Programs to reduce central line–associated bloodstream infections (CLABSIs) have improved the safety of hospitalized patients. Efforts are underway to disseminate these successes broadly to reduce other types of hospital-acquired infectious and noninfectious preventable harms. Unfortunately, the ability to broadly measure and prevent other types of preventable harms, especially infectious harms, needs enhancement. Moreover, an overarching research framework for creating and integrating evidence will help expedite the development of national prevention programs. This article outlines a 5-phase translational (T) framework to develop robust research programs that reduce preventable harm, as follows: phase T0, discover opportunities and approaches to prevent adverse health care events; phase T1, use T0 discoveries to develop and test interventions on a small scale; phase T2, broaden and strengthen the evidence base for promising interventions to develop evidence-based guidelines; phase T3, translate guidelines into clinical practice; and phase T4, implement and evaluate T3 work on a national and international scale. Policy makers should use this framework to fill in the knowledge gaps, coordinate efforts among federal agencies, and prioritize research funding.

As we mark the 10-year anniversary of the To Err is Human report, limited progress has been made in reducing patient harm [1–3]. Although the rates of certain adverse health care–associated events have recently declined [4, 5], it has been difficult to document overall improvement in patient outcomes [6]. Moreover, measures to evaluate health care performance are not widely used or not available for many adverse events, implementation of evidence-based patient care practice remains incomplete, and consumer access to outcome data is limited [3]. Improved strategies for monitoring and improving patient outcomes are needed.

Fortunately, successful models for translating evidence into prevention practice exist. For example, the approaches to reducing CLABSIs in the Michigan [7] and Pittsburgh initiatives [8] have helped shift national expectations regarding CLABSI prevention. Although the Centers for Disease Control and Prevention (CDC) reported declining CLABSI rates among hospitals reporting data between 1997 and 2007 [4], the Michigan and Pennsylvania collaboratives demonstrated a larger preventable fraction for CLABSIs than previously appreciated and major reductions in a relatively short time frame across a broad spectrum of health care facilities. These observations influenced widespread adoption of the goal of eliminating bloodstream infections [9]. Similar successes have subsequently been reported, and efforts are currently underway to replicate the model used in Michigan throughout all 50 states [10, 11]. The attention garnered by these programs has also spurred interest in creating statewide and national programs to reduce other health care–associated infections (HAIs) [12]. To
optimize the success of similar endeavors, it is important to first carefully examine the factors we believe contributed to the recent dramatic reductions in CLABSI.

First and foremost, a substantial number of scientific contributions made these recent successes possible, including (1) epidemiologic studies leading to hypotheses about new prevention strategies; (2) efficacy and effectiveness studies that were the foundation for evidence-based guidelines; (3) research to refine and translate guidelines to optimize the feasibility of implementation; (4) advances in strategies to overcome obstacles to evidence-based practice; (5) development and availability of robust yet feasible outcome measures; and (6) development of an infrastructure and partnerships for dissemination. These contributions plus the public health burden of this patient safety problem made CLABSI an attractive target for prevention. They provided a clear evidence base from which key interventions focused on a specific procedure (eg, catheter insertion) could be effectively and efficiently applied using innovative implementation strategies to increase practice compliance and a method to measure outcomes accurately. It is tempting to assume that the CLABSI prevention models used in Michigan and Pittsburgh can be immediately and directly applied to other HAIs or noninfectious preventable harms with similar success. However, these models may not directly apply to other prevention targets, because the scientific evidence base for measurement and prevention of other types of harm is, unfortunately, not as robust as that for CLABSI. Moreover, other strategies besides checklists may reduce other types of preventable harm [13–15]. To achieve similar successes in preventing other types of HAIs, it is imperative to devote adequate attention and resources when translating the “basic” science of health care epidemiology into reliable implementation of evidence-based care at the bedside. In this article, we propose a framework for developing national research programs to increase the extent to which patients receive evidence-based practices that prevent HAI and other noninfectious patient harms.

FRAMEWORK FOR CREATING EVIDENCE AND TRANSLATING IT INTO PRACTICE

Researchers have specified 5 phases through which basic scientific discoveries are translated into improved population health. These phases are analogous to those of new drug development and provide a useful framework for researchers, clinicians, and policy makers to understand and address the complexity of creating and implementing evidence-based strategies for preventing adverse health care events [16–19]. In this context of preventing HAI, the “basic” discoveries that require translation for better patient care occur through laboratory, surveillance, outbreak investigation, epidemiologic studies, and technologic advances. Table 1 illustrates the parallels and similarities between the translational phases for basic science, new drug development, and patient safety interventions. The recent advances in CLABSI prevention are used as an example of the 5-phase translation framework in Table 2.

Phase T0: Discovering Opportunities and Approaches to Prevent Adverse Events through Surveillance, Outbreak Investigation, Epidemiologic Studies, and Basic Science

The success of CLABSI prevention in intensive care units is founded in early outbreak investigations and observations from surveillance systems, such as the National Nosocomial Infection Surveillance System of the CDC. Findings helped identify prevention target populations by demonstrating that central venous catheters are a major risk factor for bloodstream infections, with infection rates highest among the critically ill [20]. Furthermore, epidemiologic and microbiologic research suggests that bacterial contamination of the cutaneous insertion site causes most CLABSI occurring in the first few days of catheter use [21, 22]. These observations prompted the hypothesis that improved disinfection of the insertion site might be an effective prevention strategy, setting the stage for the first phase T1 studies.

Phase T1: Using T0 Discoveries to Develop and Test Novel Candidate Interventions in a Small Sample of Patients or in Limited Health Care Settings

Investigators performed T1 hypothesis-testing epidemiologic studies of CLABSI and found evidence suggesting that stringent disinfection of the insertion site, full barrier precautions for patient and operator, and avoidance of non–subclavian vein insertion sites might reduce rates of infection [21, 23]. Moreover, studies of chlorhexidine-alcohol skin preparations suggested greater suppression of bacterial skin colonization at the insertion site than with other antiseptics [24]. Although such studies generated promising data, they did not provide the level of evidence necessary to warrant inclusion in evidence-based guidelines. They were, however, essential in setting the stage for phase T2 clinical studies.

Phase T2: Broadening and Strengthening the Evidence Base for Promising Interventions and Developing Evidence-Based Guidelines

Clinical studies in phase T2 add evidence supporting candidate T1 interventions by applying more rigorous study designs in larger and more diverse study populations and quantifying the impact of the interventions on clinical and economic outcomes. For example, observational and interventional studies demonstrated that the risk of CLABSI was reduced by using maximum sterile barrier precautions during central venous catheter insertion [25] and cleansing the skin with a chlorhexidine-based antiseptic (rather than povidone-iodine) before insertion [26–28]. Such studies provided the basis for the CDC guidelines for preventing CLABSI [33]. Notably, phase T2 research is not limited to large randomized, controlled trials. Alternative models of investigation, such as data mining, time series...
analyses, and evaluation of phased implementation of clinical initiatives, can generate useful information. Combining and summarizing evidence from various sources can also be an important component of phase T2. For example, formal systematic reviews, meta-analyses, and economic evaluations can provide robust evidence for or against infection prevention practices and have been increasingly used to inform policy [34–36]. Current evidence summaries can be laborious and slow, however, creating a barrier to implementation. Continuous and real-time summaries by communities of practice could improve the efficiency and effectiveness of this process. The T2 phase is critical because it provides the foundation for valid clinical practice guidelines and recommendations.

**Phase T3: Moving Evidence-Based Guidelines into Practice, Through Delivery, Dissemination, and Diffusion Research**

In this phase, researchers take evidence describing effective interventions and determine how to convert these interventions into practice behaviors and broadly implementable programs that demonstrate measurable improvements in patient outcomes. The importance of this phase is often underappreciated. If insufficient research is performed in this phase of the translational pathway, improved health outcomes can be delayed. The major barriers in performing T3 research include limited funding and the relative immaturity of methods to conduct implementation research. Science must guide implementation research so that the barriers to innovation uptake can be mitigated. Some of these barriers may be at the health system or leadership level rather than the clinical level, but researchers must still comprehensively address them.

Although the Michigan collaborative had limitations, we use it here as an example of T3 research that may provide a useful model [7, 37, 38]. In this project, the investigators divided phase T3 work into 3 steps. In step 1, they converted a subset of guideline recommendations (the product of T0–T2 activity) into a checklist of behaviors focused on a specific task (inserting a central venous catheter). They chose recommendations that had the most impact, posed the lowest risk to patients, and were the least burdensome or expensive to implement. They also adopted the CDC’s surveillance definitions and methods to collect, aggregate, and share data on infection.

In step 2, the investigators identified local barriers in implementing any checklist items and developed strategies to overcome them [39]. They ensured that line insertion supplies were available and employed the Comprehensive Unit-based Safety Program to address local, leadership, and organization-level culture barriers to change [40–44]. Organizational readiness, in which hospitals and clinicians are committed and competent to implement the intervention is an essential component [45].

In step 3, the investigators pilot-tested the multifaceted program and measures in a representative group of hospitals [7, 38]. Including both qualitative [46] and quantitative research...
methods, this step helped investigators obtain feedback from clinicians, revise the interventions, and determine whether the program was feasible, meaningful, and important to the clinicians, and it actually improved patient outcomes. We believe that centralized measurement and evidence summaries made this program work, along with local unit-level culture improvement and identification and mitigation of barriers to using evidence-based practices. In addition, theory of behavior change should guide the intervention [47]. Uptake of an intervention may be enhanced by management tools (eg, performance measures), social pressure (eg, Consumers Union involvement), economic incentives (eg, pay for performance), and regulatory efforts. In implementing an intervention, it is important to sustain it and, if desired, apply it to other clinical areas. Despite large-scale efforts to spread improvement efforts, little is known about factors that predict sustainability or spread [48]. This topic should be given high priority in future T3 research.

**Phase T4: National Implementation and Evaluation**

In designing national implementation programs that will be studied in phase T4, it is vital to clarify the mechanism by which the program will be broadly disseminated, coordinated, implemented, and evaluated. In current efforts to replicate the Michigan collaborative throughout the United States, the distribution network is organized by state. This approach has advantages given the number of important state-level stakeholders (hospital associations, health departments, quality improvement, and patient safety organizations) that can disseminate interventions and coordinate implementation. Federal and other national stakeholders are also involved, including the CDC, the Agency for Healthcare Research and Quality (AHRQ), the Centers for Medicare and Medicaid Services (CMS), the American Hospital Association, and professional societies, such as the Society for Healthcare Epidemiology of America and the Association for Professionals in Infection Control and Epidemiology. Recently, the CDC and AHRQ invested in the infection prevention activities of state health departments and state hospital associations, respectively, to help these groups align efforts and collaborate in achieving national HAI prevention goals [12]. For example, the CDC’s National Healthcare Safety Network (NHSN) now collects data from >4000 hospitals in 50 states, and the recent CMS rule requiring reporting to the NHSN to

### Table 2. Translational Research Contributions to Success in Preventing Central Line–Associated Bloodstream Infections

<table>
<thead>
<tr>
<th>Translational Research Phase</th>
<th>Contribution</th>
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<tr>
<td>Phase 0 (T0): discovering opportunities and approaches to prevent adverse events through surveillance, outbreak investigation, epidemiologic studies, and basic science</td>
<td>Observation that central venous catheters are the most important risk factor for bloodstream infection (National Nosocomial Infection Surveillance system data), especially in critically ill and high-risk patients [19]; microbiologic studies suggesting that contamination of cutaneous insertion site by skin flora is responsible for most early infections, leading to the testable hypothesis that improving methods for cutaneous decolonization before catheter insertion may be an effective preventive strategy [20,21]</td>
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<tr>
<td>Phase 1 (T1): using T0 discoveries to develop and test novel candidate interventions in a small sample of patients or in limited health care settings</td>
<td>Observational study showing that catheters inserted under more stringent barrier precautions had lower risk of infection [20]; evidence that non–subclavian vein insertion sites increase the risk of catheter contamination and infection [20,22]; evidence that chlorhexidine-based preparations are highly effective at sustained suppression of skin colonization [23]</td>
</tr>
<tr>
<td>Phase 2 (T2): broadening and strengthening the evidence base for promising interventions and developing evidence-based guidelines</td>
<td>Randomized, controlled single-center trial demonstrates maximal barrier precautions effective in reducing bloodstream infection [24]; randomized, controlled trials demonstrating that chlorhexidine is superior to other skin preparations in reducing bloodstream infection rates [25–27]; meta-analysis of numerous trials evaluating chlorhexidine-based skin disinfection indicating a significant reduction in bloodstream infections [29]; formal economic evaluation indicating that chlorhexidine site disinfection reduces infections and saves money compared with povidone-iodine [30]; systematic review of the few studies evaluating maximum sterile barriers indicating a likely benefit [31]; formal economic evaluation indicating that maximum sterile barriers reduce infections and save money compared with standard barriers [32]; distillation of evidence to prevent central line–associated bloodstream infection in comprehensive evidence-based guidelines [30]</td>
</tr>
<tr>
<td>Phase 3 (T3): moving evidence-based guidelines into practice, through delivery, dissemination, and diffusion research</td>
<td>Evidence that collaborative regional extension of bloodstream infection prevention “bundles” leads to significant reductions among critically ill across large and diverse populations of hospitals (ie, Michigan Keystone Initiative, Pittsburgh Regional Health care Initiative) [6,7]</td>
</tr>
<tr>
<td>Phase 4 (T4): national implementation and evaluation</td>
<td>National support to state health departments to promote bloodstream infection (and other health care–associated infection) prevention collaboratives [8], national expansion of Michigan Keystone Projects [6] (Agency for Healthcare Research and Quality); monitoring of population-based changes in outcomes (eg, through National Healthcare Safety Network surveillance [46]) and exploration of positive and negative outliers</td>
</tr>
</tbody>
</table>
receive certain Medicare hospital inpatient prospective payments should boost participation further [49], positioning NHSN as a platform for evaluating the national impact of HAI prevention programs on clinical and economic outcomes.

With any large collaborative improvement program, it is important to balance 2 tensions. The first tension is deciding what work should be standardized centrally and what should be modified locally. In general, the technical components of the work (eg, reviewing the evidence, developing measures) should be centralized, whereas implementation strategies should be modified based on local context to improve performance of evidence-based practices. The second tension is deciding how scientifically sound versus feasible to make the data collection. In general, large collaborative efforts should use systems that minimize the burden of data collection while producing high quality data that allow the public, policy makers, and providers to make well-informed conclusions about quality of care. This generally means collecting a higher quality and a lower quantity of data. A valid and standardized national measure, such as the CLABSI rate, can align national efforts toward a common goal. The collaborative distribution channels in phase T4 of the CLABSI prevention effort encouraged dialogue and learning among local prevention efforts and the opportunity to improve the central measurement system to address local, regional, and national needs.

This translational research process is usually not linear. It can be bidirectional, and different phases can occur simultaneously. For example, while phase T4 CLABSI prevention work is occurring, there is still a need for ongoing T0–T3 work. Improved bloodstream infection measurement strategies that employ electronic information systems are being studied (phase T0), which will dramatically reduce the burden of data collection and potentially improve the accuracy of interfacility comparisons. Promising phase T1 and T2 research with antimicrobial lock solutions for CLABSI prevention is ongoing [50, 51], as is additional phase T3 work to identify and overcome barriers to CLABSI prevention in settings outside the intensive care unit. Each of these efforts will inform T4 work, and gaps and questions identified in T4 evaluation efforts will guide ongoing T1–T3 research. The amount of research required in each phase may vary depending on the targeted adverse event. Interventions that can be “hardwired” into a system, making it difficult to avoid implementation, will require less T3 phase research than those requiring broad-based behavior changes. What is novel about this model is it begins with the goal of eliminating infections and works backward to fill gaps in knowledge that are important to achieve that goal.

**USING THE FRAMEWORK TO REDUCE OTHER HEALTH CARE-ASSOCIATED INFECTIONS AND PREVENTABLE HARMs**

The promise of current national efforts to prevent CLABSIs results from investments in all phases of the translational research process. One concern with efforts to reduce other HAIs or other preventable harms is the attempts to skip to phase T4 work without investing sufficiently in earlier phases of the translational process. Science must inform efforts to reduce preventable harm. Without sufficient grounding in phase T0, T1, T2, and T3 research, it is unlikely that future HAI prevention programs will realize the same broad-scale benefit to patients that the Michigan and Pittsburgh projects demonstrated. Using the drug development analogy, phase T4 is only possible because of an adequate investment in the drug development “pipeline” (phases 0–3). Investment in T0–T3 research will increase our ability to prevent patients from suffering HAIs and other preventable harms. Federal agencies should be encouraged to ensure adequate funding for all phases of translational research, to work toward eliminating HAIs and other patient harms.

In early 2009, the US Department of Health and Human Services released an Action Plan to Prevent Healthcare-Associated Infections [12]. In addition to activities to sustain the progress in preventing CLABSIs, the document made prevention of other important infections a priority, including surgical site infections, ventilator-associated pneumonia, catheter-associated urinary tract infections (CAUTIs), and infections caused by *Clostridium difficile* and methicillin-resistant *Staphylococcus aureus*. Each of these infections has important gaps in translational research that must be addressed before phase T4 activities can successfully achieve nationwide implementation. For example, there remains a critical need for phase T0 work to develop a feasible yet accurate surveillance method for ventilator-associated pneumonia and a standardized case finding strategy to detect surgical site infections, especially in the ambulatory setting. Moreover, gaps in phase T1 and T2 research include defining the appropriate role of condom catheters, investigating bacterial interference, and assessing whether newer catheter materials—such as antimicrobial coatings—reduce clinically significant outcomes in preventing CAUTIs; evaluating the impact of various environmental cleaning strategies on prevention of *C. difficile* infection; and determining optimal strategies for targeted preoperative *S. aureus* decolonization to prevent surgical site infections.

Additional phase T3 work is also essential. For example, the CDC recently published updated evidence-based guidelines for prevention of CAUTIs [52]. Given the wide variation in practices to prevent CAUTIs in US hospitals [53], coupled with the low priority given to CAUTI prevention compared with prevention of other HAIs [54], widespread implementation will be challenging without additional preliminary work. Indeed, phase T4 work to implement and evaluate a national CAUTI prevention strategy may be hampered by the lack of important T3 research activities to convert guidelines into effective translation mechanisms, identify barriers to guideline compliance, learn ways to ensure that all patients receive recommended catheter insertion and care, and ensure that outcome measures are scientifically sound and feasible. Unless translational research is viewed as a continuum that...
begins with basic and epidemiologic research and ends not just with new knowledge but with measurable improvement in population health, patients will continue to suffer preventable harm. Again, this process could start with the public health goal of eliminating CAUTI and work backward by ensuring that each phase in the translation framework is done. Similar approaches can be used to prevent decubitus ulcers or surgical complications.

Coordination among federal agencies, particularly the CDC, National Institutes of Health (NIH), and AHRQ, is important to ensure that gaps in the translational process are avoided. Each of these agencies has a primary role to play in directing translational HAI research investments. The CDC brings decades of experience in HAI epidemiologic investigation and a decisive link to the US public health infrastructure. The NIH has traditionally led basic and clinical research that supports very early discovery. Therefore, coordination of investments in phase T0, T1, and early T2 activity seems well suited to the strengths of the CDC and NIH. The AHRQ has demonstrated leadership and success in health services research that promotes implementation, diffusion, and uptake of evidence-based prevention practices. Thus, it should play a major role in coordinating late T2 and T3 research investments. Phase T4 activities that evaluate the impact on population health will require overlapping leadership in health services research approaches from AHRQ and the national HAI surveillance systems of the CDC. Although CMS is not a research agency, partnership with it ensures that payment policies and implementation strategies are appropriately aligned with the findings from T3 and T4 research activities [55–57], and performance is publicized. Such coordination among federal agencies will shorten the time required to translate research into reductions in preventable harm and the costs of care and provide the public with a better return on biomedical research investment.

In summary, the need to eliminate health care–associated preventable harm by ensuring implementation of evidence-based recommendations for patient care is essential and depends on a well-organized investment in research. We outlined a framework for developing research programs that are critical in accelerating the creation of evidence and its translation into practice. Policy makers should start with the goal of eliminating preventable harm and work backward to fill in knowledge gaps necessary for attaining that goal. For national prevention programs to be fully successful and broadly implemented, it is essential that resources are available to support and develop all phases of the translational research process. This full investment will ensure that patients actually receive the benefits of evidence-based prevention practices and reduce preventable harm.

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References
