

Prevention of Vascular Catheter-Related Bloodstream Infections



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KEYWORDS

• Bloodstream infection • Intravascular catheter • Prevention • Bacteremia

KEY POINTS

- Catheter-related bloodstream infections (CRBSI) are responsible for substantial morbidity, mortality, and excess cost; many CRBSI are preventable using current knowledge and prevention techniques.
- Evidence-based, clinical practice-oriented strategies to prevent CRBSI include appropriate education, training, and staffing levels for providers; insertion of central venous catheters (CVC) using full sterile barriers, skin disinfection with chlorhexidine; avoidance of the femoral insertion site; use of a checklist; and combining interventions together in a bundle.
- After insertion, care of patients with CVCs should include maintenance of the dressing; scrub-the-hub aseptic technique when accessing the CVC; skin antisepsis with chlorhexidine; and removal of the CVC as soon as practical.
- Technologic innovations proven to reduce CRBSI include antiseptic/antimicrobial-coated CVCs; chlorhexidine-impregnated sponge or gel pad dressings; chlorhexidine patient bathing; passive disinfection of catheter hubs/connectors; and antimicrobial/antiseptic catheter locks.

INTRODUCTION AND CLINICAL SIGNIFICANCE

Reliable access to the vascular system is a necessity for the practice of medicine and enables the delivery of medications and fluids, ready sampling of the blood for diagnostic testing, and monitoring of a patient's clinical status. Unfortunately, vascular catheter-related infection is an all-too-common event that results in substantial morbidity, mortality, and excess cost. The Centers for Disease Control and Infection

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(CDC) estimates that approximately 72,000 central line–associated bloodstream infections (CLABSI) occur annually in the United States in intensive care units and dialysis units¹ and that these infections result in an attributable mortality of 12%, an extra 7 days of hospitalization per case, and excess costs of \$45,000 per episode.^{2,3}

In this monograph, an evidence-based approach to the prevention of vascular catheter infections is summarized. Both practice-based and technology-based prevention strategies are covered. Although central venous catheters (CVCs) are emphasized, considerations regarding arterial catheters, hemodialysis catheters, and peripheral intravascular catheters (PIVCs) also are included. In recent years, several comprehensive evidence-based guidelines regarding prevention of catheter-related bloodstream infection (CRBSI) have been published,^{4–7} and it is not the intent to duplicate these guidelines here. Instead, the most critical issues are consolidated and summarized.

DEFINITIONS AND SURVEILLANCE

Unfortunately, the terms “central line–associated bloodstream infection” (CLABSI) and “catheter-related bloodstream infections” (CRBSI) are often used interchangeably. However, they have distinct meanings, with CRBSI being a clinical term that requires specific laboratory testing (catheter tip culture, quantitative blood cultures, or differential time-to-positivity testing from blood obtained from the implicated catheter and peripheral blood) in a patient who is bacteremic/fungemic to establish the source of infection, versus CLABSI, which is a surveillance term that is by design relatively sensitive but not as highly specific.

In recent years, great strides have been made in understanding the pathogenesis of CRBSI, as well as the implementation of effective preventive interventions. There is a growing realization that many, if not most, episodes of CRBSI can be prevented. The increasing expectation for prevention and the large additional costs associated with health care–associated infections has captured the attention of governmental agencies and third party payers. Hospitals have come under intense scrutiny and a variety of measures have been implemented to encourage prevention of CRBSI, such as mandatory public reporting and economic penalties. However, the CDC NHSN definition of CLABSI was intended as a surveillance tool to drive performance improvement. The CLABSI definition overestimates the true incidence of infection, lacks specificity, and, despite recent improvements, remains somewhat subjective (in assigning the source of infection).^{8–10} Further undermining the validity of the surveillance data, most institutions acknowledge use of an adjudication approach in defining CLABSI.¹¹ Clearly, modifications can be made in the surveillance definition to improve specificity and risk-stratify data. A robust data validation program should be in place to ensure accurate reporting and to discourage systematic underreporting. Surveillance systems should be expanded into non–acute care settings (eg, infusion centers, home care, long-term care)¹² and should include other intravascular catheters (arterial catheters, midline catheters, and PIVC).

PATHOGENESIS

Fig. 1 illustrates the 4 routes by which microbes gain access to a vascular catheter. For short-term, nontunneled catheters, the primary route of inoculation and infection is via the dermal surface: microbes that are resident on the skin colonize the catheter at the interface between the skin and the catheter. For tunneled catheters, and the longer a temporary nontunneled catheter remains in place, the hub and luminal surface become increasingly implicated as the major route of colonization and infection. Rarely do catheters become infected via hematogenous seeding and, with

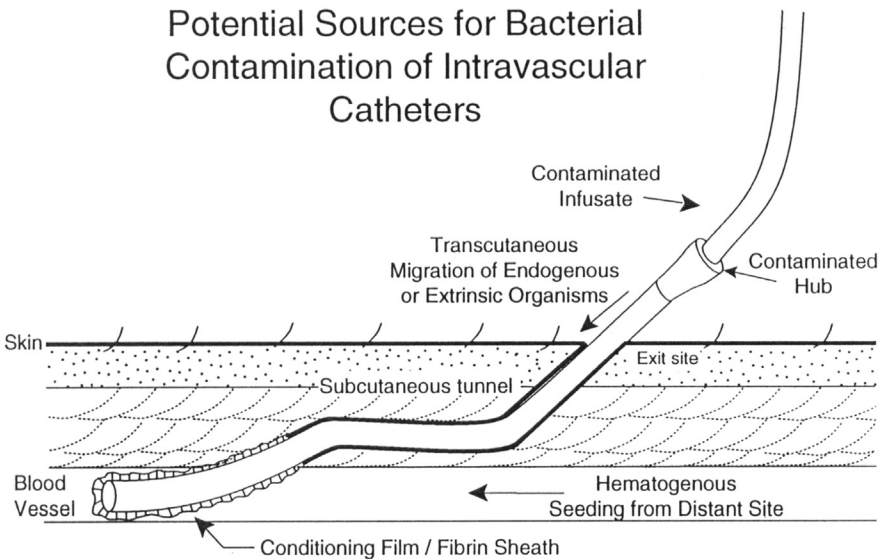


Fig. 1. Pathogenesis and routes of inoculation for catheter-related infection. Microbes gain access to the catheter by the following routes: contamination of the catheter hub, contamination of the infusate, transcutaneous migration, or hematogenous seeding. (From Rupp ME. Infections of intravascular catheters. In: Crossley KB, Archer GL, editors. *The Staphylococci in Human Disease*. New York: Churchill Livingstone; 1997. p. 381.)

appropriate manufacturing quality controls in place, rarely are catheters infected by the infusion of contaminated fluids. Once microbes gain access to the catheter, they quickly adhere to the surface, proliferate, aggregate, and form a biofilm (**Fig. 2**). Vascular catheter biofilms are subjected to a variety of local environmental

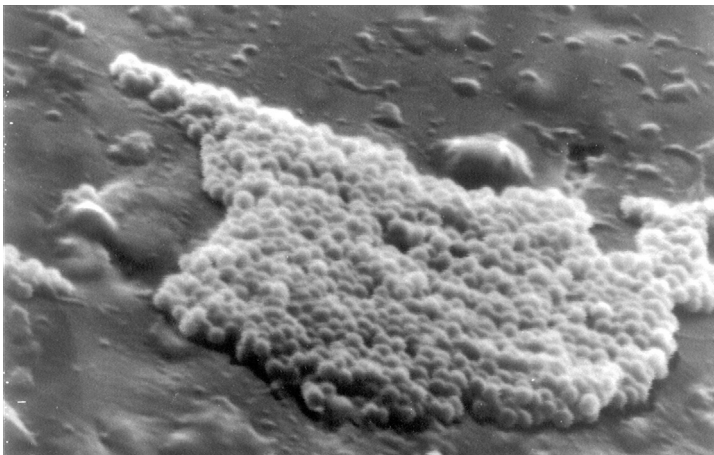


Fig. 2. Biofilm formation on an experimentally infected intravascular catheter 24 hours after inoculation with coagulase-negative staphylococci. (Reproduced from Rupp ME, Archer GL. Coagulase-negative staphylococci: pathogens associated with medical progress. *Clin Infect Dis* 1994;19:231–45.)

conditions (eg, oxygen and nutrient rich at the bloodstream interface, acidic and anaerobic at the catheter surface) and contain cells with a variety of growth and metabolic characteristics (eg, actively growing cells vs metabolically quiescent persister cells or small colony variants). Vascular catheters involved with a mature biofilm-associated infection are very difficult to treat successfully with the catheter in situ, and most infected catheters are removed to better ensure cure. Therefore, it is most advantageous to prevent infection in the first place rather than trying to salvage an infected catheter later.

Prevention of Vascular Catheter-Related Infection

Methods to prevent vascular catheter infections can be broadly grouped into 2 major categories: clinical practice-based interventions and technologic innovations (Table 1).

Clinical practice-based interventions

Peri-insertion precautions

Appropriate staffing Several outbreak investigations and studies have linked staffing levels to CRBSI.^{13–16} Most of these observations have occurred in the critical care setting. It appears that when staffing levels fall below a critical threshold, various adverse events, including CRBSI, occur more frequently. When the number of appropriately trained individuals is not sufficient to care for the number of patients in a particular setting, it is likely that infection-prevention practices and intravascular catheter care tasks are neglected, resulting in increased CRBSI. However, because patient acuity varies from unit-to-unit and from day-to-day, it is difficult to stipulate, from an infection-prevention viewpoint, minimal staffing requirements beyond a general statement that the staffing levels should be adequate to care for patient needs. To better balance patient care demands and nurse staffing levels, many institutions use various risk assessment profiles and patient classification systems.¹⁷ Similarly, implementation of physician staffing standards has resulted in decreased CRBSI.¹⁸

Table 1	
Evidence-based interventions to prevent catheter-related bloodstream infections	
Practice Interventions (Human Behavior–Oriented Interventions)	Technologic Innovations (New Devices and Technology)
Peri-catheter insertion	Antimicrobial catheter coatings (silver-sulfadiazine/chlorhexidine or minocycline/rifampin)
Appropriate staffing	Chlorhexidine-impregnated dressings (sponge dressing or gelpad dressing)
Education and training; infusion team	Passive port protectors
Use of maximal sterile barriers	Silver-impregnated connectors
Insertion site selection	Sutureless catheter securement
Cutaneous antisepsis with chlorhexidine	Antimicrobial catheter locks
Use of insertion checklist	
Bundle approach	
Post catheter insertion	Hemodialysis catheters
“Scrub-the-hub”: disinfection of hubs and needleless connectors	Antimicrobial ointment applied to the exit site
Chlorhexidine patient bathing	Tissue plasminogen activating factor weekly
Removal of unneeded catheters	
Catheter dressing maintenance	
Bundle approach	

Education and training All health care providers who insert vascular catheters, make use of the catheter, or provide catheter maintenance and care, should participate in education designed to instruct personnel regarding CVC need, catheter and site selection, proper insertion procedures, and catheter care and maintenance.^{19–21} Personnel should demonstrate competency, and those performing insertion procedures should undergo a credentialing process before performing CVC insertion. Periodic “refresher” education should be conducted and re-education should be performed whenever new products or amended procedures are introduced. Educational programs that have been linked to decreases in CRBSI have taken various guises: from simple, self-paced, written modules to more sophisticated technology-enhanced curricula. Increasingly, simulation-based training is being used to educate providers and document competency.²² Health care providers have varying preferences for optimal learning and multiple teaching strategies should be considered (eg, self-directed, small group, instructor-led) as well as multiple delivery methods tailored to individual needs. There is also growing recognition that the patient and family should be included in educational efforts to prevent CRBSI, particularly if they are to provide CVC care in the home care or ambulatory setting.^{5,12}

Some institutions have implemented vascular access teams made up of individuals with specialized training and knowledge to insert PIVCs as well as manage the insertion, maintenance, and removal of some types of CVCs.^{7,23,24} The team approach has been associated with more efficient vessel cannulation and decreased rates of infectious complications, occlusion, accidental PIVC removal, and local site adverse events (infiltration, phlebitis).^{7,23,24} In addition, infusion teams can serve as a resource in product evaluation and implementation of standardized practice.⁷

Maximal sterile barrier precautions Maximal sterile barrier precautions (sterile gloves, sterile long-sleeved gown, cap, mask, sterile head-to-toe patient drape) should be used in the insertion or guide wire exchange of CVCs.^{25–27} However, it should be noted that the relative value of the components of the barrier precautions is undefined and not all studies have demonstrated the benefit of sterile barrier precautions.²⁸ In addition, the use of maximal sterile barrier precautions for the insertion of arterial catheters has not been proven beneficial.²⁹

Insertion site In general, the subclavian site is less prone to infectious complications than the internal jugular or femoral sites.^{30,31} The femoral site may be particularly more prone to colonization and infection in obese patients.³² Due to the ease of placement with the use of ultrasound guidance, the internal jugular is the preferred site of insertion for many clinicians.³³ Ultimately, site selection should be individualized and is determined by experience of the catheter inserter, risk of complication (mechanical/infectious/thrombotic), anticipated duration of catheterization, potential need for renal replacement therapy, and other patient factors.³⁴

Cutaneous antisepsis In patients without chlorhexidine allergy, the skin should be disinfected with an alcoholic chlorhexidine solution containing more than 0.5% chlorhexidine and allowed to dry before catheter insertion.^{35,36} Although there is concern for absorption across the skin of very low birth weight neonates and potential neurotoxicity as well as contact dermatitis, clinicians in many neonatal intensive care units have formulated protocols for the use of chlorhexidine in some groups of premature infants.^{37–40}

Checklist A process to ensure adherence to appropriate insertion procedures should be in place. Many institutions have used a bedside checklist to remind

providers of appropriate procedures and to document adherence.^{41,42} A person other than the inserter should be responsible for completing the checklist and the observer should be empowered to halt the catheter insertion procedure if lapses in aseptic technique are observed.

Bundle In many institutions, a variety of interventions are combined to create a prevention “bundle.” The bundle usually concentrates on insertion practices and includes use of an all-inclusive catheter cart or insertion kit, hand hygiene before catheter placement, avoidance of the femoral site, use of maximal sterile barriers, use of alcoholic chlorhexidine for skin disinfection, and removal of unnecessary CVCs as soon as practical. A large and growing body of evidence supports this approach as effective in prevention of CRBSI, sustainable, cost-effective, and lifesaving.^{43–46} The relative importance of the components of the bundle are not defined, and in general, this approach is most effective when used in the institutional milieu of a robust patient-safety culture.

Postinsertion precautions As previously related, it is important for patients to be cared for by providers who are adequately trained in appropriately staffed units.

Disinfection of catheter hubs and needleless connectors Before accessing catheter hubs, needleless connectors, or injection ports, they should be disinfected with an appropriate antiseptic (70% alcohol, alcoholic chlorhexidine, povidone iodine) for an adequate period of time and allowed to dry. The amount of time the hub should be scrubbed is dependent on the degree of contamination and the hub/connector design, and in general, is undefined for most connectors.⁴⁷ Monitoring compliance with hub disinfection practices is difficult and subject to the Hawthorne effect. Therefore, some institutions have adopted passive port protectors, which are discussed in greater detail later in this monograph. Some connectors have been associated with outbreaks of bloodstream infection^{48,49} and the introduction of a new connector into an institution should be preceded by health care provider education and a plan to closely monitor catheter-related adverse events postintroduction. The optimal design for catheter connectors is not defined, but they should be easy to use, readily cleaned and disinfected (ie, smooth interface between housing and diaphragm), and be transparent so that personnel can easily visualize the effectiveness of flushing and exclude retained blood products, lipids, and so forth.⁵⁰

Chlorhexidine patient bathing Several studies have demonstrated a significant decrease in CLABSI associated with bathing patients with chlorhexidine.^{51–55} These studies, which were primarily performed in intensive care unit settings, showed additional benefit in preventing the transmission of multidrug-resistant organisms, such as methicillin-resistant *Staphylococcus aureus* and VRE. However, as is true with most infection-prevention efforts, not all studies have shown a beneficial effect.^{56,57} In addition, there is concern that widespread use of chlorhexidine will promote the emergence of chlorhexidine resistance.

Removal of unneeded intravascular catheters and potentially contaminated central venous catheters The need for CVCs should be assessed on at least a daily basis and unnecessary vascular catheters should be promptly removed. Unfortunately, several studies document that vascular catheters are often left in place after they are no longer needed.^{58–60} Various types of interventions (eg, audits, reminders, multicomponent programs) have proven successful in decreasing patient exposure to unnecessary vascular catheters.^{61,62} In certain circumstances (emergent “code-blue” catheter

insertion), CVCs may be inserted without use of appropriate aseptic technique. In such circumstances, the catheter should be replaced as soon as the patient's condition allows (within 24–48 hours).⁴ If an audit system or daily assessment checklist is not in place, it is easy for such potentially contaminated catheters to be overlooked.

Catheter dressing integrity and administration set replacement For nontunneled CVCs, the insertion site should be cleaned with a chlorhexidine-containing antiseptic at the time of dressing changes, which should occur at weekly intervals for transparent dressings and every 2 days for gauze dressings.^{4,7} Because dressing integrity is an important risk factor for catheter-related infection,⁶³ dressings should be changed as frequently as needed if they become soiled, damp, or loosened. Routine administration sets should be changed at intervals of 96 hours, whereas those used for blood products or lipid administration should be changed at 24-hour intervals.^{4,7} Tubing used to administer propofol should be changed every 6 to 12 hours.⁴

Postinsertion bundles Similar to insertion bundles, many institutions have instituted postcatheter insertion care bundles that emphasize catheter removal, dressing integrity, and “scrub-the-hub” aseptic accessing technique, and these programs have been associated with a decrease in infectious complications.^{64–66}

Technologic Innovations

The preceding material was directed at clinical practices that involve human behavior. Unfortunately, “to err is human” and it can be anticipated that health care providers will continue to have lapses in infection-prevention practices such as hand hygiene, scrub-the-hub, dressing changes, and so forth. Therefore, a particularly attractive option may be the use of vascular access–related devices that decrease the risk of CRBSI and do not require a change in human behavior (see [Table 1](#)). The following discussion concerns marketed devices that have supporting evidence for benefit.

Antimicrobial-coated intravascular catheters

Intravascular catheters coated on both the external and luminal surfaces presumably prevent infection through action at both the dermal interface and the hub/luminal route of inoculation. A large body of evidence supports the effectiveness of certain antimicrobial-coated catheters in the prevention of CRBSI.^{67–70} The anti-infective coatings associated with the greatest amount of clinical experience and utility are silver-sulfadiazine/chlorhexidine and minocycline/rifampin. It is suggested that antimicrobial or antiseptic-impregnated central venous catheters be used in patients in whom the CVC is expected to remain in place at least 5 days when routine efforts to prevent CRBSI have proven disappointing.^{4,5} These stipulations on CVC dwell time and application of basic aseptic techniques are applicable to all technologic approaches to CRBSI prevention. Although there is some concern that antimicrobial-coated devices will promote the emergence of resistance, available data are very reassuring.⁷¹ Fewer data are available to support use of CVCs coated with other agents.^{67,70}

Chlorhexidine-impregnated dressings

Similar to antimicrobial-coated CVCs, there are substantial supporting data for the use of chlorhexidine-impregnated dressings.^{72–74} Chlorhexidine dressings presumably act by preventing organisms that are resident on the skin from gaining access to the external/dermal surface of the catheter. Both the sponge dressing and gelpad dressing appear to be very effective.^{73,74} Due to concerns regarding dermal intolerance,

systemic absorption, and neurotoxicity, there is reluctance to use chlorhexidine dressings in low birth weight neonates, and they are marketed for infants older than 2 months.

Passive port protectors

Unfortunately, maintaining strict adherence to aseptic technique when accessing CVCs requires ongoing vigilance and is difficult to monitor. It appears that contamination of the catheter connector is a common event.^{47,75} Therefore, passive catheter port disinfection is an increasingly used strategy to prevent CRBSI. Although data from adequately powered, randomized controlled trials are lacking, increasing data from quasi-experimental trials indicate that antiseptic-containing port protectors are effective in preventing CRBSI.^{76–79}

Antiseptic-impregnated needleless connectors

Needleless connectors were developed to reduce to the use of needles in the vascular access system and thus decrease the risk of needlestick injury. As previously mentioned, some needleless connectors have been associated with an increased risk of bloodstream infection. To decrease the risk of microbial colonization of the connector, connectors impregnated with silver have been developed. Silver-impregnated connectors appear to decrease bacterial colonization and biofilm formation^{80,81} and may decrease the risk of CRBSI.⁸²

Antimicrobial/antiseptic locks

A large amount of literature supports the use of antimicrobial lock solutions to prevent CRBSI.^{83–86} The antimicrobial lock technique consists of filling the lumen of a catheter with a highly-concentrated antimicrobial solution and allowing it to dwell for a set period of time. A wide variety of antibiotics and antiseptics, in combination with various anticoagulants and other constituents, have been used in lock solutions.^{83,84} Despite the large body of supporting data, numerous questions remain regarding the use of antimicrobial lock solutions; issues concern optimal solution, minimal required dwell time, catheter material compatibility and potential adverse catheter effects, and microbial resistance. In general, antimicrobial locks are being increasingly used in patients requiring long-term catheterization (ie, chronic total parenteral nutrition/short-gut syndrome, hemodialysis) particularly in those patients with a history of CRBSI despite maximal aseptic practices. Antimicrobial locks are also useful in the treatment of CRBSI, but this is beyond the scope of this monograph.

Antibiotic/antiseptic ointments

A variety of topical antimicrobial ointments have been applied at the catheter exit site to decrease microbial burden and prevent CRBSI.⁴ This technique has been most carefully studied in hemodialysis patients with utility demonstrated for 10% povidone iodine⁸⁷ or bacitracin/gramicidin/polymyxin B.^{88–90}

Catheter securement

There is concern that injury to dermal structures associated with suture securement of CVCs results in increased microbial colonization^{91–94} and there is are few data to indicate that sutureless securement of CVCs is associated with a decreased occurrence of bloodstream infection.^{91–93} Data are lacking on whether catheter securement with tissue adhesives has a beneficial effect on catheter-related infection.

Practices not recommended

There are several interventions that have been studied and discredited and are thus specifically not recommended as standard practice (HICPAC, SHEA).^{4,5}

1. Do not administer systemic antimicrobial prophylaxis to prevent CRBSI either at the time of CVC placement or during their use.
2. Do not routinely exchange or replace CVCs.

Other Types of Vascular Catheters

Arterial catheters

Arterial catheters are often regarded as being less likely to result in infectious complications and are generally not included in surveillance programs for CRBSI. However, most studies on the subject conclude that arterial catheters are associated with essentially the same risk of CRBSI as CVCs and they should be inserted and maintained with the same degree of attention to infection prevention.^{95–100} Unfortunately, appropriate barrier precautions and aseptic technique are frequently neglected when arterial catheters are inserted.¹⁰¹

Hemodialysis catheters

Patients receiving hemodialysis via an intravascular catheter are much more likely to experience CRBSI than those undergoing hemodialysis via an arteriovenous fistula or graft. Like other tunneled vascular catheters, tunneled hemodialysis catheters are less prone to infection than nontunneled hemodialysis catheters. Special measures to prevent hemodialysis CRBSI include application of antimicrobial ointment at the exit site as previously related^{87,90} as well as administration of recombinant tissue plasminogen activating factor weekly.¹⁰²

Peripheral intravenous catheters

In many acute care hospitals, nearly all patients have a PIVC. It is estimated that approximately 330 million PIVCs are used in the United States yearly.¹⁰³ Approximately 0.1% of PIVCs (0.15 per 1000 catheter days) result in CRBSI.⁹⁵ Although the risk of infection is much less than that associated with CVCs, when the very large number of PIVCs is taken into account, it is evident that PIVCs result in a substantial burden of infection. At present, many institutions routinely replace PIVCs every 3 to 4 days.⁴ However, with the growing realization that PIVCs can remain in place until a change is clinically indicated,^{104,105} the dwell time of PIVCs will undoubtedly lengthen. It will be increasingly important for institutions to standardize practice and ensure appropriate aseptic precautions are used in the insertion and maintenance care of PIVCs.

Due to the work of countless investigators, our understanding of the pathogenesis of CRBSI and our ability to prevent CRBSI, through both clinical practice-oriented interventions and innovative technology, has greatly expanded. CRBSI prevention is a success story with the nationwide rate of infection falling by 50% between 2008 and 2014.¹ Evidence-based recommendations for prevention of CRBSI have been summarized in several guidelines^{4–7}; however, translating knowledge into sustained changes in practice requires a systematic and integrated approach to address both technical and adaptive issues.¹⁰⁶ Briefly, successful institutional change necessitates mobilization of multidisciplinary teams and creation of a culture of safety. Providers at all levels must be armed with an appropriate fund of knowledge through a variety of educational efforts; care practices should be standardized and streamlined; and performance should be measured, widely reported, and sustained. Realistic and concrete expectations should be articulated and resources must be made available to achieve the stated goals. Wise stewardship of resources is desirable and efforts associated with a diminishing return on investment should be curtailed. Accurate reporting of CRBSI rates and data validation are a must. A balanced reliance on both outcomes and process measures should be in place. In addition, the data should be primarily used to encourage ongoing performance improvement, not penalties.

Although great progress has been achieved in recent years in the prevention of CRBSI, numerous questions remain and efforts to develop safer intravascular catheters and better ways to use them should continue.

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REFERENCES

1. Centers for Disease Control and Prevention (CDC). National and state health-care associated infections progress report. 2014. Available at: <http://www.cdc.gov/HAI/pdfs/progress-report/hai-progress-report.pdf>. Accessed June 13, 2016.
2. Zimlichman E, Henderson D, Tamir O, et al. Health care-associated infections: a meta-analysis of costs and financial impact on the US health care system. *JAMA Intern Med* 2013;173(22):2039–46.
3. Umscheid CA, Mitchell MD, Doshi JA, et al. Estimating the proportion of healthcare-associated infections that are reasonably preventable and the related mortality and costs. *Infect Control Hosp Epidemiol* 2011;32(2):101–14.
4. O'Grady NP, Alexander M, Burns LA, et al. Guidelines for the prevention of intravascular catheter-related infections. *Am J Infect Control* 2011;39(4 Suppl 1): S1–34.
5. Marschall J, Mermel LA, Fakhri M, et al. Strategies to prevent central line-associated bloodstream infections in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol* 2014;35(Suppl 2):S89–107.
6. Barnes S, Olmsted RO, Monsees E, et al. Guide to preventing central line-associated bloodstream infections. 2015. Available at: http://apic.org/Resource_TinyMceFileManager/2015/APIC_CLABSI_WEB.pdf. Accessed June 8, 2016.
7. Gorski L, Hadaway L, Hagle ME, et al. Infusion therapy standards of practice. *J Infus Nurs* 2016;39(Suppl 1):S1–178.
8. Scheithauer S, Hafner H, Schroder J, et al. Simultaneous placement of multiple central lines increases central line-associated bloodstream infection rates. *Am J Infect Control* 2013;41(2):113–7.
9. Lin MY, Hota B, Khan YM, et al. Quality of traditional surveillance for public reporting of nosocomial bloodstream infection rates. *JAMA* 2010;304(18): 2035–41.
10. Sexton DJ, Chen LF, Moehring R, et al. Casablanca redux: we are shocked that public reporting of rates of central line-associated bloodstream infections are inaccurate. *Infect Control Hosp Epidemiol* 2012;33(9):932–5.
11. Beekmann SE, Diekema DJ, Huskins WC, et al. Diagnosing and reporting of central line-associated bloodstream infections. *Infect Control Hosp Epidemiol* 2012;33(9):875–82.
12. Nailon R, Rupp ME. A community collaborative to develop consensus guidelines to standardize out-of-hospital maintenance care of central venous catheters. *J Infus Nurs* 2015;38(2):115–21.
13. Fridkin SK, Pear SM, Williamson TH, et al. The role of understaffing in central venous catheter-associated bloodstream infections. *Infect Control Hosp Epidemiol* 1996;17(3):150–8.

14. Stone PW, Pogorzelska M, Kunches L, et al. Hospital staffing and health care-associated infections: a systematic review of the literature. *Clin Infect Dis* 2008;47(7):937–44.
15. Robert J, Fridkin SK, Blumberg HM, et al. The influence of the composition of the nursing staff on primary bloodstream infection rates in a surgical intensive care unit. *Infect Control Hosp Epidemiol* 2000;21(1):12–7.
16. Leistner R, Thurnagel S, Schwab F, et al. The impact of staffing on central venous catheter-associated bloodstream infections in preterm neonates—results of nation-wide cohort study in Germany. *Antimicrob Resist Infect Control* 2013;2(1):11.
17. Pappas S, Davidson N, Woodard J, et al. Risk-adjusted staffing to improve patient value. *Nurs Econ* 2015;33(2):73–8, 87; [quiz: 79].
18. Parikh A, Huang SA, Murthy P, et al. Quality improvement and cost savings after implementation of the leapfrog intensive care unit physician staffing standard at a community teaching hospital. *Crit Care Med* 2012;40(10):2754–9.
19. Coopersmith CM, Rebmann TL, Zack JE, et al. Effect of an education program on decreasing catheter-related bloodstream infections in the surgical intensive care unit. *Crit Care Med* 2002;30(1):59–64.
20. 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(5):1612–8.
21. 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(8):641–8.
22. Barsuk JH, Cohen ER, Potts S, et al. Dissemination of a simulation-based mastery learning intervention reduces central line-associated bloodstream infections. *BMJ Qual Saf* 2014;23(9):749–56.
23. Holzmann-Pazgal G, Kubanda A, Davis K, et al. Utilizing a line maintenance team to reduce central-line-associated bloodstream infections in a neonatal intensive care unit. *J Perinatol* 2012;32(4):281–6.
24. Secola R, Azen C, Lewis MA, et al. A crossover randomized prospective pilot study evaluating a central venous catheter team in reducing catheter-related bloodstream infections in pediatric oncology patients. *J Pediatr Oncol Nurs* 2012;29(6):307–15.
25. Raad II, Hohn DC, Gilbreath BJ, et al. Prevention of central venous catheter-related infections by using maximal sterile barrier precautions during insertion. *Infect Control Hosp Epidemiol* 1994;15(4 Pt 1):231–8.
26. Hu KK, Veenstra DL, Lipsky BA, et al. Use of maximal sterile barriers during central venous catheter insertion: clinical and economic outcomes. *Clin Infect Dis* 2004;39(10):1441–5.
27. Central Line Associated Bacteraemia in NSW Intensive Care Units (CLAB ICU) Collaborative, Burrell AR, McLaws ML, et al. Aseptic insertion of central venous lines to reduce bacteraemia. *Med J Aust* 2011;194(11):583–7.
28. Ishikawa Y, Kiyama T, Haga Y, et al. Maximal sterile barrier precautions do not reduce catheter-related bloodstream infections in general surgery units: a multi-institutional randomized controlled trial. *Ann Surg* 2010;251(4):620–3.
29. Rijnders BJ, Van Wijngaerden E, Wilmer A, et al. Use of full sterile barrier precautions during insertion of arterial catheters: a randomized trial. *Clin Infect Dis* 2003;36(6):743–8.

30. Parienti JJ, Mongardon N, Megarbane B, et al. Intravascular complications of central venous catheterization by insertion site. *N Engl J Med* 2015;373(13):1220–9.
31. Merrer J, De Jonghe B, Golliot F, et al. Complications of femoral and subclavian venous catheterization in critically ill patients: a randomized controlled trial. *JAMA* 2001;286(6):700–7.
32. Parienti JJ, Thirion M, Megarbane B, et al. Femoral vs jugular venous catheterization and risk of nosocomial events in adults requiring acute renal replacement therapy: a randomized controlled trial. *JAMA* 2008;299(20):2413–22.
33. Randolph AG, Cook DJ, Gonzales CA, et al. Ultrasound guidance for placement of central venous catheters: a meta-analysis of the literature. *Crit Care Med* 1996;24(12):2053–8.
34. Marik PE, Flemmer M, Harrison W. The risk of catheter-related bloodstream infection with femoral venous catheters as compared to subclavian and internal jugular venous catheters: a systematic review of the literature and meta-analysis. *Crit Care Med* 2012;40(8):2479–85.
35. Chaiyakunapruk N, Veenstra DL, Lipsky BA, et al. Chlorhexidine compared with povidone-iodine solution for vascular catheter-site care: a meta-analysis. *Ann Intern Med* 2002;136(11):792–801.
36. Maiwald M, Chan ES. The forgotten role of alcohol: a systematic review and meta-analysis of the clinical efficacy and perceived role of chlorhexidine in skin antisepsis. *PLoS One* 2012;7(9):e44277.
37. Tamma PD, Aucott SW, Milstone AM. Chlorhexidine use in the neonatal intensive care unit: results from a national survey. *Infect Control Hosp Epidemiol* 2010;31(8):846–9.
38. Taylor JE, McDonald SJ, Tan K. A survey of central venous catheter practices in Australian and New Zealand tertiary neonatal units. *Aust Crit Care* 2014;27(1):36–42.
39. Chapman AK, Aucott SW, Milstone AM. Safety of chlorhexidine gluconate used for skin antisepsis in the preterm infant. *J Perinatol* 2012;32(1):4–9.
40. Sathiyamurthy S, Banerjee J, Godambe SV. Antiseptic use in the neonatal intensive care unit - a dilemma in clinical practice: an evidence based review. *World J Clin Pediatr* 2016;5(2):159–71.
41. Berenholtz SM, Pronovost PJ, Lipsett PA, et al. Eliminating catheter-related bloodstream infections in the intensive care unit. *Crit Care Med* 2004;32(10):2014–20.
42. Centers for Disease Control and Prevention (CDC). Checklist for prevention of central line associated bloodstream infections. 2011. Available at: <http://www.cdc.gov/HAI/pdfs/bsi/checklist-for-CLABSI.pdf>. Accessed June 13, 2016.
43. 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(26):2725–32.
44. Blot K, Bergs J, Vogelaers D, et al. Prevention of central line-associated bloodstream infections through quality improvement interventions: a systematic review and meta-analysis. *Clin Infect Dis* 2014;59(1):96–105.
45. Lipitz-Snyderman A, Steinwachs D, Needham DM, et al. Impact of a statewide intensive care unit quality improvement initiative on hospital mortality and length of stay: retrospective comparative analysis. *BMJ* 2011;342:d219.
46. 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.

47. Rupp ME, Yu S, Huerta T, et al. Adequate disinfection of a split-septum needleless intravascular connector with a 5-second alcohol scrub. *Infect Control Hosp Epidemiol* 2012;33(7):661–5.
48. Rupp ME, Sholtz LA, Jourdan DR, et al. Outbreak of bloodstream infection temporally associated with the use of an intravascular needleless valve. *Clin Infect Dis* 2007;44(11):1408–14.
49. Jarvis WR, Murphy C, Hall KK, et al. Health care-associated bloodstream infections associated with negative- or positive-pressure or displacement mechanical valve needleless connectors. *Clin Infect Dis* 2009;49(12):1821–7.
50. Tabak YP, Jarvis WR, Sun X, et al. Meta-analysis on central line-associated bloodstream infections associated with a needleless intravenous connector with a new engineering design. *Am J Infect Control* 2014;42(12):1278–84.
51. Karki S, Cheng AC. Impact of non-rinse skin cleansing with chlorhexidine gluconate on prevention of healthcare-associated infections and colonization with multi-resistant organisms: a systematic review. *J Hosp Infect* 2012;82(2):71–84.
52. Popovich KJ, Hota B, Hayes R, et al. Effectiveness of routine patient cleansing with chlorhexidine gluconate for infection prevention in the medical intensive care unit. *Infect Control Hosp Epidemiol* 2009;30(10):959–63.
53. Bleasdale SC, Trick WE, Gonzalez IM, et al. Effectiveness of chlorhexidine bathing to reduce catheter-associated bloodstream infections in medical intensive care unit patients. *Arch Intern Med* 2007;167(19):2073–9.
54. Climo MW, Yokoe DS, Warren DK, et al. Effect of daily chlorhexidine bathing on hospital-acquired infection. *N Engl J Med* 2013;368(6):533–42.
55. Huang SS, Septimus E, Kleinman K, et al. Targeted versus universal decolonization to prevent ICU infection. *N Engl J Med* 2013;368(24):2255–65.
56. Popovich KJ, Hota B, Hayes R, et al. 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(5):854–8.
57. Noto MJ, Domenico HJ, Byrne DW, et al. Chlorhexidine bathing and health care-associated infections: a randomized clinical trial. *JAMA* 2015;313(4):369–78.
58. Tiwari MM, Hermsen ED, Charlton ME, et al. Inappropriate intravascular device use: a prospective study. *J Hosp Infect* 2011;78(2):128–32.
59. Lederle FA, Parenti CM, Berskow LC, et al. The idle intravenous catheter. *Ann Intern Med* 1992;116(9):737–8.
60. Cload B, Day AG, Ilan R. Evaluation of unnecessary central venous catheters in critically ill patients: a prospective observational study. *Can J Anaesth* 2010;57(9):830–5.
61. Parenti CM, Lederle FA, Impola CL, et al. Reduction of unnecessary intravenous catheter use. Internal medicine house staff participate in a successful quality improvement project. *Arch Intern Med* 1994;154(16):1829–32.
62. Seguin P, Laviolle B, Isslame S, et al. Effectiveness of simple daily sensitization of physicians to the duration of central venous and urinary tract catheterization. *Intensive Care Med* 2010;36(7):1202–6.
63. Timsit JF, Bouadma L, Ruckly S, et al. Dressing disruption is a major risk factor for catheter-related infections. *Crit Care Med* 2012;40(6):1707–14.
64. Guerin K, Wagner J, Rains K, et al. Reduction in central line-associated bloodstream infections by implementation of a postinsertion care bundle. *Am J Infect Control* 2010;38(6):430–3.
65. Rinke ML, Chen AR, Bundy DG, et al. Implementation of a central line maintenance care bundle in hospitalized pediatric oncology patients. *Pediatrics* 2012;130(4):e996–1004.

66. Exline MC, Ali NA, Zikri N, et al. Beyond the bundle—journey of a tertiary care medical intensive care unit to zero central line-associated bloodstream infections. *Crit Care* 2013;17(2):R41.
67. Casey AL, Mermel LA, Nightingale P, et al. Antimicrobial central venous catheters in adults: a systematic review and meta-analysis. *Lancet Infect Dis* 2008;8(12):763–76.
68. Lai NM, Chaiyakunapruk N, Lai NA, et al. Catheter impregnation, coating or bonding for reducing central venous catheter-related infections in adults. *Cochrane Database Syst Rev* 2016;(3):CD007878.
69. Ramritu P, Halton K, Collignon P, et al. A systematic review comparing the relative effectiveness of antimicrobial-coated catheters in intensive care units. *Am J Infect Control* 2008;36(2):104–17.
70. Wang H, Huang T, Jing J, et al. Effectiveness of different central venous catheters for catheter-related infections: a network meta-analysis. *J Hosp Infect* 2010;76(1):1–11.
71. Ramos ER, Reitzel R, Jiang Y, et al. Clinical effectiveness and risk of emerging resistance associated with prolonged use of antibiotic-impregnated catheters: more than 0.5 million catheter days and 7 years of clinical experience. *Crit Care Med* 2011;39(2):245–51.
72. Ho KM, Litton E. Use of chlorhexidine-impregnated dressing to prevent vascular and epidural catheter colonization and infection: a meta-analysis. *J Antimicrob Chemother* 2006;58(2):281–7.
73. Timsit JF, Mimoz O, Mourvillier B, et al. Randomized controlled trial of chlorhexidine dressing and highly adhesive dressing for preventing catheter-related infections in critically ill adults. *Am J Respir Crit Care Med* 2012;186(12):1272–8.
74. Timsit JF, Schwebel C, Bouadma L, et al. Chlorhexidine-impregnated sponges and less frequent dressing changes for prevention of catheter-related infections in critically ill adults: a randomized controlled trial. *JAMA* 2009;301(12):1231–41.
75. Sherertz RJ, Karchmer TB, Palavecino E, et al. Blood drawn through valved catheter hub connectors carries a significant risk of contamination. *Eur J Clin Microbiol Infect Dis* 2011;30(12):1571–7.
76. Wright MO, Tropp J, Schora DM, et al. Continuous passive disinfection of catheter hubs prevents contamination and bloodstream infection. *Am J Infect Control* 2013;41(1):33–8.
77. Kamboj M, Blair R, Bell N, et al. Use of disinfection cap to reduce central-line-associated bloodstream infection and blood culture contamination among hematology-oncology patients. *Infect Control Hosp Epidemiol* 2015;36(12):1401–8.
78. Merrill KC, Sumner S, Linford L, et al. Impact of universal disinfectant cap implementation on central line-associated bloodstream infections. *Am J Infect Control* 2014;42(12):1274–7.
79. Sweet MA, Cumpston A, Briggs F, et al. Impact of alcohol-impregnated port protectors and needleless neutral pressure connectors on central line-associated bloodstream infections and contamination of blood cultures in an inpatient oncology unit. *Am J Infect Control* 2012;40(10):931–4.
80. Maki DG. In vitro studies of a novel antimicrobial luer-activated needleless connector for prevention of catheter-related bloodstream infection. *Clin Infect Dis* 2010;50(12):1580–7.
81. Casey AL, Karpanen TJ, Nightingale P, et al. Microbiological comparison of a silver-coated and a non-coated needleless intravascular connector in clinical use. *J Hosp Infect* 2012;80(4):299–303.

82. Jacob JT, Chernetsky Tejedor S, Dent Reyes M, et al. Comparison of a silver-coated needleless connector and a standard needleless connector for the prevention of central line-associated bloodstream infections. *Infect Control Hosp Epidemiol* 2015;36(3):294–301.
83. Zacharioudakis IM, Zervou FN, Arvanitis M, et al. Antimicrobial lock solutions as a method to prevent central line-associated bloodstream infections: a meta-analysis of randomized controlled trials. *Clin Infect Dis* 2014;59(12):1741–9.
84. Snaterse M, Ruger W, Scholte Op Reimer WJ, et al. Antibiotic-based catheter lock solutions for prevention of catheter-related bloodstream infection: a systematic review of randomised controlled trials. *J Hosp Infect* 2010;75(1):1–11.
85. Oliveira C, Nasr A, Brindle M, et al. Ethanol locks to prevent catheter-related bloodstream infections in parenteral nutrition: a meta-analysis. *Pediatrics* 2012;129(2):318–29.
86. Maiefski M, Rupp ME, Hermsen ED. Ethanol lock technique: review of the literature. *Infect Control Hosp Epidemiol* 2009;30(11):1096–108.
87. Levin A, Mason AJ, Jindal KK, et al. Prevention of hemodialysis subclavian vein catheter infections by topical povidone-iodine. *Kidney Int* 1991;40(5):934–8.
88. Battistella M, Bholra C, Lok CE. Long-term follow-up of the hemodialysis infection prevention with polysporin ointment (HIPPO) study: a quality improvement report. *Am J Kidney Dis* 2011;57(3):432–41.
89. James MT, Conley J, Tonelli M, et al. Meta-analysis: antibiotics for prophylaxis against hemodialysis catheter-related infections. *Ann Intern Med* 2008;148(8):596–605.
90. Lok CE, Stanley KE, Hux JE, et al. Hemodialysis infection prevention with polysporin ointment. *J Am Soc Nephrol* 2003;14(1):169–79.
91. Ullman AJ, Cooke ML, Mitchell M, et al. Dressings and securement devices for central venous catheters (CVC). *Cochrane Database Syst Rev* 2015;(9):CD010367.
92. Yamamoto AJ, Solomon JA, Soulen MC, et al. Sutureless securement device reduces complications of peripherally inserted central venous catheters. *J Vasc Interv Radiol* 2002;13(1):77–81.
93. Cotogni P, Pittiruti M, Barbero C, et al. Catheter-related complications in cancer patients on home parenteral nutrition: a prospective study of over 51,000 catheter days. *JPEN J Parenter Enteral Nutr* 2013;37(3):375–83.
94. Karpanen TJ, Casey AL, Whitehouse T, et al. Clinical evaluation of a chlorhexidine intravascular catheter gel dressing on short-term central venous catheters. *Am J Infect Control* 2016;44(1):54–60.
95. Maki DG, Kluger DM, Crnich CJ. The risk of bloodstream infection in adults with different intravascular devices: a systematic review of 200 published prospective studies. *Mayo Clin Proc* 2006;81(9):1159–71.
96. Lorente L, Santacreu R, Martin MM, et al. Arterial catheter-related infection of 2,949 catheters. *Crit Care* 2006;10(3):R83.
97. Koh DB, Gowardman JR, Rickard CM, et al. Prospective study of peripheral arterial catheter infection and comparison with concurrently sited central venous catheters. *Crit Care Med* 2008;36(2):397–402.
98. Traore O, Liotier J, Souweine B. Prospective study of arterial and central venous catheter colonization and of arterial- and central venous catheter-related bacteremia in intensive care units. *Crit Care Med* 2005;33(6):1276–80.
99. Lucet JC, Bouadma L, Zahar JR, et al. Infectious risk associated with arterial catheters compared with central venous catheters. *Crit Care Med* 2010;38(4):1030–5.

100. Safdar N, O'Horo JC, Maki DG. Arterial catheter-related bloodstream infection: incidence, pathogenesis, risk factors and prevention. *J Hosp Infect* 2013; 85(3):189–95.
101. Cohen DM, Carino GP, Heffernan DS, et al. Arterial catheter use in the ICU: a national survey of antiseptic technique and perceived infectious risk. *Crit Care Med* 2015;43(11):2346–53.
102. Hemmelgarn BR, Moist LM, Lok CE, et al. Prevention of dialysis catheter malfunction with recombinant tissue plasminogen activator. *N Engl J Med* 2011; 364(4):303–12.
103. Hadaway L. Short peripheral intravenous catheters and infections. *J Infus Nurs* 2012;35(4):230–40.
104. Rickard CM, Webster J, Wallis MC, et al. Routine versus clinically indicated replacement of peripheral intravenous catheters: a randomised controlled equivalence trial. *Lancet* 2012;380(9847):1066–74.
105. Webster J, Osborne S, Rickard CM, et al. Clinically-indicated replacement versus routine replacement of peripheral venous catheters. *Cochrane Database Syst Rev* 2015;(8):CD007798.
106. Septimus E, Yokoe DS, Weinstein RA, et al. Maintaining the momentum of change: the role of the 2014 updates to the compendium in preventing healthcare-associated infections. *Infect Control Hosp Epidemiol* 2014; 35(Suppl 2):S6–9.