

Preventing Healthcare-Associated Infections: Beyond Best Practice

Internal Medicine Grand Rounds

Pranavi Sreeramoju, MD, MPH

July 15, 2011

This is to acknowledge that Pranavi Sreeramoju, M.D., M.P.H. has not disclosed any financial interests or other relationships with commercial concerns related directly or indirectly to this program. Dr. Sreeramoju will not be discussing off-label uses in her presentation.

Pranavi Sreeramoju, MD, MPH
Assistant Professor, Medicine-Infectious Diseases
UT Southwestern Medical Center
Chief of Infection Prevention, Parkland Health and Hospital System
Dallas, TX
Email: Pranavi.sreeramoju@utsouthwestern.edu

My research program is focused on evaluating the clinical epidemiology of healthcare-associated infections, particularly central line-associated bloodstream infections, surgical site infections and methicillin-resistant *Staphylococcus aureus*, and evaluating the effectiveness of interventions to reduce healthcare-associated infections. Ongoing studies include a cluster-randomized trial to evaluate the effectiveness of positive deviance, an observational study to evaluate post-operative clinical risk factors for development of surgical site infection, and the development of a predictive electronic medical record-based risk model for surgical site infection. The overall goal of the research program is to enhance patient safety, quality of care and disease outcomes related to healthcare-associated infections.

The Parkland hospital epidemiology and infection prevention program is designed to identify patients with healthcare-associated infections, educate caregivers on mitigating infection risk, and reduce the risk of developing these infections among patients and employees. Recent improvements in infrastructure include rep-PCR lab for strain typing within the Parkland microbiology laboratory, and acquisition of data mining software specifically targeted for infection control and antimicrobial stewardship. Additional complementary processes for data refinement include the increased use of data from electronic medical records, the Patient Safety Net[®], and the University HealthSystem Consortium[®]. The program also serves as the core site for mandatory hospital epidemiology rotation for fellows in Infectious Diseases beginning this academic year. The program is poised to be a center for infection prevention excellence in the community and beyond.

Learning Goal and Objectives:

The goal is to evaluate best practices for preventing healthcare-associated infections and to identify opportunities beyond best practice. Achieving an infection-free hospital stay for patients will require integration of infection prevention into routine bedside clinical care. The objectives are:

1. To be aware of best practices for prevention of healthcare-associated infections
2. To recognize the limitations of known best practices and approaches to implement them
3. To understand rationale and to identify opportunities for newer approaches beyond best practices to prevent healthcare-associated infections

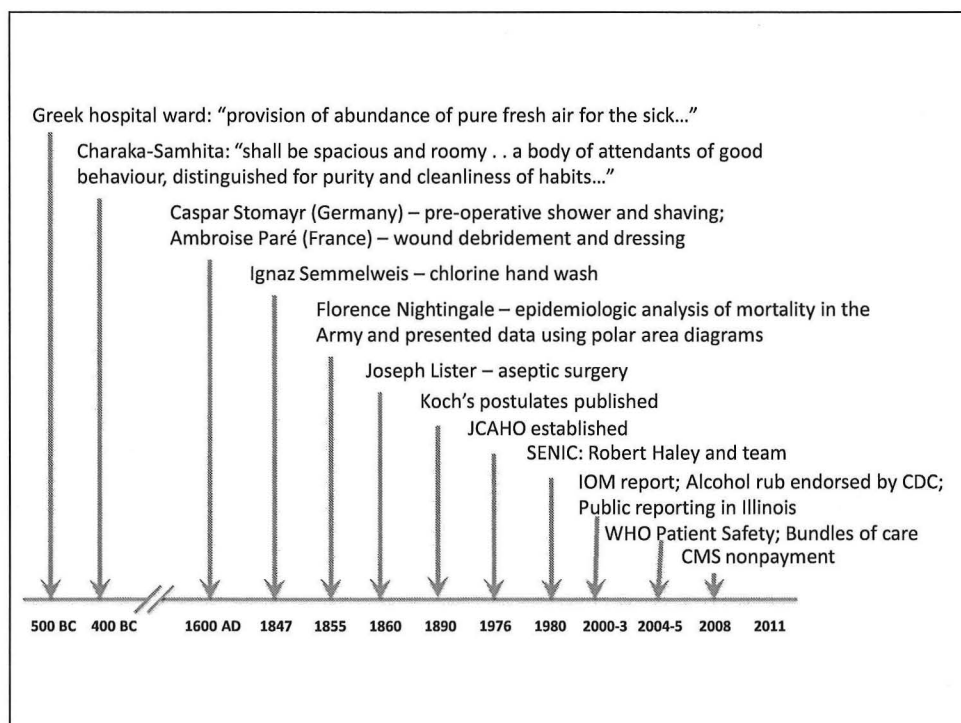
Introduction

In the United States, approximately 1.7 million healthcare-associated infections (HAI) occur every year leading to 99,000 deaths¹ per estimates from the Centers for Disease Control and Prevention (CDC). These infections result in excess healthcare costs of \$28-33 billion annually.² Of these 1.7 million HAI, 33% are urinary tract infections, 17% are surgical site infections, and 14% each are pneumonia and bloodstream infections. Twenty five percent of these infections occurred in the intensive care units (ICUs) while the remaining 75% occurred outside of the ICUs.¹

History of Infection Prevention

The history of HAI prevention is over two thousand five hundred years old.³ Historians who described the hospital wards in Greece in the 5th Century BC described that they provided for an abundance of pure fresh air for the sick. The Charaka Samhita, ancient Indian textbook on medicine stated that a building caring for the sick shall be spacious and roomy, and the attendants for the sick should be distinguished for cleanliness of habits. There are several examples of infection prevention measures in European history of the medieval and the renaissance period. In 16th century AD, a German surgeon called Caspar Stomayr advocated for pre-operative shower and shaving to 'cleanse' the body prior to surgery, while a French surgeon Ambroise Pare` advocated for use of wound debridement and simple dressings instead of using boiling oil and red-hot iron to prevent wound infection. The historical milestones are outlined in figure 1 below.

Figure1. Historical milestones in infection prevention and control



The introduction of chlorine hand wash by Ignaz Semmelweis in 1847 and subsequent demonstration of decreased mortality rates due to puerperal sepsis was a landmark in the history of infection prevention and control. A few years later in 1854-56, Florence Nightingale studied the epidemiology of mortality in the army and presented data graphically using polar area diagrams. She drew attention to the finding that majority of deaths were caused by “preventable or mitigable zymotic (infectious) diseases”. In 1860, Joseph Lister discovered the antiseptic properties of carbolic acid and demonstrated reduction in post-operative mortality with surgical antisepsis. It was only much later in 1890 that Koch’s postulates were published and the germ theory of disease gained better acceptance in the medical community.

In the 20th century, antimicrobial agents were discovered that revolutionized treatment and prevention of infections. With the establishment of the Joint Commission for Accreditation of Healthcare Organizations in the late 1970s, regulatory standards were stipulated for hospital infection prevention in the United States.⁴ Hospitals incorporating four essential components in their infection control programs reduced rates of HAI by 32%, per the pioneering work done by Robert Haley and colleagues at the CDC. The four essential components per the Study on Efficacy of Nosocomial Infection Control (SENIC)⁵⁻⁶ are (i) surveillance with feedback of infection control rates to hospital staff, (ii) enforcement of preventative practices, (iii) a supervising infection preventionist to collect and analyze surveillance data, and (iv) the involvement of a physician or microbiologist with specialized training in infection prevention and control.

The 21st century has been characterized by heightened scientific, social and legislative attention to healthcare-associated infections. The Institute of Medicine report⁷ published in 2001 played a critical role in raising everyone’s awareness on the magnitude of preventable errors. Alcohol-based hand rub was endorsed by the CDC in 2002. Illinois became the first state to require public health reporting of HAI in 2003. Currently, thirty-two states including Texas require mandatory reporting of HAI. In 2004, the World Health Organization launched the World Patient Safety program to coordinate, disseminate and accelerate improvements in patient safety worldwide.⁸ The five moments for hand hygiene campaign was launched in 2005, as a major global effort to improve hand hygiene in healthcare.⁹ In the United States, beginning with the deficit reduction act in 2005, several financial incentives and disincentives were created to increase accountability of hospitals in preventing HAI. Concurrently, several advances have been made in research related to HAI and their prevention.

Terms and Definitions

The CDC defines healthcare-associated infection as a localized or systemic condition resulting from an adverse reaction to the presence of an infectious agent(s) or its toxin(s).¹⁰ There must be no evidence that the infection was present or incubating at the time of admission to the acute care setting. HAIs may be caused by infectious agents from endogenous or exogenous sources. Endogenous sources are body sites, such as the skin, nose, mouth, gastrointestinal (GI) tract, or vagina that are normally inhabited by microorganisms. Exogenous sources are those external to the patient, such as

patient care personnel, visitors, patient care equipment, medical devices, or the healthcare environment.¹⁰

The National Health Safety Network (NHSN) is the branch of the CDC that oversees surveillance for HAI in the United States. It has over 4000 participating hospitals. The NHSN establishes surveillance definitions for HAI. Briefly, central line-associated bloodstream infection (CLABSI)¹⁰⁻¹¹ is defined as occurrence of bloodstream infection in the presence of a central venous catheter within the 48-hours prior to the development of infection. Catheter-associated urinary tract infection (CAUTI)¹⁰⁻¹¹ is defined as the occurrence of clinical signs and symptoms of urinary tract infection and a positive urine culture meeting pre-specified criteria, in a patient with an indwelling urinary catheter within 48-hours prior to onset of infection. Surgical site infection (SSI)¹⁰⁻¹¹ is defined as occurrence of one of the following within 30 days (one year if prosthesis present) from the date of the surgery: development of purulent drainage, fever ($>38^{\circ}\text{C}$), redness and tenderness, positive wound culture from aseptically obtained specimen, development of abscess or diagnosis of surgical site infection by a surgeon or attending physician. Healthcare-associated pneumonia (HAP) and ventilator-associated pneumonia (VAP) are also defined per the CDC-NHSN criteria.¹⁰⁻¹¹ Briefly, to meet the definition, a patient must have radiographic evidence of a new or progressive infiltrate, consolidation or cavitation; fever ($>38^{\circ}\text{C}$), white blood cell count $<4000/\text{mm}^3$ or $>12000/\text{mm}^3$, and new onset of purulent sputum, cough or shortness of breath or increasing oxygen requirements. For VAP, the patient must have been on a ventilator during the 48-hour period prior to the onset of symptoms of pneumonia. Clostridium difficile infection (CDI)¹² is defined as presence of symptoms of diarrhea or toxic megacolon combined with a positive result of a laboratory assay and/or endoscopic or histopathologic evidence of pseudomembranous colitis.

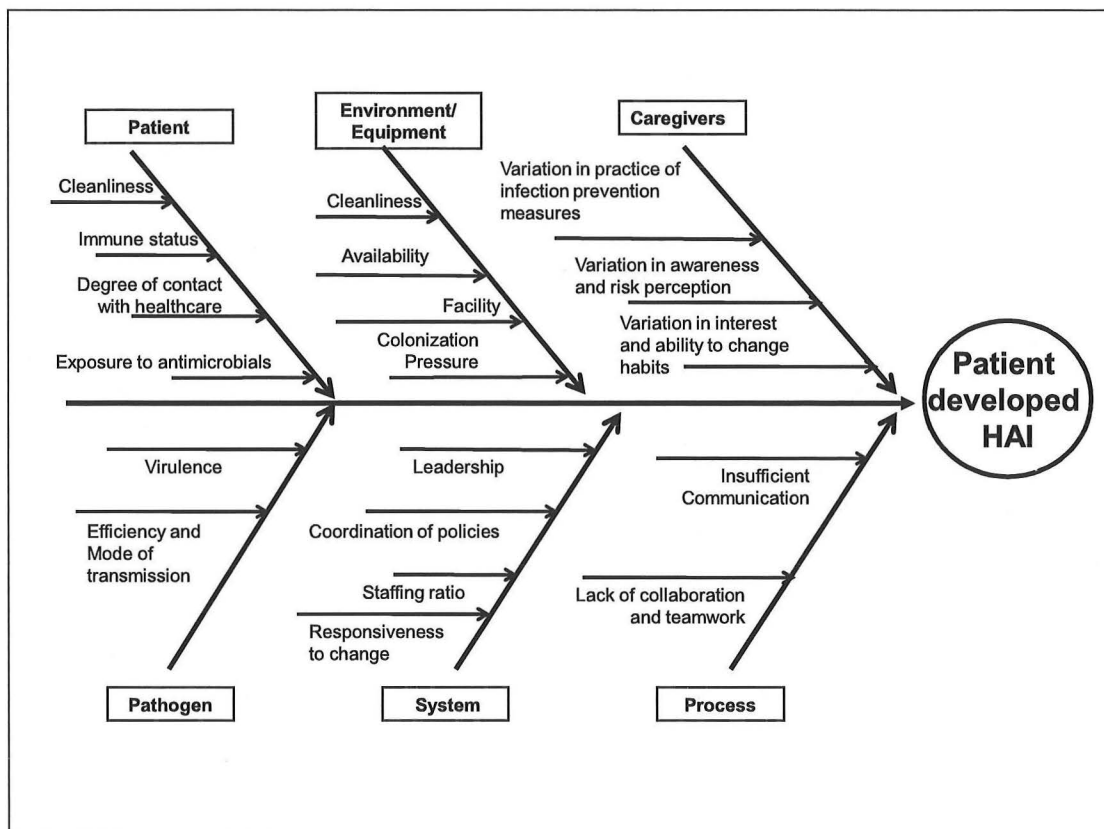
Best Practice is a method or technique that has consistently shown results superior to those achieved with other means, and that is used as a benchmark. A bundle¹³ is a set of 3-5 best practices that are effective in preventing a specific HAI. The Institute for Healthcare Improvement is one of the main drivers of this concept. A checklist is a tool modeled after its successful use in the airline industry, which serves as a reminder to use bundled best practices during patient care including performing procedures. The surgical safety checklist¹⁴ and the central line checklist¹⁵ are excellent implementation tools that have led to decreased rates of HAI.

Brief Overview of Etiology of Healthcare-Associated Infections

Many pathogens cause HAI. They include bacterial, fungal, viral and parasitic pathogens, bacterial causes being the most common. Methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), multi-drug resistant gram-negative bacilli, and *Clostridium difficile* are of particular interest. *Candida spp.* also cause significant HAI. Although there are multiple modes of transmission of pathogens in the hospital setting, the most common mode of transmission is via touch. Touching any part of the patient or an indwelling device with contaminated hands or equipment places the patient at risk for pathogen acquisition.

Inappropriate antimicrobial use leads to acquisition of drug-resistant bacteria in two different ways. Firstly, antimicrobial agents remove normal flora and leave the patient vulnerable to acquire a different, often drug-resistant pathogen introduced by contaminated hands or equipment. Secondly, they apply selection pressure and allow growth of drug-resistant bacteria previously present in small inoculums. The pathogenesis of HAI involves a complex interplay of multiple factors as outlined in figure 2 below. The list of factors in the figure is not all-inclusive. Teams of caregivers and institutions differ in their ability to prevent HAI even when the patient and pathogen factors remain constant.

Figure2: Predisposing factors for development of HAI



Best Practices to Prevent Healthcare-Associated Infections

Standard-of-Care Infection Prevention and Control Approach

The typical approach to infection prevention consists of focused surveillance for HAI and implementation of preventive measures driven by the infection control department and hospital leadership. Infection prevention interventions are usually best practices recommended by professional organizations. Implementation efforts are designed as 'projects' or 'initiatives' targeted against a particular type of infection and led by a project

leader who is an infection preventionist or a quality improvement professional. These project leaders run the risk of being viewed by frontline caregivers as 'external people'. The projects may have pre-specified reduction goals and associated with financial and social incentives. Ownership lies frequently with the infection prevention and control department and transfer of ownership to local units upon completion of these projects is often a challenge.

Best Practices

Hand hygiene,^{9, 16} standard precautions, isolation precautions and prudent antimicrobial use are fundamental measures to prevent HAI. Evidence for effectiveness of these measures in preventing HAI is based primarily on biologic plausibility and experience with HAI and outbreak control. These measures, particularly hand hygiene, are explicitly included in the bundled interventions to prevent HAI.

In recent years, bundles of care have emerged as a key concept in infection prevention and control. It is not necessary for the components of any given bundle to be constant. These components are evidence-based and typically selected by experts and endorsed by professional organizations. Hospital programs may modify the components of a given care bundle per institutional or regional needs. For example, the 'European ventilator care bundle'¹⁷ is different from the bundle commonly used in the United States. It consists of the following components: 1) no ventilator circuit tube changes unless specifically indicated, 2) strict hand hygiene practice with the use of alcohol-based hand rub, 3) appropriately educated and trained staff, 4) sedation vacation and weaning protocol, and 5) oral care with the use of chlorhexidine.

Figure3: Best practices to prevent HAI

Fundamental Infection Prevention Practices	Surgical Care Improvement Project
Hand Hygiene	Perioperative antimicrobial prophylaxis
Standard Precautions	-timing
Isolation Precautions	-choice
Prudent Antimicrobial Use	-duration
	Clippers or no shaving
Central Line Bundle	Perioperative normothermia
Hand Hygiene	Glucose control
Subclavian site	Urinary catheter removal
Chlorhexidine Skin Prep	
Maximal Sterile Barrier Precautions	Urinary Catheter Bundle
Daily review of necessity	Aseptic insertion and maintenance
	Bladder ultrasound
Ventilator Bundle	Condom or intermittent catheterization
Head of Bed elevation 30-45°	Do not use unless you must!
Sedation Vacation	Early removal
Venous thromboembolism prophylaxis	
Gastrointestinal bleed prophylaxis	

Implementation of the central line bundle has resulted in reduction of CLABSI in several hospitals. One of the most prominent examples is the Keystone study conducted by Peter Pronovost et al^{15, 18} in over a hundred intensive care units in Michigan. With the implementation of central line bundle in these ICUs, the mean and median rates of CLABSI decreased from 7.7 and 2.7 (interquartile range 0.6-4.8) at baseline to 1.3 and 0 (0-2.4) at 16-18 months and to 1.1 and 0 (0.0-1.2) at 34-36 months post-implementation. Another notable demonstration of the effectiveness of the central line bundle came from the Pittsburgh Regional Healthcare Initiative.¹⁹ In this initiative, the pooled mean rate of CLABSI per 1,000 central line days in participating ICUs decreased by 68%, from 4.31 to 1.36 ($p < 0.001$) over a four-year period.

Berenholtz and colleagues²⁰ conducted a collaborative study among 112 ICUs to reduce VAP using the ventilator bundle. They reported decrease of overall median VAP rate from 5.5 cases (mean, 6.9 cases) per 1,000 ventilator-days at baseline to 0 cases (mean, 3.4 cases) at 16–18 months after implementation ($P < 0.001$) and 0 cases (mean, 2.4 cases) at 28–30 months after implementation ($P < 0.001$). The components of the ventilator bundle used in their study were semi-recumbent positioning to decrease the risk of VAP, stress ulcer prophylaxis to decrease gastrointestinal bleeding, prophylaxis to decrease deep venous thrombosis, adjustment of sedation until the patient can follow commands, and daily assessment of readiness to extubate. Several other studies reported similar results.²¹⁻²²

In a national collaborative effort to prevent surgical site infections, the Surgical Care Improvement Project (SCIP)²³ was designed and implemented nationally in the United States. In a large study reported by Stulberg et al²⁴ including 405,720 hospital discharges after surgery, demonstrated adherence to SCIP was associated with a decreased likelihood of developing a postoperative infection from 14.2 to 6.8 postoperative infections per 1000 discharges (adjusted odds ratio 0.85; 95% confidence interval 0.76-0.95). In a multi-hospital collaborative study²⁵ with forty-four hospitals that reported data on 35,543 surgical cases, hospitals improved in measures related to appropriate antimicrobial agent selection, timing, and duration; normothermia; oxygenation; euglycemia; and appropriate hair removal. Concurrently, the rate of SSI decreased 27%, from 2.3% to 1.7% during the 9-month study period.

Bundled care practices to prevent CAUTI are relatively new in infection prevention. Computerized reminders to discontinue urinary catheters have been shown to be very effective in preventing healthcare-associated CAUTI. In a systematic review and meta-analysis of reminder systems to discontinue urinary catheters,²⁶ the rate of CAUTI (episodes per 1000 catheter-days) was reduced by 52% ($P < .001$) with the use of a reminder or stop order. The intervention resulted in 2.6 fewer days of catheterization (a 37% reduction) per patient compared to the control population. In a study by Topal et al.,²⁷ the CAUTI rate decreased by 73% (36/1000 catheter-days to 11/1000 catheter-days; $P < .001$) and 81% reduction in device use over 2 years with use of computer order entry and a nurse directed protocol for insertion and maintenance of urinary catheters. The components of the 'urinary catheter bundle' or the 'bladder care bundle', are shown in figure 3 above.

Limitations of Best Practice Approach

As discussed in the preceding section, best practices are extremely important in preventing healthcare-associated infections. However, the best practice approach has significant limitations. There are critical gaps in the scientific evidence base of pathophysiology and prevention of HAI.²⁸⁻²⁹ One of the obvious limitations of the bundled best practices approach is that if effective, it is not possible to know the relative effectiveness of different components. Some of the key limitations of best practice based infection prevention approach are discussed in the following sections.

Wide Variation in Rate of Infections

The rates of HAI vary among the different types of patient care units, presumably due to differences in patient population. However, there is a wide inter-hospital variation in rates of HAI in any given type of patient care unit, among hospitals of similar type and size. A review of the rate of CLABSI reported by several hundreds of participating hospitals to the Centers for Disease Control – National Health Safety Network (CDC-NHSN) illustrates this variation. The interquartile range for rate of CLABSI in medical-surgical intensive care units (ICUs) in major teaching hospitals reported in 2002-04, 2006-08, and 2009 was 2.6-5.1, 0.6-2.9, and 0.3-2.4 CLABSI per 1000 catheter days.³⁰⁻³² In the Keystone Michigan ICU project,¹⁵ teaching hospitals and larger hospitals had less improvement in rates of infection in response to the intervention, i.e., the use of central line bundle. For teaching hospitals in the study, the interquartile range was 1.3-4.7 at baseline and it improved to 0-2.7 after 16-18 months of implementation. For non-teaching hospitals, the interquartile range was 0-4.9 at baseline and it improved to 0-1.2 after 16-18 months of implementation. This study did not discuss the changes in rate of CLABSI in outlier hospitals or the characteristics of those hospitals. The magnitude of this variation directs one's attention to the role of organizational complexity in the rates of HAI and their responsiveness to interventions. Several experts have noted that complexity within organizational environment and the patient safety climate³³⁻³⁵ present challenges to successful implementation and uptake of recommended preventive strategies.

Best Practices do not Always Lead to Better Outcomes

Process measures and outcome measures do not always correlate with each other. There is significant ambiguity in evidence-based guidelines.³⁶ Moreover, some studies have shown that implementation of best practices and prevention guidelines have not yielded desired results. In a study conducted at a public academic hospital among patients undergoing hysterectomy, colon surgery, neurosurgery and vascular surgery, patients who received peri-operative antimicrobials per recommended SCIP guidelines (figure 3) did not have a lower rate of infections.³⁷ The rate of SSI in patients who received peri-operative antimicrobials per recommended guidelines was 6.9% (42/611) vs. 3.3% (5/152) in those who did not (P value = 0.13). This lack of difference remained even after performing stratified analyses by their NHSN risk index category¹⁰ for developing SSI. The NHSN risk index categories are based on three major risk factors –

operation duration lasting more than the duration cut point hours for the type of surgery, contaminated or dirty/ infected wound class and American Society of Anesthesiologists score of 3 or higher. Interestingly, the SSI rate in patients undergoing colon surgery who received the recommended peri-operative antimicrobial prophylaxis was significantly higher (34.2% vs. 13.9%; $p=0.03$). Pastor et al³⁸ reported that in patients undergoing colorectal surgery, the rate of SSI (19%) did not change significantly when compliance with all SCIP measures per patient improved significantly from 40% to 68%. A larger study among 211 hospitals participating in the American College of Surgeons National Surgical Quality Improvement Project showed that hospital-level compliance with recommended practices to prevent SSI ranged from 60% to 100%. Of the 16 correlations, 15 demonstrated non-significant associations with risk-adjusted outcomes. The exception was the relationship between choice of peri-operative antimicrobial agent and SSI ($p = 0.004$).³⁹

Local Practices may Complement or Override Best Practice

Locally prevalent practices that do not frequently receive attention in national guidelines also play a significant role in causing or preventing HAIs. An example of complementary practice would be the presence of a unit manager who ensures adequate infection prevention supplies on any given unit. An example of local practice that contributed to occurrence of CLABSI at one hospital is the use of a central 0.9% saline solution bag at the bedside for drawing flushes for intravenous catheters.⁴⁰ These local practices may partly explain why process measures and outcome measures do not always correlate with each other.

Changing Human Behavior and Practice is Complex

Behavior change is a complex process. Human factors contribute significantly to the development of adverse events in healthcare.^{33, 41} Incorporation of guideline recommendations is a slow and complex process.^{34-36, 42} A recent study conducted by Huskins and colleagues to prevent transmission of MRSA and VRE⁴³ illustrated these complexities. The study was a cluster-randomized trial among 18 ICUs in large academic medical centers, 10 ICUs in the intervention arm and 8 ICUs in the control arm. The intervention was active surveillance cultures for MRSA and VRE, universal gloving while awaiting results and contact isolation precautions if cultures were positive for MRSA or VRE. The mean (\pm -standard error) ICU-level incidence of events of colonization or infection with MRSA or VRE per 1000 patient-days at risk, adjusted for baseline incidence, did not differ significantly between the intervention and control ICUs (40.4 \pm 3.3 and 35.6 \pm 3.7 in the two groups, respectively; $P=0.35$). The use of infection prevention measures was suboptimal in all the participating ICUs in the study. In the intervention ICUs, when contact precautions were specified, gloves were used for a median of 82% of contacts, gowns for 77% of contacts, and hand hygiene was practiced after 69% of contacts. When universal gloving was specified, gloves were used for a median of 72% of contacts and hand hygiene was practiced after 62% of contacts. In addition, the results of active surveillance cultures were available to the providers after a mean duration of 5 days from the date of culture. The study concluded that the

intervention was not effective in reducing the transmission of MRSA or VRE. The CDC interactive hand hygiene training module and educational flyers were used to increase healthcare worker adherence to hand hygiene and use of barrier precautions. The education was clearly not effective in improving adherence to infection prevention practices.

Hawe et al⁴⁴ have also reported lack of effectiveness of passive implementation of guidelines in changing caregiver practices. When the ventilator bundle was implemented in the ICU in a relatively passive manner with adoption of a policy, display of laminated copies of the bundle prominently at the bedside and encouragement to practice the components of the bundle, the rate of VAP did not improve. However, when the implementation was changed to an active process including staff education, process and outcome measurement, feedback to staff and organizational change, the rate of VAP improved from 19.2 VAP per 1000 ventilator-days during the passive implementation period to 7.5 per 1000 ventilator-days during the active implementation period.

Opportunities for Cross-contamination

Cross-contamination occurs between different body sites within a patient, between patients and between the patient and environment. An observational study involving 286 patients who underwent cardiac surgery⁴⁵ found that patients who remained on a ventilator in the post-operative period and had endotracheal colonization with gram-negative bacteria at 1 week after surgery were more likely to develop subsequent infection compared to those without colonization (8 of 23 vs. 4 of 40; relative risk 2.3 [95% confidence interval, 1.3– 4.1; *P* value <.05]). The species of gram-negative bacilli causing infection was the same as the species causing the colonization in the eight patients. Two pairs of available isolates were strain typed using Pulsed-field gel electrophoresis analysis. The isolates causing infection (1 CLABSI and 1 SSI) were indistinguishable from the isolates causing endotracheal colonization. The underlying mechanism of development of infection was either autogenous or due to extrinsic contamination of the surgical wound and central venous catheter ports with respiratory secretions in these patients.

A different study by Sethi et al⁴⁶ on patients with *C.difficile* infection found that the frequencies of skin (groin, chest, abdomen and hands) contamination and environmental shedding were high at the time of resolution of diarrhea (60% and 37%, respectively), were lower at the end of treatment (32% and 14%, respectively), and again increased 1–4 weeks after treatment (58% and 50%, respectively). Best practice approaches do not account for the various different opportunities to transmit pathogens, which may lead to development of HAI.

Outbreak investigations have identified innumerable sources of potential contamination for the patients.⁴⁷⁻⁴⁸ Without sophisticated data mining systems, hospitals are unable to detect small temporo-spatial clusters.⁴⁹ Outbreaks with emerging strains of bacteria such as the carbapenem-resistant *Enterobacteriaceae* are increasingly reported in the

literature.⁵⁰⁻⁵¹ Control measures during outbreaks and some times between outbreaks do need to go beyond known best practices for obvious reasons.

Do Patient Safety Practices Unrelated to Infection have a Role?

In an observational cohort with nested case-control study to identify predictive factors for development of MRSA infection among patients nasally colonized with MRSA,⁵² the factors that were independently associated with development of subsequent infection are development of pressure ulcer during hospital stay [Adjusted Odds Ratio 5.82; 95% Confidence Intervals 2.21 – 15.31; *p-value* = 0.000] and pre-admission steroid therapy [AOR 13.2 (2.44 – 70.97); *p-value* = 0.003]. This study is limited by being a single institutional study with a small number of patients. However, the suggestion that other patient safety practices may influence development of HAI appears plausible, because the patient safety climate is a common denominator for all patient safety events.

Infection Prevention Approaches Beyond Best Practice

Recommendations to reduce HAI fall into two broad categories – technical and adaptive. Technical strategies constitute the majority; notable examples are use of alcohol hand rub for hand hygiene,⁵³ and use of perioperative antibiotics to prevent surgical site infections (SSI).⁵⁴ Most best practices are based on technical strategies, some of which have existed for over three decades. Variability in success and sustainability of these strategies is typical.

One major reason for this variability is that healthcare organizations are complex adaptive systems.⁵⁵⁻⁵⁶ An adaptive system is a set of interacting or interdependent entities that respond to internal or external stimuli for change. Adaptive HAI prevention strategies account for organizational and cultural complexity in healthcare systems. Approaches such as bundles^{13, 54, 57-59} and checklists^{33, 60} reduce mental workload and increase adherence and reliability. Further strategies to increase staff engagement while factoring in local organizational and cultural characteristics are necessary. Novel, promising, adaptive approaches that address these complexities in healthcare are comprehensive unit based safety program (CUSP)⁶¹ and positive deviance (PD).^{33, 62-63}

Table 1. Examples of different approaches to HAI prevention

	Technical	Adaptive
Vertical ⁶⁴⁻⁶⁵ (pathogen- specific)	Active Surveillance for MRSA ⁶⁶	Positive deviance approach to reduce HAI caused by MRSA ⁶⁷
Horizontal ⁶⁴⁻⁶⁵ (pathogen non-specific)	Alcohol hand rub for hand hygiene ⁵³	PD for improvement of hand hygiene, ⁶⁸⁻⁶⁹ CUSP for reduction of CLABSI ^{18, 70}

The recently published results of the national Veterans Affairs initiative demonstrated a significant reduction in HAI caused by MRSA in VA hospitals.⁶⁷ The intervention was an 'MRSA bundle' consisting of active surveillance for MRSA, placement in contact precautions if a patient is found to have MRSA, hand hygiene, and an institutional culture change strategy whereby infection control became the responsibility of everyone who had contact with patients. This culture change strategy was an adaptation of positive deviance. The study used a quasi-experimental before-after design. Nearly 2 million admissions, transfers, or discharges in 150 hospitals with 196 ICUs and 428 non-ICUs were included in the data. Between October 2007, when the MRSA bundle was fully implemented, and the end of June 2010, the rates of healthcare-associated MRSA infections declined by 62% in intensive care units (ICUs) and by 45% in non-ICUs. The study also reported a reduction in HAIs caused by VRE and *C. difficile*, indicating that infection prevention approaches used might have had a cross-protective effect.

Positive Deviance

Positive Deviance (PD)^{33, 62, 67} is a novel asset-based, problem-solving, bedside provider-driven approach. The PD approach learns from the natural variation in experiences, practices, strategies and behaviors of individual staff members. PD is based on appreciative inquiry techniques.⁷¹ *Positive deviant practices and behaviors* that arise from local collective intelligence are identified. *Positively deviant individuals* who have comprehended infection prevention principles are also identified. Their PD behaviors and practices are amplified within the local population to cause improved outcomes. The PD approach is effective in redesigning work practices and fostering organizational change.⁷²⁻⁷³ This approach has been used effectively to improve adherence to hand hygiene^{68-69, 74} in addition to reduction of HAI caused by MRSA.^{67, 75-78}

PD approaches have also been used successfully in other quality improvement studies to improve smoking cessation,⁷⁹ weight loss⁸⁰ and outcomes related to other chronic health conditions.⁸¹ Because of reliance on locally available resources, the approach may be cost-effective although previous studies have not addressed this issue.

PD is in contrast to the Toyota production system (TPS) or lean management approach⁸² to quality improvement. TPS approach is the traditional approach to infection prevention in most hospitals, and it is based on failure or defect analysis. The shared strengths between PD and TPS are attention to organizational culture, leadership support, norms of behavior, intergroup dynamics, and power relations in the setting they are implemented. The two major differences between the approaches are that PD assumes that the effective practices already exist and the source of these practices is within the organization (the focus is on learning from exceptional examples). The PD approach turns the conventional failure analysis approach on its head and focuses on analysis of success, the converse of Reason's Swiss Cheese Model for an adverse event.^{41, 83}

Comprehensive Unit-based Safety Program (CUSP)

The comprehensive unit-based safety program (CUSP) is used to improve culture and guide organizations in learning from mistakes that are important, but cannot be measured as rates.⁸⁴ The components of CUSP are educating staff on science of safety, identifying defects, engaging executives, learning from defects and implementing teamwork tools. 'On the CUSP: stop BSI' (Principal Investigator: Peter J Pronovost) is an ongoing national study funded by the Agency for Healthcare Research and Quality (AHRQ) on implementation of CUSP to reduce CLABSI. An interim report released on April 5, 2011 by the AHRQ stated that a 35 percent reduction in CLABSI (from 1.8 to 1.17 infections per 1000 central line days) has been achieved among adult intensive care units that are participating in this project. Currently, over 1100 hospitals from 45 states are participating in this project. On the CUSP: stop CAUTI (PI: Sanjay Saint) is another ongoing study funded by the AHRQ.

Technical Solutions, Social Media and Data Systems

In today's technology-driven world, there are several technical advances being made in infection prevention and control. Use of daily chlorhexidine bathing of patients in the ICU,⁸⁵⁻⁸⁶ use of antimicrobial impregnated catheters,⁸⁷⁻⁸⁸ advanced environmental disinfection systems,⁸⁹⁻⁹⁰ specially engineered textiles,⁹¹⁻⁹² radio frequency identification technology,⁹³ etc. have an important role to play in prevention of HAI. Discussion of these strategies is beyond the scope of this article. Use of technology alone is inadequate in solving patient safety problems.

Social media websites such as YouTube, Facebook, Twitter, Second Life, have radically altered the way people communicate and interact with each other. They are excellent platforms for engaging and educating people.⁹⁴ Newer electronic data systems offer new possibilities for surveillance and subsequent prevention of healthcare-associated infections.⁹⁵

Horizontal vs. Vertical Approaches to Prevent HAI

There is a strong debate in infection prevention on whether horizontal (pathogen non-specific) approaches to prevent HAI or vertical (approaches targeted against a single pathogen, e.g., MRSA) approaches are more efficient. As resources are limited in most settings, horizontal approaches are considered by some experts to be more cost-effective.^{64-65, 96} There have been a recent shift in global health funding towards horizontal programs.⁹⁷

Rationale for Comprehensive Horizontal Approaches

During every patient's hospital stay, each encounter between patient and healthcare provider presents numerous opportunities for contamination with pathogens (Figure 4).⁹⁸

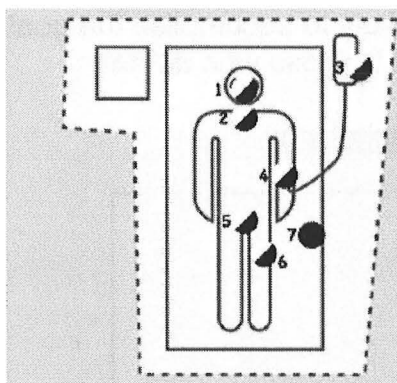


Figure 4. Numerous opportunities for contamination of patient with pathogens. Image from Sax, H. et al. (Am J Infect Control 2009;37:827-34). Examples of critical sites associated with infectious risks for the patient and/or body fluid exposure risks for healthcare worker (HCW): 1, mucous membranes of eyes and mouth; 2, tracheostoma; 3, infusion access port; 4, peripheral venous line access port; 5, urogenital mucosa; 6, wound; 7, bed linen soiled with blood. The black-and-white disks represent critical sites associated with risks for both patient and HCW; the black disk, critical sites with body fluid exposure risk for the HCW.

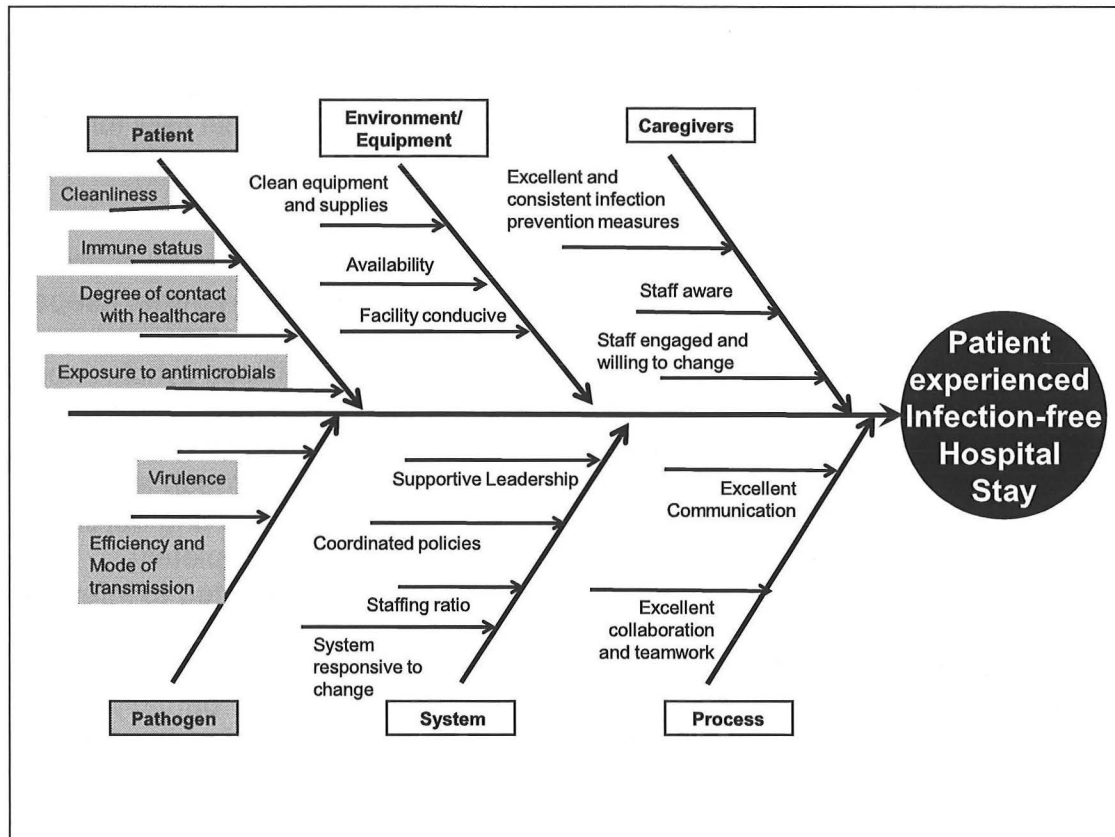
These opportunities for contamination are dynamic during a patient's hospital course. For this reason, multiple infection prevention practices including hand hygiene, asepsis during procedures such as venous catheter placement, clean catheter care, environmental hygiene and prudent use of antimicrobials must be utilized synchronously for all patients at all times. Achieving simultaneous use of all the multiple infection prevention practices during routine clinical care is challenging. HAI reduction is currently limited by addressing each type of HAI individually. The traditional approach tends to allow healthcare workers to think of individual HAI as completely distinct and unrelated entities. (e.g., catheter-associated urinary tract infection (CAUTI) is completely unrelated to CLABSI; infections caused by MRSA are completely unrelated to infections with gram-negative bacteria.) This notion is reinforced by prevention guidelines that address individual HAIs. Although this traditional perspective is helpful for some aspects of prevention (e.g., making central line insertion kits available), it is only partially applicable during day-to-day patient care. The underlying mechanisms for development of HAI, i.e., alteration of skin, gastrointestinal or respiratory flora due to antibiotic therapy, contamination of indwelling devices such as central venous catheter, peripheral venous or arterial catheter, urinary catheter, or contamination of non-intact skin (e.g., surgical incision, wounds) are similar. The underlying principles of transmission for different pathogens (e.g., *C.difficile*, MRSA, gram-negative bacteria) are also similar. For these reasons, a comprehensive, horizontal (pathogen non-specific) approach to infection prevention is necessary and relatively novel. Firstly, it is important from a patient perspective. Secondly, it is important from the perspective of a healthcare worker providing direct patient care.

Infection-free Stay for Hospital Inpatients:

Unless an infection was incubating or present at admission, an admitted patient should be infection-free through the duration of hospitalization. This concept of an infection-free hospital stay is consistent with a patient-centered approach⁷ to improving quality of care for patients including HAI prevention. National patient safety goals⁹⁹ and national guidelines¹⁰⁰ discuss specific HAIs. However, this concept of an infection-free hospital stay is not widely discussed in published literature. It is possible that healthcare workers who are able to integrate several different, but related infection prevention measures such as hand hygiene, standard precautions, isolation precautions, antimicrobial

stewardship, etc. into their daily work processes are more likely to accomplish the goal of an infection-free hospital stay for their patients compared to those who do not.

Figure5: Factors potentially leading to an infection-free hospital stay



(Boxes in grey show factors that are largely non-modifiable by caregivers)

Conclusion

Currently known best practices to prevent healthcare-associated infections have resulted in substantial improvements. However, they have significant limitations. Next level infection prevention approaches should be patient-centered and integrated into overall clinical care. The approaches must factor in scientific, social, organizational, cultural, regulatory and economic factors that influence HAI prevention. Approaches that account for organizational complexities will further improve patient safety, save lives and decrease healthcare costs.

References

1. Klevens RM, Edwards JR, Richards CL, Jr., et al. Estimating health care-associated infections and deaths in U.S. hospitals, 2002. *Public Health Rep* 2007;122:160-6.
2. Scott RD. The Direct Medical Costs of Healthcare-Associated Infections in U.S. Hospitals and the Benefits of Prevention. Atlanta, GA: Centers for Disease Control and Prevention; 2009.
3. Selwyn S. Hospital infection: the first 2500 years. *J Hosp Infect* 1991;18 Suppl A:5-64.
4. Sydnor ER, Perl TM. Hospital epidemiology and infection control in acute-care settings. *Clin Microbiol Rev* 2011;24:141-73.
5. Haley RW, Culver DH, White JW, et al. The efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals. *Am J Epidemiol* 1985;121:182-205.
6. Haley RW, Morgan WM, Culver DH, et al. Update from the SENIC project. Hospital infection control: recent progress and opportunities under prospective payment. *Am J Infect Control* 1985;13:97-108.
7. Baker A. Crossing the Quality Chasm: A New Health System for the 21st Century. Washington, DC: National Academy Press; 2001.
8. World Health Organization Patient Safety. (Accessed July 6, 2011, 2011, at <http://www.who.int/patientsafety/en/>.)
9. WHO guidelines on hand hygiene in health care. World Health Organization; 2009.
10. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control* 2008;36:309-32.
11. Centers for Disease Control and Prevention. The National Healthcare Safety Network (NHSN) Manual: Patient Safety Component Protocol. In. Atlanta, GA; 2010.
12. Dubberke ER, Gerding DN, Classen D, et al. Strategies to prevent clostridium difficile infections in acute care hospitals. *Infect Control Hosp Epidemiol* 2008;29 Suppl 1:S81-92.
13. Bundles of care. Institute for Healthcare Improvement. (Accessed August 7, 2010, 2010, at <http://www.ihl.org/IHI/Topics/CriticalCare/IntensiveCare/Changes/>.)
14. Haynes AB, Weiser TG, Berry WR, et al. A surgical safety checklist to reduce morbidity and mortality in a global population. *N Engl J Med* 2009;360:491-9.
15. Pronovost P, Needham D, Berenholtz S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med* 2006;355:2725-32.
16. Measuring hand hygiene adherence: overcoming the challenges Oak Brook, Illinois, USA: The Joint Commission; 2009.
17. Rello J, Lode H, Cornaglia G, Masterton R. A European care bundle for prevention of ventilator-associated pneumonia. *Intensive Care Med* 2010;36:773-80.
18. Pronovost PJ, Goeschel CA, Colantuoni E, et al. Sustaining reductions in catheter related bloodstream infections in Michigan intensive care units: observational study. *BMJ* 2010;340:c309.
19. Reduction in central line-associated bloodstream infections among patients in intensive care units--Pennsylvania, April 2001-March 2005. *MMWR Morb Mortal Wkly Rep* 2005;54:1013-6.
20. Berenholtz SM, Pham JC, Thompson DA, et al. Collaborative cohort study of an intervention to reduce ventilator-associated pneumonia in the intensive care unit. *Infect Control Hosp Epidemiol* 2011;32:305-14.
21. Resar R, Pronovost P, Haraden C, Simmonds T, Rainey T, Nolan T. Using a bundle approach to improve ventilator care processes and reduce ventilator-associated pneumonia. *Jt Comm J Qual Patient Saf* 2005;31:243-8.
22. Bonello RS, Fletcher CE, Becker WK, et al. An intensive care unit quality improvement collaborative in nine Department of Veterans Affairs hospitals: reducing ventilator-associated

- pneumonia and catheter-related bloodstream infection rates. *Jt Comm J Qual Patient Saf* 2008;34:639-45.
23. Bratzler DW, Hunt DR. The surgical infection prevention and surgical care improvement projects: national initiatives to improve outcomes for patients having surgery. *Clin Infect Dis* 2006;43:322-30.
 24. Stulberg JJ, Delaney CP, Neuhauser DV, Aron DC, Fu P, Koroukian SM. Adherence to surgical care improvement project measures and the association with postoperative infections. *JAMA* 2010;303:2479-85.
 25. Dellinger EP, Hausmann SM, Bratzler DW, et al. Hospitals collaborate to decrease surgical site infections. *Am J Surg* 2005;190:9-15.
 26. Meddings J, Rogers MA, Macy M, Saint S. Systematic review and meta-analysis: reminder systems to reduce catheter-associated urinary tract infections and urinary catheter use in hospitalized patients. *Clin Infect Dis* 2010;51:550-60.
 27. Topal J, Conklin S, Camp K, Morris V, Balczak T, Herbert P. Prevention of nosocomial catheter-associated urinary tract infections through computerized feedback to physicians and a nurse-directed protocol. *Am J Med Qual* 2005;20:121-6.
 28. Henderson DK, Palmore TN. Critical gaps in knowledge of the epidemiology and pathophysiology of healthcare-associated infections. *Infect Control Hosp Epidemiol* 2010;31 Suppl 1:S4-6.
 29. Kirkland KB. From best to good: can we "right-size" approaches to reducing healthcare-associated infections? *Infect Control Hosp Epidemiol* 2010;31:784-5.
 30. Edwards JR, Peterson KD, Mu Y, et al. National Healthcare Safety Network (NHSN) report: data summary for 2006 through 2008, issued December 2009. *Am J Infect Control* 2009;37:783-805.
 31. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. *Am J Infect Control* 2004;32:470-85.
 32. Dudeck MAH, T.C.; Peterson, K.D.; Bridson, K.A., Morrell, G.C., Pollock, D.A., Edwards, J.R. National Healthcare Safety Network (NHSN) Report, Data Summary for 2009, Device-associated Module. Atlanta, Georgia, USA: Centers for Disease Control and Prevention; 2010.
 33. Anderson J, Gosbee LL, Bessesen M, Williams L. Using human factors engineering to improve the effectiveness of infection prevention and control. *Crit Care Med* 2010;38:S269-81.
 34. Davis DA, Taylor-Vaisey A. Translating guidelines into practice. A systematic review of theoretic concepts, practical experience and research evidence in the adoption of clinical practice guidelines. *CMAJ* 1997;157:408-16.
 35. Grol RG, J. From best evidence to best practice: effective implementation of change in patients' care. *Lancet* 2003;362:1225-30.
 36. Gurses AP, Seidl KL, Vaidya V, et al. Systems ambiguity and guideline compliance: a qualitative study of how intensive care units follow evidence-based guidelines to reduce healthcare-associated infections. *Qual Saf Health Care* 2008;17:351-9.
 37. Lee FM TS, Tucker C, Krizan J, Ayeni A, Sreeramaju P. Surgical site infections among patients receiving care per Surgical Care Improvement Project. Abstract. In: Fifth Decennial International Conference on Healthcare Associated Infections; 2010; Atlanta, GA; 2010.
 38. Pastor C, Artinyan A, Varma MG, Kim E, Gibbs L, Garcia-Aguilar J. An increase in compliance with the Surgical Care Improvement Project measures does not prevent surgical site infection in colorectal surgery. *Dis Colon Rectum* 2010;53:24-30.
 39. Ingraham AM, Cohen ME, Bilimoria KY, et al. Association of surgical care improvement project infection-related process measure compliance with risk-adjusted outcomes: implications for quality measurement. *J Am Coll Surg* 2010;211:705-14.
 40. Chodoff A, Pettis AM, Schoonmaker D, Shelly MA. Polymicrobial gram-negative bacteremia associated with saline solution flush used with a needleless intravenous system. *Am J Infect Control* 1995;23:357-63.

41. Reason J. Understanding adverse events: human factors. *Qual Health Care* 1995;4:80-9.
42. Grilli R, Lomas J. Evaluating the message: the relationship between compliance rate and the subject of a practice guideline. *Med Care* 1994;32:202-13.
43. Huskins WC, Huckabee CM, O'Grady NP, et al. Intervention to reduce transmission of resistant bacteria in intensive care. *N Engl J Med* 2011;364:1407-18.
44. Hawe CS, Ellis KS, Cairns CJ, Longmate A. Reduction of ventilator-associated pneumonia: active versus passive guideline implementation. *Intensive Care Med* 2009;35:1180-6.
45. Sreeramoju PV, Garcia-Houchins S, Bova J, Kelly CC, Patterson JE, Weber SG. Correlation between respiratory colonization with gram-negative bacteria and development of gram-negative bacterial infection after cardiac surgery. *Infect Control Hosp Epidemiol* 2008;29:546-8.
46. Sethi AK, Al-Nassir WN, Nerandzic MM, Bobulsky GS, Donskey CJ. Persistence of skin contamination and environmental shedding of *Clostridium difficile* during and after treatment of *C. difficile* infection. *Infect Control Hosp Epidemiol* 2010;31:21-7.
47. Srinivasan A. Influential outbreaks of healthcare-associated infections in the past decade. *Infect Control Hosp Epidemiol* 2010;31 Suppl 1:S70-2.
48. Siegel JD, Rhinehart E, Jackson M, Chiarello L. Management of multidrug-resistant organisms in health care settings, 2006. *Am J Infect Control* 2007;35:S165-93.
49. Huang SS, Yokoe DS, Stelling J, et al. Automated detection of infectious disease outbreaks in hospitals: a retrospective cohort study. *PLoS Med* 2010;7:e1000238.
50. Carbonne A, Thiolet JM, Fournier S, et al. Control of a multi-hospital outbreak of KPC-producing *Klebsiella pneumoniae* type 2 in France, September to October 2009. *Euro Surveill* 2010;15.
51. Gupta N, Limbago BM, Patel JB, Kallen AJ. Carbapenem-resistant enterobacteriaceae: epidemiology and prevention. *Clin Infect Dis* 2011;53:60-7.
52. Sreeramoju, P.; De Marco, B.; Ortegon, A.; Ramarathnam, V.; Ayeni, A.; Kemp, D.; Luby, J. Risk factors for methicillin-resistant *Staphylococcus aureus* (MRSA) infection among hospitalized patients with nasal MRSA colonization. Abstract. In: Fifth Decennial International Conference on Healthcare Associated Infections; 2010; Atlanta, GA 2010.
53. Boyce JM, Pittet D. Guideline for Hand Hygiene in Health-Care Settings. Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. Society for Healthcare Epidemiology of America/Association for Professionals in Infection Control/Infectious Diseases Society of America. *MMWR Recomm Rep* 2002;51:1-45, quiz CE1-4.
54. Anderson DJ, Kaye KS, Classen D, et al. Strategies to prevent surgical site infections in acute care hospitals. *Infect Control Hosp Epidemiol* 2008;29 Suppl 1:S51-61.
55. Plesk P. Redesigning health care with insights from the science of complex adaptive systems. In: *Crossing the quality chasm: A new health system for the 21st century*. Washington, D.C.: Institute of Medicine, National Academy Press; 2001:322-35.
56. Plsek PE, Greenhalgh T. Complexity science: The challenge of complexity in health care. *BMJ* 2001;323:625-8.
57. Lo E, Nicolle L, Classen D, et al. Strategies to prevent catheter-associated urinary tract infections in acute care hospitals. *Infect Control Hosp Epidemiol* 2008;29 Suppl 1:S41-50.
58. Marschall J, Mermel LA, Classen D, et al. Strategies to prevent central line-associated bloodstream infections in acute care hospitals. *Infect Control Hosp Epidemiol* 2008;29 Suppl 1:S22-30.
59. Coffin SE, Klompas M, Classen D, et al. Strategies to prevent ventilator-associated pneumonia in acute care hospitals. *Infect Control Hosp Epidemiol* 2008;29 Suppl 1:S31-40.
60. Duane TM, Brown H, Borchers CT, et al. A central venous line protocol decreases bloodstream infections and length of stay in a trauma intensive care unit population. *Am Surg* 2009;75:1166-70.

61. Sawyer M, Weeks K, Goeschel CA, et al. Using evidence, rigorous measurement, and collaboration to eliminate central catheter-associated bloodstream infections. *Crit Care Med* 2010;38:S292-8.
62. Pascale RS, Jerry. Sternin, Monique. *The Power of Positive Deviance: How Unlikely Innovators Solve the World's Toughest Problems* Boston, MA: Harvard Business Press; 2010.
63. Singhal AB, Prucia. Lindberg, Curt. . *Inviting Everyone: Healing Healthcare through Positive Deviance*. Bordentown, New Jersey: PlexusPress; 2010.
64. Wenzel RP. Minimizing surgical-site infections. *N Engl J Med* 2010;362:75-7.
65. Wenzel RP, Edmond MB. Infection control: the case for horizontal rather than vertical interventional programs. *Int J Infect Dis* 2010;14 Suppl 4:S3-5.
66. Calfee DP, Salgado CD, Classen D, et al. Strategies to prevent transmission of methicillin-resistant *Staphylococcus aureus* in acute care hospitals. *Infect Control Hosp Epidemiol* 2008;29 Suppl 1:S62-80.
67. Jain R, Kralovic SM, Evans ME, et al. Veterans Affairs initiative to prevent methicillin-resistant *Staphylococcus aureus* infections. *N Engl J Med* 2011;364:1419-30.
68. Marra AR, Guastelli LR, de Araujo CM, et al. Positive deviance: a new strategy for improving hand hygiene compliance. *Infect Control Hosp Epidemiol* 2010;31:12-20.
69. Marra AR, Reis Guastelli L, Pereira de Araujo CM, et al. Positive deviance: A program for sustained improvement in hand hygiene compliance. *Am J Infect Control* 2011;39:1-5.
70. Pronovost PJ, Marsteller JA, Goeschel CA. Preventing bloodstream infections: a measurable national success story in quality improvement. *Health Aff (Millwood)* 2011;30:628-34.
71. Carter CA, Ruhe MC, Weyer S, Litaker D, Fry RE, Stange KC. An appreciative inquiry approach to practice improvement and transformative change in health care settings. *Qual Manag Health Care* 2007;16:194-204.
72. Marsh DR, Schroeder DG, Dearden KA, Sternin J, Sternin M. The power of positive deviance. *BMJ* 2004;329:1177-9.
73. Pascale RT, Sternin J. Your company's secret change agents. *Harv Bus Rev* 2005;83:72-81, 153.
74. Rupp ME, Kalil AC. Positive deviance and hand hygiene: more questions than answers. *Infect Control Hosp Epidemiol* 2010;31:978-9; author reply 9-80.
75. Aston G. Fresh approaches stem MRSA tide. *Mater Manag Health Care* 2009;18:22-5.
76. Lindberg C, Clancy TR. Positive deviance: an elegant solution to a complex problem. *J Nurs Adm* 2010;40:150-3.
77. Lindberg C NP, Munger MT, DeMarsico C, Buscell P. . *Letting Go,Gaining Control: Positive Deviance and MRSA Prevention*. Clinical Leader 2009.
78. Singhal A. Communicating what works! Applying the positive deviance approach in health communication. *Health Commun* 2010;25:605-6.
79. Awofeso N, Irwin T, Forrest G. Using positive deviance techniques to improve smoking cessation outcomes in New South Wales prison settings. *Health Promot J Austr* 2008;19:72-3.
80. Stuckey HL, Boan J, Kraschnewski JL, Miller-Day M, Lehman EB, Sciamanna CN. Using positive deviance for determining successful weight-control practices. *Qual Health Res* 2011;21:563-79.
81. Schubart JR, Stuckey HL, Ganeshamoorthy A, Sciamanna CN. Chronic health conditions and internet behavioral interventions: a review of factors to enhance user engagement. *Comput Inform Nurs* 2011;29:TC9-20.
82. Shannon RP, Frndak D, Grunden N, et al. Using real-time problem solving to eliminate central line infections. *Jt Comm J Qual Patient Saf* 2006;32:479-87.
83. Reason J. *Human Error*. Cambridge: Cambridge University Press; 1990.
84. Pronovost PJ, Berenholtz SM, Goeschel CA, et al. Creating high reliability in health care organizations. *Health Serv Res* 2006;41:1599-617.

85. Kassakian SZ, Mermel LA, Jefferson JA, Parenteau SL, Machan JT. Impact of chlorhexidine bathing on hospital-acquired infections among general medical patients. *Infect Control Hosp Epidemiol* 2011;32:238-43.
86. Popovich KJ, Hota B, Hayes R, Weinstein RA, Hayden MK. Daily skin cleansing with chlorhexidine did not reduce the rate of central-line associated bloodstream infection in a surgical intensive care unit. *Intensive Care Med* 2010;36:854-8.
87. Gilbert RE, Harden M. Effectiveness of impregnated central venous catheters for catheter related blood stream infection: a systematic review. *Curr Opin Infect Dis* 2008;21:235-45.
88. Di Filippo A, Casini A, de Gaudio AR. Infection prevention in the intensive care unit: review of the recent literature on the management of invasive devices. *Scand J Infect Dis* 2011;43:243-50.
89. Nerandzic MM, Cadnum JL, Pultz MJ, Donskey CJ. Evaluation of an automated ultraviolet radiation device for decontamination of *Clostridium difficile* and other healthcare-associated pathogens in hospital rooms. *BMC Infect Dis* 2010;10:197.
90. Shapey S, Machin K, Levi K, Boswell TC. Activity of a dry mist hydrogen peroxide system against environmental *Clostridium difficile* contamination in elderly care wards. *J Hosp Infect* 2008;70:136-41.
91. Hsu BB, Klibanov AM. Light-activated covalent coating of cotton with bactericidal hydrophobic polycations. *Biomacromolecules* 2011;12:6-9.
92. Gross R, Hubner N, Assadian O, Jibson B, Kramer A. Pilot study on the microbial contamination of conventional vs. silver-impregnated uniforms worn by ambulance personnel during one week of emergency medical service. *GMS Krankenhhyg Interdiszip* 2010;5.
93. Radio-frequency identification: its potential in healthcare. *Health Devices* 2005;34:149-60.
94. Bennett GG, Glasgow RE. The delivery of public health interventions via the Internet: actualizing their potential. *Annu Rev Public Health* 2009;30:273-92.
95. Woeltje KF, Lautenbach E. Informatics and epidemiology in infection control. *Infect Dis Clin North Am* 2011;25:261-70.
96. Wenzel RP, Bearman G, Edmond MB. Screening for MRSA: a flawed hospital infection control intervention. *Infect Control Hosp Epidemiol* 2008;29:1012-8.
97. Barnighausen T, Bloom DE, Humair S. Going horizontal--shifts in funding of global health interventions. *N Engl J Med* 2011;364:2181-3.
98. Sax H, Allegranzi B, Chraiti MN, Boyce J, Larson E, Pittet D. The World Health Organization hand hygiene observation method. *Am J Infect Control* 2009;37:827-34.
99. National Patient Safety Goals. In: Accreditation Program: Hospital: The Joint Commission; 2010.
100. Yokoe DS, Mermel LA, Anderson DJ, et al. A compendium of strategies to prevent healthcare-associated infections in acute care hospitals. *Infect Control Hosp Epidemiol* 2008;29 Suppl 1:S12-21.