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An Intervention to Decrease Catheter-Related Bloodstream Infections in the ICU

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ABSTRACT

BACKGROUND

Catheter-related bloodstream infections occurring in the intensive care unit (ICU) are common, costly, and potentially lethal.

METHODS

We conducted a collaborative cohort study predominantly in ICUs in Michigan. An evidence-based intervention was used to reduce the incidence of catheter-related bloodstream infections. Multilevel Poisson regression modeling was used to compare infection rates before, during, and up to 18 months after implementation of the study intervention. Rates of infection per 1000 catheter-days were measured at 3-month intervals, according to the guidelines of the National Nosocomial Infections Surveillance System.

RESULTS

A total of 108 ICUs agreed to participate in the study, and 103 reported data. The analysis included 1981 ICU-months of data and 375,757 catheter-days. The median rate of catheter-related bloodstream infection per 1000 catheter-days decreased from 2.7 infections at baseline to 0 at 3 months after implementation of the study intervention ($P \leq 0.002$), and the mean rate per 1000 catheter-days decreased from 7.7 at baseline to 1.4 at 16 to 18 months of follow-up ($P < 0.002$). The regression model showed a significant decrease in infection rates from baseline, with incidence-rate ratios continuously decreasing from 0.62 (95% confidence interval [CI], 0.47 to 0.81) at 0 to 3 months after implementation of the intervention to 0.34 (95% CI, 0.23 to 0.50) at 16 to 18 months.

CONCLUSIONS

An evidence-based intervention resulted in a large and sustained reduction (up to 66%) in rates of catheter-related bloodstream infection that was maintained throughout the 18-month study period.

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CATHETER-RELATED BLOODSTREAM INFECTIONS are common, costly, and potentially lethal.^{1,2} Each year in the United States, central venous catheters may cause an estimated 80,000 catheter-related bloodstream infections and, as a result, up to 28,000 deaths among patients in intensive care units (ICUs). Given that the average cost of care for a patient with this infection is \$45,000,³ such infections could cost up to \$2.3 billion annually. According to the National Nosocomial Infections Surveillance (NNIS) system of the Centers for Disease Control and Prevention (CDC), the median rate of catheter-related bloodstream infection in ICUs of all types ranges from 1.8 to 5.2 per 1000 catheter-days.^{3,4} Interventions aimed at decreasing the infection rate are needed to reduce the serious public health consequences of this hospital-acquired infection.

How many of these infections are preventable is unknown. Several single-hospital studies and two multicenter studies have shown reductions in the rates of catheter-related bloodstream infection.⁵⁻¹² To build on this research, we studied the extent to which these infections could be reduced in Michigan, using an intervention as part of a statewide safety initiative regarding patients in ICUs, known as the Michigan Health and Hospital Association (MHA) Keystone Center for Patient Safety and Quality Keystone ICU project, which was funded predominantly by the Agency for Healthcare Research and Quality (AHRQ). The objective of the study was to evaluate the effect of the intervention up to 18 months after its implementation.

METHODS

THE INTERVENTION

All Michigan hospitals with ICUs for adults were invited to participate in the Keystone ICU project, launched in October 2003. Hospitals were not asked to provide reasons for not participating. Five out-of-state hospitals of a health system with its corporate headquarters in Michigan participated at the request of the senior executive of the health system. Between March 2004 and September 2005, each ICU implemented several patient-safety interventions, according to a prospective cohort study design, and monitored the effect of these interventions on specific safety measures.

In addition to the intervention to reduce the rate of catheter-related bloodstream infection, the

ICUs implemented the use of a daily goals sheet to improve clinician-to-clinician communication within the ICU,¹³ an intervention to reduce the incidence of ventilator-associated pneumonia,¹⁴ and a comprehensive unit-based safety program to improve the safety culture.^{15,16} The period necessary for implementation of each intervention was estimated to be 3 months. Hospitals started with implementation of the unit-based safety program and use of the daily goals sheet and then, in any order, implemented the other two interventions during the subsequent 6 months.

Before implementing any of the components of the study intervention, the ICUs were asked to designate at least one physician and one nurse as team leaders.¹⁷ The team leaders were instructed in the science of safety and in the interventions and then disseminated this information among their colleagues. Training of the team leaders was accomplished through conference calls every other week, coaching by research staff, and statewide meetings twice a year. The teams received supporting information on the efficacy of each component of the intervention, suggestions for implementing it, and instruction in methods of data collection (described in detail in Appendix A of the Supplementary Appendix, available with the full text of this article at www.nejm.org). Team leaders were partnered with their local hospital-based infection-control practitioners to assist in the implementation of the intervention and to obtain data on catheter-related bloodstream infections at the hospital.

The study intervention targeted clinicians' use of five evidence-based procedures recommended by the CDC and identified as having the greatest effect on the rate of catheter-related bloodstream infection and the lowest barriers to implementation.¹ The recommended procedures are hand washing, using full-barrier precautions during the insertion of central venous catheters, cleaning the skin with chlorhexidine, avoiding the femoral site if possible, and removing unnecessary catheters.

Strategies to increase the use of these procedures have been described elsewhere.¹⁰ Briefly, clinicians were educated about practices to control infection and harm resulting from catheter-related bloodstream infections, a central-line cart with necessary supplies was created, a checklist was used to ensure adherence to infection-control practices, providers were stopped (in nonemergency situations) if these practices were not be-

ing followed, the removal of catheters was discussed at daily rounds, and the teams received feedback regarding the number and rates of catheter-related bloodstream infection at monthly and quarterly meetings, respectively. In April 2004, a letter and a baseline survey were sent to the chief executive officers (CEOs) of the participating hospitals. The letter outlined the evidence supporting the use of chlorhexidine¹ and asked the CEOs to stock chlorhexidine in their hospitals before implementing the study intervention.

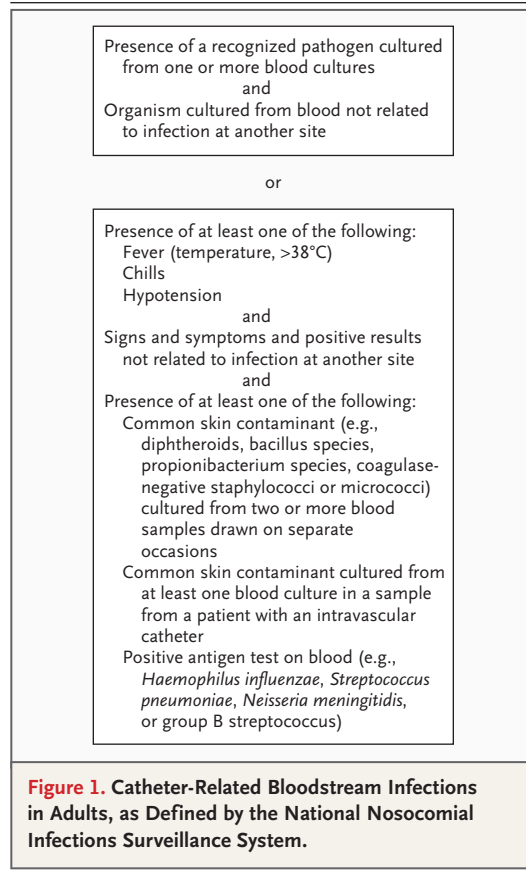
MEASUREMENT AND CATEGORIZATION OF DATA

Throughout the study, data on the number of catheter-related bloodstream infections and catheter-days were collected monthly from a trained, hospital-based infection-control practitioner. Hospitals were given the NNIS definition of catheter-related bloodstream infection (Fig. 1). Study investigators asked members of the teams to adhere to the NNIS definition of catheter-related bloodstream infection during the study period. Three ICUs changed the definition used from their own to that of the NNIS. Infection-control staff at the hospitals adjudicated contaminated cultures before submitting data for the study. We defined a central catheter as a catheter that ends at or near the heart or in a great vessel close to the heart, and the teams were explicitly instructed to exclude peripherally inserted central catheters and to count the use of multiple lines in one patient as 1 catheter-day, in accordance with the NNIS guidelines. To simplify data collection, the average duration of catheter use in individual patients was not monitored.

To coincide with the implementation periods for the study intervention, monthly data were aggregated into 3-month periods (quarters). The quarterly rate of infection was calculated as the number of infections per 1000 catheter-days for each 3-month period. Quarterly rates were assigned to one of eight categories on the basis of when the study intervention was implemented: at baseline, during the implementation period, or during one of six 3-month intervals occurring up to 18 months after implementation. We did not collect data on who inserted the central catheters. To our knowledge, no other infection-reducing practices were implemented during our study.

EXPOSURE, OUTCOMES, AND STUDY HYPOTHESES

We modeled exposure to the study intervention, after full implementation, according to six categori-



cal temporal variables, comparing values for those variables with baseline values. The outcome was the quarterly rate of catheter-related bloodstream infection. The analysis included three characteristics of the hospitals, obtained from the American Hospital Association database: teaching status (a binary variable), bed size (a continuous variable), and geographic region (eight categories). Teaching hospitals were required to be members of the Council of Teaching Hospitals Health Systems and to have been approved for residency training by the Accreditation Council for Graduate Medical Education or the American Osteopathic Association. The primary study hypothesis was that the rate of catheter-related bloodstream infection would be reduced during the first 3 months after implementation of the study intervention as compared with baseline. A secondary hypothesis was that the observed decrease in the rate of infection between 0 and 3 months after implementation of the study intervention would be sustained during the subsequent observation period. We did not evaluate the relative effectiveness of the separate components of the intervention.

STATISTICAL ANALYSIS

Because of the nonnormal distribution of the data on catheter-related bloodstream infections, medians and interquartile ranges were used to summarize the data. Medians were compared with baseline values with the use of a two-sample Wilcoxon rank-sum test. To explore the exposure–outcome relationship, we used a generalized linear latent and mixed model^{18,19} with a Poisson distribution for the quarterly number of catheter-related bloodstream infections. In the model, we used robust variance estimation and included two-level random effects to account for nested clustering within the data, catheter-related bloodstream infections within hospitals, and hospitals within the geographic regions included in the study.^{18,20} The addition of a third level of clustering for a potential ICU effect (catheter-related bloodstream infections within ICUs, ICUs within hospitals, and hospitals within the geographic regions) did not change the results. We adjusted for the hospital's teaching status and bed size in the model and explored interactions between the effect of the study intervention (modeled as a continuous variable) and teaching status and bed size. We conducted a sensitivity analysis of these results in which only ICUs with continuous data, including baseline (preimplementation) data, were included. All reported P values are two-sided; a P value of 0.05 or less was considered to indicate statistical significance. We used Stata software (version 9.1) for the analysis. The study was approved by the institutional review board of Johns Hopkins University School of Medicine. Informed consent was waived because the study was considered exempt from review.

The AHRQ provided financial support for the Keystone ICU project but had no role in the design or conduct of the study; the collection, management, analysis, or interpretation of the data; the preparation, review, or approval of the manuscript; or the decision to submit the manuscript for publication. The MHA provided support for the biannual statewide meetings but had no influence on the design, implementation, analysis, or results of the study. The authors had full access to the data and vouch for the accuracy and completeness of the data and the analysis.

RESULTS

Five of 108 participating ICUs were excluded: 4 because they did not track or report catheter-related bloodstream infections, catheter-days, or both, and 1 because it merged with another participating ICU, so that the combined data were used in the analysis. The data were obtained from 67 hospitals, of which 52% were teaching facilities. The types of ICU included medical, surgical, cardiac medical or surgical, neurologic, and surgical trauma units and one pediatric unit. The ICUs represented 1625 (85%) of all ICU beds in Michigan. Of 34 hospitals in Michigan that did not participate in the study, 27 (79%) had fewer than 100 beds; the total number of beds in the ICUs not included in the study was 268.

Thus, 103 ICUs reporting data for 1981 ICU-months and 375,757 catheter-days were included in the final analysis. The characteristics of the ICUs according to the study period are summarized in Table 1. Baseline data on catheter-related bloodstream infections at the participating ICUs

Table 1. Characteristics of 103 Participating ICUs, According to the Period of Implementation of the Intervention to Reduce the Rate of Catheter-Related Bloodstream Infections.

| Period | No. of ICUs | No. of Catheter-Days per Month | Teaching Hospital % | No. of Beds |
|----------------------------|-------------|---------------------------------|------------------------|---------------------------------|
| | | median (interquartile range) | | median (interquartile range) |
| March to May 2004* | 40 | 154 (94–258) | 83 | 404 (268–609) |
| June to August 2004 | 35 | 146 (72–228) | 57 | 336 (218–610) |
| September to November 2004 | 17 | 181 (80–275) | 59 | 299 (190–393) |
| After November 2004 | 11 | 172 (48–279) | 73 | 288 (181–917) |

* Baseline data were not collected by ICUs implementing the study intervention during the baseline (preimplementation) period.

are summarized in Table 2, according to the teaching status and bed size of the hospitals. When the Keystone ICU project was launched, 13 of the 67 hospitals (19%) included chlorhexidine in the central-line kits used in the ICUs. Six weeks after the study letter was sent to CEOs at the 67 participating hospitals, 56 (84%) stocked chlorhexidine, 46 (69%) stocked the agent in the ICU, and 43 (64%) stocked it in central-line carts.

The total number of catheter-days changed little during the study. In ICUs that implemented the study intervention during the 3 months (June to August 2004) after baseline data were collected (Table 1), the mean number of catheter-days per month was 4779. During the follow-up period, the mean number of catheter-days per month ranged from 4757 at 4 to 6 months after implementation of the intervention to 5469 at 10 to 12 months after implementation.

The overall median rate of catheter-related bloodstream infection decreased from 2.7 (mean, 7.7) infections per 1000 catheter-days at baseline to 0 (mean, 2.3) at 0 to 3 months after implementation of the study intervention ($P \leq 0.002$) and was sustained at 0 (mean, 1.4) during 18 months of follow-up (Table 3). A significant decrease was observed in both teaching and nonteaching hospitals and in small hospitals (<200 beds) and large hospitals (≥ 200 beds) (Table 3).

The multilevel Poisson regression model showed a significant decrease in rates of catheter-related

bloodstream infection during all study periods as compared with baseline rates, with incidence-rate ratios continuously decreasing from 0.62 (95% confidence interval [CI], 0.47 to 0.81) at 0 to 3 months to 0.34 (95% CI, 0.23 to 0.50) at 16 to 18 months after implementation of the study intervention (Table 4). There was a significant interaction between the intervention and bed size: the intervention was modestly more effective in small hospitals, with an incidence-rate ratio of 0.97 (95% CI, 0.96 to 0.99; $P < 0.001$) for each 100-bed decrease in the size of the hospital. The results of a sensitivity analysis of data from the 53 ICUs reporting data continuously from baseline onward were similar to those of the primary analysis, with incidence-rate ratios decreasing from 0.62 (95% CI, 0.46 to 0.85) at 0 to 3 months to 0.15 (95% CI, 0.07 to 0.32) at 16 to 18 months of follow-up.

DISCUSSION

The goal of the MHA Keystone ICU project was to improve patient safety in ICUs in Michigan. The analysis was focused on an intervention to reduce the rate of catheter-related bloodstream infection that was implemented in 103 ICUs in Michigan in 2004. Within 3 months after implementation, the median rate of infection was 0, a rate sustained throughout the remaining 15 months of follow-up. All types of participating hospitals realized a similar improvement.

Table 2. Baseline Data.

| Characteristic | No. of ICUs | Baseline Period | | |
|-----------------|-------------|-------------------|--|--|
| | | No. of Infections | Catheter-Days <i>median (interquartile range)</i> | No. of Infections per 1000 Catheter-Days |
| All hospitals | 55* | 2 (1–3) | 511 (220–1091) | 2.7 (0.6–4.8) |
| Teaching status | | | | |
| Teaching | 33 | 2 (1–4) | 744 (377–1134) | 2.7 (1.3–4.7) |
| Nonteaching | 22 | 1 (0–2) | 306 (194–608) | 2.6 (0–4.9) |
| No. of beds | | | | |
| <200 | 13 | 1 (0–1) | 247 (75–377) | 2.1 (0–3.0) |
| 200–299 | 12 | 2 (1–6) | 595 (338–1670) | 3.2 (0.3–4.3) |
| 300–399 | 12 | 2 (1–3) | 902 (184–1376) | 2.7 (1.7–5.8) |
| ≥ 400 | 18 | 2 (1–3) | 616 (424–1102) | 2.0 (1.3–4.7) |

* Of the 103 participating ICUs, 48 did not contribute baseline data — 40 because they implemented the intervention at the initiation of the study and 8 because they did not report baseline data.

Table 3. Rates of Catheter-Related Bloodstream Infection from Baseline (before Implementation of the Study Intervention) to 18 Months of Follow-up.*

| Study Period | No. of ICUs | No. of Bloodstream Infections per 1000 Catheter-Days | | | | |
|-----------------------|-------------|--|-------------------|----------------------|-------------|---------------|
| | | Overall | Teaching Hospital | Nonteaching Hospital | <200 Beds | ≥200 Beds |
| Baseline | 55 | 2.7 (0.6–4.8) | 2.7 (1.3–4.7) | 2.6 (0–4.9) | 2.1 (0–3.0) | 2.7 (1.3–4.8) |
| During implementation | 96 | 1.6 (0–4.4)† | 1.7 (0–4.5) | 0 (0–3.5) | 0 (0–5.8) | 1.7 (0–4.3)† |
| After implementation | | | | | | |
| 0–3 mo | 96 | 0 (0–3.0)‡ | 1.3 (0–3.1)† | 0 (0–1.6)† | 0 (0–2.7) | 1.1 (0–3.1)‡ |
| 4–6 mo | 96 | 0 (0–2.7)‡ | 1.1 (0–3.6)† | 0 (0–0)‡ | 0 (0–0)† | 0 (0–3.2)‡ |
| 7–9 mo | 95 | 0 (0–2.1)‡ | 0.8 (0–2.4)‡ | 0 (0–0)‡ | 0 (0–0)† | 0 (0–2.2)‡ |
| 10–12 mo | 90 | 0 (0–1.9)‡ | 0 (0–2.3)‡ | 0 (0–1.5)‡ | 0 (0–0)† | 0.2 (0–2.3)‡ |
| 13–15 mo | 85 | 0 (0–1.6)‡ | 0 (0–2.2)‡ | 0 (0–0)‡ | 0 (0–0)† | 0 (0–2.0)‡ |
| 16–18 mo | 70 | 0 (0–2.4)‡ | 0 (0–2.7)‡ | 0 (0–1.2)† | 0 (0–0)† | 0 (0–2.6)‡ |

* Because the ICUs implemented the study intervention at different times, the total number of ICUs contributing data for each period varies. Of the 103 participating ICUs, 48 did not contribute baseline data. P values were calculated by the two-sample Wilcoxon rank-sum test.

† P≤0.05 for the comparison with the baseline (preimplementation) period.

‡ P≤0.002 for the comparison with the baseline (preimplementation) period.

This study showed that a large-scale project focused on reducing the incidence of catheter-related bloodstream infection is feasible and can have important public health consequences. Current efforts to improve patient safety in the United States are fragmented, with few large-scale improvements documented.^{21–23} The ability to measure and evaluate the effect of interventions to increase patient safety is still underdeveloped.^{21,24} In this project, monitoring catheter-related bloodstream infection rates was possible because of the existence of an infrastructure — specifically, congressional funding to develop and maintain the NNIS and a staff of hospital-based infection-control practitioners. Similar infrastructure does not exist for most other issues related to patient safety.

Important reductions in morbidity and health care costs could be achieved if the intervention to reduce catheter-related bloodstream infections could be introduced successfully nationwide or worldwide. Given the results of the study, many of the estimated 80,000 infections, up to 28,000 deaths, and \$2.3 billion in costs attributed to these infections annually in the United States could be reduced. The intervention was implemented without the use of expensive technology or additional ICU staffing. However, the MHA and AHRQ funded this intervention, and the partici-

pating hospitals provided staff to implement it. The estimated costs associated with catheter-related bloodstream infections vary, ranging from \$11,971 to \$54,000 per infection.^{3,25} Given that the participating ICUs had reported 695 catheter-related bloodstream infections annually before the study, implementing the study intervention offers a strategy to improve clinical outcomes and reduce costs.

The study has several limitations. First, the design reduces the ability to make a causal connection between the intervention and reduced rates of catheter-related bloodstream infection. Randomized assignment of the intervention and of the time of implementation was not feasible, because all the ICU teams wanted to implement the intervention and to decide for themselves when to do so. However, several factors support a true and strong association between the intervention and a reduction in rates of catheter-related bloodstream infection: variability in the timing of implementation reduced any effect of seasonal trend on the baseline rates of infection, reduced infection rates were sustained and fell further with continued exposure to the intervention, and similar large decreases in infection rates were not observed outside Michigan during the study period.

Second, potential underreporting of catheter-related bloodstream infections and the lack of

baseline data from ICUs that immediately implemented the intervention when the project was launched could have created a measurement bias that exaggerated the results. However, the infection rates were collected and reported according to the guidelines of the NNIS by hospital infection-control practitioners who were independent of the ICU staff implementing the intervention. Furthermore, a sensitivity analysis showed little change in the association between the intervention and outcomes when only ICUs for which complete data (including baseline data) were available were included.

Third, data on the organisms causing catheter-related bloodstream infections were not collected, limiting insight into the mechanism of the observed benefit. Fourth, we did not evaluate compliance with the study intervention, because limited resources prevented observation of central-line placements. Fifth, we could not evaluate the relative importance of individual components of the multifaceted intervention or of the safety-culture intervention. However, our goal was maximal improvement of patient safety, and the study program offered the greatest probability of reducing catheter-related bloodstream infections. Sixth, we did not obtain data on catheter-related bloodstream infection rates from nonparticipating ICUs. Nevertheless, the ICUs that participated in the study accounted for 85% of ICU beds in Michigan. Last, we studied ICUs in only one state, which may limit the ability to generalize our findings. Nevertheless, a wide variety of types of hospital and ICU were studied.

In summary, catheter-related bloodstream infections are expensive, prevalent, and often fatal. As part of the Michigan statewide patient-safety initiative, we implemented a simple and inexpensive intervention to reduce these infections in 103 ICUs. Coincident with the intervention, the median rate of infection decreased from 2.7 per 1000 catheter-days at baseline to 0 within the first 3 months after the implementation of the intervention. The benefit from the intervention was sustained, and there was a reduction in the rate of catheter-related bloodstream infection of 66%

Table 4. Incidence-Rate Ratios for Catheter-Related Bloodstream Infections.*

| Variable | Incidence-Rate Ratio (95% CI) | P Value |
|-------------------------|-------------------------------|---------|
| Study period | | |
| Baseline | 1.00 | |
| During implementation | 0.76 (0.57–1.01) | 0.063 |
| After implementation | | |
| 0–3 mo | 0.62 (0.47–0.81) | 0.001 |
| 4–6 mo | 0.56 (0.38–0.84) | 0.005 |
| 7–9 mo | 0.47 (0.34–0.65) | <0.001 |
| 10–12 mo | 0.42 (0.28–0.63) | <0.001 |
| 13–15 mo | 0.37 (0.20–0.68) | 0.001 |
| 16–18 mo | 0.34 (0.23–0.50) | <0.001 |
| Teaching hospital | 1.34 (0.73–2.46) | 0.35 |
| Bed size (per 100 beds) | 1.03 (0.97–1.09) | 0.33 |

* Incidence-rate ratios were calculated with the use of a generalized linear latent and mixed model (Rabe-Hesketh and Skrondal¹⁸), with robust variance estimation and random effects to account for clustering of catheter-related bloodstream infections within hospitals and clustering of hospitals within geographic regions. Rates of catheter-related bloodstream infection during and after implementation of the study intervention were compared with baseline (preimplementation) values, adjusted for the hospital's teaching status and number of beds.

at 16 to 18 months after implementation. Broad use of this intervention could significantly reduce morbidity and the costs of care associated with catheter-related bloodstream infections.

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REFERENCES

- Mermel LA. Prevention of intravascular catheter-related infections. *Ann Intern Med* 2000;132:391-402. [Erratum, *Ann Intern Med* 2000;133:5.]
- Burke JP. Infection control — a problem for patient safety. *N Engl J Med* 2003; 348:651-6.
- O'Grady NP, Alexander M, Dellinger EP, et al. Guidelines for the prevention of intravascular catheter-related infections. *MMWR Recomm Rep* 2002;51(RR-10): 1-29.
- National Nosocomial Infections Surveillance System. National Nosocomial Infections Surveillance (NNIS) System re-

- port, data summary from January 1992 through June 2004, issued October 2004. *Am J Infect Control* 2004;32:470-85.
5. Warren DK, Zack JE, Mayfield JL, et al. The effect of an education program on the incidence of central venous catheter-associated bloodstream infection in a medical ICU. *Chest* 2004;126:1612-8.
 6. Sherertz RJ, Ely EW, Westbrook DM, et al. Education of physicians-in-training can decrease the risk for vascular catheter infection. *Ann Intern Med* 2000;132:641-8.
 7. Eggimann P, Harbarth S, Constantin MN, Touveneau S, Chevrolet JC, Pittet D. Impact of a prevention strategy targeted at vascular-access care on incidence of infections acquired in intensive care. *Lancet* 2000;355:1864-8.
 8. Cohran J, Larson E, Roach H, Blane C, Pierce P. Effect of intravascular surveillance and education program on rates of nosocomial bloodstream infections. *Heart Lung* 1996;25:161-4.
 9. Monitoring hospital-acquired infections to promote patient safety — United States, 1990–1999. *MMWR Morb Mortal Wkly Rep* 2000;49:149-53. [Erratum, *MMWR Morb Mortal Wkly Rep* 2000;49:189-90.]
 10. Berenholtz SM, Pronovost PJ, Lipsett PA, et al. Eliminating catheter-related bloodstream infections in the intensive care unit. *Crit Care Med* 2004;32:2014-20.
 11. 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.
 12. Warren DK, Cosgrove SE, Deikema DJ, et al. A multicenter intervention to prevent catheter-associated bloodstream infections. *Infect Control Hosp Epidemiol* 2006;27:662-9.
 13. Pronovost P, Berenholtz S, Dorman T, Lipsett PA, Simmonds T, Haraden C. Improving communication in the ICU using daily goals. *J Crit Care* 2003;18:71-5.
 14. Berenholtz SM, Milanovich S, Faircloth A, et al. Improving care for the ventilated patient. *Jt Comm J Qual Saf* 2004;30:195-204.
 15. Pronovost P, Weast B, Rosenstein B, et al. Implementing and validating a comprehensive unit-based safety program. *J Patient Saf* 2005;1:33-40.
 16. Pronovost PJ, Weast B, Bishop K, et al. Senior executive adopt-a-work unit: a model for safety improvement. *Jt Comm J Qual Saf* 2004;30:59-68.
 17. Pronovost P, Goeschel C. Improving ICU care: it takes a team. *Healthc Exec* 2005;20:14-6, 18, 20 passim.
 18. Rabe-Hesketh S, Skrondal A. Multi-level and longitudinal modeling using Stata. College Station, TX: Stata Press, 2005.
 19. Skrondal A, Rabe-Hesketh S. Generalized latent variable modeling: multilevel, longitudinal, and structural equation models. Boca Raton, FL: Chapman & Hall/CRC, 2004.
 20. Panageas KS, Schrag D, Riedel E, Bach PB, Begg CB. The effect of clustering of outcomes on the association of procedure volume and surgical outcomes. *Ann Intern Med* 2003;139:658-65.
 21. Leape LL, Berwick DM. Five years after *To Err Is Human*: what have we learned? *JAMA* 2005;293:2384-90.
 22. Altman DE, Clancy C, Blendon RJ. Improving patient safety — five years after the IOM report. *N Engl J Med* 2004;351:2041-3.
 23. Wachter R. The end of the beginning: patient safety five years after *'To Err Is Human.'* *Health Aff (Millwood)* 2004;23: Suppl 2 Web Exclusives:W4-534–W4-545.
 24. Brennan TA, Gawande A, Thomas E, Studdert D. Accidental deaths, saved lives, and improved quality. *N Engl J Med* 2005;353:1405-9.
 25. Warren DK, Quadir WW, Hollenbeak CS, Elward AM, Cox MJ, Fraser VJ. Attributable cost of catheter-associated bloodstream infections among intensive care patients in a nonteaching hospital. *Crit Care Med* 2006;34:2084-9.

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