders.[2,6]

As bar coding has the potential to substantially increase productivity and accuracy, one would expect it to be applied to important patient safety practices. Unfortunately, the published literature contains very little evidence regarding health care applications. In this chapter we focus on 4 areas in which bar coding shows promise for improving patient safety: patient identification, medication dispensing and administration, specimen handling, and medical record keeping.[2,7-10]

Practice Description

Patient Identification

Machine-readable patient ID systems could replace conventional wrist-banding, and might reduce patient ID errors ranging from specimen collection to medication and blood product administration. Attempts to create such machine-readable ID systems were reported in the blood banking literature as early as 1977.[11] Transfusion Medicine is particularly attuned to issues of patient identification, as specimen collection and blood product administration account for the majority of preventable transfusion errors.[12,13]

Most scenarios for patient identification involve the substitution or supplementation of the traditional wristband for one with a unique bar code patient identifier. All patient specimens, medications and released blood products then receive the patient's unique bar code ID. No

procedure or treatment can occur unless the patient's ID is scanned with a portable scanner and matched with a bar code generated by the doctor's order. For example, a phlebotomist would carry the scanner, check the patient's ID against a bar coded specimen label or collection list, and draw blood only in the event of a match. Similarly, for administration or treatment, the patient's ID and the intended therapeutic would be scanned at the bedside with a portable reader. If a match exists, the transfusion or medication is allowed and the time and date are recorded and even transmitted directly to the hospital computer system. The nurse's bar code ID can also be scanned and a timed administration record can be created. If there is no match, an alarm is sounded, and the administration delayed until the problem is resolved. [9,14]

Other technological means to reduce error in patient identification have been examined in the transfusion literature. Several researchers explored the use of a system providing a mechanical barrier to transfusion through a series of locks.[15] This system appears to be cumbersome and easily circumvented. In addition, electronic blood banking, with point-of-care crossmatching and computer-controlled release of blood, has been examined for high volume transfusion areas such as the operating room or intensive care unit.[16] Due to major barriers to large-scale implementation, these practices will not be discussed further.

Specimen handling

Clinical laboratories have integrated bar codes in specimen handling with a great deal of success.[3,8] Several authors have described the development of central laboratory information systems (LIS) that employ bar code technology. Collection list and label software can be modified to integrate and produce bar coded information. Confirmation of labeling and patient ID occurs at the bedside. Specimen sorting and aliquoting in the laboratory can be shortened or eliminated by various setups. At Rush-Presbyterian Hospital in Chicago, a central receiving station rapidly sorts and aliquots bar coded samples as they move on a conveyor belt.[3] At the University of Kansas Medical Center, the collection tubes are also used for analysis, thus eliminating the need for aliquoting samples. Additionally, the computer sends the bar code-coordinated orders to each of the 2 chemistry analyzers. Because a sample can then be appropriately processed at either analyzer, the need for sorting samples has also been eliminated.[8] Clinical labs also employ bar code technology in harder-to-automate processes. For instance, the University of Utah uses bar codes to replace common keystrokes for text reporting of microbiology results—eg, a technician might use a bar code "pick list" to scan the single bar code that means "no growth for 24 hours" and eliminate the need to type this phrase.[17,18]

Medication dispensing and administration

The use of bar codes is uniquely suited to the dispensing and administration stages of the medication process.[19] Bar coding may be used to simplify the patient cassette (the medicine tray for bedside delivery) filling and verification process.[20] For instance, a technician fills a cassette according to a computerized, bar coded medication schedule and completes a quick verification by scanning the label of each unit-dose that has been placed in it with a handheld scanner. The computer can generate an error message if an incorrect medication is entered. The administration of bar coded medications can also be tracked at the point-of-care using a portable scanner and compared against the hospital computer's medication orders.[9,21] Bar coded medication administration has the added capability of creating a record of the administration (ie, RN, date, time) and a bill. This type of system could be integrated with a patient identification system in an attempt to eliminate errors resulting in administration of medication to the wrong patient.

Medical record keeping

Radiology and medical records departments use bar code technology to track the location and status of studies and charts.[22-24] Even more creative use of bar coded information has been reported in the emergency medicine and pharmacy literatures. As with the applications in the microbiology lab, bar codes can be used to replace frequently used text for the creation of medical records. "Pick lists" of bar codes with their text equivalents can be employed in circumstances requiring speed and accuracy. Several uses of bar coded scripts have been examined in resuscitation events, and in mass casualty recording.[10,25-27] The use of bar code "pick lists" for the documentation of pharmacists' clinical activities has also been explored.[28-30]

Prevalence and Severity of the Target Safety Problem

Bar code technology may be used to address any number of patient safety issues in medicine. For this discussion, we will define the target safety problem as patient identification in general, using transfusion medicine as a specific example.

Patient identification remains a challenge in hospitals because of the number of complex interventions that occur to patients ranging from meals to surgeries. These interventions occur in a variety of locations and are provided by large teams of staff who work in shifts. In addition, sick patients, or those who have a language barrier, are not always capable of responding to questions about their identity or treatment plans. Hospitals generally rely on standardized wristbands containing the patient's name and other identifying information such as medical record number or date of birth. Unfortunately, conventional wristbands are not reliable sources of patient identification. A 1991 national sample of 712 hospitals estimated error rates for conventional patient identification wristbands to be 5.5%.[31] In half of the errors, the patient's wristband was absent altogether. The error rates were significantly lower in hospitals where phlebotomists had responsibility for monitoring wristband accuracy, as the phlebotomy staff would not perform routine lab work unless the band was corrected. Other errors included more than one wristband with conflicting data (18.3%); wristbands with incomplete (17.5%), erroneous (8.6%), or illegible data (5.7%); and rarely, patients wearing wristbands with another patient's data (0.5%). As patient identification data are only as good as the information entered at registration, the use of bar coded ID data could not be expected to correct certain types of errors such as a wristband with incorrect data entered at admission, although it is potentially beneficial in eliminating other types of errors such as illegible data.

Even when wristbands are free of errors, protocols for patient identification (such as dual witness verification of identification for blood transfusion) are easily circumvented or performed incorrectly.[32] In an analysis of major transfusion errors reported to the FDA over a 10-year period from 1976-1985, Sazama found 10 patient deaths where the actual and intended patients shared the same last name, and 5 deaths where the 2 shared the same hospital room.[13] Consequently, automatic patient identification systems have been proposed as a technological solution to remove human factors (Subchapter 41.1) from the patient identification process.

Despite technical improvements in testing for blood group identification, fatal ABO-incompatible transfusions in the United States continue to occur at a rate ranging from approximately 1:600,000 to 1:800,000, with as many as two dozen fatalities in the US annually.[12,13] Thus, the chance of a patient suffering a fatal transfusion reaction due to ABO-incompatibility is roughly equivalent to the risk of acquiring HIV infection from a blood transfusion.[33,34] Patient misidentification represents the most common cause of ABO-incompatible transfusion, accounting for 46-57% of these errors.[12,13] Since the rate of patient and

donor having blood group compatibility *by chance* is approximately 60%, it is estimated that the total number of ABO-incompatible transfusions is much higher than the rate of fatal errors. A study from New York State estimated that as many as one in 12,000 transfusions involve administration of a blood product intended for another patient or release of blood of an incorrect group.[*12]

Opportunities for Impact

The implementation of automatic patient identification may present a large opportunity to bring transfusion medicine and other hospital interventions closer to the goal of zero risk. According to a survey conducted by the American Society of Hospital-System Pharmacists, 1.1% of responding hospitals use bar coding of drug products in conjunction with bar coding on the patient's identification tag.[35]

Study Designs

Multiple reports of the use of bar codes appear in the medical literature, but most of these relate to inventory management. Few authors examine bar codes for patient identification. Only one of these studies was a prospective evaluation, and in the study bar coded patient identification comprised only one small part of the intervention.[10] One observational study examined a bar code patient ID system for medication administration.[9] In the study, however, routine patient ID scanning was easily circumvented and the actual error rate was not provided. The remainder of the reports are descriptive in nature.[14,36,37] Therefore, error rates in automated patient identification could not be readily compared to usual practice.

The use of bar coding in other clinical care applications (aside from inventory control) has been examined prospectively in trauma recording[27] and in documenting pharmacists' interventions.[28] One additional observational study examined bar coding in pharmacy dispensing.[20]

*This is based on a reported error rate of 1/19,000 transfusions. The authors estimate a 64% chance that a random transfusion to an unintended recipient would be compatible and assume 100% reporting of incompatible erroneous transfusions

Study Outcomes

Some of the studies report error rates in transfusion or medication errors (Level 2), while others report related outcomes such as speed of data entry (Level 3), transcription errors (Level 2) in a variety of experimental and clinical settings, and user satisfaction (Level 3).

Evidence for Effectiveness of the Practice

A point-of-care information system for medication management was implemented at a tertiary care center in Colorado.[9] The system provided online patient and medication data that verified medication administration at bedside using hand-held scanners to record patient ID, nurse ID, and medication unit-dose bar codes. When intervention data were compared with historical controls, the pre-intervention medication error rate of 0.17% dropped to 0.05%, sustained over 3 years for an overall decrease of 71% (p value not reported). There was a 33% decrease in "wrong drug" errors, a 43% decrease in "wrong time" errors, and a 52% decrease in "omitted dose" errors. There was a 47% decrease in "transcription/order-entry" errors. There was no change in "wrong patient" errors or "wrong dosage" errors, perhaps because the component of the multifaceted intervention most likely to mitigate these errors, the use of the scanners for patient ID, was easily and frequently circumvented. It is unclear if bedside scanning added an unwanted layer of work for the nurses, or if they were uncomfortable performing this task in front of patients and families. Computerized pharmacy and bar code tracking of medications led to qualitative improvements in documentation time, scheduling of administration, nursing-pharmacy communications, and pharmacist drug monitoring. However, the contribution of bar coding to the decreased error rate is not distinguishable from that of the entire intervention. It also appears that the point-of-care patient ID portion of the intervention was easily bypassed, and was therefore not adequately evaluated.[9]

On a large medical ward of a university hospital, the satellite pharmacy was reconfigured to implement bar code technology for drug dispensing.[20] The hospital bar coded all medications, patient medication cassettes, patient wristbands, and employees. Standard dispensing time was estimated at 8.24 seconds, while dispensing time for bar coded medications was 6.72 seconds (p value not reported). Accuracy of the standard cassette fill system was 99.6% (equivalent to one error in 250 doses), while the accuracy of bar coded cassette fill was reported to be 100% (based on 0 errors in about 20,000 doses). The pharmacists were freed to do other work as the burden of dispensing was shifted to pharmacy technicians.

As pharmacists have begun to use bar code technology for medication distribution, 2 pharmacy groups described the use of bar codes in recording their clinical interventions.[28, 29] One group found bar code documentation to have lower overall error rates compared to manual documentation, while the marginal cost of implementing bar coding was less than $100 (factoring in savings in labor costs related to manual entry).[28] These data were limited by the small number of operators who differed on their preferences for manual versus bar code recording.

A prospective trial reviewed bar code technology in trauma recording. Experienced emergency room nurses found bar coded pick lists to be easy to use and produced fewer errors per record compared with handwriting (2.63 ± 0.24 vs. 4.48 ± 0.3, $p<0.0001$) for videotaped trauma resuscitations.[27] In a prospective study of simulated mass casualty incidents in The Netherlands, bar coded computer registration produced 25% fewer inaccuracies than handwritten medical charts.[10]

The limitations of these studies are numerous, including their small sample sizes and lack of generalizability. However they demonstrate that bar code technology is generally easy for operators to use, can be applied in a variety of creative ways, and produces easy-to-demonstrate gains in accuracy and efficiency.

Potential for Harm

There is no clear detriment to patient identification with a bar code system. However, as with the addition of any new technology, the possibility exists that the complexity of the information system, especially if it grows, could create more routes for potential failure. For instance, an error during patient registration might be perpetuated throughout the hospitalization by the information systems, and be more difficult to correct than with conventional systems. The system's data are only as accurate as that entered by fallible humans.

Costs and Implementation

Significant barriers need to be overcome before the full potential of bar coding can be exploited in the clinical setting. The process of medication dispensing and administration highlight several examples of these barriers. First, pharmaceutical manufacturers have yet to adopt a universal bar code standard like the UPC system used in grocery store inventory.[38] As of yet, there has been no regulatory mandate by the FDA to serve as an incentive, although the American Society of Hospital-System Pharmacists recently urged the FDA to take action.[39] Second, placing bar codes on unit-doses of medications often requires major changes in packaging (such as an increase of the package size to accommodate the bar coded label). Bar code tracking systems would have difficulty with unusual doses such as halved tablets. IV doses would still require bar code labeling in the pharmacy when prepared.

At this point, implementation of bar coding requires a commitment on the part of the hospital to relabel every unit-dose of medication using a hospital standard. The hospital pharmacies that have implemented these systems have repackaged and relabeled many unit-doses at considerable cost.[9,20] One health system estimated costs at $119,516 annually, with the per dose costs of bar code labeling estimated at 2.73 cents.[20] The bottom line is that, at present, the costs of implementing bar coding in an entire pharmacy inventory are significant and the logistics complex.

The use of bar coding in simpler clinical scenarios (ie, using a blood transfusion wristband for patient identification) may be implemented with very modest outlay of resources (estimated to be less than 5 cents per wristband).[36] The costs of the scanners themselves are moderate. A new model scanner, software and recharger were priced at about $1100 in 1997.[28]

Comment

Bar coding is a fast and accurate method of automated data capture that in experimental settings provides qualitative improvements in speed and accuracy of data entry. Bar code technology might be creatively applied to any number of data-driven processes in medicine. As the rapid and accurate transfer of data is paramount in health care, the thoughtful application of appropriately piloted and evaluated bar code technology is likely to be well received and deserves further investigation.

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Subchapter 43.2. Strategies to Avoid Wrong-Site Surgery

Background

Operating on the wrong site or body part represents a potentially devastating event for all parties involved. Cases of “wrong-site surgery” frequently attract considerable media attention[1-4] and foment malpractice lawsuits. Claims for wrong-site orthopedic surgeries result in indemnity

payments in 84% of cases, compared with only 30% of orthopedic claims overall.[5,6] Although orthopedics represents the largest source of legal claims, the Physician's Insurance Association of America (PIAA) has handled wrong-site surgery litigation from the entire range of surgical specialties and subspecialties.[6] Common factors identified in wrong-site surgery include the involvement of multiple surgeons on a case, the performance of multiple procedures during a single trip to the operating room, unusual time constraints, and unusual anatomy or patient characteristics, such as physical deformity or morbid obesity.[7,8]

Based upon careful review of 43 cases reported through its Sentinel Event Policy[9] over a 3-year period, the Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) issued the following recommendations for avoiding wrong-site surgery:[7,8]

- *Mark the operative site and involve the patient in this process*
- *Require oral verification of the correct site in the operating room by each member of the surgical team*
- *Follow a verification checklist that includes all documents and medical records referencing the intended operative procedure and site*
- *Directly involve the operating surgeon in the informed consent process*
- *Engage in ongoing monitoring to ensure verification procedures are followed*

Among these recommendations, marking the operative site has received the most attention and is the focus of this chapter.

Practice Description

In 1998, the American Academy of Orthopaedic Surgeons endorsed a program of preoperative surgical site identification called "Sign your Site," modeled on the "Operate through your initials" campaign instituted by the Canadian Orthopaedic Association from 1994-96.[5,10] Both organizations recommend that the operating surgeon initial the intended operative site, using a permanent marker, during a scheduled preoperative visit. For spinal surgery, the recommendations additionally endorse the use of intra-operative x-rays for localization of the pathologic spinal level before proceeding with the procedure. Many surgeons already employ their own techniques for surgical site identification such as marking an "X" on the operative site or marking "No" on the wrong limb.[5,11,12] While these practices are commendable, they have theoretical drawbacks including lack of standardization across operating rooms and institutions. These alternative strategies will not be evaluated further in this chapter.

Prevalence and Severity of the Target Safety Problem

From January 1995 to March 2001, JCAHO reviewed voluntary reports of 1152 "sentinel events." Wrong-site surgery accounted for 114 (9.9%) of these reports and included procedures in neurosurgery, urology, orthopedics, and vascular surgery.[13] Despite the high profile of JCAHO's Sentinel Event Policy,[9] under-reporting by health care organizations almost certainly affects these statistics. Only 66% of the 1152 total events were "self-reported" by the institutions involved. The remainder came from patient complaints, media stories and other sources.[13] In fact, using a mandatory reporting system, the New York State Department of Health received 46 reports of wrong-site surgery from April 1, 1998 through March 31, 2000[4] (F. Smith, personal communication, May 2001), compared with the 114 cases JCAHO received nationally over a

period 3 times longer.[13] This suggests that voluntary incident reporting may underestimate the true incidence by a factor of 20 or greater.[14]†

The PIAA reviewed claims data from 22 malpractice carriers representing 110,000 physicians from 1985 to 1995.[5] These claims included 331 cases of wrong-site surgery. The complete PIAA database documents almost 1000 closed malpractice claims involving wrong-site surgery.[6] However, this figure also underestimates the prevalence of wrong-site surgery, as every case does not result in a claim. Most wrong-site surgeries involve relatively minor procedures such as arthroscopy,[10,15] rather than limb amputations or major neurosurgical procedures. Consequently sequelae are minimal. The State Volunteer Mutual Insurance Company (Tennessee) released a series of 37 wrong-site surgery claims from 1977 to 1997.[15] Performing the correct procedure on the wrong side constituted the most common error (eg, arthroscopic knee surgery on the wrong knee in 15 of the 37 cases). Twenty-six of the patients experienced no sequelae beyond a scar, and only three patients suffered permanent disability. Given the rarity of significant harm, estimates of the incidence of wrong-site surgery derived from litigation data likely underestimate the true prevalence of this problem, as do estimates based on incident reports.

Opportunities for Impact

Some surgeons have developed their own methods for surgical site identification,[11,12] but routine preoperative evaluation and marking of the intended surgical site by the attending surgeon has yet to become standard practice in orthopedics or any surgical specialty. One year after its "Sign Your Site" campaign, the American Academy of Orthopaedic Surgeons surveyed its membership. Among the 2000 orthopedic surgeons surveyed, 77% responded that the idea was a good one, but only 40% stated that they complied with the recommended practice. Only one-third stated that their principal hospitals had a “Sign Your Site” or similar program in place, although many anticipated initiation of one in response to the campaign.[16,17]

Study Designs

The published literature includes no studies in which the adoption of a practice related to surgical site identification is analyzed in the setting of a controlled observational design or clinical trial. One report described the experience of 4 orthopedic surgeons in private practice,[18] but included no comparable observations from a control group. The experience of the Canadian Orthopaedic Association remains unpublished, and the observed effect is based entirely on litigation statistics[10] (B. Lewis, personal communication, March 2001).

Study Outcomes

Given the egregious and distressing nature of wrong-site surgery, the error itself represents the outcome of interest, regardless of the clinical outcome. Unfortunately, in the absence of observational studies that include controls, the number of malpractice claims for wrong-site surgery represents the most widely cited outcome.

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† Mandatory New York reporting system (NYPORTS) documented 46 events in 24 months. New York State has a population roughly 1/15th of the entire country. Thus, had JCAHO captured wrong-site surgeries with the same sensitivity, one would expect 2484 wrong site surgeries to have been reported during the 87 months covered by the JCAHO sentinel event policy. This figure is 21 times the actual figure of 114 cases.

Evidence for Effectiveness of the Practice

The Canadian Medical Protective Association reported a baseline level of litigation for wrong-site surgery at 7% of all orthopedic surgery settlements before 1994 when the Canadian Orthopaedic Association instituted their "Operate Through Your Initials" policy.[10] Currently, there are no known wrong-site surgery claims against orthopedic surgeons in Canada. (B. Lewis, personal communication, March 2001) Interpreting the difference in the rates of litigation of a rare occurrence is difficult, however, especially without an accurate estimate of the denominator (ie, the total number of relevant procedures performed during the time periods involved). Moreover, the degree to which Canadian surgeons complied with the policy is unknown. As mentioned above, only 40% of responding American orthopedists reported adoption of preoperative site identification in routine practice.[16]

In a North Dakota private practice that used preoperative site identification with indelible ink, there was one incidence of wrong-site surgery (pinning of the wrong phalanx in a hand) in 15,987 consecutive cases.[18] Even assuming that the sole detected case represents the only wrong-site surgery in this sample, interpreting this low event rate is impossible without a control group. Comparing this result with national data is also problematic. National data on the number of orthopedics procedures performed each year might generate an estimate of an appropriate "denominator," but the nationwide "numerator" is unknown. Because we do not know the extent to which incident reporting and malpractice litigation underestimate the incidence of wrong-site surgery, we cannot accurately estimate the baseline rate of wrong-site surgeries for comparison with results of a case series such as the North Dakota report cited above.[18]

Potential for Harm

Some surgeons may worry that marking the surgical site increases the risk of contamination, but this concern appears unwarranted.[15,18] More concerning is the potential harm that may arise from confusion caused by practice variability in "signing the site." Although the original recommendations called for surgeons to initial the intended operative site, some surgeons and hospitals mark the site with an "X."[15,16] Still others use an "X" or "No" to mark the limb or site that should not be operated upon.[11,12] In addition, there are reports of patients crossing their legs before the ink is dry and producing an identical mark on the contralateral knee, thus subverting the intended effect of the intervention.[10] Confusion may also ensue if operating room personnel cover the mark with surgical drapes prior to the start of the surgery.[10]

Costs and Implementation

The costs of marking a surgical site are negligible. Marking procedures that require the presence of the surgeon in the preoperative area prior to the initiation of anesthesia may require a culture shift among surgeons and involve the costs of surgeons' time. Implementation strategies designed to more efficiently utilize the operating surgeon's time could be designed. For hospitalized patients, implementation might involve the operating surgeon initialing the intended operative site at the time consent is obtained, thus requiring that the physician be present at the time of consent. The nurse/anesthetist, anesthesiologist or other responsible party in the preop area would then be required to contact the operating surgeon only in cases where the operative site has not already been initialed.

Comment

While "signing the site" represents a low-tech solution with high face validity, no evidence supports a particular version of this practice. Additionally, the existence of different versions of the "signing the site" practice may cause confusion to the point of increasing the likelihood of error. Strategies that focus only on a single aspect of the identification problem, without considering the preoperative and operative processes as a whole may fail to avert error. For instance, protocols that rely on review of key preoperative x-rays in the operating room creates a new mandate to ensure that the correct patient's x-rays are brought to the operating room.[6]

Practices to successfully reduce (and eventually eliminate) wrong-site surgeries will likely combine a standard method of marking the intended site with collaborative protocols for verification of the intended procedure and operative site by all members of the operating room staff.[7] Straightforward as each of these processes may appear, successful implementation may require substantial investments of time and resources for protocol development and team training. Whatever multifaceted practice is developed should be implemented within the setting of a planned observational study.

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Chapter 44. Crew Resource Management and its Applications in Medicine

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Background

Patient care, like other technically complex and high risk fields, is an interdependent process carried out by teams of individuals with advanced technical training who have varying roles and decision-making responsibilities. While technical training assures proficiency at specific tasks, it does not address the potential for errors created by communicating and decision making in dynamic environments. Experts in aviation have developed safety training focused on effective team management, known as Crew Resource Management (CRM). Improvements in the safety record of commercial aviation may be due, in part, to this training.[1] Over the past 10 years, lessons from aviation's approach to team training have been applied to patient safety, notably in intensive care unit (ICU) and anesthesia training.[2,3] This chapter reviews the literature on Crew Resource Management, also known as Cockpit Resource Management, and describes adaptations of this training framework to medicine.

Practice Description

Crew Resource Management in Aviation

Crew Resource Management has been widely used to improve the operation of flight crews. The concept originated in 1979, in response to a NASA workshop that examined the role that human error plays in air crashes.[4] CRM emphasizes the role of human factors in high-stress, high-risk environments. John K. Lauber, a psychologist member of the National Transportation Safety Board, defined CRM as "using all available sources—information, equipment, and people—to achieve safe and efficient flight operations."[5,6] CRM encompasses team training, as well as simulation (also referred to as *Line-Oriented Flight Training*, or LOFT), interactive group debriefings, and measurement and improvement of aircrew performance.

There is no universal CRM training program. The Federal Aviation Administration (FAA) allows air carriers to customize their CRM programs to best suit the needs of individual organizations. Therefore, training programs vary somewhat from carrier to carrier, making it difficult to describe operational components. Furthermore, these programs continue to evolve as aviation technology changes and more is learned about group dynamics.

One CRM model focuses on the elements of human effectiveness.[7] The 3 primary components of effective crew management are safety, efficiency, and morale. Specific factors related to aircrew performance are categorized, and serve as the basis for training and research. These factors include materials, organization, individual, and group process variables associated with performance.[8] Examples of outcomes that result from these input variables are safety, efficiency, and customer satisfaction.

Subsequently, Helmreich and colleagues proposed a modified conceptual framework for CRM, termed the "Error Troika,"[9] to display a hierarchy of 3 error countermeasures. At the first

level, CRM includes training on how to avoid errors. At the second level, potential errors are "trapped" before they are committed. At the third level, mitigation of error consequences occurs.

From a practical standpoint, CRM programs typically include educating crews about the limitations of human performance.[10] Trainees develop an understanding of cognitive errors, and how stressors (such as fatigue, emergencies, and work overload) contribute to the occurrence of errors. Multi-day CRM training programs typically require participants to assess personal and peer behavior. Operational concepts stressed include inquiry, seeking relevant operational information, advocacy, communicating proposed actions, conflict resolution and decision making.

Prevalence and Severity of the Target Safety Problem

The field of aviation has a substantial history of collecting and analyzing safety-related data. Historically, human error has caused or contributed to over 50% of aviation accidents. In an analysis of 35,000 reports of incidents over 7.5 years, almost 50% resulted from a flight crew error, and an additional 35% were attributed to air traffic controller error.[11] Root cause analyses (Chapter 5) by safety experts have found that errors frequently occur because flight crews fail to effectively manage the resources available to them (eg, fail to verify information when uncertain about it, fail to plan for contingencies).[11] Naval aviation reports provide similar results, with one study reporting 59% of "Class A mishaps" (serious consequences including fatality, destroyed aircraft, and major injury) attributed to some degree to aircrew factors.[12] These and similar analyses have catalyzed tailored prevention strategies including CRM for commercial aviation,[1] and "aircrew coordination training" (ACT) for Naval aviators.[12]

Study Design and Outcomes

Measures

Although the most obvious and meaningful measure of CRM effectiveness would appear to be airline accident or "near miss" rates, these objective measures have not been used in commercial aviation studies. Helmreich suggests that it is not possible to use these measures, because accident rates are very low and "near misses" are voluntarily reported.[10] Furthermore, the content and structure of CRM training programs are variable.[10]

In response, researchers have developed tools that assess the effectiveness of CRM in other ways. These tools include attitudinal surveys and peer performance rating questionnaires, including the NASA/University of Texas Line/LOS Checklist (LINE/LOS Checklist),[13] the Cockpit Management Attitudes Questionnaire (CMAQ), and the Flight Management Attitudes Questionnaire (FMAQ). The LINE/LOS Checklist is used to rate crew performance on critical behaviors during specific segments of flight (eg, not rushing through briefing period, exhibiting high levels of vigilance in both high and low workload conditions, etc). Ratings on each behavioral element (ie, model for teamwork) range across 4 levels from poor to outstanding.

In contrast, CMAQ is used to evaluate the attitudes of crewmembers within and between organizations, pre- and/or post-CRM training. Results are intended to serve as a proxy for measuring crew process and performance.[14] The instrument has been validated by comparing self-reported attitudes with performance ratings made by experienced Check Airmen, experts trained in peer evaluation.[15] The FMAQ is a revised version of the CMAQ that was developed by Helmreich and colleagues in response to attitudinal differences observed in flight crews from different countries.[16]

Observation of crew performance in simulated flights has also been used.

Representative Studies

Several studies have utilized proxy tools to test the effectiveness of CRM.[8,12,17] One study by Helmreich and colleagues consisted of an assessment of the attitudes before versus after CRM training (pre-test versus post-test).[17] Crew behaviors were noted by a trained observer using the NASA/University of Texas Line/LOS Checklist.[18] More than 2000 line flights and LOFT sessions were included in the analysis. Overall performance of crews was classified as "below average," "average," or "above average" by Check Airmen and LOFT instructors.

As a result of the CRM training, the percentage of crews rated as "above average" increased while the percent rated "below average" decreased. Performance ratings differed between fleets and airlines. Superior pilots also shared many common attitudes, (for example, they were aware of their personal limitations and diminished decision-making capacity during emergencies). In addition, they encouraged crewmembers to question their decisions and actions, were sensitive to the personal problems of other crewmembers, and recognized the need to verbalize plans and to train other crewmembers.

A second study by Barker and colleagues compared the effectiveness of 17 CRM-trained flight crews on military mission simulators, divided according to whether they were "fixed" or "formed" crews.[8] Nine of the crews were defined as "fixed" since they had flown together for six months or longer; the remaining 8 were "formed," as they had flown together for less than 6 months. Each crew was asked to participate in a simulated mission. The first leg of the mission was programmed to be problem-free, but the second leg required crews to address a safety issue. As with the earlier study, crew behaviors were observed using the NASA/University of Texas Line/LOS Checklist. Surprisingly, the formed crews committed fewer minor errors, but the number of major errors did not differ significantly between the groups.[8] The authors concluded that formed crews may experience less ineffective coordination than fixed crews, as the latter might be more complacent from the routine of working together, but that further research was needed.

A third study evaluated rates of naval aviation mishaps, and the role of CRM failures.[12] While the study primarily compared crew performance in 2 types of equipment, the aircrew performance deficits were also compared with those seen during an earlier time period, prior to implementation of aircrew coordinating training (ACT) programs (the specific form of CRM used). Analysis of data from the post-ACT implementation period across the fleet revealed that 70% of human error mishaps were connected with aircrew factors, and that 56% of these resulted from at least one CRM failure. The authors noted that these percentages were similar to those reported in a separate study prior to ACT implementation. Because of a lack of controls or adjustments for potential confounders, no conclusions about effectiveness of the ACT program can be drawn.[12]

Comparison to Medicine

Sexton and colleagues compared flight crews with operating room personnel on several measures, including attitudes toward teamwork.[19] The study included more than 30,000 cockpit crew members (captains, first officers, and second officers) and 1033 operating room personnel (attending surgeons, attending anesthesiologists, surgical residents, anesthesia residents, surgical nurses, anesthesia nurses). Data from the crew members were obtained from previous administrations of the CMAQ and FMAQ to major airlines around the world (over a 15-year period). The operating room participants were mailed an analogous questionnaire (CMAQ modified[20]), administered over a period of 3 years at 12 teaching and non-teaching hospitals in the United States and abroad (Italy, Germany, Switzerland, and Israel).

The level of teamwork perceived by attending surgeons compared with other operating room staff differed markedly. A majority of surgical residents (73%) and attending surgeons (64%) reported high levels of teamwork, but only 39% of attending anesthesiologists, 28% of surgical nurses, 25% of anesthesia nurses, and 10% of anesthesia residents reported high levels of teamwork. A bare majority (55%) of attending surgeons rejected steep hierarchies (determined by whether they thought junior team members should question the decisions of senior team members). In contrast, 94% of airline crew members preferred flat hierarchies.

It was also noted that medical participants were far more likely to agree with the statement "Even when fatigued, I perform effectively during critical times." Seventy percent of attending surgeons agreed with this statement, as well as 56% of surgical residents, 60% of surgical nurses, 57% of anesthesia residents, 55% of anesthesia nurses, and 47% of attending anesthesiologists. In contrast, 26% of pilots agreed with this statement.

Applications of CRM Principles in Medicine

The Sexton study and other analyses suggest that safety-related behaviors that have been applied and studied extensively in the aviation industry may also be relevant in health care. We identified CRM applications in several dynamic decision-making health care environments: the operating room, labor and delivery, and the emergency room.[3,21,22] In addition, Gaba has noted that some other domains (eg, cardiac arrest response teams) that have active simulation training are currently incorporating a broader range of CRM-like training methods.[23] (Simulators are covered in more detail in Chapter 45).

Practice Description

Crew Resource Management in Health Care Settings

As with aviation, the medical application of CRM has required tailoring of training approaches to mirror the areas in which human factors contribute to mishaps. In anesthesiology 65-70% of safety problems (accidents or incidents) have been attributed at least in part to human error. In response, several anesthesiologists from the VA Palo Alto Health Care System and Stanford University, with funding from the Anesthesia Patient Safety Foundation, developed *Anesthesia Crisis Resource Management* (ACRM), modeled on CRM.[3,23] The original demonstration courses consisted of didactic instruction, videotape of a reenactment of an aviation disaster, videotape of an actual anesthetic mishap, simulation training and a debriefing session. Ongoing courses include the use of a textbook that catalogues 83 critical events (eg, acute hemorrhage, bronchospasm, seizures), and approaches to managing them.[24] Currently, there are 3 ACRM courses offering progressively more challenging material, a Working Group

on Crisis Management Training in Health Care formed by the developers of ACRM that has initiated formal ACRM instructor training, and thoughtful consideration of pragmatic approaches to evaluating ACRM.[23]

Helmreich and Schaefer have also advanced CRM theory in the operating room environment by adapting their model of team performance. This framework describes the team performance inputs that are critical to essential team functions that in turn lead to desired outcomes (defined as patient well-being). Examples of inputs include individual aptitudes, physical environment, and culture (professional, organizational, and national). Performance functions consist of team formation and management, surgical procedures, communications, decision processes, and situational awareness.[18]

Another application of CRM to the health environment is the *MedTeams behavior-based teamwork system*, developed by Dynamics Research Corporation, and sponsored by the Army Research Laboratory. It aims to adapt research in team performance and training from military helicopter aviation to emergency medicine.[22,25,26] Thus far, specific applications have been developed for Emergency Department care and labor and delivery units.[27] The system is implemented through courses and assessment tools. The Emergency Team Coordination Course (ETCC) includes 5 team dimensions or goals (ie, maintain team structure and climate, facilitate planning and problem-solving, enhance communication among team members, facilitate workload management, improve team-building skills). Each goal is tied to specific teamwork tasks. For example, tasks for the first goal (maintain team structure and climate) include "establish team leader," "form the team," "set team goals," and "assign roles and responsibilities."[22] Like the CRM approach to the "Error Troika," the MedTeams approach is based on avoiding errors, trapping them as they occur, and mitigating the consequences of actual errors. Principles underlying the MedTeams approach include:

- Team responsibility for patients
- A belief in clinician fallibility
- Peer monitoring
- Team member awareness of patient status, team member status and institutional resources

Peer monitoring is a fundamental component of the MedTeams system, as well as a feature of the ACRM and aviation field's CRM approaches. Along with his or her clinical responsibilities, each team member undertakes the intermittent process of peer monitoring or "check" actions, engaging in this check cycle as frequently as possible. The teamwork check cycle begins with each team member monitoring his or her own situation awareness and cross-monitoring the actions of other teammates. If during the monitoring mode the *monitoring* teammate observes a suspected error in progress, that individual intervenes with a direct question or offer of information. The erring teammate may then acknowledge the lapse, correct it and continue working. Alternatively, the *monitoring* teammate may have lost situation awareness. The non-erring *monitored* colleague can then provide feedback to correct the peer's situation awareness. If team members are in strong disagreement about how patient care should proceed, advocacy, assertion and perhaps third-party involvement may be used to resolve the situation. Over time, the check cycle becomes habitual, resulting in hundreds of team checks daily, all with the potential to break the error chain.

Recently, ACRM has been extended to a full-day course on neonatal resuscitation training for neonatologists and pediatricians.[21] Called "NeoSim", the course combines traditional

training methods with reviews of literature and didactic instruction with simulation. Debriefing follows, using videotape of the simulation. As with the other examples, the emphasis of teaching behavioral teamwork skills along with technical content is the hallmark of CRM interventions in health care.

Evidence for Effectiveness of the Practice

The most thoroughly studied of the medical CRM applications is ACRM, although as with the aviation examples, rigorous evaluations are challenging to design. Few studies utilize a control group, although researchers have reported assessment methods for determining both technical and behavioral performance from simulator videotapes[28] (see also Chapter 45). A before-after ACRM training analysis (Level 3 Study Design) of trainees' knowledge-base (Level 3 Outcome) for crisis yielded mixed results.[3] The average score on the post-test was significantly greater than the pre-test for one trainee class, composed mostly of residents. For the other class of experienced anesthesiologists, the test scores did not change and were at the same level as the post-test scores of class of residents. Subjective data evaluating the course indicated that trainees "uniformly felt that the ACRM course was an intense, superior form of training related to an important, but inadequately taught, component of anesthesia practice."[3] Another study of ACRM at Harvard also found that participants rated the course favorably, with over 80% responding that they felt the course should be taken every 24 months or less.[29]

As with aviation, the incremental value of this form of training is difficult to link to improvements in teamwork performance and better safety records. At the time of this literature assessment, there were no published data to describe the effects on medical error rates of the MedTeams approach. The NeoSim course participants provided positive responses to open-ended questions about their satisfaction with the course.[21]

Costs and Implementation

Helmreich has noted some of the limitations associated with CRM.[10] At this time, the evidence connecting CRM approaches to improving patient safety does not exist, notwithstanding the face validity of the approach. Nevertheless, a long history of variants of the approach offers health care a reasonable foundation from which to draw practical and evidenced-based resources[30] for further development and adaptation of CRM, as well as measurement methods to ascertain its effectiveness.

At a minimum, implementation of the CRM approach in health care settings requires customization of tools and techniques for each specific care venue, as is illustrated by adaptations implemented thus far. This customization comes at considerable cost and cannot be expected to immediately reap safety benefits. At the time of this review, approximate costs for implementing the MedTeams system ranged from $15,000-$35,000, with additional costs for ongoing activities (such as continuing education) that ranged from $8,000-$20,000 (R. Simon, personal communication, April 2001). Similarly, marginal costs for CRM-like training based on the ACRM experience are estimated at $800 to $2,000 per participant per day (D. M. Gaba, personal communication, June 2001). These costs do not include the overhead of starting a program (eg, simulator investment, training instructors), nor do they factor in the cost of reduced practice work hours, if these are above those devoted to current training time.

Cultural shifts in medicine are also necessary if the CRM approach is truly to take root. CRM applications are relatively novel in health care, a field in which professional training and education have traditionally focused on developing technical proficiency rather than facilitating human interaction. Although communication and decision making are central to medical

practice, relatively little about this topic has appeared in medical literature, despite the fact that information flow is critical, particularly in high acuity venues such as the operating room and emergency departments. Ideas must be elicited, debated and evaluated without discrimination based on the status of the staff person offering the information.[31]

Paradoxically, the attachment to hierarchy may be the reason that a small percentage of participants can be expected to reject CRM training. Research has shown that some resistance is rooted in personality characteristics. Crew members lacking in achievement motivation and interpersonal skills are more likely to reject the training. Additionally, CRM practices decay over time, even with repeated training, requiring continuing expenditures to retain the hoped-for gains.[10]

Comment

CRM has evolved in the airline industry for more than 20 years, and has been extensively applied during the past decade. Although no definitive data link CRM to decreased aviation error *per se*, the industry has accepted the face validity of the practice, and it is now an integral part of training. Over time, survey data from thousands of civilian and military participants in the United States and abroad has been accrued. These data indicate that most flight crew members accept CRM training, and find it both relevant and useful.[7]

The studies reviewed provide some support for the notion that CRM is worth further investigation in health care. However, it cannot yet be concluded that CRM is a practice that can reduce medical errors. Additional research in this area is warranted, although measurement and study design are particularly challenging. As noted, although the evidence from aviation, where CRM is well-established, has shortcomings, data are easier to capture since CRM assessments can be grafted onto mandatory, ongoing, yearly pilot assessments conducted both in simulators and in real flights (D. M. Gaba, personal communication, June 2001). In medicine, where ongoing assessments are not the norm, capturing relevant data will be more difficult logistically and much more expensive than in aviation. Consequently, and for the analogous reasons that aviation has adopted CRM based on face validity, health care decision makers may wish to consider face validity in lieu of massive research investments.

Nonetheless, evaluations of CRM that focus on intermediate outcomes (eg, trainee performance) are feasible, and instructive for optimizing components of CRM programs. CRM design and evaluation resources are becoming more widely available,[30] and health care should continue to consult these sources, building on the advances made in other fields.

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Chapter 45. Simulator-Based Training and Patient Safety

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Background

For a number of years, simulators have been used in aviation, nuclear power, military flight operations and other industries as a training tool and method to assess performance. Their use is nearly universal in high reliability organizations.[1] Recently the use of simulation in medicine has increased markedly, in part due to greater awareness of the importance of patient safety.

Defined broadly, a simulator replicates a task environment with sufficient realism to serve a desired purpose.[1] In medical training, simulators can substitute for actual patients and can be as simple as utilizing pigs' feet to practice suturing, or as complex as virtual reality machines and re-creations of actual clinical environments for surgeons, radiologists and anesthesiologists. In a general sense, they improve patient safety by allowing physicians to become better trained without putting patients at risk. For example, in a randomized controlled trial, Peugnet and colleagues used a virtual reality simulator to train physicians to perform retinal photocoagulation and found that surgeons who trained with the simulator performed the procedure as well as those who trained with patients.[2] Gaba lists several other advantages of simulation, among them[3]:

- Presentation of uncommon but critical scenarios in which a rapid response is needed (eg, malignant hyperthermia, which occurs once in every 40,000 anesthesia cases).[4] To conduct systematic training about managing such critical events there is little alternative but to use simulation.
- Errors can be allowed to occur and reach their conclusion—in real life a more capable clinician would have to intervene—so participants can see the results of their decisions and actions.
- With mannequin-based simulators clinicians can use actual medical equipment, exposing limitations in the human-machine interface.
- Complete interpersonal interactions with other clinical staff can be explored and training in teamwork, leadership, and communication provided. In a number of medical fields, simulation has been used in crew resource management (CRM) training[1] (see Chapter 44), where the focus is on behavioral skills such as inter-team communication during critical incidents.

Human error is a leading cause of adverse anesthesia events that lead to poor patient outcomes[5] and may play an important role in surgical errors as well.[6] However, it may be difficult to demonstrate improved patient outcomes from simulation because adverse events are unusual and there are an extreme number of potential confounders. Given these difficulties, performance has been used as a surrogate outcome, despite concerns that it may be a less than perfect measure. It is yet unclear which attributes of performance matter most to patient outcomes. Additionally, the methods (eg, reliability and consistency) and timing (eg, duration of

follow-up) by which performance is measured also remain ill-defined.[1] Studies of the effectiveness of simulators often are limited in that they measure performance using the same training simulator, which may favor those who have trained on the simulator itself. In other words, seemingly improved performance may not translate to actual patient care. Of the studies that have extended laboratory simulation to patient care, few have evaluated the impact on medical error or established a clear link between simulator training and patient outcomes.

This chapter reviews the evidence regarding the use of simulators in the training and ongoing education of health care providers as a patient safety measure. Not included in this review is the use of simulators in the planning or preparation of diagnostic or therapeutic interventions in specific patients (eg, calculation of radiotherapy doses using computer simulations, planning a surgical procedure for a specific patient using 3-D simulations based on the anatomical data from the actual patient). While these kinds of simulation clearly decrease the morbidity and mortality associated with their particular procedures, they are omitted here because they focus on unique characteristics of individual patients that may not be generalizable to other patients. Other uses of simulators beyond the scope of this discussion include simulators to measure worker proficiency,[7-10] to identify areas for educational intervention, and to target improvements in training.[11,12]

Simulators in Anesthesia

Patient simulators have been most widely studied in anesthesia where human error may account for over 80% of critical incidents.[5] Simulators range from simple mannequins to high-fidelity simulators that recreate the operating room experience. According to one study, 71% of medical schools in Canada, the United Kingdom and other western nations used mannequins or some other form of simulator to teach anesthesia to medical students.[13] There is a growing body of literature on the different roles that simulators can play in anesthesia training.[14]

Studies have found that simulators can effectively identify errors and appropriateness of decision making in anesthesia. For example, during 19 comprehensive anesthesia simulations, DeAnda et al documented 132 unplanned incidents, of which 87 (66%) were due to human error and 32 (27%) were considered critical incidents.[15] Schwid and O'Donnell have also used simulators to document the type of errors that anesthesiologists make in critical incidents, finding errors in monitor usage (37%), airway management (17%), ventilator management (13%), and drug administration (10%).[16] Gaba and colleagues studied both the appropriateness of decisions and response time of anesthesia trainees to simulated critical incidents.[8] They found great individual variability as well as variability by incident in the accuracy and timeliness of response. Some simulated incidents, such as cardiac arrest, had major errors in management a majority of the time. Based on these studies, patient simulators can be used to identify areas for further education or training of anesthesia providers.

We identified 2 studies of the effect of simulators on anesthetists' performance. Schwid and colleagues studied the impact of a computer screen-based anesthesia simulator in a randomized, controlled trial of 31 first-year anesthesia residents.[17] Residents that had trained on the simulator with individualized debriefing responded better to critical events on a mannequin-based simulator than those who received standard training without the simulator. Using a randomized, controlled design, Chopra and colleagues studied management of simulated critical situations by 28 resident or staff anesthesiologists.[18] The performance of subjects who trained on the simulator was superior to that of subjects who did not receive that training.

Another setting where simulators may play an important role is in crew resource management (CRM). Though establishing the effectiveness of simulation in CRM training may

be difficult,[19] initial work has been done on reliably and consistently rating performance.[10] CRM is discussed further in Chapter 44.

Proficiency on a simulator does not ensure proficiency in clinical settings. Simulator fidelity (ie, how accurately the simulator replicates reality) is imperfect. It is much more difficult to "re-create" a human being than to do so for, say, an airplane. This limitation is illustrated by a study conducted by Sayre and colleagues. They studied emergency medical technicians (EMT) who learned intubation techniques on anesthesia mannequins.[20] After successfully intubating the mannequins 10 times, they were permitted to intubate patients in the field, where their proficiency was only 53%. Other factors can inhibit optimum learning using simulation or the applicability of learning to real practice. Some participants may be more vigilant than usual during simulator sessions. Others may be unable to "suspend disbelief," may treat the simulation only as a game, or act in a cavalier fashion, knowing that the simulator is not a real patient.[21] Refinement of simulators to make them more sophisticated and life-like may help to improve the quality of the training that simulators can provide. Appropriate construction of curricula and debriefings can also minimize the potential problems of simulation training.

Simulators in Radiology

The number of radiologic examinations that require sedation, analgesia, or contrast media has increased rapidly in recent years.[22] Despite their rarity, serious medication reactions do occur and require prompt, appropriate management. Some evidence of suboptimal management[23] has prompted the creation of computer-based simulators to improve training in these areas.[24] Simulators have also been used to measure the effectiveness of strategies to teach trainees about critical incidents, but studies have not reported the effectiveness of simulators as adjuncts to training. Sica and colleagues developed a computer-based simulator that was used to study the effectiveness of a lecture and videotape-based intervention on critical incidents for radiology housestaff.[25] Those residents who underwent the intervention scored better on the simulator than those that had only received basic, standard training. The authors concluded that the simulator was an effective way of assessing the utility of the educational course.

Simulators in Surgery

As surgical technique and expertise has changed drastically over recent decades, some methods used to train surgeons have evolved as well. Simulators in the surgical setting are aimed at improving surgeons' technical skills and dexterity. Training on simulators and virtual reality machines, though still in its nascent stages, is becoming increasingly accepted.[26,27] Surgical simulators have been developed for a variety of procedures: endovascular repair of abdominal aortic aneurysms,[28] sinus surgery[29,30] gynecologic surgery,[31] orthopedic surgery,[32] prostatic surgery,[33] amniocentesis procedures,[34] and oral surgery.[35] Nonetheless, many of these have yet to be formally evaluated in terms of efficacy in improving physician performance in patient care.

We identified several studies that evaluated physician performance after training on a surgical simulator. Derossis evaluated surgical residents and attendings in a randomized study and found that those trained with a simulator had greater proficiency in suturing, transferring, and mesh placement, when tested on the simulator, than did the control group.[36] They subsequently found that when tested *in vivo* in pigs, surgeons (both attendings and residents) who had been randomized to the simulator arm were more proficient at the same skills.[37] Scott and colleagues studied the impact of a video-trainer on laparoscopic cholecystectomy skills.[38] They randomized surgical residents to training on a video-trainer versus no formal training over

a 30-day period. At the end of the period, when tested on pre-specified tasks on the video trainer, those who trained on the video trainer did uniformly better.

Intuitively, improved technical skills should lead to fewer complications during surgery. Wallwiener and colleagues developed a surgical trainer that, when used in conjunction with other improvements in their training program, led to lower rates of hysteroscopic complications.[39,40] However, for most simulators the link between improvements in technical skills and dexterity from simulator training and prevention of adverse events has yet to be established and deserves formal investigation. Further, problem-based surgical simulation (eg, avoiding inadvertent ligation of the ureter during hysterectomy) may improve patient safety not only by improving skills, but also by training surgeons to better anticipate and avoid complications and to manage them should they occur.

Simulators in Gastroenterology

Simulators have been developed to train physicians in the technical skills required in endoscopy.[41-43] We identified one study that evaluated the effect of simulator training on physician performance. In a small randomized controlled trial enrolling 10 residents, Tuggy and colleagues found residents who trained for flexible sigmoidoscopy using a virtual reality simulator were faster, visualized a greater portion of the colon, and made fewer directional errors in actual patients.[44]

Simulators in Cardiology

Cardiology training has long used a variety of simulators from audiocassettes of heart tones to full patient simulators. Two simulators have been evaluated. Champagne and colleagues demonstrated that a heart sound simulator could increase medical students' recognition of pathologic heart sounds.[45] Ewy and colleagues studied the efficacy of "Harvey," a cardiology patient simulator.[46] In a study enrolling 208 senior medical students at 5 medical schools, participants were randomized to receive training on Harvey versus a standard cardiology curriculum during their cardiology elective. Students who had been trained with Harvey performed skills better both when tested with the simulator and when tested with real patients. Some physicians have expressed concern that training on simulators may decrease professionalism. In this study, there was no difference in the way patients perceived the professionalism of the students trained on Harvey compared with students who received standard training.

Systems that simulate the cardiovascular anatomy and physiology have also been developed. Swanson and colleagues created a cardiovascular simulator to train physicians on the workings of mechanical valves and balloon assist devices, and to recognized diseased vessels.[47] As cardiac procedures have become more invasive, simulators to train cardiologist in these procedures have become more common,[48, 49] but their effect on resident performance has not been evaluated formally.

Comment

Although simulators have been used for many years in a variety of settings, data on their efficacy are still emerging. While there is currently no evidence that simulation-based training leads to improved patient outcome, it may prove difficult to conduct such studies. These would require large cohorts of patients to be followed during and after care by clinicians who were randomized to have undergone different cumulative amounts of simulation training. Because adverse events are uncommon, and there are a large number of patient-based and system-based

factors that contribute to negative outcomes, any such study would have to be massive and prolonged. Instead, provider performance, with its known limitations, has been and will continue to be used as a surrogate outcome. Nonetheless, as Gaba has asserted "…no industry in which human lives depend on skilled performance has waited for unequivocal proof of the benefits of simulation before embracing it."[50] Certain benefits are clear. In training for procedures, simulators have high face validity because they ease trainees' transition to actual patients, which seems inherently beneficial as a means to avoid adverse events. Further, procedural success is related to the experience of the operator, known as the volume-outcome relationship[51, 52] (see Chapter 19). As simulators become more advanced, they may be reasonable substitutes to improve proficiency of both trainees and low volume physician operators. This increase in proficiency may have an important impact in patient outcomes. Future studies of the link between simulator-based training and performance on actual patients will improve our ability to better assess the appropriate role of simulators in training and patient safety.

The costs of simulators vary widely and need to be considered. "Home-made" or simple trainers are far less expensive than complex simulators or full-scale simulation centers. The average cost of high-fidelity patient simulators is on the order of $200,000. Medium fidelity simulators may be as little as $25,000. Establishing a dedicated simulation center can cost up to $1,000,000 (including the simulator) depending on the amount of space, the type of clinical equipment to be used, the extent of renovations needed, and the sophistication of the audio-visual equipment. However, such capital costs are amortized over a long period of time, and such centers typically are used for a wide variety of training curricula for diverse target populations. Further, for most simulation training the dominant cost is that of instructor time. Another indirect cost is that of removing clinical personnel from revenue producing work to undergo training. The health care industry currently does not fully embed time or costs of training into the system, but instead often leaves these costs for the individual clinicians to bear.

There are potential risks to simulation-based training. Where the simulator cannot properly replicate the tasks or task environment of caring for patients, there is a risk that clinicians might acquire inappropriate behaviors (negative training) or develop a false sense of security in their skills that could theoretically lead to harm. Although there are no data to suggest that this currently happens, such risks will have to be weighed and evaluated as simulators become more commonly used.

In summary, although there is currently little evidence that simulation training improves patient care, the experience with simulation in other industries and the high face validity of their applications in health care has led many institutions to adopt the technology. It is likely that simulators will continue to be used and their role in training of medical personnel will grow. Definitive experiments to improve our understanding of their effects on training will allow them to be used more intelligently to improve provider performance, reduce errors and ultimately, promote patient safety. Although such experiments will be difficult and costly, they may be justified to determine how this technology can best be applied.

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Chapter 46. Fatigue, Sleepiness, and Medical Errors

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Introduction

Fatigue may contribute to the human error component of medical errors.[1-3] Hospitals function around the clock, which necessitates shift work for many personnel. Physicians, especially those in training, typically work long hours and are often sleep deprived.[4] Personnel who work during evenings and at night experience disruptions in circadian rhythms, which may aggravate fatigue. Although little research has focused specifically on fatigue in hospital personnel and its relationship to medical error, studies outside the medical field demonstrate the intuitive link between fatigue and degradation in performance and suggest some safety practices that may be adopted in medicine. Although both acute and chronic fatigue may have detrimental effects on the health of medical practitioners,[5-7] this chapter focuses on fatigue's direct effects on patient safety. We review the literature on problem sleepiness among medical personnel, its impact on performance, and interventions to address sleep deprivation: limiting work hours, changes in shift scheduling, napping, and pharmaceutical aids. Although beyond the scope of this chapter, factors that contribute to fatigue beyond sleepiness, such as job stress and work load, should be considered as part of a multifaceted strategy to combat fatigue.

Background

Fatigue and sleepiness may affect patient safety in several ways. Physicians and nurses need good attention, sound judgment, and often quick reaction time, especially in emergency situations. Whether evaluating an electrocardiogram for signs of myocardial ischemia or monitoring a patient during general anesthesia, degradation of attention, memory, or coordination may affect performance and lead to adverse events. Research suggests that sleep requirements and patterns are idiosyncratic, with wide variation across populations. In order to design interventions that will effectively decrease or prevent these events, it is important to understand the signs, prevalence, and impact of sleep deprivation and problem sleepiness.

Sleep Deprivation

Individuals differ in their optimal sleep requirements. Most sleep experts agree that adults typically need between 6 and 10 hours of sleep per 24-hour period, with most people requiring approximately 8 hours of sleep per day.[8,9] When adults get less than 5 hours of sleep over a 24-hour period, peak mental abilities begin to decline.[2] For short periods of time (2-3 days), adult who get 4 hours of sleep can function reasonably well, but below peak levels.[2] However, even with sleep deprivation of just a couple of days, slower response times and decreased initiatives are observed.[10] After one night of missed sleep, cognitive performance may decrease 25% from baseline.[11,12] After the second night of missed sleep, cognitive performance can fall to nearly 40% of baseline.[12]

With ongoing sleep deprivation (getting 2 to 3 hours less sleep than optimal), people develop a *sleep debt*.[2] If the sleep debt continues over 5 to 10 days, they are rarely maximally

alert and at some point general performance, and particularly cognitive performance, become verifiably worse. Sleep debt also leads to slower response times, altered mood and motivation, and reduced morale and initiative. A meta-analysis of the effect of sleep deprivation on performance by Pilcher et al found that humans who are chronically sleep deprived function at the 9th percentile of non-sleep-deprived subjects. Further, sleep deprivation affected mood more than it did cognitive function; both were more affected than motor function.[9]

Night-Shifts and Shift Rotation

Shift work usually refers to a schedule in which some employees begin work at times other than the morning. In hospitals, up to 35% of nurses may be required to work at times other than the day shift.[13] A report by the Association of Professional Sleep Societies concluded that night-time operators' fatigue contributed to 4 well known disasters: Exxon Valdez, Bhopal, Chernobyl, and Three Mile Island.[14] Fatigue has also been implicated in aircraft accidents[15] and in poor driving and accidents among truck drivers.[16] It is well documented that shift workers have disturbances in their circadian rhythm, as measured by changes in their melatonin and cortisol levels.[17] Sleep after night work tends to be shorter than sleep after day work, leading to greater cumulative sleep deprivation.[18-20] Shift workers have poorer quality of sleep, marked by less REM sleep, and are less likely to feel refreshed after awaking. Between 60 and 70 percent of shift workers complain of sleeping difficulties or problem sleepiness.[21] Several surveys of shift workers have found that those who work during night shifts are more likely to report sleepiness at work.[18,19,22,23] Alertness on the job is also affected, with employees showing less alertness during nighttime shifts.[24] In addition, shift workers tend to perform less well on reasoning and non-stimulating tasks than non-shift workers.[22,23]

Prevalence and Severity

Fatigue and sleep deprivation are common among medical personnel. Long work-hours are a tradition during residency,[25] with most interns and residents working 80 to 100 hours a week, often 36 hours at a time.[26] During these shifts their sleep is limited, and is usually interrupted.[27] In a 1991 national survey, second-year residents reported an average of 37.6 hours as the largest number of hours without sleep during their first postgraduate year and roughly 25% of the residents reported being on call in the hospital over 80 hours per week.[26] A movement in the late 1980s, prompted partly by the death of a young woman,[28] led to regulations in New York State dictating that residents could work a maximum of 80 hours per week, with a maximum of 24 consecutive hours of patient care, and a minimum of 8 hours off duty between shifts (see also chapter 55).[29] Despite these regulations, unannounced inspections of 12 teaching hospitals in New York State in March 1998 found 37% of all residents worked more than 85 hours per week, 20% of all residents and 60% of surgical residents worked more than 95 hours per week, and 38% of all residents and 67% of all surgical residents worked more than 24 consecutive hours.[30] In 2000, 8% of programs and institutions reviewed by the Accreditation Council for Graduate Medical Education were cited as being in violation of their work-hour requirements.[31] Work-hour violations were noted in general surgery (35%), pediatrics (16%), internal medicine (10%) and other training programs as well.[31]

Long hours and sleep deprivation continue after residency. Health care providers, particularly those still in training or who have recently completed training, occasionally work extra shifts to increase their income ("moonlighting"). One recent survey found that nearly half of all emergency medicine residents moonlight.[32] As many as 65% of internal medicine residents and fellows moonlight[33] and moonlighting is common among other residencies and

fellowships.[34, 35] These shifts are often at odd hours, and therefore are disruptive to normal sleep patterns. Among surgical staff, fatigue is common, especially since surgical teams can be involved in long, complicated operative cases that can take 12 to 20 hours at a time.[36,37]

Multiple studies have documented the impact of fatigue on medical personnel performance.[38] However, these studies have been limited by poor study designs or outcomes that may not correlate well with medical error. One study of nursing fatigue suggests that it may play a role in increased error. Gold and colleagues administered a questionnaire to nurses at a large academic hospital and found that nurses who worked a rotating schedule, when compared with nurses who predominantly worked day shifts, were more likely to fall asleep at work and get less sleep over all, and were nearly twice as likely to report committing a medication error.[39]

Using standardized testing, investigators have found that after a night of call, sleep deprived physicians may have worse language and numeric skills,[40] retention of information,[41] short-term memory,[42] and concentration.[43] Performance on standardized tests may not reflect performance in medical situations. Taffinder et al studied the impact of sleep deprivation on surgical residents previously trained on a simulator and found that after a night without sleep, surgeons were slower and more prone to errors on the simulator than those who had a normal night of sleep.[44] Similarly, Denisco et al studied anesthesia residents after a night of sleep deprivation and found that those who had been on call and were sleep deprived scored less well on simulated critical events.[45] Smith-Coggins et al compared cognitive and motor performance of emergency physicians and found that, as the 24-hour study period progressed, physicians were more likely to make errors during a simulated triage test and while intubating a mannequin.[19] However, other studies have failed to find an effect of sleep deprivation on cognitive performance by resident physicians.[46-48] Simulators may not reflect actual medical performance (see chapter 45). Though psychomotor performance seems to be affected by sleep deprivation, data are inconsistent as to fatigue's impact on cognitive function and there are inadequate data assessing its impact on clinical performance.

Few studies have looked at the impact of fatigue in hospital personnel on adverse events. A retrospective study by Haynes et al of 6371 surgical cases, found that the risk of postoperative complications among patients undergoing surgery was not increased when the surgical resident was sleep deprived.[49] These results may not be surprising for several reasons. First, the authors did not measure the residents' error rate, which may have been higher with sleep deprivation. Second, the study did not measure the role attending physicians or other operating room personnel may have played in averting adverse events when residents erred. The supervisory aspect of system design can (and should) reduce both the frequency of individual mistakes (*error prevention*) and the likelihood of adverse events given that errors are inevitable (*error absorption*).[1] Finally, the rate of adverse events, including those that did not result in operative complications ("near misses"), may have been higher but under reported. Well-designed studies that evaluate the effects of fatigue among medical personnel on rates of medical errors or adverse events would be useful. In the meantime, the lack of convincing data linking fatigue with poor patient outcomes should not deter us from tackling the issue of fatigue among medical personnel.

Practice Descriptions

Hours of Service

We reviewed the evidence for 2 potential safety practices concerning hours of service: 8-hour versus 12-hour length shifts and regulations limiting maximum shift length and/or total hours worked. Most observational studies on optimal shift length to reduce fatigue and maximize

performance are in non-medical settings and present inconsistent findings. In a study of work-place accidents in Germany, Hanecke et al found accident risk increased exponentially after the 9th hour at work and was highest among workers whose shift began in the evening or night.[50] The authors concluded that shifts that last longer than 8 hours might lead to more worker fatigue and higher risk of accidents. Axelsson and colleagues studied workers at a power plant and found no difference in sleepiness or performance between those who worked 8-hour shifts and those who worked 12-hour shifts.[51] Another group found that switching from 8- to 12-hour shifts led to increased alertness on the job and improved recovery time after night shifts.[52] Overland has proposed that work that requires complex cognitive tasks may be ill suited for longer shifts, whereas work with limited cognitive demands may be well suited for longer shifts.[53] Because the components of work vary dramatically within and across industries, shift durations that maintain performance in one setting may be ineffective in another.

We identified 9 observational studies comparing 8- versus 12-hour shifts for medical personnel. Two studies of nursing care on 10 wards found that quantity[54] and quality[55] of care were significantly lower with 12-hour shifts. Six studies of nurses[56-61] and one of physicians[62] measured outcomes including self-reported alertness, self-reported performance, and/or worker satisfaction. While 2 nurse studies found that self-reported alertness, performance, and satisfaction wane with longer shifts,[56,57] Urgovics and Wright found that ICU nurses reported higher job satisfaction and subjectively improved clinical performance with 12-hour shifts.[60] The 3 remaining studies in nurses found no difference in either satisfaction or self-reported performance between 8- and 12-hour shifts.[58,59,61] A survey of emergency department physicians found that those who worked 12-hour shifts were less likely to be satisfied than those who worked 8-hour shifts.[62] The relationship between these subjective outcomes measures and medical error is not clear.

Hours of service regulations as an effort to reduce errors due to fatigue are standard in some non-medical fields. Truck drivers are typically allowed to work no more than 10 hours at a time and no more than 60 hours in one week. Airline pilots and air traffic controllers work regulated hours and some data suggest waning performance as work-hours increase.[24,63-65] Although most health care personnel are not subject to work-hour standards, many physicians-in-training are, either by statutory regulations or by being in an accredited training program. In a retrospective cohort study, Laine and colleagues found the aforementioned New York State regulations limiting resident work-hours had no effect on patient outcomes such as mortality or transfers to the intensive care unit but were associated with increased rates of medical complications and delays in diagnostic tests.[66] These negative effects may have been related to discontinuity of care and/or fewer physician-hours per patient. As the authors noted, "better care may be provided by a tired physician who is familiar with the patient than by a rested physician who is less familiar with the patient."[66] In a case-control study, Petersen and colleagues found that when patients were cared for by a physician other than their primary resident, they were 6 times as likely to suffer a preventable adverse event.[67] Thus, fewer physician work hours may lead to more physician discontinuity and potentially, more adverse events and poorer outcomes for patients.

On the other hand, Gottlieb studied changes in a medical service staffing schedule that allowed for reduced sleep deprivation, improved distribution of admissions throughout the week, and improved continuity of inpatient care.[68] After these changes were instituted, patients had shorter lengths of stay, fewer ancillary tests, and fewer medication errors. Although it is difficult to ascribe the improvements to changes in work-hours because several other changes were made as well, it does appear that changes in work-hours can be made without adversely affecting

patient outcomes. Any effort to change duty hours for health care personnel in an effort to reduce fatigue should factor in and continuously monitor numerous variables, including the potential costs of discontinuity, medical complications and unnecessary hospital days, to ensure that the measures do not compromise patient care. The costs needed to maintain adequate staffing in face of lost physician work-hours has been estimated to be $360 million in New York State alone.[69] However, the difficult task of estimating other costs and potential savings from implementing these regulations has not been accomplished.

Finally, some authors have expressed concern that restriction of resident physician work-hours may lead to poorer quality training and decreased professionalism among doctors.[70] They argue that restricted working hours will decrease a sense of obligation to patients and will sanction self-interest over the well-being of patients. However, there are no data to substantiate these concerns.

Direction and Speed of Rotation of Shift Work

The direction of s*hift rotation* may impact worker fatigue. For workers who change from one shift to another, a forward rotation of shift work (morning shifts followed by evening shifts followed by night shifts) may lead to less fatigue on the job than backward rotation (day shift to night shift to evening shift).[71-74] Forward rotation appears easier to tolerate physiologically since the natural circadian rhythm tends to move forward and it is more difficult to fall asleep earlier than the normal bedtime. Several studies in non-medical personnel have shown that forward rotation allows for better acclimation of the circadian rhythm.[2,12,75] However, 2 other studies found no significant difference in forward versus backward shift rotation.[76,77] None of these studies measured worker performance or error rates and we found no studies that evaluated direction of shift work rotation among medical personnel.

Another variable in scheduling is the speed of shift work rotation. Studies suggest that slow rotation (eg, changing from one shift to another every one to two weeks) may allow for better adaptation of the circadian rhythm than fast rotation (eg, changing shifts every 2-3 days).[71,73,78,79] Slow shift rotation results in greater sleep length at home, less sleepiness on the job, better self-reported performance, and fewer errors.[74,79] In some cases, fast rotation may increase worker satisfaction[80] but the effects of such satisfaction on safety have not been assessed. Shift rotation at an extremely slow rate approximates fixed, non-rotating shifts (permanent night shifts, permanent day shifts). Permanent shifts are associated with better adaptation to changes in the circadian rhythm[78] and better performance than rotating shifts.[79] However, daytime commitments and social obligations often prevent workers from completely adapting to permanent night shifts and worker satisfaction is poor.[71]

Improving Sleep: Education about Sleep Hygiene

Good sleep hygiene, including the avoidance of alcohol and caffeine before bedtime, and maintaining a healthy sleep environment, may aid in decreasing sleep debt and fatigue. Studies of sleep hygiene have focused on treatment of persons with insomnia or other chronic sleep disorders.[81-83] We found no clinical studies that measure the efficacy of good sleep hygiene among shift workers. Generally, most employers cannot dictate how their workers spend their hours off-duty and compliance with recommendations may be poor. One study of law-enforcement officers working rotating shifts found significant increases in awareness and knowledge after a training session on sleep hygiene practices but no change on a post-sleep

inventory assessed at one-month follow-up.[84] The effectiveness of educational programs about sleep hygiene to improve shift worker performance requires further study.

Lighting at Work

The body's regulation of circadian rhythm is mediated by the effects of light and darkness. A 1986 survey found that 7.3 million Americans work at night.[71] These employees, who work during dark hours and sleep during daylight hours, are often chronically sleep deprived and may suffer adverse health effects,[85] partially due to poor synchrony of circadian rhythm to work schedule. Since scheduled light exposure can produce a phase shift in the endogenous circadian rhythm,[71, 86] investigators have studied changes in lighting at work and home to improve adjustment to the shift cycle. Foret et al studied 8 young men in a sleep lab and found exposure to bright lights during the night produced a beneficial effect on subjective alertness.[87] Czeisler and colleagues found that subjects who were exposed to bright light at night and nearly complete darkness during the day had better cognitive performance and subjective alertness, and longer daytime sleep (7.7 vs. 5.7 hours, p=0.01).[88]

Manipulation of light and dark is much easier in sleep labs than in the field,[89] where unintended exposure to bright light is common and may adversely impact attempts to alter workers' circadian rhythm.[90] The National Aeronautics and Space Administration (NASA) has studied the efficacy of bright lights on shuttle astronauts. Their encouraging results suggest that alterations in circadian rhythm can be obtained upon on exposure to light at night.[89,91] The United States Nuclear Regulatory Commission has also implemented bright lighting for its night workers and found less fatigue and better alertness on the job.[92] Field studies are needed to determine how bright artificial light affects objective measures of performance in health care workers and medical error. Bright light may not be appropriate for all areas of the hospital. For example, Bullough and Rea have noted that while bright light might help workers in neonatal care units, it may also be detrimental to patients.[93]

Nonetheless, lighting can be a relatively inexpensive intervention using existing equipment. Keeping lights bright at night, and educating workers about using heavy shades at home may have an important impact on worker performance on night shifts.

Napping

Napping is common among shift workers and is perceived as a way to combat fatigue.[94,95] One study of shift workers in a steel plant found that over half reported napping at home either before or after their shifts.[94] The efficacy of naps has been studied in 3 settings: prior to periods of sleep deprivation (*prophylactic naps*), during periods of sleep deprivation (*therapeutic naps*) and during work hours (*maintenance naps*). Most studies have been conducted in sleep labs in healthy, young, male subjects.

A number of studies in the non-medical literature have studied the efficacy of prophylactic napping. Gillberg and colleagues studied 8 male subjects who were allowed only 4 hours of sleep at night. When subjects took a 30-minute nap in the middle of the prior day, they had better subjective alertness, 20% improvement in vigilance performance, and less overall sleepiness than when they had not been allowed to nap.[96] Others have also found benefits of prophylactic naps on subjective and objective measures of alertness and performance in healthy volunteers undergoing extended periods of sleep deprivation.[97-100] Bonnet and Arand studied prophylactic versus therapeutic naps in 12 healthy young men who underwent 24 hours of sleep deprivation to simulate sleep patterns of medical housestaff.[101] One group of subjects had a 4-

hour prophylactic nap in the evening and caffeine during the 24 hours, while the second group had four, 1-hour naps during the 24-hour work period and no caffeine. Those in the prophylactic nap and caffeine group had a 15% increase in reasoning and overall improved subjective alertness compared with the group that had only short naps. There was no impact on mood. We identified one study of napping by medical personnel. Harma and colleagues studied 146 female hospital nurses and nurses' aides and found that those who napped prior to their night shifts were less likely to report on the job fatigue.[95]

Most studies evaluating the efficacy of therapeutic napping during prolonged periods of sleep deprivation have found beneficial effects when compared with no napping.[102-108] On the other hand, Gillberg and colleagues found no difference in simulated driving between the 2 groups of sleep deprived truck drivers, one group having taken a 30-minute nap during the middle of the previous night.[109]

Maintenance naps are naps that occur on the job, during the shift. These naps could compensate for daytime sleep deprivation or could bridge the nighttime low point in circadian somnolence.[110] Many Japanese industries have provided their employees with the option of on the job napping and nearly half of nighttime shift workers take advantage of this opportunity.[111] Though no systematic studies of the impact of maintenance naps exist in shift workers, one investigation found that short naps in the middle of the night improved performance for the rest of the shift.[98] Napping over several successive shifts has not been studied.[110]

An important consideration in napping is the phenomena of *sleep inertia*, a period of transitory hypo-vigilance, confusion, disorientation of behavior and impaired cognitive performance that immediately follows awakening.[112] Sleep inertia is well documented[112-116] and lasts up to 30 minutes after awakening.[116-118] The duration of deep sleep and the time of the nap, relative to the circadian cycle, seem most related to the severity of sleep inertia.[8] Strategies for napping on the job to reduce fatigue should be designed to avoid possible detrimental effects of sleep inertia. Another potential negative effect of lengthy naps is that they can disrupt the quantity and quality of later sleep periods.[119]

In summary, there is strong evidence that therapeutic naps and maintenance naps combat the effects of fatigue and sleep loss. They can help subjects adapt better to circadian rhythm disturbances and perform better during acute sleep deprivation. Their application in the medical field is not well known. While prophylactic and therapeutic napping result in loss of social time at home, maintenance napping results in loss of work time. Costs associated with naps have not been reported. The financial impact of reduced worker fatigue due to napping has not been evaluated in medicine.

Medical Therapies

Melatonin is the major hormone responsible for circadian rhythm regulation. James et al studied the effect of oral melatonin supplementation on circadian rhythm and adaptation to night shifts among medical personnel.[120] They and others have found no effect among medical shift workers.[121-123] Though melatonin continues to be studied for chronic insomnia and other conditions, there currently is insufficient evidence to recommend its use to combat the fatigue associated with changing workshifts.

Some studies have looked at the potential benefits of benzodiazepines and other sedatives for short-term insomnia associated with shift work, but no data exist on long-term use. Stimulants and caffeine can boost performance acutely but do not address the underlying sleep deprivation,[124] and thus are not a viable long-term solution. Furthermore, concern over side

effects, addiction, and performance degradation with current pharmacologic interventions makes their use as a safety practice unlikely.

Comment

Sleep deprivation and disturbances of circadian rhythm lead to fatigue, decreased alertness, and poor performance on standardized testing. Although data from non-medical fields suggest that sleep deprivation leads to poor job performance, this link has not yet been established in medicine. Although the link with fatigue seems intuitive, promoting interventions designed to combat medical errors should be evidence-based. Limits on physician duty hours must account for potentially detrimental effects of discontinuity in patient care. Forward rather than backward shift rotation, education about good sleep hygiene, and strategic napping before or during shifts may reduce fatigue and improve performance. High face validity, low likelihood of harm, and ease of implementation make these promising strategies, although more evidence of their effectiveness in medicine is warranted. Studies on the use of bright light in the medical workplace are needed before it can be embraced.

As Gaba points out,[125] in most high-hazard industries the assumption is that fatigue and long, aberrant work hours lead to poor performance, and the burden of proof is in the hands of those who believe that such work practices are safe. In medicine, concerns over discontinuity of care, and difficulties in changing medical culture have pushed the burden of proof into the hands of those who wish to change the *status quo*. Given that medical personnel, like all human beings, probably function suboptimally when fatigued, efforts to reduce fatigue and sleepiness should be undertaken, and the burden of proof should be in the hands of the advocates of the current system to demonstrate that it is safe.

Finally, fatigue among medical personnel may not be fully remediable and human errors are, in the end, inevitable. The ultimate solution for health care organizations will likely require a systems-based approach that both limits the potential for human error and intercepts errors that do occur before they reach patients.

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Chapter 47. Safety During Transport of Critically Ill Patients

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Background

The care of acutely ill patients routinely includes transportation, both within a given hospital to undergo tests and procedures, and between hospitals, as patients may require transfer to other facilities for specialized services. Critically ill patients in particular commonly require such transfers and are at high risk for complications en route.[1-4] Developing practices to reduce or minimize this necessary risk represents a potentially important area of patient safety research. This chapter focuses on transportation of critically ill patients by health professionals (paramedics, nurses, physicians and/or respiratory therapists) between hospitals (to receive higher levels of care) and within the hospital (for diagnostic or therapeutic procedures).

Stabilization before transport, in the field or in the transferring hospital, and the mode of transferring patients from the field to specialized centers also present important research and policy questions.[5] However, we regarded these issues as clinical research topics and quality improvement issues for the fields of pre-hospital and emergency medicine, rather than patient safety in general, and so do not review this literature here.

Practice Description

Intrahospital transport refers to transportation of patients within a hospital for the purpose of undergoing diagnostic or therapeutic procedures or transfer to a specialized unit. In the context of this chapter, this generally involves movement of critically ill patients from intensive care areas of the hospital (including intensive care units, emergency departments, operating theaters and recovery rooms) to areas typically not involved in the delivery of such care (eg, a hospital radiology department). Equipment and staffing used for intrahospital transport varies by hospital, clinical service and patient acuity. Studies of intrahospital transport have mainly focused on the adequacy of patient monitoring and ventilator support. The specific practices evaluated in this chapter include:

- The continued use of mechanical ventilation instead of switching to manual ventilation. Manual ventilation involves a self-inflating bag with or without a volumeter, while mechanical ventilation consists of a portable, time-cycled, volume-constant transport ventilator.
- The use of specialized transfer units during intrahospital transport. The unit is attached to the patient's bed and contains all equipment necessary to meet the patient's needs (ventilation, monitoring and infusion of drugs) in the ICU and during transport. The unit works as a stand-alone unit.

Interhospital transport refers to transportation of patients between hospitals by ground or air ambulance. Interhospital transport teams vary widely in composition, training and experience. The transport team does not always include a physician; even when a physician is present, his or her training may not include skills necessary for this task.[6-8] Nurses and respiratory therapists frequently accompany critically ill patients during interhospital transport. Some paramedics

receive special training in skills necessary for the interhospital transport of critically ill patients.[9] As with physicians, the training of nurses and respiratory therapists assigned responsibility for interhospital transport varies widely. Equipment used during interhospital transport also varies widely,[6,7] but the practices evaluated in the literature mainly relate to the use of *specialized transport teams*.

Specialized transport teams characteristically receive consistent and high levels of training and experience in the transportation of critically ill patients,[10-12] compared with teams assembled *ad hoc*. Further details of the composition of these teams are presented in connection with the specific studies reviewed below (see Table 47.1). Because of the relative paucity of studies of practices for improving the safety of patient transport, we have reviewed the pediatric and adult literature together.

Prevalence and Severity of the Target Safety Problem

Adverse events during transport of critically ill patients fall into two general categories: mishaps related to intensive care (eg, lead disconnections, loss of battery power, loss of intravenous access, accidental extubation, occlusion of the endotracheal tube, or exhaustion of oxygen supply), and physiologic deteriorations related to critical illness (eg, worsening hypotension or hypoxemia). Unfortunately many studies do not distinguish clearly between these 2 categories. Further complicating assessments of patient transport as a safety problem is the confounding effect of patient selection, as patents requiring intra- or interhospital transport likely represent a sicker patient population than unselected critically ill patients. In fact, one case-control study reported no differences in adverse events (equipment-related or physiologic) in critically ill adults during the period of intrahospital transportation as compared to matched subjects in the ICU.[13]

Death during transport is a rare event. The majority of studies reported no mortality during intrahospital transport[13-17] or interhospital transport,[18,19] and some do not mention deaths.21-23,24

For intrahospital transport of critically ill patients, reported rates of adverse events range from 5.9% to 66%.[13,14,16,21,22,25] (We could find no comparable reports of event rates for critically ill children.) Much of this variation undoubtedly reflects definitional differences, but differences in patient populations also contribute to this wide range. For instance, a prospective study of 50 high-risk adult cardiac patients reported arrhythmias in 84% of patients, with 52% of these arrhythmias providing an indication for emergency treatment.[17] These event rates are clearly much higher than would be observed in an unselected population of critically patients. Similarly, Insel et al showed a significantly higher incidence of hemodynamic changes requiring therapeutic intervention when intrahospital transport involved transfers from the operating room to the ICU compared with patients transported from the ICU to diagnostic procedures.[26]

In contrast to the above, the literature on adverse events during interhospital transport has generally involved critically ill children, not adults. Reported rates of adverse events during pediatric interhospital transport range from 0 to 75%.[2,10-12,19,24,27-29] In one of these studies, a prospective cohort design reported a morbidity ratio of 1.85 (95% CI: 1.12-3.06) for pediatric patients transported from another hospital to the pediatric ICU (PICU) as compared with those admitted directly (emergency room and wards). Importantly, this increased morbidity reflected an increased rate of “intensive care events” such as plugged endotracheal tubes and loss of intravenous access, not an increase in physiologic events. Patients experiencing such adverse events tended to have higher morbidity scores (on the PRISM scale) and lower therapy level (TISS) scores prior to transport. Thus, as noted above, confounding of differences in patient

sickness and intensity of therapy could account for much of the observed variation in transport-associated morbidity.[24]

Opportunity for Impact

A survey conducted in 1990 to review voluntary compliance with the American Academy of Pediatrics (AAP) recommendations to include physicians with higher level of training (at least 3rd year residency) reported that only 28% of hospitals with a pediatric critical care transport team met this recommendation. All teams included a nurse with pediatric experience and a varying degree of training, and 50% of teams included a respiratory therapist.[7]

Subchapter 47.1. Interhospital Transport

Study Designs and Outcomes

We identified 3 studies with at least a Level 3 study design and Level 2 outcomes (see Table 47.1). Two of these studies[10,12] involved pediatric patients. One12 reported the prospective comparison of outcomes for high-risk pediatric patients admitted to two different ICU's, one of which employed a specialized transport team, while the other followed the standard practice of using non-specialized teams. The specialized team consisted of a second-year pediatric resident and a pediatric ICU nurse, both trained in pediatric advanced life support, and a respiratory therapist with pediatric experience. Non-specialized teams varied in composition—a physician was not always present and level of training in pediatric care for other personnel was not standardized. The other pediatric study, from England,[10] retrospectively compared outcomes using a specialized team for the transport of intubated newborns from hospitals within 80 miles to a NICU at a referral center to outcomes during a control period in which transport was performed by *ad hoc* doctor/nurse teams. The specialized teams included physicians with more years of experience and dedicated transport nurses with specialized training, as well as slight equipment improvements (humidifier for ventilator and invasive/noninvasive blood pressure monitoring).

The third study (the one involving adults) describes the experience of a London teaching hospital that receives critically ill patients from other facilities by two methods: either accompanied by the receiving hospital's special retrieval team consisting of an ICU physician, nurse, and medical physics technician (a technician to fix and maintain equipment) or standard ambulance transport, with an escorting physician supplied by the referring hospital.

The 2 pediatric studies[10,12] reported adverse events during transportation. We counted adverse events related to intensive care (eg, accidental extubation) as Level 2 and physiologic events (eg, ph < 7.2) as Level 3. (A case could be made for classifying both types of adverse events as Level 3, as neither has a clearly established relationship to adverse events of interest). All studies provided information on case mix in the study and control groups.

Evidence for Effectiveness of the Practice

Although of theoretical and practical concern, the literature to support the scope, frequency and outcome of adverse events during transportation is sparse and methodologically weak. Most studies are small descriptive studies of local practices. Factors that limit comparability between studies include a variety of definitions for transport-related adverse events, unclear descriptions of transport team training and experience, diverse equipment

availability and different scoring systems for severity of illness (APACHE II, APACHE III, Glasgow Coma Scale, PRISM, etc). Many confounders affect the evaluation of transportation of a critically ill patient, among them selection bias, the intervention received at primary hospital, time spent at primary hospital, adequate stabilization before transport and duration of transport.

As shown in Table 47.1, 2 studies involving pediatric populations revealed reductions in intensive care-related adverse events through the use of specialized teams for interhospital transport.[10, 12] In one of the studies, patients transported by the standard (non-specialized) team were older and more likely to have trauma as a diagnosis.12 This difference in patient populations clearly limits the ability to interpret the results, although the direction of bias this might introduce is not clear. The other pediatric study [10] reported no significant differences in basic clinical and demographic factors between the 2 patient populations, but did not report PRISM scores.

The single study in adults did not report intensive care-related adverse events, but did observe significant reductions in surrogate physiologic markers and a non-significant reduction in mortality within 12 hours of arrival at the receiving facility. Although an observational study, there were no differences in the patient populations in terms of demographic factors, basic physiology measurements (FiO_2, PaO_2, $PaCO_2$, PaO_2/FiO_2, MAP, heart rate and temperature) or sophisticated measures of severity of illness (APACHE II, Simplified Acute Physiological Score-SAPS II).

Studies were underpowered to detect significant mortality differences.

Potential for Harm

A delay in the transfer of critically ill patients to referral hospitals because the specialized team is not available in timely fashion could create a potential for harm although one study showed no delay or cancellation due to unavailability of specialist team.[11]

Costs and Implementation

Although no firm recommendation can be made, the costs and implementation requirements may only be feasible for tertiary centers that have enough volume to justify the investment in human and physical resources. Time out of hospital will vary depending on the time required to stabilize the patient—not the focus of our study. (One study reported an increase in stabilization time from 80-105 minutes ($p<0.0001$) after the implementation of a specialized team[10] and another reported no difference in duration of transport between non-specialized and specialized team.[12]) The third study did not mention duration of transport.

Comment

This practice has high face validity, and what little evidence exists does support the practice. No direct potential for harm exists, but adopting this practice without further study might unnecessarily strain scarce health care resources. Moreover, if adopted as a standard of care, lack of timely availability of designated transport personnel may become a factor in delaying inter-facility transfers. For some critically ill patients, the time lost in assembling the transport team may have a greater negative impact than the safety gained by their eventual presence. Further research on this topic is required, fundamentally controlling for confounders and improving outcome measures to include morbidity. Two areas that have evolved enormously over the last 2 decades are training requirements of health personnel and the quality of transport monitoring and ventilation equipment.

Subchapter 47.2. Intrahospital Transport

Study Designs and Outcomes

As shown in Table 47.2, the 3 studies of manual versus mechanical ventilation employed a randomized (or quasi-randomized) controlled design. Randomization procedures were not described in two studies[30, 31] and used the last digit of the patient record in one study.[32] The quasi-randomized study[32] implemented a crossover design using manual ventilation or transport ventilator on one leg of the journey and vice-versa on the other leg.

Two studies reported on Level 2 and 3 outcomes[30, 32] and one on level 3 outcomes,[31] venous pressure, oxygen saturation, $PetCO_2$ and mean airway pressure during transport. All studies report on before-after variation, one study[30] also reported on minute variations during the first 8 minutes of transport (see Table 47.2). Only one study reported scores for severity of illness (PRISM).[30] Case-mix was inadequately reported in one study[31] and not reported in another.[32]

It is worth briefly noting a third practice which involves the use of mobile bed/monitor units versus standard procedure for intrahospital transportation. Studies on this topic are limited to descriptive experiences of local practice with no definition or systematic evaluation of adverse events,[17,33-35] so these practices were not reviewed further.

Evidence for Effectiveness of the Practice

The clinical significance of the hyperventilation observed in manually ventilated patients during intrahospital transportation has yet to be determined. Mechanical ventilation was associated with respiratory alkalosis when precision of ventilatory settings was inaccurate. No adverse effect, (ie, morbidity) was observed as a result of the method of ventilation. Use of a volumeter when manually ventilating a patient reduced the risk of hyperventilation. Studies were underpowered to detect significant mortality differences.

Potential for Harm

Inadequate maintenance and/or precision of transport ventilator may create an opportunity for harm.

Costs and Implementation

Portable mechanical ventilators are much more expensive, require more hours of training to manipulate and frequent use to maintain experience. Costs were not mentioned.

Comment

One randomized controlled trial in pediatric postoperative cardiac patients showed an increase in markers of hyperventilation for patients in the manually-ventilated group. Otherwise, manual ventilation appears to achieve results comparable to portable mechanical ventilation. Use of a volumeter when manually ventilating patients, and the addition of a blender to reduce FiO_2 when manually ventilating neonates,[30] may adequately reduce the risks of hyperventilation, rendering mechanical ventilation during intrahospital transport unnecessary.

Table 47.1. Specialized transport teams versus standard care for interhospital transport

Study Setting	Study Design, Outcomes	Main Results
Critically ill children transported to two PICU's in Albany, NY (specialized transport team) and Syracuse, NY (standard care): 1992-94[12]	Level 3, Level 2	Significant decrease adverse event related to intensive care for patients transported with specialized team compared to standard care: 1/47 (2%) vs. 18/92 (20%), $p<0.05$ For physiologic adverse events the decrease was minimal and not significant: 5/47 (11%) vs. 11/92 (12%) $p>0.05$
Intubated newborns transported by specialized doctor/nurse team (increased training and experience) to NICU in Nottingham, England: 1994-95, and historical control period during which non-specialized (*ad hoc*) doctor/nurse team transported patients to the same NICU: 1991-93[10]	Level 3, Levels 2&3†	Nonsignificant reduction in endotracheal tube-related events (blocked or dislodged endotracheal tubes): 0/146 (95% CI: 0-3.2%) patients transported by specialized teams vs. 3/73 (4.1%, 95% CI: 1.1-12.3%) by ad hoc teams Reductions also observed in adverse physiologic end-points; such as abnormal ph ($p<0.05$) and abnormal temperature ($p<0.001$)
Critically ill adults transported to a university ICU in London: 1996-1997; specialist team with mobile ICU compared with emergency ambulance with medical escort[11]	Level 3, Levels 1&3	Mortality within 12h of arrival at the receiving facility: 5/168 (3%, 95% CI: 1.1-7.2%) vs. 7/91 (7.7%, 95% CI: 3.4-15.7%) 70% reduction in number of patients arriving in serious metabolic acidosis when transported by a specialist team ($p=0.008$): pH<7.1: 5/168 (3%) vs. 10/91 (11%) 50% reduction in number of patients arriving in a dangerously hypotensive state when transported by a specialist team ($p=0.03$): MAP<60mmHg 15/168 (8.9%) vs. 16/91 (17.6%)

Table 47.2 Manual versus mechanical ventilation for intrahospital transportation

Study Setting	Study Design, Outcomes	Main Results
30 ventilator dependent, critically ill adults in ICU: manually ventilated with self-inflating bag group, manually ventilated self-inflating bag with volumeter, and mechanically ventilated group (Federal Republic of Germany)[31]	Level 1, Level 3	Pre/post transport: $PaCO_2$ decreased from 41±2 to 34±2 ($p<0.01$) and pH increased from 7.40±0.02 to 7.46±0.03 ($p<0.05$) after manual ventilation, and $PaCO_2$ decreased from 40±1 to 35±2 ($p<0.01$) and pH increased from 7.42±0.01 to 7.47±0.01 ($p<0.01$) after using transport ventilator. No differences were observed in the group that received manual ventilation with a volumeter.
28 critically ill adults and adolescents transported from emergency department for diagnostic procedures in a University Hospital: manual ventilation versus transport ventilator (US)[32]	Level 1, Level 2&3	Pre/post transport: $PaCO_2$ decreased from 39±4 to 30±3 ($p<0.05$) and pH increased from 7.39±0.03 to 7.51±0.02 ($p<0.05$) after manual ventilation as compared to conventional ventilation. No differences between transport mechanical ventilation and conventional ventilation. No significant changes in oxygenation, heart rate or blood pressure in either group. 2/14 patients had supraventricular tachycardia (no clinical significance) during transport in the manually ventilated group and none in the transport ventilator group.
51 pediatric postoperative cardiac surgery patients who were transported within hospital while intubated: manually ventilated versus mechanically ventilated (US)[30]	Level 1, Level 2&3	Pre/post transport: Statistically significant decrease in $PetCO_2$ [32±1.6 to 26±1.4] in manually ventilated as compared to mechanically ventilated [35±1.1 to33±1.7] patients ($p=0.02$). No significant difference in other ventilatory parameters, airway pressure and hemodynamic parameters. Minute-to-minute variations: greater amount of fluctuation and lower mean values in $PetCO_2$ ($p<0.05$) in the manually ventilated group when compared to the mechanically ventilated group. No clinical changes reported.

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Section H. Role of the Patient

Chapter 48. Procedures For Obtaining Informed Consent

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Background

The process of obtaining informed consent, whether a written document or an oral communication is one means of ensuring that patients understand the risks and benefits of a treatment or medical intervention. Rooted in medical ethics and codified as a legal principle, it is based on the assertion that a competent individual has the right to determine what will or will not be done to him or her.[1] The American Medical Association (AMA) Code of Medical Ethics establishes informed consent as an ethical obligation of physicians.[2] In addition to being an ethical obligation of physicians, legislation in all 50 states requires that patients be informed of all important aspects of a treatment and/or procedures, although the details of these laws and statutes differ greatly.[2] Failure to obtain adequate informed consent renders a physician liable for negligence or battery[3] and constitutes medical malpractice.

To date, studies of informed consent have not investigated outcomes related to the adequacy of the communication, insofar as this may impact patient safety.[4,5] Physician-patient communication styles have been linked to lower rates of malpractice claims.[6] Nonetheless, as noted by Levinson, malpractice claims do not reflect the actual rate of negligence. While some have hypothesized that better informed consent could improve the patient-physician relationship, establish trust, increase patient compliance, and provide information that could reduce medical error, this has not been shown.[7,8] In the absence of a direct link between adequate informed consent and the reduction of medical error, the "patient safety outcome" reviewed in this chapter is the patient's provision of adequate informed consent.

Practice Description

Informed consent is a process through which a physician informs a patient about the risks and benefits of a proposed therapy and allows the patient to decide whether the therapy will be undertaken.[9] It may be received in one sitting, or over a period of time,[7] either orally or in writing or a combination of the two. Informed consent procedures have been instituted in both research and clinical medicine. In the former case, Federal regulations establish strict guidelines for informed consent that are monitored by a special board at each institution (Institutional Review Board). In addition, risks and adverse events that occur while research is in progress are followed closely and reported. As such informed consent in the research setting differs greatly from informed consent in the clinical setting.[10]

In clinical practice, formal efforts, such as the signing of a consent form, (presumably preceded by adequate exchange of information), are only undertaken in some circumstances, notably prior to major invasive procedures such as radiologic procedures and surgery. Less well appreciated is that all medical care, including pharmacy prescriptions or laboratory tests, requires informal informed consent, except when the patient is incompetent to make a decision or relinquishes the right to provide it.[3] Studies suggest that in practice only minimal formal efforts are made to obtain informed consent for routine interventions.[11, 12]

Legislation governing the requirements of, and conditions under which, consent must be obtained varies greatly from State to State. General guidelines, such as those proposed by the AMA require patients to be informed of the nature of their condition and the proposed procedure, the purpose of the procedure, the risks and benefits of the proposed treatments, the probability of the anticipated risks and benefits, alternatives to the treatment and the associated risks and benefits, and the risks and benefits of not receiving the treatment or procedure.[2,3,13]

As discussed below, procedures to obtain informed consent may not adequately promote the patient's comprehension of the information provided, rendering the consent not truly "informed." Interventions that may prove beneficial in improving and ensuring the patient's understanding include redrafting of consent forms to reduce complexity, providing written materials to accompany oral conversations, using multimedia or other techniques to improve comprehension, and asking patients to recap discussions about the procedure.

Prevalence and Severity of Target Safety Problem

Procedures to obtain consent must ensure that the patient understands his or her condition, as well as the risk and benefits of treatment, and its alternatives. It has been estimated that less than half of the US population understands commonly used medical terms.[14,15] This "health literacy" problem may impact the ability of the patient to understand any attempts to obtain information. In addition to lack of comprehension, procedures to obtain informed consent may be incomplete.

Several studies have noted the various insufficiencies in procedures to obtain informed consent. Three studies examined the completeness of physician-patient conversations in obtaining informed consent. Braddock et al[12] focused on outpatient discussions. Recognizing that some procedures may require more discussion than others, they created a three-tiered evaluation procedure, in which the completeness of patient-physician discussion differ according to the complexity of the decision being discussed. Basic decisions, such as laboratory tests, require the least in-depth discussion, covering only the patient's role, the clinical nature of the decision, and exploration of patient preferences. Intermediate decisions, such as changes in medication, require a moderate depth of discussion, incorporating the Tier 1 subjects, and adding a discussion of alternative treatments, the risks and benefits of the alternatives, and an assessment of the patients understanding. Complex decisions such as surgery require a discussion of the uncertainties associated with the decision, in addition to all of the aforementioned steps. Analyzing audiotaped conversations between 1057 patients and 59 primary-care physicians and 65 surgeons, Braddock et al found that 17.2% of basic decisions contained all required components, while none of the intermediate decisions and only one of the complex decisions contained all of the required components. Applying only the Tier 1 basic consent standards, 20.5% of basic decisions, 21.9% of intermediate decisions, and 38.2% of complex decisions met all the criteria.

In a study of informed consents of surrogates for pediatric patients undergoing surgery, coders examined audiotaped conversations with surrogates, as well as structured interview and questionnaire data regarding the conversations. They noted that patients' recall of the conversations with physicians often omitted key components, such as the risks and benefits of the procedures.[16]

Bottrell et al[13] examined the completeness of 540 consent forms from 157 hospitals nationwide. Of these, 26.4% included all four of the basic elements (risks, benefits, alternatives, and other important aspects of the procedure). Eighty-seven percent noted the general possibility of risk, but less than half provided specific information. Alternatives were noted in 56.9% of the

forms, and benefits appeared in 37%, though most of these were general references rather than specific information. Although 74% of consent forms were deemed incomplete, it is unknown whether physician-patient discussions that preceded the signing of the consent form included the missing information.

A study by Mark et al[9] found that 82.4% of 102 participants reported that they understood everything that their physicians had described about a procedure and indicated that all of their questions had been answered. Eighteen patients had remaining unanswered questions. Half of this group requested more time to speak with their physicians, while the other 9 felt that their questions were not important.

In a study by Lavelle-Jones,[17] 69% of patients admitted that they did not read a consent form before signing it. In addition, approximately half of the patients awaiting treatment were unhappy with the amount of information they received, with 21% stating that most of the information they obtained about their surgical treatment was obtained outside of the hospital.

Consent forms have been targeted for their lack of readability. Patients with limited reading ability are at increased risk for medical errors, due to problems reading medication bottles, appointment slips, self-care instructions, and health education brochures.[18] These patients may also have trouble reading materials intended to aid in obtaining informed consent. According to the National Adult Literacy Survey of 1993, approximately 40-44 million Americans were functionally illiterate, defined as the inability to complete basic reading tasks required to function as a member of society.[19] In addition, even in educated adults, the highest grade-level completed may not reflect actual reading comprehension level. A study of 100 adult cancer patients found that most read at a mean grade-level equivalent of between 10th and 11th grade. The authors suggest that forms and educational materials be written at a grade-level three levels below the highest level of education completed by a patient.[20]

Several studies have examined the readability of procedure consent forms. Two studies examined consent forms for radiologic procedures using computer generated “readability” scores. Consent forms for use with iodinated contrast media found that 12.35 years of education were required to read consent forms.[21] A similar study of general radiologic procedure consent forms found that they required a mean of 15 years of education. Only 16% of forms could be understood by patients with a high-school education.[11] Another Hopper et al study[22] found that general hospital consent forms were written at a grade level of 12.6. Just over half could be understood by a patient with a high school education, less than a third by patients with a 10th grade reading level, and just over 5% by patients with an 8th grade reading level.

Opportunities for Impact

While informed consent is a well-established practice, it often fails to meet its stated purpose. Several methods of improving the procedures of obtaining informed consent have been proposed, including improving the readability of consent forms,[22] asking patients for recall to establish understanding,[3,23] adding additional stimuli, such as multimedia presentations[24] and providing written information.[17]

Lavelle-Jones[17] found that elderly patients (over 60 years of age) had poorer recall than younger patients. In addition, patients with internal locus of control—those who believed their health was in their own control—were better informed than those with an external locus of control. Patients with above average IQ exhibited better recall. These findings could indicate “at-risk” groups that interventions may target.

One author argues that an important opportunity for impact is to change the model of implementing informed consent from a single event approach to a process approach.[7] Currently

obtaining informed consent often revolves around the signing of the consent form. Although this approach clearly delineates the responsibility of health care providers, provides documentation of the consent, and fits easily into the current provider structure, it often results in patients failing to actually comprehend the information and reinforces physicians' conception that the consent ritual is futile. In contrast, a process model involves the physician providing information over time, establishing a better patient-physician relationship and better comprehension of medical care. As of yet there is no data to support these suppositions.

Since the definition of adequate informed consent is debatable, the number of individuals currently not receiving interventions to obtain adequate informed consent is likely to be quite high, but is not known.

Study Design, Outcomes and Effectiveness of Various Approaches

Improving Readability of Consent Forms and Education Materials

In order to ensure that patients understand the procedure to which they are consenting, it is important that all materials be presented in a comprehensible manner. Consent forms are written with relatively complex sentence structure and vocabulary, making it difficult for the average adult to interpret the information. In addition, providing consent forms in the primary language of patients may improve consent procedures. However, we located no studies examining the effectiveness of such practices.

Structured Discussions

Informed consent is often obtained during informal discussion between physicians or nurses and patients, and (as discussed above), these discussions frequently do not cover all of the relevant information.[12] Two studies examined the use of a structured interview format in providing information to patients. Solomon et al[25] studied 36 patients receiving cardiac catheterization for the first time at a Veterans hospital. Patients were randomized into two groups (Level 1 design). Both groups were briefed by a cardiologist regarding the procedure (standard care). In addition, the experimental group received a 30-minute structured teaching session with a nurse to discuss all aspects of the procedure, including the purposes, techniques, sensations, risks and benefits. Patients in the experimental group also received an illustrated guide to cardiovascular procedures and an educational pamphlet. All subjects were tested using a 13-item questionnaire covering the information that should have been imparted during informed consent procedures (Level 3 outcome). The intervention group scored significantly better than the control group (11.5 vs. 8.9).

In a later study, Dawes et al[26] studied 190 hospitalized patients undergoing ENT surgery. Patients were assigned to one of 4 groups. Groups 1 and 2 were assigned at different times (Level 2 design), while groups 3 and 4 were randomly assigned (Level 1 design). Group 1 had no consent interview until after assessment at the conclusion of the study. Group 2 engaged in an informal interview with a physician (reflecting current practice), during which the number of complications discussed was recorded. Group 3 engaged in a structured interview with a physician, covering the purpose and technique of the procedure, complications, sensations, alternatives, and benefits (a checklist was used as a guide). The final group, Group 4, engaged in the same structured interview, except that the patient was provided with a copy of the checklist and allowed to take it with them after the interview. Patient anxiety was assessed following consent using a visual analog scale, then reassessed at an interview, given 4 hours later. At the later interview, patients were asked to recount orally the operation name, describe what would be

done, list complications, and state whether they understood the information given to them (Level 3 outcome). All but Group 1 (control group) patients showed a drop to normal anxiety after informed consent. Group 2 (informal discussion) remembered proportionately more complications mentioned in the informal interview, although fewer complication were covered. Groups 3 and 4 recalled more total complications than Group 2. There was no differences between Groups 3 and 4 (structured interviews).

Asking for Recall

A simple method of determining whether a patient understands information regarding a procedure is to ask the patient to recount what he or she has been told.[3] Two studies examined this intervention, using a randomized controlled trial design (Level 1 design). In the first study, informed consent was solicited from 50 patients undergoing percutaneous lung biopsy.[23] Twenty-seven patients in the control group were offered the standard procedure for obtaining informed consent: approximately 30 minutes prior to the procedure, the physician described the procedure in detail, including its risks and benefits. Four complications were specifically described, along with their relative risks. Patients were asked to sign a standard consent form. Twenty-three patients received the same procedure, but in addition, they were asked to describe all 4 potential complications. The procedure was repeated until all patients in the intervention group could recount all of the complications. This modified procedure usually took less than 5 minutes extra compared with the traditional approach. Patients were interviewed 2 hours after the procedure was completed. Patients in the modified consent group had better recall (Level 2 outcome) than patients in the control group (56% vs. 14% with high recall (recalling 3-4 out of 4 risks), and 13% vs. 44% with low recall (recalling 0-1 out of 4 risks)).

A second study examined verbalization in 20 patients undergoing anterior cruciate ligament (ACL) reconstruction.[27] Patients were randomly assigned to 2 groups. Both groups received the standard education for ACL reconstruction, which included the use of a 3-D model of the knee, discussion with a physician about the procedure, and obtaining informed consent. The experimental group (8 subjects) also were asked to repeat back the risks of the procedure until they could accurately recall all risks discussed. One-month later, recall regarding the information received was tested using a 3-item questionnaire (Level 2 outcome). All 8 in the experimental group answered all questions correctly, while only four out of the 12 in the control group answered all questions correctly ($p=0.03$).

Use of Visual or Auditory Learning Aids

Adding additional stimuli may increase the ability of the patient to understand information being conveyed or increase retention of that information. For instance, use of visual diagrams may make a procedure easier to understand. Multi-media may also promote better comprehension. Three studies have examined the addition of visual stimuli for informed consent. One study of patients undergoing back surgery examined the impact of a diagnosis-specific videodisk program on patient outcomes.[24] Patients (n=393) who were candidates for elective back surgery (primarily for herniated disc and spinal stenosis) were randomized to two education groups (Level 1 design). The control group received a written booklet regarding the surgical and non-surgical treatments for herniated disc and spinal stenosis, a description of expected outcomes, and a short self-test on the booklet information. Patients in the experimental group also received the booklet, but in addition viewed a videodisk program. The program allowed a patient to enter their diagnosis and age and receive customized information on the alternative treatments, discussion of the diagnoses (and the ambiguities of diagnosis), and interviews from

patients that had been treated surgically and non-surgically. At the end the patient was provided with a printout of outcome probabilities. Patients in the experimental group were slightly more likely to report that they had all the information they wanted (Level 3 outcome). Rates of patients consenting to surgery for herniated disk (32% vs. 47%) and other diagnoses (5.4% vs. 14.0%) were lower in the videodisk group.

Hopper et al[28] also tested an interactive video program, although the tested program was computer based. One-hundred and sixty outpatients referred for IV contrast media studies were stratified by age, sex, and previous exposure to contrast media, then randomized to receive either a written consent form, or an interactive computer-based video (Level 1 design). Subjects in the control group received a consent form designed to be read at an eighth grade reading level. Subjects in the experimental group viewed a video in which a physician used identical words as the consent form to inform subjects about the procedure and risks. Subjects then had an option of hearing more about the risks. If subjects chose not to hear additional information, they were provided with printouts of the risks (with the minimal information already given). Otherwise subjects were provided with printouts certifying that they had completed the program. All subjects were tested using a 7-item questionnaire regarding the procedure and risks (Level 2 outcome). Patients that viewed the video responded correctly more often than the control group when asked about general aspects of the procedure. Female patients in the video group also responded correctly more often to questions about risks, although this finding did not hold for male patients. The video did take approximately 1.6 minutes of additional time to complete, and there was no difference in patients desire for additional knowledge between the groups (Level 3 outcome).

One final study did not use an interactive video, but tested whether providing information via video was superior to providing information via an informal discussion with the physician (standard practice).[29] Two-hundred and twenty four subjects referred for colonoscopy were stratified into previous or no previous colonoscopy, then randomized into 3 groups (Level 1 design). The control group had a structured discussion with a physician, in which the physician covered the same information covered in the video according to a checklist. The video-only group watched a 5-minute videotape, in which a physician described the procedure, and its risk and benefits. The third group (video and discussion), watched the video and then engaged in a structured discussion with a physician. All patients were tested using a 13-item questionnaire (Level 2 outcome). Both video groups gave more correct responses than the discussion-only group, although they did not differ from each other. In addition, patient anxiety levels were measured using the State-Trait Anxiety Inventory (Level 3 outcome). There were no differences among the 3 groups.

Providing Written information to Patients

Providing written information to patients regarding their diagnoses, proposed treatments, and other information given during informed consent discussion allows the patient to refer back to such information, and possibly increases comprehension. One early study compared the then-common practice, informal interview between patient and doctor, with provision of a written consent form.[30] Eighty patients, referred for a first excretory urography, were randomly assigned to 2 groups (Level 1 design). The control group received standard care, the informal interview. The experimental group received the same interview along with a detailed written consent form to read and sign. Patient clinical reactions and side effects were monitored (Level 1 outcome). One to 3 days after the procedures, patients retrospectively rated discomfort, fear or apprehension, and understanding of the procedure (Level 3 outcome). Patients also completed an

8-item knowledge examination covering the information on the consent form (Level 2 outcome), or in the informal interview. Experimental subjects scored significantly better ($p=<0.01$) than control subjects for the knowledge exam (scoring 73% vs. 48%), but did not differ in their discomfort, perception of the procedure, or anxiety.

Some investigators have proposed that patients should receive written consent forms days before receiving a procedure. Neptune et al[31] studied 160 subjects referred for a contrast media radiology exam. The patients were stratified by age, sex, and previous exposure to constrast media, and then were randomized within the strata into 2 groups (Level 1 design). The control group received a simple consent form (designed such that it could be read with an eighth grade education), 15-60 minutes before the procedure, consistent with standard care. Patients in the experimental group received the same consent form 24-72 hours before the procedure, and were called one day in advance to remind them to read the form. Subjects' knowledge concerning their procedures was tested using a 7-item questionnaire (Level 2 outcome). Overall, there were no significant differences between the two groups on either a knowledge or satisfaction score.

In a British study,[17] 265 patients undergoing intrathoracic, intraperitoneal, or vascular procedures, were assigned to one of 2 consent groups (Level 2 design). The control group was provided with an oral explanation of their disease and the proposed procedures. Members in the experimental group were provided with the same information, and also provided with an "operation card" detailing the same information. Patients were given 30 minutes to review the cards before signing the consent form. Patients were interviewed for recall (Level 2 outcome) immediately after consent (1 hour), the day of discharge, 4-6 weeks post-discharge, and at 6 months post-discharge. Control and experimental groups did not differ, except on the day of discharge ($p<0.0001$). The only significant factor in predicting recall was the age of the patient, as older patients had poorer recall than younger patients, even when controlling for psychological factors. Written information did not appear to aid in recall for older patients at any time point.

Two other studies provided written information to patients, although this was combined with structured teaching programs. These studies are reviewed under "Structured Discussions" above.[25, 26]

Comment

While much has been written regarding informed consent and the ethical obligations of providers to obtain proper informed consent, serious shortcomings have been reported. However, very little literature has examined the impact of different procedures for obtaining informed consent on the quality of the consent obtained. The weight of the literature suggests that the value of informed consent can be modestly enhanced by augmenting standard provider-patient discussions with additional learning and retention aids (written or videodisk materials). Moreover, the process of consent can be mildly improved by using structured interviews and by asking patients to recall and re-state key elements of the discussion. In addition to the ethical imperative of informed consent, it may be that informed patients are less likely to experience medical errors by acting as another layer of protection (as when a patient is able to inform providers about his or her correct medications or the correct surgical procedure he or she is to undergo). More research is needed to establish the best practices to improve informed consent, and to test the impact of such practices on patient safety.

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Chapter 49. Advance Planning For End-of-Life Care

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Background

Physicians and other health care workers have long struggled with decisions regarding care for patients at the end of life. An important component of this care involves assessing and understanding patient preferences for care through ongoing discussions with competent adult patients and/or their family members or surrogates. Advance care planning protects patient autonomy and helps to assure that their health and medical treatment wishes are implemented. Good communication at the end of life can also help patients achieve closure and meaning in the final days of their life.

Over the past 20 years, public consciousness regarding planning for end-of-life care has been raised through several seminal court cases, such as those involving Karen Ann Quinlan and Nancy Cruzan. These cases and the public interest they helped engender led to legislation promoting patients' rights to determine their care at the end of life. For example, Natural Death Acts (statutes passed by State legislatures that assert a person's right to make decisions regarding terminal care) have helped promote the use of living wills (described below).[1] In addition, in 1990 the Federal Patient Self-Determination Act (PSDA) was passed by Congress to encourage competent adults to complete advance directives. The PSDA requires hospitals, nursing homes, health maintenance organizations, and hospices that participate in Medicare and Medicaid to ask if patients have advance directives, to provide information about advance directives, and to incorporate advance directives into the medical record.[2]

Advance directives are any expression by a patient intended to guide care, should they lose their medical decision making capacity. Although both oral and written statements are valid, the added effort required to complete written statements gives them greater weight. In addition to their use when patients lose competence, advance directives also help patients consider the type of care they would want in the future, even if they retain decision making capacity. Advance directives have legal validity in almost every State.

There are 2 principal forms of written advance directives: living wills and durable powers of attorney for health care. A *living will* is a document that allows an individual to indicate the interventions he or she would want if he or she is terminally ill, comatose with no reasonable hope of regaining consciousness, or in a persistent vegetative state with no reasonable hope of regaining significant cognitive function. A *durable power of attorney for health care* (DPOA-HC) is a more comprehensive document that allows an individual to appoint a person to make health care decisions for him or her should he or she lose decision making capacity.

Prevalence and Severity of the Target Safety Problem

Respecting patient preferences regarding end-of-life care requires a well-coordinated approach. Problems can arise in both documenting patient preferences and ensuring that preferences are available and respected at the time they are needed. In addition, inadequate communication with patients can compromise the goal of respecting patient preferences for end-of-life care through a variety of mechanisms.

Failure to Document Preferences

The PSDA was a legislative solution (see Chapter 55) designed to increase rates of completed advance directives. Although there was initial hope that PSDA would markedly increase rates of advance directive documentation, by the early 1990s it was clear that the impact was small. At that time, a large multicenter randomized trial, the Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT), was undertaken to improve advance care planning. SUPPORT represents one of the largest and most comprehensive efforts to describe patient preferences in seriously ill patients, and to evaluate how effectively patient preferences are communicated. SUPPORT cost 28 million dollars and enrolled 9100 seriously ill patients. In SUPPORT, a trained nurse facilitator provided prognostic information to patients and medical staff, discussed patient preferences with patients and families, and facilitated communication between patients and physicians.

Neither the PSDA legislation nor the SUPPORT intervention had major impacts on the documentation of patients' preferences regarding end-of-life care. Teno et al reported on the documentation of advance directives at 3 points: before PSDA, after PSDA, and after the SUPPORT intervention. The percentage of patients with an advance directive was unchanged in all 3 groups, but documentation of those directives increased at each stage, from 6% to 35% to 78% in the SUPPORT intervention group. Despite this increase in documentation, only 12% of patients with an advance directive had talked with a physician when completing the document and only 25% of physicians were aware of their patients' advance directives.[3] SUPPORT found that only 23% of seriously ill patients had talked to their doctors about their wishes concerning cardiopulmonary resuscitation (CPR) and that patient-physician discussions and decisions were uncommon even in seriously ill patients whose death was predictable.[4] Another study that surveyed elders in community settings found that the vast majority (81%) stated their desire to discuss their preferences with their physicians if they were terminally ill, but only 11% had done so.[5] As these studies demonstrate, patients often want to talk about death and dying but expect physicians to bring up the issues.[6]

Ensuring that Preferences are Available and Respected

Even when advance directives are prepared, studies show they often do not change interventions at the end of life.[3,7] Advance directives are frequently not available, recognized or applied, nor do they help reduce hospital resource use. There are multiple reasons why advance directives may go unrecognized.[8] Admitting clerks may fail to document or incorrectly document the status of a directive on admission to the hospital. Patients and families often do not inform the hospital physician or admitting clerk about their advance directives, or fail to bring documentation to the hospital.[8] In one survey of 200 patients, only 18% had filled out an advance directive and of these, 50% had secured the only copy in a safety deposit box![9] A copy of the advance directive is often not transferred from the nursing home to the hospital on admission. In a study by Morrison, physicians documented advance directives or discussions with appointed proxies about treatment decisions in only 11% of admission notes.[8]

Although the goal of advance directives is to ensure that patients receive treatment that is consistent with their preferences, to date there is no evidence that documenting advance directives leads to this outcome. In SUPPORT, there was no evidence that increasing the rates of advance directives resulted in care more consistent with patients' preferences.[10] This finding was concordant with a study of nursing home patients and their family members regarding preferences for aggressive treatment at the end of life. There, 25% of patients received care that

was inconsistent with their previously expressed wishes.[11] The problem may not be the substance of advance directives *per se*, but rather in the manner in which clinicians approach them. Physicians may be hesitant to initiate discussions of advance directives with patients, especially early in the course of an illness.[12]

Despite these shortcomings, advance directives remain the best available approach for helping patients plan future care. These discussions, difficult as they are, help ensure that patients receive care consistent with their values and goals, spare the patient inappropriate interventions, and help maintain dignity during the dying process.

Physician Communication

In order to improve the quality of end-of-life care, physicians need to effectively communicate with their patients and understand their preferences for care. Several studies have documented imperfections in physician-patient communication.[13,14] Several studies have demonstrated that physicians often misunderstand or are unaware of their patients' preferences for care.[15,16] Furthermore, physician prediction of patients' preferences for resuscitation are no better than random.[3,14]

In summary, the published literature demonstrates significant problems in all areas crucial to advance care planning and ascertainment of patient preferences, transmission of information to appropriate care settings, and respecting those preferences. The provision of unwanted end-of-life care is an adverse event that can potentially be avoided by the implementation of effective patient safety practices.

Opportunities for Impact

Patients with chronic or life-limiting illnesses make up a large proportion of the adult primary care population. Almost three-quarters of the 2.3 million Americans that die each year are 65 years of age or older. By the year 2030, people older than 65 will compromise 20% of the total population (70 million people), compared with 13% in 1994. Today's average life expectancy is 75.5 years, and the leading causes of death are heart disease, cancer and stroke. Data from 1995 estimated that these causes accounted for 62% of all deaths and 67% of deaths for those age 65 and over.[17] The overall picture is of an aging population, with many individuals living for several decades (often with chronic diseases) after the possibility of death becomes more than theoretical.[18]

SUPPORT documented serious problems with terminal care. Physicians did not implement patients' refusals of interventions. When patients wished to forgo CPR, a do not resuscitate order was never written in about 50% of cases.[4] While 90% of Americans say they want to die at home, 4 out of 5 die in a hospital or other health care facility. The SUPPORT study showed that only 35% of the study patients had an advance directive. These patients had an approximate six month mortality rate of 50%.

Physicians and the public also commonly overestimate the effectiveness of CPR. In reality, in-hospital cardiac arrests have a survival rate of about 15%. For patients over 65 the survival rate is about 10-11%, and 3.5% for patients over age 85.[19] Elderly nursing home patients with out-of-hospital arrest only have 1-2% survival.[20] Studies have shown that when patients are aware of the real survival rates for CPR, they are less likely to desire this intervention.

Evidence for Effectiveness of the Practice

Documenting Preferences and Ensuring that they are Available and Respected

A Physician Order form for Life-Sustaining Treatment (the POLST)

In the mid-1990s, a task force of ethicists and clinicians at the Oregon Health Sciences University developed a new Do Not Resuscitate (DNR) order form called POLST (Physician Orders for Life-Sustaining Treatment). POLST is a comprehensive two-page order form that documents a patient's preference for life-sustaining treatments. The form is designed to record a patient's wishes clearly and simply. The accompanying POLST wallet card is included as Figure 49.1; the complete POLST form and materials can be obtained from the Oregon Health Sciences University's Center for Ethics in Health Care (http://www.ohsu.edu/ethics/polst.htm).

Tolle et al examined the extent to which POLST ensured that nursing home residents' wishes were honored for DNR orders, and for hospital admission only if comfort measures failed. None of the 180 patients who completed POLST received CPR, ICU care, or ventilator support, and only 2% were hospitalized to extend life. The study subjects had low rates of transfer for aggressive life-extending treatments and high levels of comfort care.[21]

Since 1995, more than 220,000 copies of POLST have been distributed throughout the State. Data from 1999 suggest, albeit circumstantially, that this initiative may be working. In 1996, Oregon's in-hospital mortality rate was 31%, compared with the national average of 56%.[22]

Lee et al studied the effectiveness of POLST in a Program of All-Inclusive Care for the Elderly (PACE) in Portland, Oregon. They retrospectively reviewed POLST instructions for each of the 58 participants and whether or not each of the treatments addressed by the POLST was administered in the final 2 weeks of life. The POLST specified DNR for 50 participants (93%); CPR use was consistent with these instructions for 49 participants (91%). The participants also designated the level of care they preferred as either comfort care, limited, advanced, or full intervention. Interventions administered were at the level specified in only 25 cases (46%), with less frequent deviations in antibiotic administration, administration of IV fluids, and placement of feeding tubes. The investigators concluded that the POLST effectively limits the use of some life-sustaining interventions, but that further investigation is needed into the factors that lead physicians to deviate from patients' stated preferences about other treatments.[23]

Administrative Initiatives to Ascertain Preferences on Admission to Hospital or Nursing Home

In addition to POLST, some medical centers have developed admission order forms to document patient preferences regarding end of life. These forms require health care personnel to inquire about advance directives, resuscitation preferences, artificial fluids and nutrition, etc. This approach, promoted by the passage of the PSDA, may be effective in promoting provider-patient discussions about end-of-life wishes and prevent unwanted treatments. However, there are no data documenting the effectiveness of this strategy.

Ascertaining Preferences in the Outpatient Setting

As with other forms of computerized decision support (Chapter 53), computer-generated reminders for primary caregivers can increase the rates of discussion of advance directives and completion of advance directive forms among elderly outpatients with serious illnesses. Dexter et al performed a randomized, controlled trial to test the effectiveness of computerized reminders. The participants were 1009 patients and 147 primary care physicians in an outpatient setting. Physicians that received computer-generated reminders that recommended discussion of one or both of 2 types of advance directives were compared with physicians who received no reminders. Physicians who did not receive reminders (controls) discussed and completed advance directives in only 4% of the patients On the other hand, physicians who received both types of reminders discussed (24%) and completed (15%) advance directives significantly more frequently.[24]

The Portability of Advance Directives between Hospitals and Nursing Homes

Ghusn et al retrospectively studied the relationship between inter-institutional communication and continuity of advance directives from hospital to nursing home settings. Having a hospital discussion about advance directives or having a hospital DNR order were associated with a higher rate of advance directive discussions in nursing homes. Hospital DNR orders were continued for 93% of patients discharged to the hospital-affiliated nursing home and 41% of patients discharged to the community nursing home. Specific communication of hospital DNR status to the receiving nursing homes was associated with better continuity of DNR orders. The authors concluded that completing advance directives before patients are discharged to nursing homes, communicating advance directives to the receiving home, and providing follow-up discussions at the nursing home might improve the continuity of advance directives between hospitals and nursing homes.[25]

<u>Practices to improve physician-patient communication and physician understanding of patient preferences</u>

Training for Physicians

Physician education is an attractive way to improve end-of-life care. Physicians often do not communicate about advance care planning because many have not been taught the relevant communication skills and have learned them only through personal experience.[26] A study by Tulsky et al revealed that when physicians discussed end-of-life issues with their patients, they spoke twice as much as they listened and did not routinely explore patients' values.[26]

Until recently, training for health care providers in palliative care and respecting patient preferences, and materials to support such training, were inadequate. For example, recent studies

have demonstrated that most medical and nursing textbooks insufficiently cover end-of-life care issues.[27] Increasingly, resources (including textbooks, palliative care journals or journal series,[28] Web sites and training programs) are filling this educational void. The American Medical Association has developed an extensive physician training program titled Education for Physicians on End-of-Life Care (EPEC).[29] This curriculum teaches fundamental skills in communication, ethical decision making, palliative care, pain and symptom management, and other end-of-life treatment issues.[30] The Robert Wood Johnson Foundation initiative, "Last Acts," is another ambitious effort to educate both patients and providers.

Other educational training programs exist for physicians and students as well.[30] Physicians can receive formal training by attending conferences on decisions near the end of life, case management meetings regarding individual patients, and seminars on communication skills with individual feedback to physicians on their performance.[31] Physicians with expertise in this area often conduct seminars to educate physicians. Buckman and Lo have developed guides for specific end-of-life discussions, such as breaking bad news and the act of active listening and empathy.[32, 33]

As attractive as these educational programs are, none have been studied for their impact on changing practice or outcomes. Although common sense might tell us that such programs are likely to be effective, the generally unimpressive relationship between professional education and outcomes or process change (Chapter 54) provides grist for uncertainty pending formal effectiveness studies.

Palliative Care Services

Specialized palliative care programs have become increasingly common in the health care system. Physicians and other health care providers, including nurses, social workers, chaplains, and others are available to coordinate care and provide consultation for terminally ill patients in hospices, hospitals, nursing homes or patient's homes. The palliative care service also plays an important role in fostering communication among providers, patients, and families. Data regarding effectiveness are lacking.

Hospitalist Systems

Hospitalist physicians may improve end-of-life care in hospitals. Hospitalists, by virtue of their large inpatient volumes, should become increasingly facile with ascertaining patient preferences regarding end-of-life care. Hospitalists have a unique opportunity to approach patients, since an admission generally signals either a worsening of the patient's current condition or a new diagnosis. The hospitalist may have more time to spend with patients and is available over consecutive hospital days to answer any questions. A routine discussion of advance directives by hospitalists can help improve the quality and efficiency of patient care.[34] On the other hand, patients may have a long-standing trusting relationship with their primary care physicians, and may have expressed their wishes to this physician prior to hospitalization. This possibility highlights the importance of hospitalist-primary care provider communication, particularly concerning end-of-life issues.[34]

One retrospective chart review study of 148 patients dying at a community teaching hospital has examined the impact of hospitalists on end-of-life care. In this study, patients cared for by hospitalists were significantly more likely to have had a documented family meeting (91% vs. 63% for patients of community-based primary physicians). About two-thirds of patients in both groups requested limitations in the level of care by the time of death. Of these, patients of hospitalists were significantly less likely to have documented pain, dyspnea, or anxiety in the 48

hours prior to death (57% vs. 75%). Whether these differences reflect differences in the quality of care, the completeness of documentation, or underlying patient differences requires further study.[35] Although the hospitalist movement holds promise for improving end-of-life discussions, more research is needed to determine whether this promise will be met.

End-of-Life Education for the Public

Extensive public awareness and educational programs are necessary to create a foundation for successful end-of-life conversations in patients with advanced illness. Broadcasts, such as the PBS-Bill Moyers special "On Our Own Terms," may help the public appreciate the experience of terminal illness, and the complex choices that are faced. Such presentations may encourage viewers to discuss how they might manage a similar situation, and explore their own fears and concerns about dying. There are no data regarding the effectiveness of public education to improve advance care planning.

Other Locally Successful Advance Care Planning Programs

Individual programs to implement patient preferences have emerged around the country. Limited data suggest that they may be effective, and bear further examination as to their portability to other programs and settings and their durability over time.

- "Respecting Your Choices" Program

Gundersen Lutheran Medical Center in La Crosse, Wisconsin has worked on community-wide programs to improve advance care planning with an initiative called "Respecting Your Choices." This program used patient and family education, community outreach, education for non-medical professionals, standard training sessions, and standard methods for documenting and tracking advance directives. Hammes et al reported that 85% of patients in the intervention group had written advance directives at death, executed on average 1.2 years before death. Of these directives, 95% were in the medical record. Virtually all patients (95%) reported that the interview process was meaningful. The patients felt that they benefited from improved communication with loved ones and with health care providers.[36]

- Dayton VA Initiative

The Dayton (Ohio) VA Medical Center aimed to increase the number of veterans who participated in advance care planning. VA patients and their families received a patient education booklet and a video on advance care planning. The VA also developed discussion guidelines for providers, initiated an advance care planning clinic, and initiated a bereavement support group. In a 12-week period, advance care planning discussions and follow-up increased from about 15% percent of charts to almost 90%.[37]

- "Let Me Decide" Program

Molloy et al examined patient satisfaction with decision making and health care costs after systematically implementing an advance directive program in nursing homes. The "Let Me Decide" program included educating staff in local hospitals and nursing homes, residents, and families about advance directives and offering competent residents or next-of-kin of mentally incompetent residents an advance directive. The researchers reported that systematic implementation of this program reduced hospitalizations and aggressive care for nursing home patients who did not want that level of intervention. It also reduced utilization of health care services without affecting satisfaction or mortality.[38]

Costs and Implementation

Estimating the cost of ascertaining and respecting patient preferences is difficult since improvements in this area may require major changes in the structure of the health care system. Institutional barriers, the culture of medicine, patient attitudes, time constraints physicians face with office visits may all play a role in implementation and may inhibit change.[26] Barriers to implementation include complacency on the part of the physician and patient, fear of political controversy, diffused responsibility, and absence (or perverse) financial incentives for providers and institutions. The surprising ineffectiveness of the SUPPORT intervention, which cost over 28 million dollars, demonstrates how difficult it is to make major improvements in this area. Nevertheless, improving our ability to respect patient preferences is valuable in its own right and may ultimately prove to be cost-effective, since some patients will choose to forego high technology and expensive care at the end of life.

Medical care at the end of life consumes 10% to 12% of the total health care budget. An estimated 40% of the Medicare budget is spent during the last 30 days of life.[39] Some have posited that increased use of hospice and advance directives and lower use of high-technology interventions for terminally ill patients will produce significant cost savings. However, the studies on cost savings from hospice and advance directives are not definitive. The 3 randomized trials of hospice and advance directives use show no overall savings, but the authors of a review suggest that the studies were either too small for confidence in their negative results or their intervention and cost accounting are flawed.[40] In the absence of a definitive study, the existing data suggest that hospice and advance directives can save between 25% and 40% of health care costs during the last month of life, but far less (and perhaps nothing) in the 3-12 months before death. Although, these savings are less than most people anticipate, they do indicate that hospice and advance directives should be encouraged because they certainly do not cost more and they provide a means for patients to exercise their autonomy over end-of-life decisions.[40] Finally, several of the promising interventions described above (eg, the POLST intervention), are relatively inexpensive. For example, 500 POLST forms can be ordered from Oregon Health Science University's Web site[41] for less than $100, although the cost of implementing the POLST program is unknown.

Comment

Preventing unwanted aggressive care at the end of life requires active communication between provider and patient, and effective strategies to transfer information regarding preferences seamlessly across care venues. The dominant strategy to improve care in this area over the past 20 years has been the promotion of advance directives. Although the enthusiasm for advance directives has not been matched by evidence of their effectiveness, SUPPORT and other studies have renewed public concern and prompted providers and policy makers to reexamine advance care planning and strive to improve it. Although we have found evidence of several potentially promising strategies (perhaps the most promising of which is the POLST form), the inevitability of death and the importance patients place on improving end-of-life care point strongly to the need for further research in this area.

Figure 49.1. POLST Wallet Card instructions

POLST WALLET CARD INSTRUCTIONS

This is an identification wallet card for the Physician Orders for Life-Sustaining Treatment (POLST) document. This card is **not** a substitute for a completed POLST document. It provides a summary of the POLST document and is expected to be honored by care providers.

The POLST document and wallet card are completed by the physician. The physician must sign **both** the POLST document and the wallet card to make the wallet card valid.

Instructions continued on other side.

_ _

Physician Orders for Life-Sustaining Treatment

Name: _____

Resuscitation (Patient has no pulse **and** is not breathing:

- Resuscitate
- Do Not Resuscitate (DNR)

Medical Interventions (has pulse and/or is breathing):

- Comfort Measures Only
- Limited Interventions
- Advanced Interventions
- Full Treatment/Resuscitation

Antibiotics:

- No antibiotics except if needed for comfort
- No invasive (IM/IV) antibiotics
- Full Treatment

Instructions continued on other side.

…continued from other side

It is recommended that the completed wallet card be laminated in plastic for durability and to prevent alteration. An existing card should be destroyed if the POLST document is changed. A new wallet card can be completed to match the new physician orders.

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Artificially Administered Fluids and Nutrition:

- No feeding tube/IV fluids
- Full Treatment
- No long term feeding tube/IV fluids

Discussed with:

- Patient
- Health Care Representative
- Court-appointed Guardian
- Spouse
- Other

I have completed the following forms:

- Advance Directive
- Court-appointed Guardian

_____ _____

Print name of Physician Phone

_____ _____

Signature of Physician Datee

Center for Ethics in Health Care *Developed in conformance with ORS 127.505 et seq.*

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Chapter 50. Other Practices Related to Patient Participation

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Background

A number of practices and resources aim to facilitate the role of patients as their own safety advocates. These practices are not intended to shift the burden of monitoring medical error to patients. Rather, they encourage patients to share responsibility for their own safety. Although these types of interventions hold promise for enhanced patient safety, there is yet insufficient evidence of their effectiveness. Therefore, this chapter is a brief, general survey of practices related to patient participation; there are few practices that have been studied with sufficient rigor to merit a full evidence-based review. This chapter explicitly excludes consumer report cards, since such tools presently are more relevant to health care quality than patient safety.[1,2] There is a substantial literature on the patient's role in quality improvement related to specific diseases - eg, self-management and general education for patients with certain chronic diseases such as asthma,[3-5] diabetes,[6-8] and rheumatoid arthritis,[9-12] as well preoperative educational and preparation programs for patients undergoing cardiac surgery. [13] This literature was not reviewed in detail, both because it falls outside our definition of patient safety practices (Chapter 1) by virtue of its disease specificity, and because the volume of material was overwhelming given the time allocated for the production of this Report. There are obvious additional opportunities to promote patient involvement in helping protect their own safety drawn from the disease-specific experiences of the past, and this should be the subject of further exposition and analysis.

Patient Education Materials Regarding Patient Safety

Books, Web sites and consumer group publications abound with health care and medical information for patients.[14] The goal of these resources is to enable consumers to arm themselves with the knowledge to protect themselves. Health care providers may wish to distribute such materials to patients to alert them of the possible problem of medical error, and encourage those that would like to take appropriate action.

The Agency for Healthcare Research and Quality[15] produces a 5-page "Patient Fact Sheet" on preventing medical errors. This fact sheet educates patients on the problem of medical error, and provides 20 tips patients may follow to avoid medical error, ranging from properly measuring liquid medications to ensuring health care employees have washed their hands.

Proprietary educational materials have also been developed. For instance, DoctorQuality, Inc., a quality management company that provides products and services to health care consumers, purchasers, and providers, has developed online and offline tools that providers and patients can use to improve care,[16] including patient safety workbooks and quality guides for a variety of diagnoses and surgical procedures. The books describe the key events that patients should anticipate at each step of diagnosis and treatment, identify high-risk points in the treatment plan where mistakes are more likely occur,[14] and provide tips as to how to avert common errors.

Patients may also find resources in the popular literature. In *Lerner's Consumer Guide to Health Care*, the authors coach readers on questions to ask their physicians and ways to avoid

medical mistakes.[17] Dr. Robert Arnot's book, *The Best Medicine*,[18] educates patients about specific procedures (eg, coronary artery bypass surgery, cesarean section, hysterectomy, and carotid endarterectomy). Potential complications of each of these procedures are described, and volumes, average lengths of stay, and complication rates of major hospitals are presented.

Health information on the Web has increased patients' desire for medical information and raised significant issues regarding patient safety and the manner in which patients approach their doctors for information.[19] A recent study revealed that many physicians believe that Web resources can distance patients from physicians and have an adverse effect on patient safety. Specifically, there is concern that patients can receive and believe misinformation, or read of treatments and procedures unfamiliar to physicians, and in both instances lower their trust in physician recommendations.[20] Other physicians see the Web as a positive development in patient safety because when patients approach their doctors prepared with questions, office visits run more smoothly, and the physician's counsel may be better received.[20]

Similar issues surround the topic of direct-to-consumer (DTC) marketing by pharmaceutical companies.[21] In 1997 the Food and Drug Administration relaxed restrictions on television and advertising for prescription medication. Drug companies responded with an explosion of marketing in all forms of media. DTC advertising may stimulate discussion between patients and their doctors about treatment options, but it also drives patients to demand newer and costlier medications, when less expensive treatments might be effective.[22] When doctors resist, 46% of patients try to persuade them to change the original recommendation and another 24% attempt to obtain the requested drugs from another physician.[22] These sort of interactions erode the physician-patient relationship and may jeopardize safety by promoting polypharmacy.

Practices to Improve Non-compliance

Compliance with medical advice is widely discussed in the literature and non-compliance with treatment may result in adverse drug events.[23] The frequency of non-compliance is higher than many health care professionals realize.[24] Non-compliance may arise from misunderstandings regarding instructions for drug use, self-care, or other factors. In addition, some of these misunderstandings may arise from remediable factors, such as language barriers[25] or low health literacy.[26,27] Simple solutions, such as using a trained interpreter instead of a family member or untrained volunteer, and providing self-care and other literature in multiple languages and bilingual versions may improve patient understanding. Other interventions, such as patient education publications, have been proposed to reduce adverse drug events due to non-compliance.[28]

Access to Medical Records

Although patient access to their own medical records is regulated in some states, these statutes differ across the United States.[29] Some states mandate certain levels of access for patients; others limit access or allow the provider to deem access appropriate or inappropriate. Other countries, such as Britain, have passed legislation requiring that providers allow patients to have complete access to their medical records.[30] Some argue that access to medical records may encourage patients to take a more active role in their own health care, allow patients to become better informed about their care, and increase rapport. Others argue that staff may modify medical records due to concerns about offending the patient, and will be diverted by the time needed to explain information contained in the records. Finally, still others express concern that patients may be unnecessarily worried by what they read.[30] No studies in the United States have

analyzed these competing views, and therefore it is not clear whether cultural norms reported in studies from other countries are applicable here, and whether allowing patients to review their own charts will have the intended effect of reducing errors.

Comment

With the growing level of consumerism in health care,[31] patients may wish to take a more active role in reducing their chance of experiencing a medical error. However, the research regarding the ways in which providers can facilitate this role for patients who desire it is lacking. More research is needed on the efficacy of these interventions regarding medical error reduction and on patients' willingness and ability to use them.

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PART IV. PROMOTING AND IMPLEMENTING SAFETY PRACTICES

Chapter 51. Practice Guidelines

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Background

Practice guidelines are among the most widely employed methods of modifying physician behavior. Defined as "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical conditions,"[1] guidelines may affect both the process and the outcome of care. Although guideline development and implementation have traditionally focused on ensuring a perceived standard of care, increasing emphasis has been placed on patient outcomes and patient safety. In this regard, thousands of guidelines have been promulgated on a great variety of clinical topics ranging from the prevention of falls in the elderly to the proper use of bone marrow transplantation.[2,3]

Practice Description

Guidelines vary greatly in terms of both method of development and format. Some consist of relatively straightforward statements that advocate a particular clinical practice, whereas others represent a series of complex algorithms that require the input of multiple clinical variables. Many guidelines are developed by specialty and advocacy organizations with attention paid to rigorously conducted systematic reviews.[4] Others may simply reflect a local standard of care.

Guidelines should only be considered a potential source of information and are effective at modifying physician behavior only when coupled with appropriate implementation strategies. Guidelines disseminated using a multifaceted approach that provides for peer influence and management support, for example, are more likely to be successful in influencing provider behavior than strategies that depend solely on the passive dissemination of printed materials.[5]

Prevalence and Severity of Target Safety Problem/Opportunities for Impact

Practice guidelines have the potential to greatly impact patient safety as they may facilitate widespread dissemination of practices that effectively reduce medical errors. It is well established in other medical fields that known tenets of effective health care are not practiced on a universal basis despite overwhelming evidence supporting their use. According to an audit of Medicaid charts in Connecticut, for example, only 50% of patients presenting with an acute myocardial infarction received aspirin and beta-blockers on the day of admission despite substantial evidence that these practices reduce mortality.[6] A second report estimated that 3500 infarctions would be averted and 4300 lives saved annually if beta-blockers were appropriately prescribed in patients with coronary artery disease.[7] Guidelines could help rectify similar shortcomings in the field of patient safety with corresponding reductions in medical errors.

Study Design

There are no well-designed studies that specifically evaluate the effect of practice guidelines on patient safety. However, research regarding their effectiveness in modifying physician behavior and improving patient outcomes is plentiful. The most comprehensive review evaluating general utility of guidelines involved an extensive search of MEDLINE and other electronic databases, the gray literature and the bibliographies of pertinent articles. Its analysis included 59 reports consisting of both controlled time series and before-after studies in addition to randomized trials.[8]

A second systematic review, limited to computer-based guidelines, reported the results of a search of several electronic databases (MEDLINE and CINAHL) complemented by a limited bibliography search. It included 25 studies detailing the use of 20 guideline systems. In this group, there were 10 time series studies (all without external controls) and 10 controlled trials, 9 of which were randomized.[9]

A final systematic review, limited to the primary care setting, also searched MEDLINE and several other electronic databases and included a limited bibliography search.[10] This review included only randomized trials that reported clinical outcomes associated with the treatment of patients with established diagnoses and identified 13 studies for inclusion. In keeping with these criteria, trials of the use of guidelines to promote preventive health care and proper diagnostic evaluations were excluded.

Several studies not represented in the above systematic reviews also provide valuable information on the effectiveness of practice guidelines. Two multicenter studies, for example, evaluated the impact of guidelines on the treatment of patients admitted for pneumonia and certain surgical procedures, respectively. Both of these were prospective before-after trials.[11,12] A prospective controlled trial of the implementation of a diabetes guideline using problem-based learning was also completed,[13] as were 2 randomized controlled trials of the local implementation of nationally developed guidelines.[14,15] Other recently completed works include an evaluation of a guideline for the outpatient treatment of cystitis with concurrent and historical controls, and a prospective before- after investigation of a guideline for the treatment of upper gastrointestinal hemorrhage.[16,17]

Study Outcomes

Very few of the reviewed studies report outcomes specifically linked to patient safety. Those that do (such as guidelines to prevent falls in the elderly (Chapter 26) and to promote hand washing (Chapter 12)) are of less than robust design.[2,18,23] A few of the studies included in the systematic reviews do report the effect of guidelines on surgical site infections and vaccination rates, but results are reported in terms of the process of care rather than the outcome of care. The systematic review from Worrall et al is an exception, as it only analyzed studies that reported direct clinical variables.[10] Among the other studies, however, the most commonly reported variables were length of stay, rates of provider adherence to guidelines, complication rates and the rates of the appropriate use of diagnostic testing.

Evidence for Effectiveness of Practice

Despite the inherent methodologic problems of many of the cited studies, there is substantial evidence that practice guidelines may be effective in influencing provider behavior and patient outcomes. In the seminal review from Grimshaw and Russell, 9 of 11 studies reporting clinical outcomes noted some degree of improvement while the process of care was found to improve in 55 of 59 studies.[8] This review did include several trials with marginal study design, but the authors argued for the inclusion of the time series and before-after studies on the premise that the magnitude of effect seen in many of the studies overwhelmed any potential bias that may have been attributable to study design. They additionally noted that the randomized trial may not represent the best method for evaluating practice guidelines.

The systematic review investigating the utility of computer-based guidelines is similarly encouraging.[9] Fourteen of 18 studies found guidelines increased provider adherence to the tenets of care promoted by the guidelines. Of the 8 studies that evaluated patient outcomes, 3 found improvements. These results mirror those of Grimshaw and Russell and reinforce the supposition that guidelines, at least in the studies completed to date, are more effective at influencing the process rather than the outcome of care.

The systematic review of controlled trials reporting clinical outcomes in the primary care setting is significantly less optimistic.[10] Only 5 of the 13 trials analyzed showed improvements in the defined clinical outcomes. None did so across all of the study groups or for an extended period of time. These results cast doubt on the utility of guidelines, particularly since this paper only included rigorously conducted trials reporting clinical outcomes, in contrast to the larger review by Grimshaw and Russell. However the authors correctly assert that many of these studies likely used guidelines that were not evidence-based and which may not have been sensitive enough to discern small improvements in clinical outcomes. In addition, it is likely that improvements in the process of care represents a reasonable surrogate endpoint for clinical outcomes given the size of the studies that would need to be conducted to show a beneficial outcomes effect of guidelines. To exclude all studies using this surrogate endpoint may be an extreme and unnecessary measure.

The studies of guidelines that have been published since the completion of the above systematic reviews are similarly conflicting. The multicenter study of the pneumonia guideline, for example, showed no effect on the length of stay or complication rates whereas the study of the postoperative surgical guidelines showed a significant decrease in the length of stay in 2 of the 3 groups.[11,12] Additionally, studies of the implementation of nationally developed guidelines yielded conflicting results, perhaps as a function of the implementation strategies used in each study. The study of the Agency for Healthcare Policy and Research (AHCPR, now the Agency for Healthcare Research and Quality, AHRQ) guideline for cessation of smoking in pregnant woman, which was a rigorously conducted randomized controlled trial, used extensive implementation strategies and showed a marked and statistically significant increase in the smoking cessation rate in the intervention group.[15] In contrast, the trial using continuous quality improvement measures and academic detailing to promote the AHCPR depression guideline showed little effect.[14] Yet several other studies, all of reasonable design and well-controlled, demonstrated improvements in the process of care[13,16,17] with one also reporting a marked clinical benefit in improving glycemic control in diabetics.[13]

Potential for Harm

It has been theorized that practice guidelines, if improperly developed or implemented, could actually be detrimental to the process of care or worsen clinical outcomes. A study of guidelines in the use of neurodiagnostic testing in patients with low back pain found the tests were more frequently utilized in an improper fashion than at baseline when clinicians were given a set of guidelines that were relatively narrow in focus.[19] Another study of patients treated for congestive heart failure found the guidelines actually increased the length of stay beyond that which was clinically necessary.[20] Although neither of these studies revealed worsened patient outcomes due to the guidelines, that potential certainly exists. In addition, the promulgation of guidelines with imprudent advice could also result in widespread harm to patients.

Costs and Implementation

Developing and implementing practice guidelines is expensive. When developed for a complex clinical problem by a national organization, for example, they consume tremendous resources, often tens of thousands of dollars.[21] In addition, some of the more successful implementation strategies, such as academic detailing (Chapter 54), also require a substantial measure of effort and financial outlay.

The manner in which practice guidelines are implemented is at least as important as the content of the guidelines themselves. Several systematic reviews have investigated both the strategies that are associated with successful institution of guidelines and the specific barriers to implementation.[5, 22, 23] These reviews concluded that the deterrents vary by practice location and that strategies to circumvent these barriers must be devised on an individual and local basis. In general, however, the number and intensity of the implementation strategies employed generally corresponds with the ultimate success of the guideline.

Comment

There is convincing but by no means overwhelming evidence that practice guidelines are effective in positively influencing the process and, to a lesser extent, the outcome of care. Many of the completed studies are plagued by methodologic shortcomings that reflect the difficulty inherent in studying the impact of guidelines. Although evidence specific to the use of guidelines in patient safety is scanty, they are likely to be as effective in this area as any other. It thus appears that well-constructed guidelines could play a significant role in ensuring patient safety and reducing medical errors. The effectiveness of guidelines, however, is dependent on many factors outside of their content. In particular, specific attention must be focused on utilizing appropriate implementation strategies if the full potential of guidelines is to be realized.

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Chapter 52. Critical Pathways

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Background

Burgeoning concerns regarding patient safety, variable health care quality and increasing health care costs have led to the introduction of clinical management tools that have their origins outside of the traditional health care sector. Primary among these innovations has been the implementation of critical pathways, administrative models that streamline work and production processes.[1] Critical pathways have been utilized extensively in several different business sectors including the construction and automotives industries.[2-4] It is theorized that the adaptation of pathways to health care, particularly inpatient care, may help ensure the delivery of quality care and decrease the occurrence of medical errors.

Practice Description

Although closely related to clinical practice guidelines (Chapter 51), pathways more directly target the specific process and sequence of care, frequently plotting out the expected course of an illness or procedure with associated prompts for appropriate interventions. Also known as clinical pathways and care maps, pathways are generally multidisciplinary by design and may incorporate the responsibilities of physicians and nurses with those of ancillary medical providers including pharmacists, physical therapists and social workers.[5] They are regularly intercalated into the point-of-care and may, in some cases, incorporate or even replace traditional chart documentation. In addition, pathways are often evidence-based and may even be integrated with locally or nationally developed clinical practice guidelines. Most pathways, however, are locally developed and are most frequently implemented at the level of the hospital or medical center as part of a cost-containment or quality assurance initiative.

Prevalence and Severity of the Problem/Opportunities for Impact

It is well established that the methods currently used to disseminate medical information are both cumbersome and inefficient. Even medical advances that are well entrenched in the literature and of unquestionable value are not routinely or universally implemented. A study of patients treated for myocardial infarction in Connecticut, for example, revealed only 50% of patients received the most basic beneficial treatments (aspirin and beta-blockers) at the time of admission.[6] A second report suggested that 3500 myocardial infarctions would be averted and 4300 lives would be saved annually if all eligible patients with coronary artery disease were prescribed beta-blockers.[7] Critical pathways, if able to beneficially alter health care provider performance and ensure that effective patient safety strategies were practiced on a widespread basis, could be powerful agents in the prevention of medical errors, in addition to any beneficial impact they might have on overall health care quality.

Study Design

There is a dearth of well-designed studies analyzing the extent to which critical pathways change physician behavior and patient outcomes. Even fewer relate specifically to the topic of patient safety. There are no systematic reviews of pathways and most of the published work describes the non-randomized implementation of pathways in which it is often difficult to differentiate effects of the pathway from secular trends. The vast majority of these studies describe the implementation of a pathway for a specific surgical procedure and use historical controls with a retrospective before-after study design.[8-19]

Four randomized controlled trials investigated the impact of the implementation of pathways.[20-23] There are also several studies with non-randomized concurrent controls with enrollment in the intervention arms being completed at the request of the attending physician.[24,25] The latter group of studies also included historical control groups. There is one prospective before-after trial in which the control group actually shifted to receive the intervention after a washout period.[26] Finally one study used historical controls and concurrent controls from other hospitals in the region.[27] Table 52.1 describes the salient features of these papers.

Study Outcomes

The great majority of the cited studies reported at least one clinical outcome (Level 1) with the most commonly reported variable being diagnosis-related complications. Very few of the studies reported more definitive endpoints, such as mortality. Most of the included studies reported surrogate clinical end-points (Level 2) as the major study outcome variables, usually length of stay and re-admission rates. The relative utilization of certain interventions including medications, laboratory tests and radiology studies was also commonly reported. In addition, most of the studies also included an analysis of the changes in costs associated with instituting the pathway. Some of the studied pathways did include other recommendations for interventions germane to the field of patient safety, including the use of indwelling urinary catheters (Chapter 15) and prophylactic preoperative antibiotics (Chapter 20.1), but these outcomes were rarely reported.

Evidence for Effectiveness of the Practice

Several of the randomized controlled trials provide at least some evidence that critical pathways can be effective in influencing health care provider behavior. One study evaluated the effectiveness of a pathway for the treatment of asthma in children admitted to a non-ICU hospital setting.[22] Those patients treated under the pathway, when compared to the control group undergoing "usual care," had a shorter length of stay as well as decreased hospital charges and medication usage, but no change in complication rates. Although the results are somewhat promising, the study was likely skewed by a significant Hawthorne effect, as patients treated under the pathway were placed on a separate clinical ward than those undergoing usual care (although the same physicians cared for both groups of patients). This study found no impact on the rate of complications, which provides little encouragement regarding the ability of pathways to reduce medical errors and enhance patient safety.

A second randomized trial investigated the utility of a pathway for the treatment of patients undergoing knee and hip replacement at an academic medical center in Australia.[21] Implementation of the pathway was followed by significant decreases in the length of stay and shorter times to patient mobilization and ambulation. More importantly, it showed a decrease in the incidence of medical complications, including readmission rates (although this change did

not reach statistical significance). The study, although fairly small at 163 total patients, represents some of the most convincing evidence that pathways may be effective in decreasing complications.

A third randomized trial, performed by the same Australian group, evaluated the effect of a pathway for the treatment of patients with hip fracture.[20] Implementation of this pathway, which provided recommendations regarding medications, laboratory and radiology testing and discharge planning, resulted in a significantly shorter lengths of stay without any concomitant change in complication rates. The study was rigorously conducted and complication rates were meticulously documented, but no information regarding the effort needed from clinicians to comply with the pathway was presented.

A final trial used cluster randomization to investigate the effectiveness of a critical pathway for the treatment of community-acquired pneumonia in 19 Canadian hospitals.[23] The pathway, which was initiated upon presentation of the patient to the emergency department, included recommendations for the use of a specific antibiotic and provided a clinical prediction tool to aid in decisions regarding hospital admission. Following admission, a study nurse also regularly placed guideline-based recommendations in the chart regarding changing to oral antibiotic therapy and discharge planning. The pathway showed impressive results in terms of cost containment, with a shorter length of stay and a smaller percentage of inappropriate admissions. However, there were no significant changes in the clinical parameters measured, including mortality and complication rates. In addition, it is difficult to dissect the effect of the pathway from that of the other elements of the multifaceted intervention.

The second strata of studies were less encouraging. A prospective before-after evaluation of the implementation of a pathway for the administration of supplemental oxygen for hospitalized patients showed the pathway was associated with markedly elevated costs without any significant clinical benefit.[26] This study, which used an intensive 3-tiered strategy including an oxygen order form, the posting of the pathway in patient rooms and a research nurse providing immediate audit and feedback, doubled the cost of providing supplemental oxygen. Although it did change some of the physician prescription practices, this alteration in practice resulted in no appreciable clinical effect.

At least 2 other studies compared an intervention group with a non-randomized concurrent control group (thus introducing the possibility of selection bias) as well as to historical controls. In a study evaluating the impact of a critical pathway on the treatment of patients undergoing neck dissection, the length of stay and total costs were significantly lower for the pathway group when compared with those of the historical controls. However, the differences disappeared when the concurrent control group was used.[25] In the other, a study of a pathway for the treatment of asthma exacerbations, the pathway resulted in improvements in resource utilization that were significant compared to both historical and concurrent controls.[24] However no changes were noted between the groups in readmission rates or medical outcomes.

Finally, there are a great number of observational before-after studies of pathways, the vast majority of which relate to specific surgical procedures.[8-19] Few of these studies account for secular trends and their capacity for judging the effectiveness of critical pathways is limited, at best. In addition, a recent evaluation of pathways for patients undergoing a variety of surgical procedures compared the intervention group to both historical controls and to patients from similar hospitals in the same region in an attempt to correct for such secular trends. Although implementation of the pathways resulted in significant decreases in length of stay when compared to the historical controls, these differences disappeared when the pathway groups were compared to the concurrent control groups from the other hospitals.[27] An additional study of the

effect of a pathway on the treatment of acute myocardial infarction demonstrated that the improvements seen in the intervention group were likely secondary to secular trends and not an independent effect of the pathway.[6] These powerful results cast a great deal of doubt over those studies that demonstrated effectiveness of the pathways in comparison to historical controls alone.

Potential for Harm

There are theoretical concerns that pathways may result in adverse patient outcomes as a result of shortened length of stay and a dependence on "cookbook medicine," although there is little support for this in the literature.

Costs and Implementation

Although many studies report cost savings associated with instituting pathways, very few detail the costs of developing and implementing them. One report attempted to put a dollar figure on the development of a pathway for the treatment of patients undergoing knee replacement surgery; however the reported estimate ($21,000) did not account for the time staff physicians spent on the project.[14] The expense of developing critical pathways in terms of physician time commitment and actual financial outlay is unknown. In addition, most pathways are developed on the local level and require a great deal of initiative and expertise on the part of the hospital or medical center. Whether most centers have access to these resources is unclear.

Physicians and other providers are also not universally welcoming of critical pathways. They are considered intrusive by some providers and evidence of "cookbook medicine" by others. The developers of pathways must be careful to allow for clinical judgment and flexibility in the pathways or they are likely to be ignored or applied too rigidly.

Comment

There is conflicting evidence regarding the efficacy of critical pathways as a method to modify health care provider behavior and a means of implementing patient safety initiatives. Although a few studies suggest they may impact physician practice and, to a lesser extent, complication rates and other clinical outcomes, the data are inconsistent and more studies are needed. Additionally it is unclear whether the costly development and implementation of pathways represents an appropriate use of limited health care resources. Finally, there is very little information on the application of pathways to patient safety.

Table 52.1. Key features of studies of critical pathways

Study Setting	Design, Outcomes	Clinical Outcomes (p value)	Non-Clinical Outcomes (p value)
Children with an asthma exacerbation admitted to an academic medical center: patients randomized to pathway group or usual care group[22]	Level 1, Level 1	Shorter duration of intensive nebulizer treatment (0.02), length of stay (0.01)	Lower room charges (0.001) and therapy charges (0.001)
Patients undergoing hip or knee replacement surgery at an academic medical center in Australia: patients randomized to pathway group or usual care group[21]	Level 1, Level 1	Shorter length of stay (0.011) and time to mobilization (0.001) and ambulation (0.02)	
Patients being treated for hip fracture at an academic medical center in Australia[20]	Level 1, Level 2	Shorter length of stay (0.03)	
Patients presenting to the emergency department with pneumonia at 19 medical centers across Canada: hospitals were randomized to pathway group or usual care group[23]	Level 1, Level 1	Lower rates of bed-days per patient (0.04), shorter length of stay (0.01) and shorter duration of IV therapy (0.01)	
Patients in need of supplemental oxygen therapy: prospective before-after analysis with washout period[26]	Level 2, Level 1	More frequent appropriate oxygen discontinuation orders (0.001)	Increased costs (0.02)
Patients undergoing unilateral neck dissection at an academic medical center: pathway group compared to historical controls and non-randomized concurrent controls[25]	Level 2, Level 1	Length of stay decreased compared to historical controls (0.001) but not concurrent controls	Total costs decreased compared to historical controls (0.001) but not concurrent controls
Patients admitted to a community teaching hospital for the treatment of an asthma exacerbation: pathway group compared to historical controls and non-randomized concurrent controls[24]	Level 2, Level 1	More appropriate antibiotic use and conversion to nebulizer treatment (0.002 for historical controls, 0.05 for concurrent controls)	
Patients undergoing one of several defined surgical procedures over a seven year period at an academic medical center: pathway group compared to historical controls as well as to patients from other similar hospitals in the same region[27]	Level 2, Level 2	Decreased lengths of stay for the pathway group compared to the historical controls, but not compared to the concurrent control group	

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Chapter 53. Clinical Decision Support Systems

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Background

Integrating medical knowledge and advances into the clinical setting is often difficult due to the complexity of the involved algorithms and protocols. Clinical decision support systems (CDSS) assist the clinician in applying new information to patient care through the analysis of patient-specific clinical variables.[1] Many of these systems are used to enhance diagnostic efforts and include computer-based programs such as Dxplain™ that provide extensive differential diagnoses based on clinical information entered by the clinician.[2] Other forms of clinical decision support systems, including antibiotic management programs and anticoagulation dosing calculators, seek to prevent medical errors and improve patient safety.[3-5]

Practice Description

Clinical decision support systems vary greatly in their complexity, function and application.[1] These clinical tools differ from practice guidelines (Chapter 51) and critical pathways (Chapter 52) in that they require the input of patient-specific clinical variables and as a result provide patient-specific recommendations. Guidelines and pathways, in contrast, may not require the input of such information and provide more general suggestions for care and treatment. Although many clinical decision support systems are now computer-based, some are relatively simple, with no inherently complex internal logic systems. Among the most common forms of support systems are drug-dosing calculators, computer-based programs that calculate appropriate doses of medications after clinicians input key data (eg, patient weight, indication for drug, serum creatinine). These calculators are especially useful in managing the administration of medications with a narrow therapeutic index (see Chapter 9). More complex systems include computerized diagnostic tools that, although labor intensive and requiring extensive patient-specific data entry, may be useful as an adjunctive measure when a patient presents with a confusing constellation of symptoms and an unclear diagnosis. Other systems, both simple and complex, may be integrated into the point-of-care and provide accessible reminders to clinicians regarding appropriate management based on previously entered data. These systems may be most practical when coupled with computerized physician order entry and electronic medical records (see Chapter 6). Finally, through their integration with practice guidelines and critical pathways, decision support systems may provide clinicians with suggestions for appropriate care, thus decreasing the likelihood of medical errors. For example, a guideline for the management of community-acquired pneumonia may include a clinical tool that, after the input of patient-specific data, would provide a recommendation regarding the appropriateness of inpatient or outpatient therapy.[6]

Prevalence and Severity of the Target Safety Problem/Opportunities for Impact

A great variety of patient safety issues may be affected by clinical decision support systems. Since the systems are typically intercalated at the point-of-care, they are likely to have their greatest effect on problems related to the individual patient. Some of the best studied applications of decision support systems are those that seek to prevent adverse drug reactions and inappropriate drug dosing as well as those that facilitate the appropriate use of effective prophylactic measures, such as those for venous thromboembolic disease (see Chapter 31).[4,5] Decision support systems may also help ensure a minimum standard for quality of care as part of the implementation of practice guidelines by providing patient-specific recommendations after the input of certain clinical variables. This combination of decision support systems and guidelines may be especially effective in conjunction with the use of the electronic medical record.[7] To date no high quality studies have examined the impact of widespread institution of decision support, but local studies suggest that it may be substantial. An evaluation of an antibiotic management system in a single 12-bed Intensive Care Unit over a 3 year period revealed that use of the system resulted in 24 fewer adverse drug reactions and 194 fewer cases of antibiotic-susceptibility mismatch.[4] These results and others suggest that national implementation of decision support systems could markedly improve patient safety.

Study Design

The functionality and effectiveness of clinical decision support systems has been evaluated in a number of systematic reviews. The seminal review, last updated in 1998, investigated the use of computer-based systems in all clinical settings.[3] The authors completed an exhaustive search of electronic databases and the bibliographies of pertinent articles and found 68 prospective trials on the subject. The vast majority of these studies (90%) were randomized trials. The articles were rated on a 10-point scale for quality. The scale assessed the design features of the trials, including method of randomization, baseline comparability of the study groups, allocation unit, outcome measures, and degree of follow-up. The mean score on this validity scale was 6.4 for studies published prior to 1992 and 7.7 for subsequent studies.

Another systematic review evaluated the use of computer-based decision aids in the provision of outpatient preventive care.[8] This study, which was based on a search of electronic databases including MEDLINE, found 16 trials that met the pre-defined inclusion criteria. Only randomized controlled studies were included. Those that used only historical controls were excluded. The acceptable studies were then evaluated using weighted mixed effects model regression analysis.

Yet another systematic review investigated the utility of computer systems in the primary care setting.[9] A detailed search of several electronic databases and a hand search of bibliographies and conference proceedings yielded 30 studies that met criteria for inclusion. These papers were ranked by the same validity score utilized in the systematic review of computer-based decision supports systems described above. The average validity score of the included trials was 6.7 on the 1-10 scale.

Most relevant to patient safety *per se* is a fourth systematic review of the utility of computers in medication dosing.[10] This review, which located studies in the Cochrane Collaboration on Effective Clinical Practice, was also based on an extensive search of electronic databases, supplemented by a bibliography search and consultation with experts. Of 16 relevant studies, all but one were randomized controlled clinical trials. Time series studies were not included. The included trials were then evaluated using a random effects model.

A final systematic review analyzed the utility of computers in the implementation of practice guidelines which, in such a setting, may be considered clinical decision support systems.[11] A structured search of MEDLINE, CINAHL, bibliographies and books found 25 papers detailing the use of 20 such systems. In this group, there were 10 time series studies (all without external controls) and 10 controlled trials, 9 of which were randomized.

Two well-designed studies have been published since the above systematic reviews. One is a cluster randomized trial of the use of a decision support system in the treatment of patients with hypertension.[12] The second is a prospective time series investigation of a decision support system for the prevention of thromboembolic disease in post-surgical patients.[4]

Study Outcomes

Most of the reviewed studies reported results in terms of patient outcomes and provider performance. The most common clinical outcomes (Level 2) included the relative adherence to specific recommendations and the degree to which prospectively described tenets of "appropriate practice" were followed. Examples of such principles included whether clinicians followed medication dosage recommendations and delivered appropriate preventive health care measures. Several studies reported even more definitive clinical data (Level 1) including the degree of blood pressure reduction, the incidence of adverse drug reactions, the control of postoperative pain and percentage of patients with therapeutic drug blood levels.

Evidence for Effectiveness of Practice

The majority of the systematic reviews portray clinical decision support systems in a positive light. The seminal systematic review of computer-based decision support systems, for example, found that 43 of the 65 investigated studies showed at least some benefit in either the process of care or patient outcomes.[3] Most impressively, 74% of the studies of preventive health care reminder systems and 60% of the evaluations of drug dosing models reported a positive impact. In addition, 6 of the 14 studies that reported actual patient outcomes reported a beneficial effect. However only one of the five diagnostic aids, a model used to predict postoperative pulmonary complications, showed encouraging results. The others, including systems designed to aid diagnostic efforts in patients with chest and abdominal pain, were ineffective. This review was rigorously conducted and only those papers with robust study design were included. Overall it provides compelling evidence for the effectiveness of specific decision support systems.

These results are supported by the review of systems to aid the delivery of preventive health care.[8] By applying weighted mixed effects model regression analysis to the 16 identified studies, the authors found decision support systems resulted in significantly improved rates of delivery of preventive health care (OR 1.77, 95% CI: 1.38-2.27). Computer systems, however, were not statistically superior to manual reminder systems. Although this study reviewed many of the same papers that were evaluated in the reviews discussed above, it provides further evidence of the utility of these systems in improving the process of care.

The review of clinical decision support systems in the outpatient setting provided similarly encouraging results.[9] All of the 21 studies that examined processes of care found improvements. Results were somewhat less impressive in the articles reporting more definitive clinical outcomes including level of blood pressure reduction and patient satisfaction. Only one of three such studies found significant benefit.

The systematic review of the use of computer models to determine drug doses provides some of the most compelling evidence for application of decision support systems to patient safety and error avoidance efforts.[10] Seven of the 11 studies showed a beneficial effect on drug

dosing, and more significantly, 4 of 6 showed a decrease in adverse drug effects. Five of six also reported direct positive effects on the patient, including one that reported improved control of postoperative pain. Since the majority of the analyzed studies were randomized controlled trials, this review provides powerful evidence that decision support systems may prevent medical errors and other adverse events. A more recent study of an antibiotic management program also supports this contention.[5] In this prospective before-after trial, the use of the decision support system resulted in a substantial and significant decrease in the incidence of adverse drug reactions ($p=0.018$) and prescriptions for medications contraindicated by allergy ($p<0.01$). The system was also popular among the health care providers, cut costs and saved time (see also Chapter 6).

Finally, clinical decision aids were useful in implementing practice guidelines. The systematic review of this subject found favorable effects on guideline adherence in 14 of the 18 papers studied.[11]

The impact of decision support systems on the outcomes of care for discrete disorders has also been studied. These results are mixed. For example, the recent randomized controlled trial of a computer-based system in the treatment of patients with hypertension failed to show any benefit, and the system was actually out-performed by a paper-based system.[12] These findings corroborated those of a systematic review that questioned the utility of CDSS for treating hypertension.[13]

In summary, clinical decision support systems may provide significant benefits in the process of care, preventing medical errors and prompting physicians to provide appropriate preventive care measures. Their utility in guiding the treatment of individual clinical disorders (such as hypertension) remains a matter of study.

Potential for Harm

Most studies show no major adverse effects from the use of CDSSs. Although one study demonstrated that they may increase a physician's consultation time (thus decreasing the time spent on direct patient care),[14] others suggest that they may improve efficiency, especially in terms of data recall.[5] The usefulness and efficiency of such systems is clearly dependent on the programmed logic. As such they must be with developed with extremely high quality control standards. A system that provides erroneous information and guidance, for example, has the potential to cause broad deleterious impact.

Costs and Implementation

Very few studies specifically address the cost of developing and implementing decision support systems. We posit that the costs may be substantial as the majority of systems are now computer-based and require significant hardware, most commonly placed at the point-of-care. In addition, many of the successful systems were integrated with computerized medical record systems and physician order entry (Chapter 6), which are not yet in universal use. The development and frequent updating of system software is also likely to be very expensive. Despite these concerns, the widespread implementation of successful systems is feasible and will likely become even more so as providers and systems increasingly shift to computerized medical record systems.

Comment

The preponderance of evidence suggests that clinical decision support systems are at least somewhat effective. Their highest utility has been demonstrated in the prevention of medical errors, especially when coupled with a computerized medical record and directly intercalated into the care process. Unlike more passive methods such as education and feedback, decision support systems are generally able to modify physician behavior and affect the process of care. Although the results of support systems have been far less positive when used in the ongoing care of patients with chronic diseases or to help with diagnostic decision making, these capabilities may improve with further technological advances.

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Chapter 54. Educational Techniques Used in Changing Provider Behavior

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Background

A number of techniques have been used to modify the behavior of practicing physicians.[1] Continuing medical education, practice guidelines and critical pathways represent a major thrust of these efforts. The relative effectiveness of each is largely dependent on the particular strategy employed in their implementation.[2] Traditionally these strategies have focused on lectures and printed materials but other techniques have also been utilized, including audit and feedback, academic detailing, local opinion leaders and reminder systems. In addition, some have championed the use of sentinel event reporting and root cause analysis in graduate medical education programs.[3] Only recently have these various techniques been critically evaluated for their effectiveness at changing physician behavior.

This chapter reviews the evidence regarding the utility of educational-oriented techniques to improve provider behavior, particularly as they do or might pertain to patient safety practices. Incident reporting (Chapter 4), root cause analysis (Chapter 5), guidelines (Chapter 51), pathways (Chapter 52), and decision support systems (Chapter 53) are reviewed elsewhere in the Report.

Practice Description

The passive dissemination of information through the use of lectures, conferences, mailings and printed materials remains the primary method to alter physician behavior. This primacy has not been substantially challenged in practice, although more interactive techniques have increasingly been utilized. *Academic detailing*, for example, involves the process of having invested and well-informed agents for change interacting with individual physicians to promote certain tenets of practice. Alternatively, *audit and feedback* entails the review and return to the clinician of their own process of care and patient outcomes (often compared with local or national benchmarks or evidence-based standards) in the hopes it will result in more appropriate medical care.[3] *Reminder systems*, which may be computerized and embedded in the electronic medical record, prompt physicians to provide certain health care measures. They differ from *clinical decision support systems* (Chapter 53) in that they may not provide information tailored to the specific patient. Finally, *opinion leaders*, usually respected local physicians, may improve health care by championing "best practices" on a regional basis.[4, 5]

Prevalence and Severity of Target Safety Problem/Opportunities for Impact

It is well established that physicians are unable to keep abreast of the staggering volume of published medical literature. This is reflected by the many studies that demonstrate the glacial pace at which many beneficial advances are incorporated into medical practice. Practice guidelines, clinical decision support systems and programs for physician education are potential solutions to this problem, but their effectiveness is greatly dependent on the methods used in their implementation.[2] Despite the presence of comprehensive guidelines on the treatment of reactive airways disease, for example, a substantial percentage of asthmatic patients do not

receive appropriate care.[6, 7] Physician education techniques that reliably impact practice patterns may yield substantial improvements in patient care and safety.

Study Designs

The Cochrane Group completed a series of systematic reviews of physician education based on the Research and Development Base in Continuing Medical Education, a central database compiled from an extensive search of electronic databases and bibliographies and supplemented by contact with experts in the field. Although the initial review was completed in 1997, reviews are regularly updated as more pertinent data are published. One such study evaluated the role of audit and feedback and found 37 randomized controlled studies comparing this technique to non-interventional control groups.[3] An ancillary study by the Cochrane Group compared audit and feedback with other educational strategies and located 12 randomized controlled studies for analysis.[10] A second study of the effectiveness of audit and feedback was completed by a separate group that searched MEDLINE and selected bibliographies for trials investigating the strategy's utility in improving immunization rates. Fifteen studies were identified for inclusion, 5 of which were randomized controlled studies with 6 interrupted time series evaluations and 4 before-after trials.[11] A third meta-analysis of peer-comparison feedback systems used an extensive electronic database and bibliography search to locate 12 randomized controlled studies.[12]

The Cochrane Group also investigated the utility of academic detailing and found 18 randomized controlled studies.[13] A similar evaluation of local opinion leaders yielded 8 randomized controlled trials.[5]

A separate Cochrane review was completed on the utility of printed educational materials using the Cochrane Effective Practice and Organization of Care Group database. The search of this database, which was compiled in the same manner as the Research and Development Base in Continuing Medical Education, found 10 randomized controlled trials and one interrupted time series study fulfilling criteria for analysis.[14]

Study Outcomes

Few of the studies report outcomes specific to the field of patient safety. The vast majority are concerned with process of care rather than the outcomes of care. Although clinical outcomes are reported in at least one of the studies evaluated in each of the systematic reviews (with one exception), the majority relate outcomes pertaining to physician performance. Some of the more commonly described variables include the rates of appropriate provision of preventive care measures and of adherence to appropriate treatment or diagnostic protocols.

Evidence for Effectiveness of Practice

Much of the evidence for the effectiveness of educational and implementation techniques is of fair quality and the results are generally consistent across the various systematic reviews. However, methodologic concerns prevented the completion of quantitative data synthesis in the majority of the reviews. The studies are summarized in Table 54.1.

The initial comprehensive review found overall beneficial effect for 62% of interventions. In investigations of effect on patient outcomes, 48% had favorable results. Academic detailing and the use of local opinion leaders were the most effective techniques evaluated. Physician reminder systems were also effective, as 22 of the 26 evaluated studies revealed some benefit. The technique of audit and feedback was of marginal effectiveness and conferences and printed materials were found to be relatively ineffective. Of note, multifaceted

interventions with at least 3 components were associated with a 71% success rate.[8] The second comprehensive review of 102 randomized controlled studies supported these conclusions. Yet it emphasized that the degree of effect with even the most consistently effective techniques was moderate at best, and that the process of care rather than the outcome of care was the most readily influenced variable.[9]

The Cochrane reviews reported similar results. Audit and feedback was found to be effective in 62% of the studies in which it was compared with non-interventional controls, but the effect was typically small. The results were not substantially different when audit and feedback was augmented by conferences or educational materials or was part of a multifaceted intervention.[3] In the review of comparative trials, however, this technique was found to be inferior to reminder systems in 2 of the 3 trials where a direct comparison was made.[10] The second review of audit and feedback, which focused on improving immunization rates, found beneficial results in 4 of 5 randomized controlled trials evaluated. Statistically significant changes were present in at least 2 of these evaluations. However, the marginal effect was small and likely was overwhelmed by the relatively high cost of the intervention.[11] Finally the meta-analysis of the 12 randomized controlled trials investigating peer-comparison feedback systems did establish a modest benefit for the use of audit and feedback ($p<0.05$), but the magnitude of benefit was again noted to be small.[12]

The Cochrane review of academic detailing was somewhat more optimistic. All of the evaluated studies showed some degree of a beneficial effect on physician performance although only one of these studies reported patient outcomes. Most combined detailing with other techniques and there was insufficient evidence to make direct comparisons between detailing and the other techniques.[13]

The use of local opinion leaders was also found to be effective by the Cochrane group, although to a much less convincing degree than academic detailing. Two of 7 trials showed a statistically significant beneficial effect with a trend toward effectiveness in all 7 studies. One of 3 trials investigating patient outcomes demonstrated a significant benefit.[5]

Finally, the Cochrane review of the use of printed educational materials supported the findings of the previous overviews. None of the 9 studies showed a statistically significant effect when compared with controls and only one of 6 trials that included printed materials in a multifaceted approach demonstrated benefit. Of note, all of the evaluated trials were plagued by methodologic shortcomings.[14]

Potential for Harm

These educational techniques are unlikely to cause significant patient harm.

Costs and Implementation

Although the cost-effectiveness of the various educational techniques has not been explicitly studied, it is clear that several may require substantial outlay in terms of financial resources and personnel. It also appears that the forms of education that are most effective, including academic detailing and local opinion leaders, are also the most expensive to design and support. Programs of printed materials and lectures, although dramatically less effective, are substantially less expensive to implement. It is unclear whether the integration of Internet technology and computer-based education initiatives will result in substantial changes in efficacy or cost. Finally, the relative cost-effectiveness of the various techniques remains unclear.

Comment

From studies of randomized controlled trials, it appears that academic detailing and local opinion leaders are frequently associated with at least some benefit. Reminder systems are also effective in specific situations and the utility of audit and feedback has been established, although unimpressively. Traditional programs of conferences, lectures and printed materials are ineffective at inducing changes in physician behavior. None of the current techniques, however, have demonstrated a consistent ability to induce substantial and durable changes in physician behavior. The relative cost-effectiveness of the various techniques is uncertain; it remains unclear if the added cost of the more effective strategies (ie, academic detailing and local opinion leaders) is justified given their relatively small marginal increase in effectiveness. Finally there are few data regarding the specific utility of these techniques in increasing patient safety and/or the prevention of medical errors. However, techniques effective in other areas of medicine are likely to be equally effective in inducing practices changes to improve patient safety.

Table 54.1. Studies of techniques for changing physician behavior*

Study Setting	Study Design	Results
Review of 99 trials assessing the effect of educational techniques on physician performance in all clinical settings[8]	Level 1A	62% of the interventions were associated with beneficial results; academic detailing, local opinion leaders and reminder systems were the most effective while audit and feedback was less so; traditional CME programs were ineffective
Review of 102 trials assessing the effect of educational techniques on physician performance in all clinical settings[9]	Level 1A	Academic detailing and local opinion leaders were the most effective techniques; audit and feedback and reminder systems were less effective; multifaceted approaches were effective, especially at influencing the process of care
Review of 37 randomized controlled trials of the utility of audit and feedback in all clinical settings in the US, Europe and Australia[3]	Level 1A	Eight of 13 studies showed a moderate beneficial effect with audit and feedback with little change noted when other interventions were added or a multifaceted approach was used
Review of 12 trials comparing the effect of audit and feedback with other educational techniques on 2194 physicians in all clinical settings[10]	Level 1A	Two of 3 trials showed reminder systems outperformed audit and feedback; 4 studies demonstrated little benefit to adding other modalities to audit and feedback
Review of fifteen studies, of which five were randomized controlled trials, investigating the use of audit and feedback in improving immunization rates in adults and children in the outpatient setting in the US and the UK[11]	Level 1A	Twelve of the 15 studies showed a benefit with audit and feedback and of the 5 RCTs, 4 showed a beneficial trend that was significant in at least 2 of the trials
Review of 18 trials investigating the effects of academic detailing on 1896 physicians in the US, Canada, Europe, Indonesia and Australia[13]	Level 1A	All of the evaluated studies showed some degree of benefit although only one looked specifically at patient outcomes
Review of 8 randomized controlled trials investigating the effect of local opinion leaders on 296 physicians in the US, Canada and Hong Kong[5]	Level 1A	Six of the 7 studies evaluating effects on physician performance showed a beneficial effect with 2 of these being statistically significant; one of the 3 trials evaluating patient outcomes showed a significantly positive effect
Review of eleven studies evaluating the effect of printed education materials on over 1848 physicians in a variety of clinical settings[14]	Level 1A	None of the studies reported significantly improved outcomes with the use of printed educational materials

* CME indicates continuing medical education; RCT, randomized controlled trial.

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Chapter 55. Legislation, Accreditation, and Market-Driven and Other Approaches to Improving Patient Safety

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Background

Although conventional approaches to health care quality improvement based on educating providers and offering feedback have been proposed, the tremendous public and professional concerns raised by the Institute of Medicine's report on medical errors[1] have led to an unusual amount of interest in regulatory and legislative efforts to improve safety. Given the traditional American dependence on education, competition, and other non-coercive mechanisms of change, the shift toward a regulatory approach is evidence of the depth of concern this issue has engendered. As these regulatory and legislative approaches are considered, it is also worthwhile to consider the role of health care payers, hospital accreditation organizations, and professional societies, all of whom have also led safety initiatives.[2-4] This chapter considers the potential advantages and disadvantages of legislative, regulatory, professional society, and market-oriented approaches to implementing patient safety efforts, and reviews the evidence regarding their effectiveness.

Government Legislation and Regulation

The concept of patient safety has been championed by several prominent legislators in both major political parties and has become the topic of a great deal of national debate. Proposals to date include the establishment of voluntary and mandatory error reporting systems, the publication of outcomes data, and the development of several Health Care Financing Administration (HCFA) programs to prevent medical errors.[5] In addition, in 2000 the Agency for Healthcare Research and Quality (AHRQ) established a Center for Quality Improvement and Patient Safety, whose mandate in part is to fund research and demonstration projects in patient safety. Though most of these Federal efforts are in the formative stages,[6] successful Federal agency and regulatory efforts outside of medicine, most notably in workplace safety and commercial airline travel, may herald medicine's success. In these fields, the Occupational Safety and Health Administration (OSHA) and the Federal Aviation Administration (FAA) are credited with catalyzing significant improvements in safety over the past 30 years.[7, 8]

Despite a paucity of data regarding the effect of State legislation on medical errors and patient safety, there is some evidence regarding the effectiveness of State regulatory efforts to improve health care quality.[9-11] Among the most prominent set of regulations are the New York State enactments as a result of the death of Libby Zion.

The daughter of a prominent reporter, Ms. Zion died soon after being admitted to the medical service of a New York City hospital. A detailed investigation of the circumstances of her death subsequently raised concerns regarding working conditions and the supervision of resident physicians. The Bell Commission, formed at the behest of the New York State Health Commissioner, later recommended major reform in these areas and several regulations were enacted mandating dramatic changes in working conditions and supervisory oversight.[12]

These regulations markedly altered resident physician education in New York State. Although they anecdotally resulted in an improvement in resident morale and quality of life,[13]

their effect on patient safety is less certain. One retrospective cohort study demonstrated that patients treated after the work-hour limitations were instituted were more likely to suffer from complications and delays in the performance of diagnostic tests.[11] A second retrospective analysis of patient transfer-of-care, a bi-product of restricting resident work-hours, showed increased lengths of stay and utilization of laboratory testing for patients that were "handed off."[10] A third study, however, revealed exactly contradictory results. It found the work-hours limitations led to shorter lengths of stay and fewer medication errors.[9] These studies have been criticized for concentrating on the work-hour regulations when the main finding of the Bell Commission was that increased supervision of resident physicians was a more important initiative.[14] (See Chapter 46 for a more complete discussion of fatigue and work hours).

Although regulations to improve patient safety might be a more efficient way of changing practice than less coercive methods such as education or feedback, the use of government regulation in the assurance of patient safety has limitations. A primary concern is that regulations may be crafted by legislators who lack intimate knowledge of the health care system. In addition, health care in the United States is extremely heterogeneous - what may be feasible and appropriate in one setting may be inapplicable in another. The differences between the delivery of care in urban and rural settings may be particularly troublesome in this regard. Finally, it is unclear whether government agencies would provide adequate funding to assist health care organizations to comply with new regulations. For example, a cash-starved institution faced with a resident work-hours mandate might need to decrease nurse staffing or defer purchase of a computerized order entry system to meet the mandate.

Government agencies may also influence patient safety practices through means other than direct legislation. For example, the National Nosocomial Infections Surveillance (NNIS) system may serve as a template for the development of a government-sponsored safety program. Established and administered by the Centers for Disease Control and Prevention (CDC), the NNIS is a voluntary nationwide consortium of 300 hospitals that regularly report the incidence of specified nosocomial infections.[15] Through analysis of the aggregate data, benchmarks are set for the expected rates of nosocomial infection that hospitals may then strive to meet or better. There is some evidence that the NNIS has contributed to a substantial decline in the rate of nosocomial infections over the past several decades.[16] It is conceivable that a similar program could be established for broader patient safety issues. Although voluntary and lacking enforcement power, NNIS-like patient safety benchmarking could significantly improve safety, especially if the data were made available to the public or accreditation agencies.

Infection control officers, another aspect of the CDC-championed infection control movement, may also be applicable to the patient safety movement. Presently, infection control officers employed by medical centers focus on improving the system and changing practices to decrease the institutional rates of serious infections. An institutional "patient safety officer" might assume an analogous function with regard to decreasing adverse events and errors. The establishment of a patient safety officer or committee is one of the new Joint Commission on Accreditation of Healthcare Organization's (JCAHO) safety standards (discussed below). To date, there are no data regarding the effectiveness of these practices in patient safety.

Accreditation Organizations

Accreditation organizations represent another sector of the health care industry that is assuming new responsibilities in the field of patient safety. JCAHO, an outgrowth of accreditation programs initiated by the American College of Surgeons several decades ago, is the best known of these organizations. JCAHO conducts meticulous inspections of medical centers,

hospitals and other health care institutions on a triennial basis. Survey results are subsequently used in the process of obtaining Medicare certification and State licensure and to obtain bond ratings and managed care contracts. Although such inspections had previously included some elements relating to the field of patient safety (including infection control and the prevention of medication errors), they tended to focus on organizational topics including information management, institutional leadership and strategic planning.[17] In response to concerns regarding patient safety, however, JCAHO has recently launched a major patient safety initiative and implemented an entirely new set of standards in July 2001.[18]

The new JCAHO standards place a much greater emphasis on the prevention of medical errors and the process of responding to medical errors once they occur. A particular focus of the new initiative is the development of organization-specific patient safety programs. Such programs, which will undoubtedly require substantial resources to implement, are expected to have well-defined leadership, to proactively determine areas where errors are likely to occur, and to be capable of effecting significant organizational change when necessary. The key elements of these standards are listed in Table 55.1.

Although there is no published evidence that the patient safety standards previously required by JCAHO have reduced medical errors, it seems reasonable to assume they have had some salutary effect.[6] Because JCAHO reports are now publicly available and are used by a wide variety of credentialing agencies and health care purchaser organizations, many hospitals and other medical institutions will make serious and concerted efforts to meet the new standards. Although lacking the enforcement power of Federal regulations, the agencies' knowledge of, and contacts within the medical community may produce change more efficiently. Moreover, the process of accreditation involves frequent site visits between the agencies and health care organizations. These visits, in turn, may allow for interactions between institutions and accreditors which, under ideal circumstances, could allow for user input in to modifications of regulations. How often this ideal is realized is not known, and some observers have questioned JCAHO's overall effectiveness.[19-21]

Health Care Purchaser Initiatives

The business community has also reacted to the perceived crisis of safety in health care. The most prominent example is the Leapfrog Group.[3] Sponsored by a consortium of major corporate chief executive officers known as the Business Roundtable, the Leapfrog Group's stated commitment is "to mobilize employer purchasing power to initiate breakthrough improvements in the safety of health care for Americans."[22] Large volume purchasers of health care, including Aetna, ATT, IBM and many other Fortune 500 companies, have joined the group. Combined, their annual health care outlay is over $45 billion. Using their considerable financial influence, the group hopes to impact medical care by requiring or incentivizing health care providers to adhere to certain standards for the process and delivery of care.[22]

Thus far the Leapfrog consortium has chosen to promote 3 patient safety practices: the use of computerized physician order entry (Chapter 6), the involvement of critical care physicians in the care of intensive care unit patients (Chapter 38), and the use of evidence-based hospital referral systems (Chapter 18).[23] The latter practice refers to the referral of patients to hospitals with the highest volume and best outcome figures for certain elective medical procedures and treatments. These initiatives were selected because there is substantial evidence that they enhance quality of care and their implementation is both feasible and easily assessed. Initial research sponsored by the group suggests that implementing just these 3 strategies could prevent almost 60,000 deaths per year and avoid over 500,000 errors in medication

administration.[24, 25] It is anticipated that other quality-related practices (some directed at patient safety targets) will be added to the list as evidence for their effectiveness is accumulated.

The Leapfrog Group has also begun to outline a program to improve compliance with the target practices. Plans include rewarding complying providers with an increased number of patients, increasing remuneration for specific services, and providing public recognition. General quality will be assessed and publicized through the use of rankings, including those assigned by JCAHO and other accreditation organizations.[23] In addition, the employees of participating companies will be encouraged to become more active in choosing providers that meet the Leapfrog standards.

Although the Leapfrog initiative is in its nascent stages and there is presently no objective evidence that it will favorably impact patient safety, the sheer financial clout of the involved corporations may catalyze rapid and meaningful change. As with government regulation, it is unclear which sector of the health care industry will bear the brunt of the implementation costs. The institution of computerized order entry systems, for example, will require substantial financial outlays (several million dollars in hardware, software and training for the average hospital; see Chapter 6) that hospitals and medical groups may find extremely difficult to absorb without assistance. Additionally, physicians and other health care providers may resist changes forced upon them from outside medicine, or may "game the system" to create the appearance of change simply to meet the standards.[26] Finally, purchaser initiatives may create disparities in the level of patient safety among socioeconomic groups if the changes they promote are only required of health care institutions that provide care to insured members of the group.

Other Approaches

Professional Societies

Some of the earliest efforts to improve patient safety were actually directed by medical professional societies rather than outside regulators, accreditors, or legislative bodies. The American Society of Anesthesiologists (ASA), for example, formed the Anesthesia Patient Safety Foundation in 1984 and has since promulgated a number of reforms that have substantially changed the routine practice of anesthesia. Safety measures such as continuous electrocardiographic monitoring, pulse oximetry and preoperative evaluation were strongly championed by these organizations through the dissemination of quality standards and newsletters.[1] While no evidence directly links these initiatives to improved patient safety, there is little doubt that these reforms resulted in substantial advances. In fact, the standards of care promoted by the ASA have been widely adopted and now represent the recognized minimum level of appropriate care.[4] It is nonetheless difficult to separate the effects of these standards from secular trends associated with technological and clinical advances.

Although medical professional societies do not possess the regulatory might of the Federal government or the financial power of large health care purchasers, their standing in the medical community and collective clinical experience are great advantages. It is well established that physicians are more apt to follow practice guidelines sponsored by respected medical societies than those issued by the government or industry.[27] Society-based programs are also likely to allow for more provider input and may be more amenable to frequent modification. Unfortunately, because they lack the power to compel, society recommendations cannot be the sole agent of change, especially when the evidence supporting a practice is extremely strong and the stakes are high. It is important to recognize that society recommendations carry a potential

for bias, particularly when the recommended changes may have an economic impact on society members.

Publication of Performance Data

Each of the large entities described above (legislatures, accrediting bodies, purchasers, payers, and professional societies) may choose to disseminate performance data to the public as part of its quality improvement strategy. To date, most such report cards have focused on discrete quality outcomes for single diseases or procedures (eg, mortality after coronary angioplasty) rather than patient safety targets such as error or nosocomial infection rates. Nonetheless, implicit in the vigorous debate regarding mandatory error reporting systems is the question of whether public reporting of performance data is effective in either motivating provider change or facilitating informed choices by patients.

Marshall and colleagues recently reviewed the evidence regarding the impact of public reporting systems.[28] They found that such systems had a relatively small impact on patients (the potential users of the data), but a greater impact on the hospitals (the sources of the data). They posit that the impact is growing as the public becomes increasingly comfortable with both the concept and interpretation of quality reports. Although some have claimed that public reporting systems, such as New York State's Cardiac Surgery Data System (which has reported risk-adjusted coronary bypass outcomes since 1990), have led to major improvements in quality,[29] this remains controversial.[30] Proponents point to New York's falling bypass mortality rate as evidence of the value of public reporting, but there is some evidence that the fall in the rate was due to outmigration of high-risk patients to other states rather than true quality improvement.[31]

Comment

Concerns about medical errors have spurred many organizations and institutions to launch major patient safety initiatives. Perhaps because they represent a relatively recent development or because empirical measurement of such macro-changes is difficult (isolating the effects of individual interventions vs. other confounding influences), there is little objective evidence either to determine if they will result in meaningful change or to consider their relative advantages and disadvantages (Table 55.2). Yet Federal and State governments, accreditation agencies such as JCAHO, and health care purchasers such as the Leapfrog Coalition, in combination and independently, may eventually be highly effective champions of patient safety initiatives. In addition, professional medical societies, given their influential role in the medical community, are effective agents of change in certain circumstances. The work and involvement of these diverse, powerful organizations and institutions may prove to be valuable adjuncts to the more traditional mechanisms of change represented by practice guidelines, continuing medical education programs, and decision support systems.

Table 55.1. New JCAHO safety standards

-Development of a leadership individual or group to devise and implement a comprehensive patient safety program
-Development of a proactive error prevention program that includes means of identifying potentially high risk areas
-Development of systems for the reporting of errors
-Development of an error-response system including protocols for root cause analysis
-Requirement for an annual report discussing errors, the response to errors and the programs initiated to prevent future errors
-Requirement for hospital leaders to set “measurable objectives” for patient safety programs
-Requirement for educational initiatives for employees, stressing the concept of patient safety

Table 55.2. A comparison of non-local methods to promote patient safety practices

Approach	Example	Advantages	Disadvantages
Legislation	"Libby Zion" laws limiting resident work hours	-potential for widespread implementation -supported by government enforcement ability	-inflexible -limited acceptance by health care providers -potential to be developed with inadequate input from providers and experts -may be politically driven with limited applicability -may not provide for costs of implementation, leading to cost-shifting away from other beneficial patient safety practices
Accreditation	JCAHO patient safety standards	-may be more flexible and more easily modified than legislation -implemented at the level of the health care organization -health care providers may have the opportunity for input	-dependent on voluntary participation in the accreditation process -limited enforcement ability -generally assessed only every few years
Market-based	The Leapfrog Group	-uses the power of the market to induce change (may be more acceptable for many providers than regulatory solutions) -may involve carrot (eg, higher payments for better practices or outcomes) rather than stick alone to achieve impact	-potential to cause disparity in care among groups not covered by initiatives -limited acceptance by health care providers -potential for standards to develop with inadequate input from health care providers -change is not required, and therefore implementation may be limited
Professional Societies	Anesthesia Patient Safety Foundation	-readily accepted by health care providers -developed by providers themselves, leading to better "buy in" -more easily modified when new evidence or changes in practice emerge	-minimal enforcement potential; depends largely on voluntary participation by practitioners -potential for bias by professional societies

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PART V. ANALYZING THE PRACTICES

Chapter 56. Methodology for Summarizing the Evidence for the Practices

Background

The Agency for Healthcare Research and Quality (AHRQ) charged the UCSF-Stanford Evidence-based Practice Center with the task of rating or grading the patient safety practices identified and evaluated in this Report. The Report is an anthology of diverse and extensive patient safety practices, grouped by general topic (Part III, Sections A-H), and then further sorted within chapters by individual practices. Synthesis was challenging, but critical in order that readers and health care decision-makers could make judgments about practices to implement and/or research further. Keeping these two audiences in mind, we set 3 goals for "rating" the practices, as follows:

- Develop a framework for rating the main elements of practices within the constraints of the available literature, providing as much pragmatic information as possible to decision-makers who might endorse practices or fund further research in the area of patient safety interventions;
- Document the limitations of the rating method so that those "taking home" messages from the report understand the inherent limitations of making comparisons of a highly heterogeneous field of possible practices; and
- Convey the results of the ratings in an organized, visually appealing, accessible way that ensures that our cautionary notes regarding oversimplifying the ratings are clear.

Ultimately, we aimed to weight the practices, based on the evidence, on a range of dimensions, without implying any ability to calibrate a finely gradated scale for those practices in between. Proper metrics for these comparisons (eg, cost-effectiveness analysis) require more data than are currently available in the literature.

Data Inputs into the Practice Ratings

For each practice, information about various inputs into the final "roll-up", as we referred to our scoring of the practices, were prospectively determined. The decision about what information to attempt to gather was based on the potential expected uses of summary tables of practices. Three major categories of information were gathered to inform the rating exercise:

- *Potential Impact of the Practice*: based on prevalence and severity of the patient safety target, and current utilization of the practice
- *Strength of the Evidence Supporting the Practice*: including an assessment of the relative weight of the evidence, effect size, and need for vigilance to reduce any potential negative collateral effects of practice implementation
- *Implementation*: considering costs, logistical barriers, and policy issues

Further clarification of the 3 categories is in order. Authors were asked to report on *prevalence and severity of the safety target* for a given practice in order to categorize the potential impact of implementing the practice. We added to this an assessment of the practice's potential impact by reviewing evidence of its *current utilization.* If an intervention is already widely used, the room for improvement, stated in terms of additional reductions in adverse events targeted by the practice that could be achieved by wider implementation, is less than if few are currently using the practice. Thus, *potential impact of implementing the practice* is a

function of the prevalence and severity of the patient safety target (eg, medical error) and the current utilization of the practice.

Of course the actual impact of any practice is assessable only if factors related to *evidence supporting the practice* are evaluated. Since the Report represents an assemblage of the evidence for patient safety practices, the instructions to authors outlined the detailed data elements related to study design and outcomes we required them to abstract from the relevant studies (see Chapter 3). This information was used to assess, in general terms, the *overall strength of the studies* for each practice. *Effectiveness* is commonly defined as the net positive effect in routine practice. Frequently the data reported in the studies related to *efficacy*, usually the net positive effect under controlled, experimental situations. The translation from efficacy to effectiveness is not straightforward if no direct evidence is available, and is therefore based on judgments about the generalizibility of the specific research studies conducted. Also of key importance, and therefore abstracted from studies for use in the ratings, was the *effect size of the intervention*.

Finally, evidence-based reviews consider the *potential for harm* from a medical intervention, and authors were asked to report on any relevant evidence, as well as reasoned concerns, gleaned from the literature or from common knowledge about a practice.

To address the real-world environment and the desire by the public for action in the area of patient safety, practice chapters were designed to include information about cost and other potential barriers to *implementation*. While authors sometimes discussed cost savings or reported cost-effectiveness analyses, the focus was on the *start-up costs and annual outlays* for ongoing use of the practice. Although initial and ongoing costs are a function of local environments (eg, size of the health care network or institution), possible cost savings are likely to be even more subject to local conditions (eg, prevalence of the patient safety target). For major investment decisions, an assessment of tradeoffs is more appropriate at the local level. Our intention was simply to report "ballpark" estimates of initial and recurring costs. Separate from economic consequence of a particular practice implementation are the *political and technical considerations*.

For all of these data inputs into the practice ratings, the primary goal was to find the best available evidence from publications and other sources. Because the literature has not been previously organized with concurrent considerations of each of these areas, most estimates could be improved with further research and some are informed by only general and somewhat speculative knowledge. Where possible, in the summaries of these elements, we have attempted to highlight assessments made on the basis of limited data.

Rating Process

The 4-person Editorial Team developed a rating form that captured the patient safety target, practice description, and general rating categories (eg, High, Medium, Low) for some of the elements described in the section above. General heuristics were specified for each category, although individual judgment for ratings was designed into the process. The form also specified comment areas to allow raters to document their specific judgments and concerns about ratings. Each chapter was independently rated by each Editor as to the practices for which there was evidence. The Editorial Team convened for 3 days to compare scores, discuss disparities, and come to consensus about ratings–both by category and summary ratings–or the reviewed practices.

Details about Decision Rules and Judgment Considerations

Potential Impact Factor

As noted above, an assessment of potential impact considered the prevalence and severity of the patient safety target, and the current utilization of the practice being evaluated. The Editorial Team used the data from the chapters and clinical knowledge to order the potential impact as "High," "Medium," "Low," or "Insufficient Information." To qualify for the "High" score, a practice had to target a patient population of greater than 1% of hospitalized patients (about 300,000 patients per year) or target a patient safety problem that can result in death or disability. The "Low" score was used for target populations of less than 0.01% of hospitalized patients (about 3000 patient/year) who might experience reversible adverse effects if an effective practice were not available. Potential impact was deemed a "Medium" if the practice had a patient safety target that fell between the 2 other categories.

An additional decision rule was applied to the Impact rating after the initial assessment based on prevalence and severity was made. If a practice was currently widely used (>75% of hospitals), then the rating was demoted one notch (ie, from High to Medium or Medium to Low). When this situation occurred, a notation identified that the potential impact level was impacted by its high current utilization.

We reserved the "Insufficient Information" category for those cases where the prevalence and severity information was quite limited or where the patient safety target was ill-defined.

Evidence Supporting the Practice

Study strength, effect size on target(s), and need for vigilance due to potential harms were rated based more on judgment than pre-specified decision rules. In each case, raters documented their reasons for category choices.

For *study strength*, the level of study design and outcomes (see Chapter 3 for hierarchies), number of studies, numbers of patients in studies, generalizability, and other methodologic issues were specified as factors to consider in weighting the relative study strength for a particular practice. Study strength could be categorized as "High," "Medium," or "Low." The actual findings of the studies were not considered when scoring study strength because this information was captured in the assessment of effect size on target. If there was minimal or no evidence about a practice, the study strength rating was "Low" and raters did not score the remaining 2 elements of the evidence supporting the practice since that might give undue "credit" to the findings.

The assessment of *effect size on target(s)* was based on the relative risk reductions or odds ratios reported in the reviewed studies for evidence of effectiveness. The raters only used the findings reported in the practice chapters, and did not perform additional analyses (eg, meta-analysis). If all studies or, in cases where there were a large number of studies, the vast majority showed a positive and appreciable effect size (ie, greater than 15% relative risk reduction), then the positive effect size was categorized as "Robust." If there was clearly no effect or a very minimal effect (ie, less than 5% relative risk reduction), then the positive effect size was rated as "Negligible." For findings that were considered suggestive of substantive effect, but not clearly "Robust," the category used was "Modest." The final category, "Unclear," captured those practices for which the effect size results were inconsistent.

For any given practice that reduces one adverse event, it is conceivable that new problems might ensue when the practice is implemented. Thus, we subjectively rated the

concern for harm based on the *level of vigilance* necessary to ensure that the practice, if implemented, would not result in collateral negative effects. The categories available were "Low," "Medium," and "High." Thus, a practice rated as "Low" would require little to no attentiveness to potential harms, while one rated as "High" would merit heightened monitoring for potential negative effects. These ratings were made conservatively, meaning that when in doubt, a higher vigilance category was selected.

Implementation

Assuming a 3-year lead time for implementation, patient safety practices were rated for their costs and complexity. *Costs* were based on initial start-up and annual expenditures for full implementation at an average size hospital or health care organization. Potential cost savings were not considered for the rating, but were reported in the practice chapters if they were documented in the literature. If a practice was expected to require expenditures of greater than about $1 million, the rating was "High." Expenditures of approximately $100,000-$1 million were categorized as "Medium." Below this level, practices were rated as "Low" in terms of cost.

The feasibility of implementation was rated by considering potential political (eg, major shifts in who delivers care) and technical (eg, integration of legacy and newer computer systems) obstacles. Because relatively few data exist for rating implementation complexity, we used only 2 categories, "Low" and "High," meaning relatively easy and relatively difficult. In cases in which implementation could be accomplished simply with the expenditure of dollars, we gave high cost scores but low feasibility scores.

Overall Rating for Impact/Evidence

In addition, each member of the team considered the totality of information on potential impact and evidence supporting the practice to score each on a 0 to 10 scale ("Strength of the Evidence"). For these ratings, we took the perspective of a leader of a large health care enterprise (eg, a hospital or integrated delivery system) and asked the question, "If you wanted to improve patient safety at your institution over the next 3 years and resources were not a significant consideration, how would you grade this practice?" For this rating, we explicitly did *not* consider difficulty or cost of implementation in the rating. Rather, the rating simply reflected the strength of the evidence regarding the effectiveness of the practice and the probable impact of its implementation on reducing adverse events related to health care exposure. If the patient safety target was rated as "High" impact and there was compelling evidence (ie, "High" relative study strength) that a particular practice could significantly reduce (eg, "Robust" effect size) the negative consequences (eg, hospital-acquired infections), raters were likely to score the practice close to 10. If the studies were less convincing, the effect size was less robust, or there was a need for a "Medium" or "High" degree of vigilance because of potential harms, then the rating would be lower.

Overall Rating for Research Priority

Analogously, we also rated the usefulness of conducting more research on each practice, emphasizing whether there appeared to be questions that a research program might have a reasonable chance of addressing successfully ("Research Priority"). Here, our "thought question" was, "If you were the leader of a large agency or foundation committed to improving patient safety, and were considering allocating funds to promote additional research, how would you grade this practice?" If there was a simple gap in the evidence that could be addressed by a research study or if the practice was multifaceted and implementation could be eased by

determining the specific elements that were effective, then the research priority was high. If the area was one of high potential impact (ie, large number of patients at risk for morbid or mortal adverse events) and a practice had been inadequately researched, then it also would also receive a relatively high rating for research need. Practices might receive low research scores if they held little promise (eg, relatively few patients affected by the safety problem addressed by the practice *or* a significant body of knowledge already demonstrating the practice's lack of utility). Conversely, a practice that was clearly effective, low cost and easy to implement would not require further research and would also receive low research scores.

Caveats to Ratings

For all elements assessed, divergent assessments among the 4 Editor-raters were infrequent and were discussed until consensus was reached. For each final category where differences in interpretation existed and persisted after discussion, the protocol was to document a comment about these differences (see Chapter 59). Comments were also noted when specific additional information could clarify concerns about fidelity of a specific rating. In a few cases, categories that had not been specified were created for unusual circumstances and again comments to explain the category were documented.

Rating Tables

Information Captured

Ratings were recorded on a data table, and comments were footnoted. Summarizing from the previous discussion, the various data tables appearing in Chapters 57-59 captured some or all of the following 11 elements and rating categories, ordered from strongest to weakest:

1. Chapter number
2. Patient safety target(s)
3. Patient safety practice description
4. Potential Impact: High, Medium, Low, Insufficient Information
5. Study Strength: High, Medium, Low
6. Effect Size: Robust, Modest, Negligible, Unclear
7. Vigilance: Low, Medium, High
8. Implementation cost: Low, Medium, High
9. Implementation complexity (political, technical): Low, High
10. Overall rating for impact/evidence: 0 to 10 (10 is highest), in 0.5 increments
11. Overall rating for research need: 0 to 10 (10 is highest), in 0.5 increments

Information Reported

Chapter 59 presents the detailed data tables with categorization of elements 1-9 above. Reporting specific scores for the overall ratings would imply a refinement in scoring that was neither attempted nor advisable given the nature of the information available. Where applicable, caveats to the categorizations are appended in a series of endnotes.

In rating both the strength of the evidence and the research priority, our purpose was not to report precise 1-10 scores, but *to develop general "zones" or practice groupings*. As noted earlier, better methods are available for comparative ratings *when the data inputs are available*. The relative paucity of the evidence dissuaded us from using a more precise, sophisticated, but ultimately unfeasible, approach.

Chapter 57 summarizes the overall ratings for the “Strength of the Evidence" regarding their impact and effectiveness score, and subdivides the practices into 5 zones. Practices are listed from highest score to lowest score for each rating zone. The zones are “greatest strength” (score of 8-10), “high strength” (score of 6-7.5), “medium strength” (4-5.5), “lower impact/evidence scored practices” (score of 2-3.5), “lowest impact/evidence scored practices” (score of 0-1.5). Practices near the bottom of one zone may be just as appropriate to list near the top of the adjacent lower zone. Similarly, practices at the top of a zone may actually be more comparable to those in the adjacent higher zone. The cut-offs between zones are somewhat artificial, but allow a general and reasonable synthesis of the data on impact and evidence supporting (or negating) the effects of the practice. Readers can be confident that practices that fall in the highest zone do not belong in the lowest zone.

Chapter 58 summarizes the overall ratings for the “Research Priority” score, and provides examples of types of research that may be helpful. Practices are categorized in 3 zones: “Further Research Likely to be *Highly* Beneficial” (scores of 7 and higher), “Further Research Likely to be Beneficial” (scores of 4 to 6.5 inclusive), and “Low Priority for Research” (below 4). The chapter lists practices for each of the top two categories of research priority.

Chapter 57. Practices Rated by Strength of Evidence

After rating practices on a metric for potential impact, and on the strength of the evidence, we grouped them into 5 categories (Tables 57.1-57.5). These categorizations reflect the current state of the evidence. If a practice that addresses a highly prevalent or severe patient safety target receives a low rating on the impact/evidence scale, it may be because the strength of the evidence base is still weak due to lack of evaluations. As a result the practice is likely to show up at a high level on the research priority scale. However, if the practice has been studied rigorously, and there is clear evidence that its effectiveness is negligible, it is rated at the low ends of both the "strength of the evidence" (on impact/effectiveness) scale and the "research priority" scale.

For each practice listed in Tables 57.1 through 57.5, a designation for the cost and complexity of implementation of the practice is included. The ratings for implementation are "Low," which corresponds to low cost and low complexity (eg, political, technical); "Medium," which signifies low to medium cost and high complexity, *or* medium to high cost and low complexity; and "High," which reflects medium to high cost and high complexity.

Several practices are not included in the tables because they were not rated. This set of practices have long histories of use outside of medicine, but have not yet received enough evaluations for their potential health care applications:

- Promoting a Culture of Safety (Chapter 40)
- Use of Human Factors Principles in Evaluation of Medical Devices (Subchapter 41.1)
- Refining Performance of Medical Device Alarms (eg, balancing sensitivity and specificity of alarms, ergonomic design) (Subchapter 41.2)
- Fixed Shifts or Forward Shift Rotations (Chapter 46)
- Napping Strategies (Chapter 46)

Table 57.1. Patient Safety Practices with the Greatest Strength of Evidence Regarding their Impact and Effectiveness

Chapter	Patient Safety Target	Patient Safety Practice	Implementation Cost/Complex
31	Venous thromboembolism (VTE)	Appropriate VTE prophylaxis	Low
25	Perioperative cardiac events in patients undergoing noncardiac surgery	Use of perioperative beta-blockers	Low
16.1	Central venous catheter-related bloodstream infections	Use of maximum sterile barriers during catheter insertion	Low
20.1	Surgical site infections	Appropriate use of antibiotic prophylaxis	Low
48	Missed, incomplete or not fully comprehended informed consent	Asking that patients recall and restate what they have been told during informed consent	Low
17.2	Ventilator-associated pneumonia	Continuous aspiration of subglottic secretions (CASS)	Medium
27	Pressure ulcers	Use of pressure relieving bedding materials	Medium
21	Morbidity due to central venous catheter insertion	Use of real-time ultrasound guidance during central line insertion	High
9	Adverse events related to chronic anticoagulation with warfarin	Patient self management using home monitoring devices	High
33	Morbidity and mortality in post-surgical and critically ill patients	Various nutritional strategies	Medium
16.2	Central venous catheter-related bloodstream infections	Antibiotic-impregnated catheters	Low

Table 57.2 Patient Safety Practices with High Strength of Evidence Regarding their Impact and Effectiveness

Chapter	Patient Safety Target	Patient Safety Practice	Implementation Cost/Complex
18	Mortality associated with surgical procedures	Localizing specific surgeries and procedures to high volume centers	High (varies)
17.1	Ventilator-associated pneumonia	Semi-recumbent positioning	Low
26.5	Falls and fall injuries	Use of hip protectors	Low
8	Adverse drug events (ADEs) related to targeted classes (analgesics, KCl, antibiotics, heparin) (focus on detection)	Use of computer monitoring for potential ADEs	Medium
20.3	Surgical site infections	Use of supplemental perioperative oxygen	Low
39	Morbidity and mortality	Changes in nursing staffing	Medium
48	Missed or incomplete or not fully comprehended informed consent	Use of video or audio stimuli	Low
17.3	Ventilator-associated pneumonia	Selective decontamination of digestive tract	Low
38	Morbidity and mortality in ICU patients	Change in ICU structure—active management by intensivist	High
42.1	Adverse events related to discontinuities in care	Information transfer between inpatient and outpatient pharmacy	Medium
15.1	Hospital-acquired urinary tract infection	Use of silver alloy-coated catheters	Low
28	Hospital-related delirium	Multi-component delirium prevention program	Medium
30	Hospital-acquired complications (functional decline, mortality)	Geriatric evaluation and management unit	High
37.4	Inadequate postoperative pain management	Non-pharmacologic interventions (eg, relaxation, distraction)	Low

Table 57.3 Patient Safety Practices with Medium Strength of Evidence Regarding their Impact and Effectiveness

Chapter	Patient Safety Target	Patient Safety Practice	Implementation Cost/Complex
6	Medication errors and adverse drug events (ADEs) primarily related to ordering process	Computerized physician order entry (CPOE) and clinical decision support (CDSS)	High
42.4	Failures to communicate significant abnormal results (eg, pap smears)	Protocols for notification of test results to patients	Low
47	Adverse events due to transportation of critically ill patients between health care facilities	Specialized teams for interhospital transport	Medium
7	Medication errors and adverse drug events (ADEs) related to ordering and monitoring	Clinical pharmacist consultation services	Medium
13	Serious nosocomial infections (eg, vancomycin-resistant enterococcus, *C. difficile*)	Barrier precautions (via gowns & gloves; dedicated equipment; dedicated personnel)	Medium
20.4	Surgical site infections	Perioperative glucose control	Medium
34	Stress-related gastrointestinal bleeding	H_2 antagonists	Low
36	Pneumococcal pneumonia	Methods to increase pneumococcal vaccination rate	Low
37.2	Inadequate pain relief	Acute pain service	Medium
9	Adverse events related to anticoagulation	Anticoagulation services and clinics for coumadin	Medium
14	Hospital-acquired infections due to antibiotic-resistant organisms	Limitations placed on antibiotic use	Low
15.2	Hospital-acquired urinary tract infection	Use of suprapubic catheters	High
32	Contrast-induced renal failure	Hydration protocols with acetylcysteine	Low
35	Clinically significant misread radiographs and CT scans by non-radiologists	Education interventions and continuous quality improvement strategies	Low
48	Missed or incomplete or not fully comprehended informed consent	Provision of written informed consent information	Low
49	Failure to honor patient preferences for end-of-life care	Computer-generated reminders to discuss advanced directives	Medium (Varies)
9	Adverse events related to anticoagulation	Protocols for high-risk drugs: nomograms for heparin	Low

17.1	Ventilator-associated pneumonia	Continuous oscillation	Medium
20.2	Surgical site infections	Maintenance of perioperative normothermia	Low
26.2	Restraint-related injury; Falls	Interventions to reduce the use of physical restraints safely	Medium
26.3	Falls	Use of bed alarms	Medium
32	Contrast-induced renal failure	Use of low osmolar contrast media	Medium

Table 57.4 Patient Safety Practices with Lower Impact and/or Strength of Evidence

Chapter	Patient Safety Target	Patient Safety Practice	Implementation Cost/Complex
16.3	Central venous catheter-related bloodstream infections	Cleaning site (povidone-iodine to chlorhexidine)	Low
16.4	Central venous catheter-related bloodstream infections	Use of heparin	Low
16.4	Central venous catheter-related bloodstream infections	Tunneling short-term central venous catheters	Medium
29	Hospital-acquired complications (eg, falls, delirium, functional decline, mortality)	Geriatric consultation services	High
37.1	Inadequate pain relief in patients with abdominal pain in hospital patients	Use of analgesics in the patient with acute abdomen without compromising diagnostic accuracy	Low
45	Adverse events due to provider inexperience or unfamiliarity with certain procedures and situations	Simulator-based training	Medium
11	Adverse drug events (ADEs) in drug dispensing and/or administration	Use of automated medication dispensing devices	Medium
12	Hospital-acquired infections	Improve handwashing compliance (via education/behavior change; sink technology and placement; washing substance)	Low
49	Failure to honor patient preferences for end-of-life care	Use of physician order form for life-sustaining treatment (POLST)	Low
43.1	Adverse events due to patient misidentification	Use of bar coding	Medium (Varies)
10	Adverse drug events (ADEs) in dispensing medications	Unit-dosing distribution system	Low
24	Critical events in anesthesia	Intraoperative monitoring of vital signs and oxygenation	Low
42.2	Adverse events during cross-coverage	Standardized, structured sign-outs for physicians	Low
44	Adverse events related to team performance issues	Applications of aviation-style crew resource management (eg, Anesthesia Crisis Management; MedTeams)	High
46	Adverse events related to fatigue in health care workers	Limiting individual provider's hours of service	High

57.5 Patient Safety Practices with Lowest Impact and/or Strength of Evidence

Chapter	Patient Safety Target	Patient Safety Practice	Implementation Cost/Complex
23	Complications due to anesthesia equipment failures	Use of pre-anesthesia checklists	Low
42.3	Adverse events related to information loss at discharge	Use of structured discharge summaries	Low
22	Surgical items left inside patients	Counting sharps, instruments and sponges	Low
17.4	Ventilator-associated pneumonia	Use of sucralfate	Low
26.4	Falls and fall-related injuries	Use of special flooring material in patient care areas	Medium
43.2	Performance of invasive diagnostic or therapeutic procedure on wrong body part	“Sign your site” protocols	Medium
26.1	Falls	Use of identification bracelets	Low
32	Contrast-induced renal failure	Hydration protocols with theophylline	Low
47	Adverse events due to transportation of critically ill patients within a hospital	Mechanical rather than manual ventilation during transport	Low
16.4	Central venous catheter-related bloodstream infections	Changing catheters routinely	High
16.4	Central venous catheter-related bloodstream infections	Routine antibiotic prophylaxis	Medium

Chapter 58. Practices Rated by Research Priority

Further research on a number of practices would clarify a range of questions (eg, whether the practice is effective, what aspects of a multi-faceted intervention matter the most, how best to implement the practice). The conceptual framework for this categorization is described in Chapter 56. In Table 58.1 and 58.2, the practices are grouped in zones: "research likely to be highly beneficial," and "research likely to be beneficial." We also list, in the far-right column, the practices' categorization for "Strength of the Evidence" (as detailed above in Tables 57.1-57.5). For presentation in this table, this category is simplified into a 1 ("highest strength of evidence") to 5 ("lowest strength of evidence") which corresponds exactly to the groupings in Tables 57.1-5. We list these here to allow the reader to compare and contrast the research priority rankings with the evidence rankings. Practices that are not listed in either Table 58.1 or 58.2 may benefit from more research, but were not scored as highly as those included in these 2 lists.

Table 58.1 Further Research Likely to be Highly Beneficial

Chapter	Patient Safety Target	Patient Safety Practice	Strength of the Evidence (1-5 Scale; 1 is highest)
20.4	Surgical site infections	Perioperative glucose control	3
18	Mortality associated with surgical procedures	Localizing specific surgeries and procedures to high volume centers	2
20.3	Surgical site infections	Use of supplemental perioperative oxygen	2
39	Morbidity and mortality	Changes in nursing staffing	2
15.1	Hospital-acquired urinary tract infection	Use of silver alloy-coated catheters	2
6	Medication errors and adverse drug events (ADEs) primarily related to ordering process	Computerized physician order entry (CPOE) with clinical decision support (CDSS)	3
14	Hospital-acquired infections due to antibiotic-resistant organisms	Limitations placed on antibiotic use	3
20.1	Surgical site infections	Appropriate use of antibiotic prophylaxis	1
31	Venous thromboembolism (VTE)	Appropriate VTE prophylaxis	1
33	Morbidity and mortality in post-surgical and critically ill patients	Various nutritional strategies (especially early enteral nutrition in critically ill and post-surgical patients)	1
37.1	Inadequate pain relief in patients with abdominal pain in hospital patients	Use of analgesics in the patient with acute abdomen without compromising diagnostic accuracy	4

12	Hospital-acquired infections	Improve handwashing compliance (via education/behavior change; sink technology and placement; washing substance)	4
9	Adverse events related to chronic anticoagulation with warfarin	Patient self-management using home monitoring devices	1
21	Morbidity due to central venous catheter insertion	Use of real-time ultrasound guidance during central line insertion	1
38	Morbidity and mortality in ICU patients	Change in ICU structure—active management by intensivist	2
32	Contrast-induced renal failure	Hydration protocols with acetylcysteine	3
43.1	Adverse events due to patient misidentification	Use of bar coding	4
27	Pressure ulcers	Use of pressure relieving bedding materials	1
20.2	Surgical site infections	Maintenance of perioperative normothermia	3
25	Perioperative cardiac events in patients undergoing noncardiac surgery	Use of perioperative beta-blockers	1
48	Missed or incomplete or not fully comprehended informed consent	Use of video or audio stimuli	2
28	Hospital-related delirium	Multi-component delirium prevention program	2
7	Medication errors and adverse drug events (ADEs) related to ordering and monitoring	Clinical pharmacist consultation services	3
13	Serious nosocomial infections (eg, vancomycin-resistant enterococcus, *C. difficile*)	Barrier precautions (via gowns & gloves; dedicated equipment; dedicated personnel)	3
9	Adverse events related to anticoagulation	Anticoagulation services and clinics for coumadin	3
48	Missed, incomplete or not fully comprehended informed consent	Provision of written informed consent information	3
49	Failure to honor patient preferences for end-of-life care	Computer-generated reminders to discuss advanced directives	3

9	Adverse events related to anticoagulation	Protocols for high-risk drugs: nomograms for heparin	3
26.3	Falls	Use of bed alarms	3
11	Adverse drug events (ADEs) in drug dispensing and/or administration	Use of automated medication dispensing devices	4

Table 58.2 Further Research Likely to be Beneficial

Chapter	Patient Safety Target	Patient Safety Practice	Impact/ Evidence Category (1-5)
17.2	Ventilator-associated pneumonia	Continuous aspiration of subglottic secretions (CASS)	1
17.1	Ventilator-associated pneumonia	Semi-recumbent positioning	2
26.5	Falls and fall injuries	Use of hip protectors	2
30	Hospital-acquired complications (functional decline, mortality)	Geriatric evaluation and management unit	2
47	Adverse events due to transportation of critically ill patients between health care facilities	Specialized teams for interhospital transport	3
34	Stress-related gastrointestinal bleeding	H_2-antagonists	3
37.2	Inadequate pain relief	Acute pain service	3
15.2	Hospital-acquired urinary tract infection	Use of suprapubic catheters	3
26.2	Restraint-related injury; Falls	Interventions to reduce the use of physical restraints safely	3
45	Adverse events due to provider inexperience or unfamiliarity with certain procedures and situations	Simulator-based training	4
49	Failure to honor patient preferences for end-of-life care	Use of physician order form for life-sustaining treatment (POLST)	4
42.2	Adverse events during cross-coverage	Standardized, structured sign-outs for physicians	4
44	Adverse events related to team performance issues	Applications of aviation-style crew resource management (eg, Anesthesia Crisis Management; MedTeams)	4
16.2	Central venous catheter-related bloodstream infections	Antibiotic-impregnated catheters	1
17.3	Ventilator-associated pneumonia	Selective decontamination of digestive tract	2

42.4	Failures to communicate significant abnormal results (eg, pap smears)	Protocols for notification of test results to patients	3
36	Pneumococcal pneumonia	Methods to increase pneumococcal vaccination rate	3
16.3	Central venous catheter-related bloodstream infections	Cleaning site (povidone-iodine to chlorhexidine)	4
16.4	Central venous catheter-related bloodstream infections	Use of heparin	4
16.4	Central venous catheter-related bloodstream infections	Tunneling short-term central venous catheters	4
29	Hospital-acquired complications (eg, falls, delirium, functional decline, mortality)	Geriatric consultation services	4
46	Adverse events related to fatigue in health care workers	Limiting individual provider's hours of service	4
26.4	Falls and fall-related injuryies	Use of special flooring material in patient care areas	5
43.2	Performance of invasive diagnostic or therapeutic procedure on wrong body part	"Sign your site" protocols	5
42.1	Adverse events related to discontinuities in care	Information transfer between inpatient and outpatient pharmacy	2
48	Missed, incomplete or not fully comprehended informed consent	Asking that patients recall and restate what they have been told during informed consent	1
8	Adverse drug events (ADEs) related to targeted classes (analgesics, KCl, antibiotics, heparin) (focus on detection)	Use of computer monitoring for potential ADEs	2
24	Critical events in anesthesia	Intraoperative monitoring of vital signs and oxygenation	4
42.3	Adverse events related to information loss at discharge	Use of structured discharge summaries	5

Chapter 59. Listing of All Practices, Categorical Ratings, and Comments

Ch. #	Patient Safety Target	Patient Safety Practice	Impact	Study Strength	Effect Size	Vigilance	Cost	Complexity
6	Medication errors and adverse drug events (ADEs) primarily related to ordering process	Computerized physician order entry (CPOE) with clinical decision support system (CDSS)	High	Medium[1]	Modest	Medium	High[2]	High
7	Medication errors and ADEs related to ordering and monitoring	Clinical pharmacist consultation services	High	Medium	Modest[3]	Low	High	Low
8	ADEs related to targeted classes (analgesics, KCl, antibiotics, heparin) (focus on detection)	Use of computer monitoring for potential ADEs	Medium	Medium	Robust[4]	Low	Medium[5]	Low
9	Adverse events related to anticoagulation	Protocols for high risk drugs: nomograms for heparin	Medium	Medium[6]	Robust[7]	Medium	Low	Low
9	Adverse events related to anticoagulation	Anticoagulation services and clinics for coumadin[8]	High	Medium	Unclear	Low	Medium	Low
9	Adverse events related to chronic anticoagulation with warfarin	Patient self-management using home monitoring devices	High	High	Robust	Medium	Medium[9]	High[10]
10	ADEs in dispensing medications	Unit-dosing distribution system	Medium[11]	Medium	Unclear	Low	Low	Low
11	ADEs in drug dispensing and/or administration	Use of automated medication dispensing devices	High	Medium[12]	Unclear	Medium	Medium[13]	Low
12	Hospital-acquired infections	Improved handwashing compliance (via education/behavior change; sink technology and placement;	High	Medium[14]	Unclear[15]	Low	Low	Low[16]

Ch. #	Patient Safety Target	Patient Safety Practice	Impact	Study Strength	Effect Size	Vigilance	Cost	Complexity
		washing substance)						
13	Serious nosocomial infections (eg, vancomycin-resistant enterococcus, *C. difficile*)	Barrier precautions (via gowns & gloves; dedicated equipment; dedicated personnel)	High	Medium [17]	Robust	Medium [18]	Medium	Low[19]
14	Hospital-acquired infections due to antibiotic-resistant organisms	Limitations placed on antibiotic use	High[20]	Medium	Modest	Medium [21]	Low	Low
15.1	Hospital-acquired urinary tract infection	Use of silver alloy-coated catheters	High	High	Unclear[22]	Low	Low	Low
15.2	Hospital-acquired urinary tract infection	Use of suprapubic catheters	High	High	Unclear [23]	Medium	High	High
16.1	Central venous catheter-related blood infections	Use of maximum sterile barriers during catheter insertion	Medium	High	Robust	Low	Low	Low[24]
16.2	Central venous catheter-related blood infections	Antibiotic-impregnated catheters	Medium	High	Robust	Low[25]	Low	Low
16.3	Central venous catheter-related blood infections	Cleaning site (povidone-iodine to chlorhexidine)	Medium	High	Unclear	Low	Low	Low
16.4	Central venous catheter-related blood infections	Changing catheters routinely	Medium	High	Negligible ±	NA	High	High
16.4	Central venous catheter-related blood infections	Use of heparin	Medium	High	Unclear	Medium	Low	Low
16.4	Central venous catheter-related blood infections	Tunneling short-term central venous catheters	Medium	High	Unclear	Low	Low	High

± Actually, studies show a detrimental effect of practice.

Ch. #	Patient Safety Target	Patient Safety Practice	Impact	Study Strength	Effect Size	Vigilance	Cost	Complexity
16.4	Central venous catheter-related blood infections	Routine antibiotic prophylaxis	Medium	Medium	Negligible	Medium	Medium	Low
17.1	Ventilator-associated pneumonia	Semi-recumbent positioning	High	Medium	Robust[26]	Low	Low	Low
17.1	Ventilator-associated pneumonia	Continuous oscillation	High	High	Robust[27]	Medium	Medium	Low
17.2	Ventilator-associated pneumonia	Continuous aspiration of subglottic secretions (CASS)	High	High	Robust[28]	Low	Low	High[29]
17.3	Ventilator-associated pneumonia	Selective decontamination of digestive tract	High	High	Robust[30]	Medium [31]	Low	Low
17.4	Ventilator-associated pneumonia	Sucralfate	High	High	Unclear	High[32]	Low	Low
18	Mortality associated with surgical procedures	Localizing specific surgeries and procedures to high volume centers	High	Medium [33]	Varies	Medium	Varies	High
20.1	Surgical site infections	Appropriate use of antibiotic prophylaxis	Medium [34]	High	Robust	Medium [35]	Low	Low
20.2	Surgical site infections	Maintenance of perioperative normothermia	High	Medium [36]	Robust	Medium [37]	Low	Low
20.3	Surgical site infections	Use of supplemental perioperative oxygen	High	Medium [38]	Robust	Low	Low	Low
20.4	Surgical site infections	Perioperative glucose control	High	Medium	Robust	Medium	Low	High[39]
21	Morbidity due to central venous catheter insertion	Use of real-time ultrasound guidance during central line insertion	High	High	Robust[40]	Low[41]	Medium	High
22	Surgical items left	Counting sharps, instruments,	Insuff.	Low	Not rated	Not rated	Low	Low

Ch. #	Patient Safety Target	Patient Safety Practice	Impact	Study Strength	Effect Size	Vigilance	Cost	Complexity
	inside patient	sponges	Info.[42]					
23	Complications due to anesthesia equipment failures	Use of preoperative anesthesia checklists	Low[43]	Low	Not rated	Not rated	Low	Low
24	Critical events in anesthesia	Intraoperative monitoring of vital signs and oxygenation	Low[44]	Medium 45	Unclear[46]	Low	Low	Low
25	Perioperative cardiac events in patients undergoing noncardiac surgery	Use of perioperative beta-blockers	High	High	Robust	Medium	Low	Low
26.1	Falls	Use of identification bracelets	Medium	Medium	Negligible	Low	Low	Low
26.2	Restraint-related injuries; Falls	Interventions to reduce the use of physical restraints safely	Medium	Medium	Unclear[47]	Medium	Medium	Low
26.3	Falls	Use of bed alarms	Medium	Medium	Unclear	Low[48]	Medium 49	Low
26.4	Falls and fall-related injuries	Use of special flooring material in patient care areas	Medium	Low	Not rated	Not rated	High	Low
26.5	Falls and fall injuries	Use of hip protectors	Medium	High	Robust	Medium	Low[50]	Low[51]
27	Pressure ulcers	Use of pressure relieving bedding materials	High	High	Robust[52]	Low	High	Low
28	Hospital-related delirium	Multi-component delirium prevention program	High	Medium	Robust	Low	Medium	Low
29	Hospital-acquired complications (eg, falls, delirium, functional decline, mortality)	Geriatric consultation services	High	High	Varies[53]	Low	Medium	High

Ch. #	Patient Safety Target	Patient Safety Practice	Impact	Study Strength	Effect Size	Vigilance	Cost	Complexity
30	Hospital-acquired complications (functional decline, mortality)	Geriatric evaluation and management unit	High	High	Modest[54]	Low	Medium	High
31	Venous thromboembolism (VTE)	Appropriate VTE prophylaxis	High	High	Robust	Medium	Low	Low[55]
32	Contrast-induced renal failure	Use of low osmolar contrast media	Medium	High	Robust	Low	High[56]	Low
32	Contrast-induced renal failure	Hydration protocols with theophylline	Medium	High	Negligible	Low	Low	Low
32	Contrast-induced renal failure	Hydration protocols with acetylcysteine	Medium	Medium[57]	Robust	Low	Low	Low
33	Morbidity and mortality in post-surgical and critically ill patients	Various nutritional strategies	High	High	Robust[58]	Medium	Medium	Low
34	Stress-related gastrointestinal bleeding	H_2-antagonists	Medium	High	Unclear	Medium[59]	Low	Low
35	Clinically significant misread radiographs and CT scans by non-radiologists	Education interventions and continuous quality improvement strategies	Medium	Medium	Robust	Low	Low	Low
36	Pneumococcal pneumonia	Methods to increase pneumococcal vaccination rate	Medium	High	Unclear[60]	Low[61]	Low	Low
37.1	Inadequate pain relief in hospital patients with abdominal pain	Use of analgesics in patients with acute abdomen without compromising diagnostic accuracy	High	Medium[62]	Robust	Medium	Low	Low[63]
37.2	Inadequate pain relief	Acute pain service	High	Medium	Robust[64]	Low[65]	Medium	Low

Ch. #	Patient Safety Target	Patient Safety Practice	Impact	Study Strength	Effect Size	Vigilance	Cost	Complexity
37.4	Inadequate postoperative pain management	Non-pharmacologic interventions (eg, relaxation, distraction)	High	High	Unclear	Low	Low	Low
38	Morbidity and mortality in ICU patients	Change in ICU structure—active management by intensivist	High	Medium	Robust[66]	Low	Medium	High
39	Morbidity and mortality	Changes in nursing staffing	High	Medium[67]	Varies	Low	High	Low[68]
40	Any safety problem amenable to culture	Promoting a culture of safety	Insuff. Info.	**[69]			Varies	High
41.1	Medical device related adverse events	Use of human factors principles in evaluation of medical devices	Insuff. Info.	**[70]			Varies	High
41.2	Adverse events	Refining performance of medical device alarms (eg, balancing sensitivity and specificity of alarms, ergonomic design)	High[71]	**[72]			Varies	High
42.1	Adverse events related to discontinuities in care	Information transfer between inpatient and outpatient pharmacy	High	Medium	Robust	Low	Medium[73]	Low
42.2	Adverse events during cross-coverage	Standardized, structured sign-outs for physicians	Medium	Low	Not rated	Not rated	Low[74]	Low
42.3	Adverse events related to information loss at discharge	Use of structured discharge summaries	Insuff. Info	Low[75]	Not rated	Not rated	Low	Low
42.4	Failures to communicate significant abnormal results	Protocols for notification of test results to patients	Medium	Medium	Modest	Low	Low	Low

Ch. #	Patient Safety Target	Patient Safety Practice	Impact	Study Strength	Effect Size	Vigilance	Cost	Complexity
	(eg, pap smears)							
43.1	Adverse events due to patient misidentification	Use of bar coding	High[76]	Low	Not rated	Not rated	Varies[77]	High
43.2	Performance of invasive diagnostic or therapeutic procedure on wrong body part	"Sign your site" protocols	High	Low	Not rated	Not rated	Low	High
44	Adverse events related to team performance issues	Application of aviation style crew resource management (eg, Anesthesia Crisis Management; MedTeams)	High[78]	Low	Not rated	Not rated	Medium	High
45	Adverse events due to provider inexperience or unfamiliarity with certain procedures and situations	Simulator-based training	Insuff. Info[79]	Medium 80	Unclear 81	Low	Medium	Low
46	Adverse events related to fatigue in health care workers	Limiting individual provider's hours of service	Insuff. Info.	Medium	Unclear	Low	High	High
46	Adverse events related to fatigue in health care workers	Fixed shifts or forward shift rotations	Insuff. Info.	**[82]			Varies 83	Varies
46	Adverse events related to fatigue in health care workers	Napping strategies	Insuff. Info.	**[84]			High[85]	Low
47	Adverse events due to transportation of critically ill patients between health care facilities	Specialized teams for interhospital transport	Medium	Medium 86	Modest	Low	Medium	Low

Ch. #	Patient Safety Target	Patient Safety Practice	Impact	Study Strength	Effect Size	Vigilance	Cost	Complexity
47	Adverse events due to transportation of critically ill patients within a hospital	Mechanical ventilation	Medium	Medium	Negligible	Low	Low	Low
48	Missed, incomplete or not fully comprehended informed consent	Asking that patients recall and restate what they have been told during informed consent	High	Medium	Robust	Low	Low	Low[87]
48	Missed, incomplete or not fully comprehended informed consent	Use of video or audio stimuli	High	Medium	Modest	Low	Low[88]	Low
48	Missed, incomplete or not fully comprehended informed consent	Provision of written informed consent information	High	Medium	Unclear	Low	Low	Low
49	Failure to honor patient preferences for end-of-life care	Computer-generated reminders to discuss advanced directives	High	Medium	Robust	Low	Medium [89]	Low
49	Failure to honor patient preferences for end-of-life care	Use of physician order form for life-sustaining treatment (POLST)	High	Low	Not rated	Not rated	Low	Low[90]

Comments Section

[1] Medium strength of evidence for computerized physician order entry: although randomized control trials have been conducted, findings from sophisticated "home grown" systems only 2-3 sites may not be fully generalizable. In addition, the impact of the practice on adverse events has not been as well studied as for the non-clinical outcome, medication errors.

[2] Cost of CPOE is substantially higher than for most other practices in the high cost category.

[3] The impact of clinical pharmacists consultation services may be less than that of CPOE due to logistics of screening large volumes of orders to target those most prone to error or most consequential.

[4] Estimate of effect size based on single study with limited target (only antibiotic treatments).

[5] Cost influenced by whether existing computer systems are used in pharmacy services.

[6] For nomogram protocols, study strength medium because the major concern (bleeding) is not addressed in most studies.

[7] Effect size greater than 15% for surrogate markers; not bleeding or clot rate.

[8] Anticoagulation clinics: Both inpatient and outpatient venues studied, so some heterogeneity among results.

[9] Self-management of warfarin (coumadin): on average the cost per patient is low, but the aggregated cost is medium from the perspective of an insurer or integrated system.

[10] Higher complexity of implementation because self-management practice displaces locus of control out of institution and may engender debate over insurance coverage. Other countries cover this practice, but it is currently not covered by Medicare in the United States.

[11] Unit-dosing is a ubiquitous practice that has surprisingly little evidence of effectiveness; evidence is old and mixed.

[12] Study strength is affected because outcomes measured are not the major outcomes of interest - ie, ADEs.

[13] The implementation ratings are related to patient safety only, but note that institutions may also implement this practice for cost-savings due to less drug loss and better inventory control.

[14] Study design for handwashing compliance practices generally had short duration of follow-up; no randomized control trials.

[15] Unclear effect size due to mixed results and no clear pattern in a group of heterogeneous practices.

[16] Rated as low, but this practices requires behavior change on the part of the provider. Therefore, it may be more difficult to implement because its success largely rests on education (see Chapter 54) and acceptance.

[17] There are a number of studies of barrier precautions, but most are Level 3 study designs so the strength is not rated as "High."

[18] Potential decrease in provider interaction with patients may cause psychological, as well as other, effects if care from clinicians is compromised.

[19] Rated as low, but this practices requires behavior change on the part of the provider. Therefore, it may be more difficult to implement because its success largely rests on education (see Chapter 54) and acceptance.

[20] Impact upgraded from "medium" to "high" rating because of public health impact of more antibiotic-resistant pathogens.

[21] Practice requires active, ongoing monitoring and input from infection control officers to make sure proper drugs are prescribed. Also, vigilance includes need for institution-wide monitoring of pathogens.

[22] The effect size of using silver alloy catheters is unclear: a well-done meta-analysis is positive, showing decrease in bacteriuria, but more recent results of possibly better designed individual studies are mixed regarding benefit. Also, the actual strength of the link, however intuitive, between bacteriuria and clinically significant urinary tract infection is unclear.

[23] Effect size of using suprapubic catheters is unclear because of some heterogeneity in studies. Results are generally positive, but no meta-analysis yet conducted. In addition, the effect on outcome of clinically significant urinary tract infections is also unclear.

[24] Rated as low, but this practices requires behavior change on the part of the provider. Therefore, it may be more difficult to implement because its success largely rests on education (see Chapter 54) and acceptance.

[25] With antibiotic-impregnated catheters made with minocycline, there is the theoretical risk of increased antibiotic resistance.

[26] Pneumonia outcome was significantly reduced, but mortality was not.

[27] Meta-analysis of 6 randomized controlled trials showed significant and large relative risk reduction, but 2 other randomized controlled trials showed no impact.

[28] Benefit observed in prevention of ventilator-acquired pneumonia; no established benefit for mortality.

[29] High complexity for implementation since it requires retraining for a new practice.

[30] Most benefit in reducing pneumonia and mortality occurs when both IV and topical decontamination are used. Topical (by itself) only reduces ventilator-associated pneumonia. However, topical carries less potential for harm (ie, antibiotic resistance).

[31] Medium vigilance for harm because of public health concerns due to possible increase in antibiotic resistance. The Center for Disease Control and Prevention (CDC) and the American Thoracic Society (ATS) both recently reviewed this topic and did not recommend this practice.

[32] If sucralfate were used because of its possible effect on reducing risk of ventilator-acquired pneumonia, it would displace a practice that has more established benefit for GI bleeding (H_2 blockers).

[33] The study strength for localizing care to high volume centers is evaluated across a range of practices. There are large variations in evidentiary base across specific practices. Evidence is not structured to determine effect on patient safety. Although the literature includes possible benchmarks/thresholds for volume levels for specific procedures, the evidence is related more to quality enhancement than to improvements in patient safety.

[34] Relatively high current utilization of practice reduced impact by one level.

[35] Vigilance is required to monitor antibiotic overuse to prevent negative public health effects.

[36] Study strength is rated as medium because randomized clinical trial data only applies to one disease process, although may be generalizable.

[37] Medium vigilance for harm: although not studied, for certain cohorts the practice may be detrimental.

[38] Study strength is rated as medium because randomized clinical trial data only applies to one disease process, although may be generalizable.

[39] Tight perioperative glucose control requires major shift in practice style, increased vigilance, more coordination between nurses and physicians, and perhaps new policies regarding nursing care for diabetics.

[40] Effect size high, but more impressive decrease in “failed insertion attempts” than in more clinically relevant complications. Also, there is some heterogeneity in study results, and there are two different technologies assessed (plain ultrasound vs. US with doppler), and the results vary.

[41] Theoretical risk that additional manipulation/handling could increase infection risk; also concern regarding impact on providers’ abilities to place catheters emergently when ultrasound guidance is not available.

[42] Insufficient information about retained sponges: the event is highly concerning and often morbid when occurs, but the only data on frequency are from case reports.

[43] Low potential impact because anesthesia complications are already so uncommon; also difficult to determine impact of current use of some version of this practice (eg, low opportunity possible due to current utilization).

[44] Low potential impact because anesthesia complications are already so uncommon; also difficult to determine impact of current use of some version of this practice (eg, low opportunity possible due to current utilization).

[45] Although there has been a very large randomized trial of pulse oximetry, other studies covered additional aspects of intraoperative monitoring and were generally of lower study design quality.

[46] Pulse oximetry study showed no benefit, but major potential methodologic problems, such as secular trends. Complications that monitoring are designed to find are very unusual, so even a large trial may have been under-powered to detect important effects.

[47] Because the patient safety target is *reduction* of unnecessary restraints, there are multiple outcomes of interest. Although reducing unnecessary restraints does not seem to increase the risk of falls, it raises other concerns regarding disconnected IVs, elopement risk, etc., which have not been fully evaluated.

[48] Probably low, as categorized, but there is a theoretical risk that patients will not receive as much attention from nurses and other providers.

[49] Medium cost based on relatively widespread implementation of bed alarms required to impact all patients who may potentially benefit. May also impact nursing workload and staffing needs.

[50] Possibly higher cost if large numbers of patients would benefit from wearing hip protectors. There is also the question of whether these costs are borne by system/insurers or patients themselves.

[51] Implementation complexity in the hospital may be low, but implementation outside of the hospital might involve large educational campaign directed at patients who could benefit from practice.

[52] Studies compare a variety of special bedding materials to standard beds. Effect size for one special bed option versus another is not known. Unclear which particular surface works best.

[53] Effect size varies since heterogeneous outcomes, perhaps in part related to the variety of interventions, some of which involved both inpatient and outpatient components.

[54] Effect size varies due to heterogeneous results, which depend in part on the outcomes of interest (ie, functional outcomes vs. mortality).

[55] Rated as low, but this practices requires behavior change on the part of the provider. Therefore, it may be more difficult to implement because its success largely rests on education (see Chapter 54) and acceptance.

[56] Total cost, of course, depends on the extent of utilization (eg, all patients versus only targeted patients). Cost-effectiveness analyses demonstrate the importance of targeting appropriate patients.

[57] Outcome is level 2, only one study for N-acetylcystine.

[58] Varies according to specific nutritional support practice. Robust findings for early enteral nutrition in critically ill and post-surgical patients.

[59] Vigilance for harm is medium because of potential risk of increasing ventilator-associated pneumonia, and also because of possible overuse since high-risk groups are now better defined.

[60] Depends on specific intervention; standing orders have the highest effectiveness.

[61] Harm concern low, except one recent study (see Chapter 36) showed trend toward harm in HIV-positive patients.

[62] Although some studies were randomized control trials, they did not look at all clinically relevant outcomes to ensure that practice was safe. Under-powered to assess whether diagnostic capability not impaired.

[63] Rated as low, but this practices requires behavior change on the part of the provider. Therefore, it may be more difficult to implement because its success largely rests on education (see Chapter 54) and acceptance.

[64] Only studied for post-operative pain; may not apply more generally.

[65] Some speculation that care may be fragmented when applied broadly, beyond post-operative patients.

[66] Some of the positive results may be attributable to factors other than the intervention. Concern about underlying population changing (eg, secular trends).

[67] Study strength is medium despite a number of studies, because of variation in practices (eg, various measures of nurse staffing, models of care). Chapter was designed to generalize across practices regarding nursing structure versus outcomes; evidence is not structured to tell effect on patient safety, and there are no benchmarks/thresholds for nurse staffing levels.

[68] Rated as low, but this practices requires behavior change on the part of the provider. Therefore, it may be more difficult to implement because its success largely rests on education (see Chapter 54) and acceptance.

[69] Most evidence available outside of medicine; study strength not rated. These practices, drawn largely from non-health care industries, were not fully rated because of their unique nature and their relatively small evidentiary base in the health care literature.

[70] Most evidence available outside of medicine; study strength not rated. These practices, drawn largely from non-health care industries, were not fully rated because of their unique nature and their relatively small evidentiary base in the health care literature.

[71] Although alarms are ubiquitous in the hospital, it is unclear how many adverse events might be improved by improvements in alarm systems.

[72] Most evidence available outside of medicine; study strength not rated. These practices, drawn largely from non-health care industries, were not fully rated because of their unique nature and their relatively small evidentiary base in the health care literature.

[73] Costs are shared among a variety of payors including outpatient pharmacy.

[74] Cost would vary based on interventions considered—some low-tech, paper-based, or pocket computers; higher cost for full-scale computerized systems.

[75] Although one randomized trial performed, the outcomes reported were only indirectly related to patient safety outcomes.

[76] Somewhat unclear, but errors due to misidentification can be grave.

[77] Cost varies based on specific system and level of implementation.

[78] Impact is a function of how widely the practice can be used (ICU vs. ward teams vs. operating room).

[79] Insufficient information outside of anesthesia about volume of human factors errors amenable to training approaches.

[80] Limited studies with small numbers of participant and with different simulators lead to concerns about generalizability.

[81] Effect unclear since few studies with comparable simulators, and evaluated with mostly Level 3 outcomes.

[82] Most evidence available outside of medicine; study strength not rated. These practices, drawn largely from non-health care industries, were not fully rated because of their unique nature and their relatively small evidentiary base in the health care literature.

[83] Fixed shift may be more costly and difficult to implement than forward rotation.

[84] Most evidence available outside of medicine; study strength not rated. These practices, drawn largely from non-health care industries, were not fully rated because of their unique nature and their relatively small evidentiary base in the health care literature.

[85] Restructuring patient care to allow for napping while minimizing discontinuities could be expensive.

[86] Study strength is borderline-medium with three Level 3 studies.

[87] Rated as low, but this practices requires behavior change on the part of the provider. Therefore, it may be more difficult to implement because its success largely rests on education (see Chapter 54) and acceptance.

[88] Cost for video disks – assumes that off-the-shelf products exist for common procedures; would be higher if an institution has to build its own systems.

[89] Cost would be lower for health care organizations that already rely on computers for care management.

[90] Rated as low, but this practices requires behavior change on the part of the provider. Therefore, it may be more difficult to implement because its success largely rests on education (see Chapter 54) and acceptance.

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