REVIEW ARTICLE

Darren B. Taichman, M.D., Ph.D., *Editor*

Prevention of Central Line–Associated Bloodstream Infections

Naomi P. O'Grady, M.D.

From the National Institutes of Health Clinical Center, Bethesda, MD. Dr. O'Grady can be contacted at nogrady@cc.nih.gov or at the National Institutes of Health Clinical Center, 10 Center Dr., Bldg. 10, Rm. 2-2731, Bethesda, MD 20892.

N Engl J Med 2023;389:1121-31.
DOI: 10.1056/NEJMra2213296

The management of many medical and surgical conditions often involves long-term infusion of intravenous fluids, broad-spectrum antibiotics, chemotherapeutic agents for cancer, critical care therapies, antibiotics administered at home, total parenteral nutrition, or hemodialysis. For these interventions, central venous catheters (referred to as central lines by the National Healthcare Safety Network [NHSN]) provide safe and reliable vascular access. Although these devices are vital to care, they are associated with a risk of infection. Central line–associated bloodstream infection (CLABSI) may increase antibiotic exposure, the hospital stay, health care costs, and the risk of death.

A study conducted at a large, suburban, tertiary care hospital involving 1132 patients in an intensive care unit (ICU) who had undergone central venous catheterization showed the magnitude of this problem. CLABSI was associated with significant increases in the unadjusted ICU length of stay (median, 24 days, vs. 5 days for patients without a CLABSI; P<0.001), hospital length of stay (median, 45 vs. 11 days; P<0.001), mortality (51% vs. 28%, P=0.001), and total hospital costs ($83,544 vs. $23,803, P<0.001). After adjustment for other factors that may affect costs and length of stay, CLABSI resulted in an attributable cost of $11,971 (95% confidence interval [CI], $6,732 to $18,352), an additional ICU length of stay of 2.41 days (95% CI, 0.08 to 3.09), and an additional hospital length of stay of 7.54 days (95% CI, 3.99 to 11.09).[1] Although there is little debate about the excess cost of these infections, reported excess mortality has varied. However, an updated meta-analysis that included 18 studies showed an increased risk of death among patients with CLABSI as compared with those who did not have this infection (odds ratio, 2.75; 95% CI, 1.86 to 4.07),[2] findings that reaffirmed those in a smaller meta-analysis.[3]

The enormous morbidity and mortality burden associated with CLABSI and the literature showing that these infections are often preventable have made CLABSI an easy target for performance improvement. In fact, CLABSI rates have become proxies for hospital quality and patient safety and are used by the Centers for Medicare and Medicaid Services (CMS) to deny hospitals reimbursement for the care of patients who acquired these infections after admission. It is therefore not surprising that over the past 20 years, substantial efforts have been made by several governmental, public health, and professional organizations to sponsor and promote evidence-based guidelines for strategies to prevent CLABSI.[4-9] These efforts have been credited for successfully reducing the incidence of CLABSI in ICUs, acute care units, burn units, neonatal ICUs, and oncology units nationwide. The Centers for Disease Control and Prevention (CDC) reported a 58% reduction in CLABSI across all ICU types from 2001 through 2009.[10] Another analysis showed more than a 50% reduction in CLABSI rates, from 2.5 infections per 1000 catheter days in 2004 to 0.76 infections per 1000 catheter days in 2013.[11] Reductions in CLABSI rates were sustained during the Michigan Keystone ICU Project,[11] a study that included 103 ICUs in Michigan.

Several other factors may have contributed to these reported reductions in CLABSI rates, including changes in the definition of CLABSI and changes in public policy. CLABSI rates remained low nationwide until the middle of 2020, when the coronavirus disease 2019 (Covid-19) pandemic brought with it a substantial increase in infection rates, with one study showing a 51% increase in CLABSI rates during the first few months of the pandemic in 78 hospitals across 12 states in a single health care system.[12]

This review focuses on the specific strategies for which there is high-quality evidence of reduced CLABSI rates and considers how changes in both definitions of CLABSI and public policy may have indirectly contributed to the reduction in these rates, without having improved clinical outcomes. In addition, since the increase in the incidence of CLABSI during the Covid-19 pandemic revealed vulnerabilities in some infection-prevention strategies, strategies that are more resilient in the face of changing conditions in health care are highlighted.

Figure 1 (facing page). Four Routes for Catheter Contamination.

In the first route of contamination, skin pathogens can enter the cutaneous catheter tract at the insertion site and migrate down the external surface of the catheter toward the catheter tip. Insertion-site contamination can also happen when the skin microorganism density increases underneath the catheter dressing over time if the area is not decontaminated frequently. In the second route, intraluminal contamination can occur when the catheter hub is manipulated, and pathogens gain access to the intraluminal surface of the device, where they adhere and become incorporated into biofilm that allows sustained infection and hematogenous dissemination. In the third route, less commonly, catheters can become contaminated hematogenously from a secondary bloodstream infection that develops from another focus of infection (e.g., pneumonia or a urinary tract infection). Bacteria then stick to the biofilm that is formed and adhere to the internal lumen of the catheter. In the fourth route, rarely, contaminated infusate can taint the catheter (e.g., in outbreaks with contaminated injectable flushes).

DEFINITION OF CLABSI

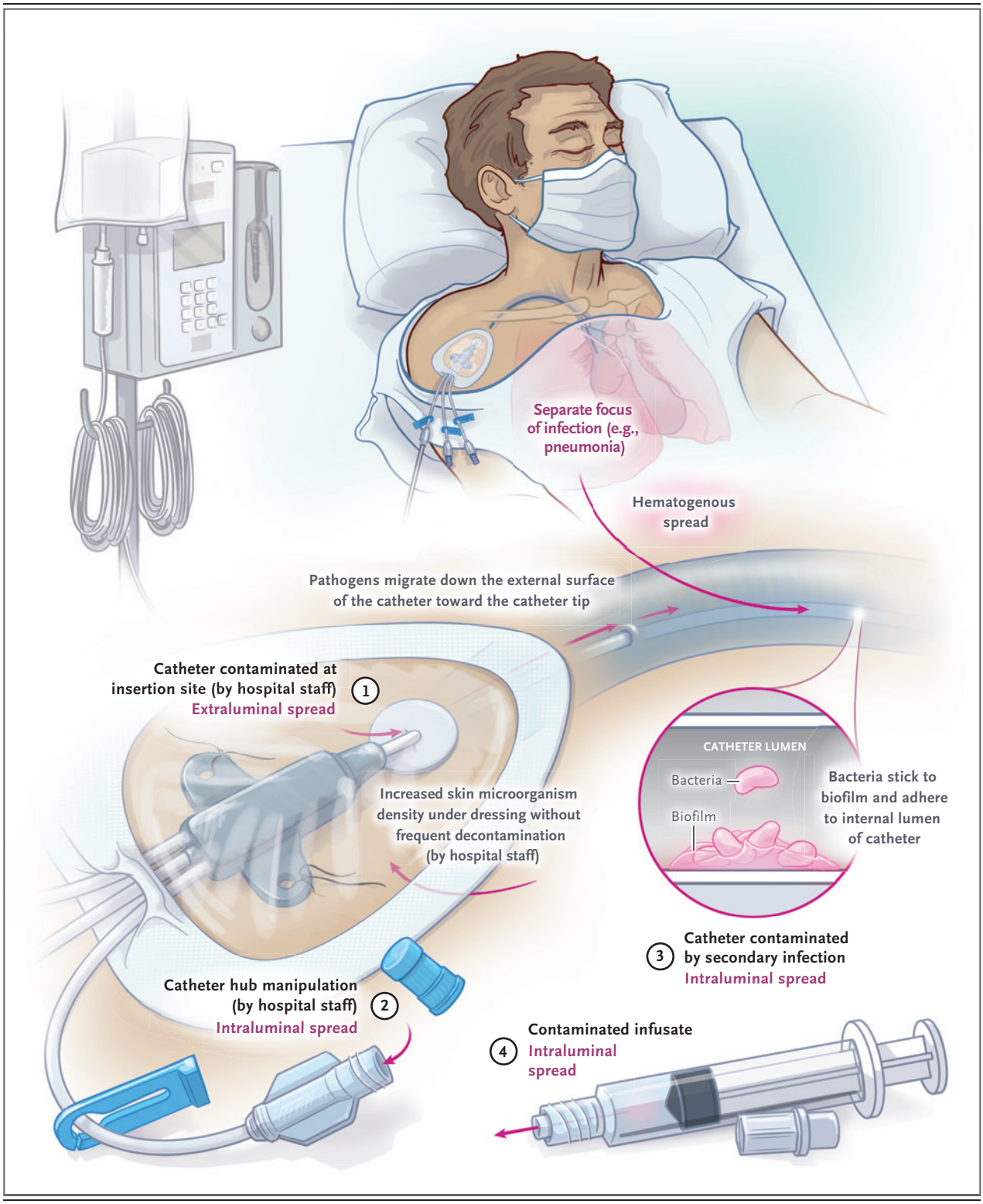
The NHSN, the widely used health care–associated infection tracking system of the CDC, defines CLABSI as a laboratory-confirmed bloodstream infection in a patient who has had a central venous catheter in place for more than 48 hours before the date on which blood was drawn for culture, if no other source of bacteremia or fungemia is identified.[13] This definition is based on surveillance rather than on a clinical presentation, with no requirement for signs or symptoms of infection. Since it is often difficult to determine whether a bloodstream infection is related to the central catheter itself or whether it has a secondary source (e.g., an abdominal abscess or pneumonia), the NHSN definition of CLABSI may overestimate the true incidence of central catheter–associated infection. This surveillance definition is used by the NHSN network because it is easy to apply to areas in the hospital where tracking the rates of CLABSI is deemed important. If this definition is applied consistently, it will provide useful information on institutional CLABSI trends.

Catheter-related bloodstream infection (CRBSI) is a clinical definition used for diagnosis and treatment. It requires specific laboratory testing that accurately identifies the catheter as the source of the bloodstream infection. In addition to meeting the criteria for the surveillance definition (i.e., CLABSI), the CRBSI definition includes signs and symptoms of infection (e.g., fever, elevated white-cell count, and erythema at the catheter exit site) when blood was drawn for culture, and it can be influenced by various other factors such as catheter removal, laboratory resources such as quantitative blood cultures or time to positivity, and submission of the catheter tip for culture.[14,15] CRBSI rates are not used for surveillance because the complex process of establishing the catheter as the source of the bloodstream infection would make broad application for epidemiologic purposes challenging.

Although there are nuanced but distinct differences between CLABSI and CRBSI, the terms are often used interchangeably, which can complicate data interpretation. In this review, I discuss studies that used either CLABSI or CRBSI as an outcome measure, recognizing that the CLABSI definition is less accurate and may affect the validity of the evidence.

PATHOGENESIS

Understanding the pathogenesis of CRBSI is pivotal for developing preventive strategies that target the entry routes of pathogens. There are



four routes for catheter contamination (Fig. 1). First, skin pathogens at the insertion site can enter the cutaneous catheter tract and migrate down the external surface of the catheter toward the tip. This most commonly happens within the first 7 days after catheter placement and is

thought to occur at the time of insertion. Insertion-site contamination can also happen when the skin microorganism density increases underneath the catheter dressing over time, if the area is not decontaminated frequently.

Second, intraluminal contamination can happen when the catheter hub is manipulated. Pathogens gain access to the intraluminal surface of the device, where they adhere and become incorporated into biofilm (an aggregate of microorganisms in a matrix of extracellular polymeric substances), which allows for sustained infection and hematogenous dissemination. This contamination typically happens more than 7 days after catheter insertion and is related to the care and maintenance of the catheter, as well as the number of times the catheter is manipulated or accessed.

Third, and less commonly, catheters become contaminated hematogenously from a secondary bloodstream infection that develops from another focus of infection (e.g., pneumonia or a urinary tract infection). Bacteria stick to the biofilm that is formed and adhere to the internal lumen of the catheter. Finally, in rare cases, contaminated infusate taints the catheter (i.e., in outbreaks with contaminated injectable flushes).[7] Knowledge of the pathogenesis of CRBSI has informed the development of strategies for prevention.

RISK FACTORS FOR CRBSI

Although most efforts to reduce CRBSIs over the past 20 years have focused on the ICU, which is perceived to be a high-risk setting, most CRBSIs now occur in non-ICU inpatient units and in the outpatient setting.[16,17] Rather than focusing on the areas of the hospital such as the ICU where the risk of acquiring CLABSI is high, some infection-prevention strategies aim to mitigate specific CRBSI risk factors that are related to characteristics of the patient, provider, or device (Table 1). Patient characteristics that increase the risk of infection include immunocompromise related to hematologic cancer, neutropenia, malnutrition, a prolonged hospital stay before device insertion, severe burns, a body-mass index (the weight in kilograms divided by the square of the height in meters) of more than 40, and prematurity in infants.[18-21]

Table 1. Risk Factors for Central Line–Associated Bloodstream Infection.

Patient factors
Immunocompromise
Neutropenia
Burns
Malnutrition
BMI >40*
Prolonged hospitalization before catheter insertion
Prematurity in infants
Limited venous access
Provider factors
Emergency catheter insertion
Incomplete adherence to aseptic technique
Multiple manipulations of the catheter
Low nurse-to-patient ratio
Failure to remove unnecessary catheter
Device factors
Catheter material
Catheter insertion site
Indications for use (e.g., for hemodialysis)

* The body-mass index (BMI) is the weight in kilograms divided by the square of the height in meters.

Provider characteristics that increase the risk include insertion of the catheter under emergency conditions, incomplete adherence to sterile insertion technique, multiple manipulations of the catheter, low nurse-to-patient ratios, and failure to remove unnecessary catheters.[22,23] Finally, device characteristics that are associated with risk include the material used to make the catheter, the site of insertion, the number of lumens, and the indication for use (e.g., hemodialysis or pulmonary-artery catheters).[24-26] Most strategies to prevent CLABSI have targeted provider and device characteristics, which are more amenable to modification than patient characteristics.

PROVEN PREVENTIVE STRATEGIES AND DEVICES

CHECKLISTS

Table 2 lists preventive strategies and devices that have been shown to reduce the incidence of CLABSI. For example, checklists consist of specific step-by-step instructions on how to insert a

Table 2. Strategies and Devices for Preventing Central Line–Associated Bloodstream Infection.

Checklists
Catheter-insertion cart or kit
Hand hygiene
Maximal sterile barrier precautions
Alcoholic chlorhexidine skin antisepsis
Selection of subclavian catheter-insertion site (in patients in the intensive care unit)
Chlorhexidine dressings
Chlorhexidine bathing
Antibiotic- or antiseptic-impregnated catheters
Manual decontamination of catheter hubs and caps before catheter insertion
Antiseptic-containing hubs and caps

catheter with the use of standard infection-prevention practices and aseptic technique. The list usually begins with hand hygiene and works through all steps related to infection control, including gowning, gloving, masking, draping the patient, and applying antiseptic agents to the patient's skin. Checklists have been shown to improve adherence to infection-control practices at the time of catheter insertion and to reduce the incidence of infection.[27,28] The checklist is usually completed by someone who is directly observing the procedure. This approach helps the members of the procedure team focus their attention on the details in the list and makes them less prone to skipping any of the small but important steps.

CATHETER-INSERTION KITS OR CARTS

The use of all-inclusive catheter-insertion kits or carts has been shown to reduce the risk of CRBSI by ensuring that everything needed for successful catheter insertion is in one place, thus making it easy to do the right thing and more difficult to make a mistake.[29] For example, choosing the correct antiseptic agent (chlorhexidine instead of povidone iodine) for the skin is no longer a decision the proceduralist needs to make if the agent comes bundled in a kit or on a catheter-insertion cart. Catheter-insertion kits should contain all the necessary components for completion of this sterile procedure, including gowns, gloves, masks, sterile drapes, and the antiseptic agent, as well as the local anesthetic, needles, trocars, catheter, and sutures needed for catheter insertion and securement.

HAND HYGIENE

Hand hygiene before insertion of a central catheter is an essential part of an infection-prevention program.[30-32] Hand hygiene can involve washing with conventional soap and water or with an alcohol-based, waterless hand rub. An alcohol-based sanitizer is preferred for hands that are not visibly soiled. Alcohol-based products should be applied according to the manufacturer's guidelines on dispensing the product. Typically, 3 to 5 ml is applied to the palm, and the hands are rubbed vigorously and thoroughly so that all surfaces on both hands are covered. All surfaces usually dry completely in 20 seconds.[33] Hand hygiene is essential before and after inserting, replacing, accessing, repairing, or dressing an intravascular catheter. Using gloves when manipulating central catheters does not preclude the need for hand hygiene. If hands are not cleaned before gloves are donned, any organisms on the hands may be transferred to the outside surface of the gloves.

MAXIMAL STERILE BARRIER PRECAUTIONS

Maximal sterile barrier precautions are defined as wearing a mask, cap, sterile gown, and sterile gloves and placing a large sterile drape that fully covers the patient's entire body. The use of maximal sterile barrier precautions during catheter placement has been associated with a reduced incidence of CLABSI, as compared with the use of sterile gloves and a small drape alone.[34]

ALCOHOLIC CHLORHEXIDINE SKIN ANTISEPSIS

Skin antisepsis with an alcoholic chlorhexidine preparation containing at least 2% chlorhexidine gluconate at the time of catheter insertion has become the standard of care, based on multiple randomized studies showing a reduced incidence of CLABSI with alcoholic chlorhexidine than with povidone iodine.[35-38] Although both antiseptic preparations have broad-spectrum antimicrobial activity, the superior clinical protection provided by chlorhexidine is probably related to more rapid action, a shorter drying time owing to the combination with alcohol, persistent activity despite exposure to blood and body fluids, and a longer residual effect at the site of catheter insertion. The available evidence provides support

for the use of an alcoholic preparation of chlorhexidine rather than its aqueous competitors.[39]

SITE SELECTION

The subclavian site is the preferred catheter-insertion site for reducing the risk of CRBSI in the ICU.[20,25,26,40,41] In the non-ICU setting, the difference in infection risk among insertion sites is less clear. The influence of the site on the risk of CRBSI is related in part to the density of skin flora at the site. Femoral catheters have higher colonization rates and, in some studies, are associated with a higher incidence of CRBSI than catheters inserted at subclavian or internal jugular sites in adults.[20,26,40] In a randomized, controlled trial that compared all three sites, catheterization of the subclavian vein was associated with a lower risk of the combined end-point event of CRBSI and symptomatic deep venous thrombosis than catheterization of the femoral vein or the internal jugular vein.[20] However, subclavian-vein catheterization was associated with an increased risk of mechanical complications such as pneumothorax and subclavian-artery cannulization. This potential for mechanical complications should be considered in weighing the risks and benefits of infectious and noninfectious complications of catheter insertion.

Site selection should be guided by patient comfort, the ability to secure the catheter, and maintenance of aseptic technique, as well as by patient-specific factors such as coagulopathies, anatomical complexity, and preexisting catheters. In patients for whom hemodialysis will probably be warranted, the subclavian site should be avoided because of the risk of subclavian stenosis.[42] The availability of bedside ultrasonography and the experience of the proceduralist should be factored into the choice of insertion site, along with a consideration of infection risk.

CHLORHEXIDINE DRESSINGS

Dressings containing chlorhexidine have been shown to reduce the risk of CLABSI and should be routinely used in patients older than 2 months of age.[43-46] These dressings are available in two forms: a gel-based chlorhexidine coating on a transparent dressing and a chlorhexidine-impregnated sponge dressing. Chlorhexidine dressings cover the top of the catheter exit site and reduce the risk of infection by targeting the extraluminal pathway, providing antimicrobial activity at the site for up to 7 days. Once secured in place, the dressings require less frequent changes than standard dressings. In patients who have well-healed access sites, it is not clear whether chlorhexidine dressings provide any additional benefit.[47,48]

CHLORHEXIDINE BATHING

Several randomized trials involving adults and children have established the role of daily chlorhexidine bathing to prevent CLABSI in critically ill patients.[49-51] However, the role of daily chlorhexidine baths is less clear in other patient populations. One study, which involved patients on general medical and surgical wards, showed that daily chlorhexidine bathing was associated with a significant decrease in the incidence of CLABSI.[52] However, some of the patients in that study received mupirocin decolonization if they were known to be carriers of methicillin-resistant *Staphylococcus aureus*, so that it was difficult to discern the role of chlorhexidine bathing alone. Chlorhexidine bathing has also been studied in patients with cancer. Some studies in this patient population showed that daily chlorhexidine bathing decreased the incidence of CLABSI among adults[53]; however, in children, similar benefits were not observed.[54]

ANTIBIOTIC- AND ANTISEPTIC-IMPREGNATED CATHETERS

Catheters impregnated with chlorhexidine–silver sulfadiazine or minocycline–rifampin have been studied for more than two decades and have been shown to be very effective in reducing the risk of CLABSI.[24,55-59] When these catheters were first introduced, they were more expensive than standard catheters, and the higher cost prevented widespread adoption, since the cost–benefit ratio was not perceived to be favorable. Over the years, the costs have decreased, and these catheters have been recommended for use in hospital units or special patient populations that have a high incidence of CLABSI despite compliance with essential preventive practices.[4,5,7,8] Many of the studies investigating the effectiveness of antibiotic- and antiseptic-impregnated catheters were performed before chlorhexidine-based skin antisepsis became the standard of care. Some data suggest that for patient care units with a very low incidence of CLABSI, the use of an anti-

microbial-impregnated catheter may not provide an additional benefit.[60]

Data are lacking from studies assessing the combined effect of chlorhexidine skin antisepsis, antimicrobial-impregnated catheters, and chlorhexidine-impregnated catheter dressings in order to determine whether all these interventions are necessary or what contribution each intervention makes individually. This lack of data has contributed to the reluctance to recommend antimicrobial-impregnated catheters for routine use in all patients.

ANTISEPTIC-CONTAINING HUBS AND CAPS

Contamination of catheter hubs and caps has long been recognized as a source of CLABSI. Manual decontamination of these hubs and caps has been the subject of "scrub the hub" campaigns, which advocate scrubbing the catheter hub or cap with an antiseptic (i.e., alcohol or chlorhexidine) for 10 to 15 seconds and then allowing it to dry before insertion.[61] Since 15 seconds plus drying time may not be achievable if rapid insertion is required, antiseptic-containing connector or cap protectors have been developed. These protectors passively bathe the access hub or cap continuously in an antiseptic, usually alcohol, providing both a physical barrier to contamination and chemical antisepsis at the access site.

Several studies have shown that antiseptic-containing hubs and caps reduce the risk of CLABSI.[62-68] However, although the use of these devices is supported by high-quality evidence, they have not been recommended for routine use because they are not viewed as superior to manual disinfection, which is considered to be an essential practice.[4] Whether manual disinfection of the hub in accessing the catheter has any additional benefit when an antiseptic-containing protective cap has been used is unknown.

NONCLINICAL FACTORS AND CLABSI

PUBLIC POLICY

In 2008, as part of an effort to encourage hospitals to strengthen infection-prevention measures, the CMS ceased reimbursement for the treatment of hospital-acquired infections that were not present on admission. This change in policy, in essence, shifted the cost of CLABSI acquired in a health care system to the hospital or nursing or rehabilitation facility. Several studies have reviewed the effects of these financial penalties on hospital CLABSI rates. One study showed no effect, another showed a decline in infection rates, and a third showed no change in infection rates but rather a change in providers' coding patterns, with an increase in codes that categorized these infections as present on admission.[69-71] These findings suggest that financial penalties may change practice patterns. One concern is that these policies may provide an incentive to stop ordering blood cultures for patients with catheters. Less testing would lower detection rates and improve hospital performance without changing clinical outcomes.

In addition to the financial penalties put forward in 2008, several states passed laws requiring public reporting of hospital-acquired infection rates. In 2004, only 4 states had such reporting requirements, but by 2022, a total of 38 states and territories mandated public reporting. It is difficult to determine how these policies affect clinical care, but they do put pressure (by design) on hospital administrators to reduce CLABSI rates within their institutions. This pressure can lead to unintended consequences such as changes in how CLABSI is defined or detected.

TRACKING METHODS

CLABSI rates depend not only on the definition used but also on the methods of tracking. Changes to either of these will alter data interpretation over time. One component of the NHSN definition of CLABSI is that there are no identifiable alternative sources of bacteremia; this component can be especially subjective. Current policies linking public reporting and financial penalties to CLABSI rates could provide an incentive for hospitals to engage in a very granular search for an alternative source of bacteremia, a practice that did not exist before the adoption of these policies. Whereas the CLABSI definition may have overestimated the true incidence of infection in years past, current tracking strategies may underestimate the incidence of CLABSI if bacteremia is attributed to alternative sources of infection. Even with rigorous application of the NHSN definition, data suggest that interrater reliability is low.[72-76]

In 2013, the CDC added another category of laboratory-confirmed bacteremia — mucosal

barrier injury. This change was intended to prevent bacteremia caused by gastrointestinal organisms in patients with neutropenia or graft-versus-host disease from being classified as a CLABSI. The new category was introduced to improve the comparability of CLABSI rates among institutions that care for large numbers of patients with cancer. Studies showed a reduction in CLABSI rates when bacteremia due to mucosal barrier injury was considered separately.[77-79] Thus, although a lower incidence of CLABSI after 2013 may reflect actual improvement in clinical outcomes, it is also possible that changes in the CLABSI classification contributed to the reported reduction. It is therefore challenging to determine the actual degree of improvement in clinical outcomes or the effect of changes in the CLABSI classification.

COVID-19 PANDEMIC AND CLABSI

The Covid-19 pandemic has had a disruptive effect on the U.S. health care system, straining hospital resources and exhausting hospital staff. The pandemic resulted in an abrupt decrease in hospital admissions for patients with common conditions and led to a disproportionate increase in the severity of illness among hospitalized patients.[80] In addition, the health care provider component of the health care system was and continues to be stressed. Since patient and provider risk factors for the development of CLABSI were substantially altered during the height of the Covid-19 pandemic, it is not surprising to see an increase in the incidence of CLABSI.[12,81-83] What is surprising, however, is how quickly and how high the incidence of CLABSI rose during the pandemic, with one study reporting an increase by 325%.[81]

Much of the increase in the incidence of CLABSI has been attributed to changes in the care and maintenance of central catheters and is related to provider-related risk factors. Some changes in care were a result of a shortage of resources such as chlorhexidine wipes used for chlorhexidine baths, whereas other changes were a result of a decrease in the amount of time that providers spent with patients in order to reduce exposure and the risk of infection. In one large health care system, qualitative feedback from infection-prevention teams regarding changes in practices after the beginning of the Covid-19 pandemic included less chlorhexidine bathing, fewer bedside checks on catheters and tubing owing to long-extension tubing and intravenous pumps placed in hallways, disturbance of catheter dressings because of prone positioning of patients, and fewer catheter accesses that complied with antiseptic protocol (manual scrubbing of the hub with antiseptic for 15 seconds).[12] Another factor affecting CLABSI rates was the increased number of traveling nurses and physicians in response to increased patient volumes; these clinicians may not have been familiar with standard preventive practices within the units they were staffing.[12]

The Covid-19 pandemic revealed other vulnerabilities in the CLABSI-prevention system when the NHSN stopped collecting data from January through June 2020 because of the strains of the pandemic and the limited number of infection-prevention professionals who were available. The NHSN has served for decades as the foundation of CLABSI surveillance, with more than 25,000 participating hospitals. This interruption in data collection has impeded comparisons among institutions and prevented individual institutions from assessing the effect of the Covid-19 pandemic on their own institutional CLABSI rates. Application of the complicated CLABSI definitions used by the NHSN requires a substantial amount of education and training. Thus, substituting new persons for the infection-prevention professionals who had been assigned to other priorities was nearly impossible.

This problem highlights the need for a new and simpler definition that allows for computerized capture of CLABSI rates with the use of artificial intelligence and the electronic health record. This simpler definition could encompass all cases of hospital-acquired bacteremia in patients with all types of vascular catheters, including peripheral intravenous catheters, midline catheters, and arterial catheters. The benefit of capturing all hospital-acquired cases of bacteremia is that bloodstream infections associated with these other catheters are not infequent.[84,85] The full extent of the problem is unknown because reporting is currently required only for CLABSI. Combining a simpler definition with an electronic solution could achieve high reliability during all conditions of health care delivery.

CONCLUSIONS

The remarkable success in reducing the incidence of CLABSI over the past two decades has been achieved with new forms of technology, new strategies, and consistent reinforcement of proven infection-prevention practices, with the recognition that part of the reduction may have been artifactual, as a result of changes in public policies and tracking methods. Despite this success, we should be circumspect, given that both 20 years of reductions in the incidence of CLABSI and our ability to collect surveillance data vanished during the first 3 months of the Covid-19 pandemic. The system we have in place for the prevention of CLABSI is clearly fragile and vulnerable to stress in the health care environment, particularly stress on the provider component of clinical care.

We need to engineer resilient infection-prevention processes that can withstand changing environmental conditions and uncertain events. Although consistent reinforcement of preventive practices such as checklists is effective, it relies on limited staff who may have competing priorities when the health care system is strained. It is time to consider combining routine use of all available CLABSI preventive strategies that do not depend on providers in order to be effective. Relying more firmly on the use of forms of technology that have been shown to be effective when used in CLABSI-prevention programs — such as antiseptic-impregnated catheters, chlorhexidine-impregnated dressings, and alcohol-bathed protective caps for every central catheter that is placed — may be a reasonable approach, even if it is not known whether each intervention is necessary. Building redundancy into the infection-prevention system increases reliability and resilience in a system that currently relies on backward-looking data to identify a problem and that cannot adapt to meet the needs imposed by new conditions in real time. Although we do not know the individual contribution of each strategy, combining them adds little cost, increases redundancy in the CLABSI-prevention program, and reduces the risk that another unexpected health care event will derail gains in CLABSI prevention that were achieved over decades.

The opinions expressed in this article are those of the author and do not represent any position or policy of the National Institutes of Health, the Department of Health and Human Services, or the federal government.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

REFERENCES

1. 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.
2. Ziegler MJ, Pellegrini DC, Safdar N. Attributable mortality of central line associated bloodstream infection: systematic review and meta-analysis. Infection 2015;43:29-36.
3. Siempos II, Kopterides P, Tsangaris I, Dimopoulou I, Armaganidis AE. Impact of catheter-related bloodstream infections on the mortality of critically ill patients: a meta-analysis. Crit Care Med 2009;37:2283-9.
4. Buetti N, Marschall J, Drees M, et al. Strategies to prevent central line-associated bloodstream infections in acute-care hospitals: 2022 update. Infect Control Hosp Epidemiol 2022;43:553-69.
5. Marschall J, Mermel LA, Fakih 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-S107.
6. Gorski LA, Hadaway L, Hagle ME, et al. Infusion therapy standards of practice, 8th edition. J Infus Nurs 2021;44:Suppl 1:S1-S224.
7. O'Grady NP, Alexander M, Burns LA, et al. Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis 2011;52(9):e162-e193.
8. 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.
9. Huang EY, Chen C, Abdullah F, et al. Strategies for the prevention of central venous catheter infections: an American Pediatric Surgical Association Outcomes and Clinical Trials Committee systematic review. J Pediatr Surg 2011;46:2000-11.
10. Vital signs: central line-associated blood stream infections — United States, 2001, 2008, and 2009. MMWR Morb Mortal Wkly Rep 2011;60:243-8.
11. Pronovost PJ, Watson SR, Goeschel CA, Hyzy RC, Berenholtz SM. Sustaining reductions in central line-associated bloodstream infections in Michigan intensive care units: a 10-year analysis. Am J Med Qual 2016;31:197-202.
12. Fakih MG, Bufalino A, Sturm L, et al. Coronavirus disease 2019 (COVID-19) pandemic, central-line-associated bloodstream infection (CLABSI), and catheter-associated urinary tract infection (CAUTI): the urgent need to refocus on hardwiring prevention efforts. Infect Control Hosp Epidemiol 2022;43:26-31.
13. Bloodstream infection event (central line-associated bloodstream infection and non-central line associated bloodstream infection). National Healthcare Safety Network, January 2023 (https://www.cdc.gov/nhsn/PDFs/pscManual/4PSC_CLABScurrent.pdf).
14. Mermel LA, Allon M, Bouza E, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 2009;49:1-45.
15. Lai YL, Adjemian J, Ricotta EE, Mathew L, O'Grady NP, Kadri SS. Dwindling utilization of central venous catheter tip cultures: an analysis of sampling trends and clinical utility at 128 US hospitals, 2009-2014. Clin Infect Dis 2019;69:1797-800.
16. Kallen AJ, Patel PR, O'Grady NP. Preventing catheter-related bloodstream infections outside the intensive care unit: expanding prevention to new settings. Clin Infect Dis 2010;51:335-41.

17. Marschall J, Leone C, Jones M, Nihill D, Fraser VJ, Warren DK. Catheter-associated bloodstream infections in general medical patients outside the intensive care unit: a surveillance study. Infect Control Hosp Epidemiol 2007;28:905-9.
18. Callister D, Limchaiyawat P, Eells SJ, Miller LG. Risk factors for central line-associated bloodstream infections in the era of prevention bundles. Infect Control Hosp Epidemiol 2015;36:214-6.
19. Jumani K, Advani S, Reich NG, Gosey L, Milstone AM. Risk factors for peripherally inserted central venous catheter complications in children. JAMA Pediatr 2013;167:429-35.
20. Parienti J-J, Mongardon N, Mégarbane B, et al. Intravascular complications of central venous catheterization by insertion site. N Engl J Med 2015;373:1220-9.
21. Zakhour R, Chaftari A-M, Raad II. Catheter-related infections in patients with haematological malignancies: novel preventive and therapeutic strategies. Lancet Infect Dis 2016;16(11):e241-e250.
22. Fridkin SK, Pear SM, Williamson TH, Galgiani JN, Jarvis WR. The role of understaffing in central venous catheter-associated bloodstream infections. Infect Control Hosp Epidemiol 1996;17:150-8.
23. Templeton A, Schlegel M, Fleisch F, et al. Multilumen central venous catheters increase risk for catheter-related bloodstream infection: prospective surveillance study. Infection 2008;36:322-7.
24. Hanna H, Benjamin R, Chatzinikolaou I, et al. Long-term silicone central venous catheters impregnated with minocycline and rifampin decrease rates of catheter-related bloodstream infection in cancer patients: a prospective randomized clinical trial. J Clin Oncol 2004;22:3163-71.
25. Parienti J-J. Catheter-related bloodstream infection in jugular versus subclavian central catheterization. Crit Care Med 2017;45(7):e734-e735.
26. Timsit J-F, Bouadma L, Mimoz O, et al. Jugular versus femoral short-term catheterization and risk of infection in intensive care unit patients: causal analysis of two randomized trials. Am J Respir Crit Care Med 2013;188:1232-9.
27. Wichmann D, Belmar Campos CE, Ehrhardt S, et al. Efficacy of introducing a checklist to reduce central venous line associated bloodstream infections in the ICU caring for adult patients. BMC Infect Dis 2018;18:267.
28. Pronovost P, Needham D, Berenholtz S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU. N Engl J Med 2006;355:2725-32.
29. 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.
30. Rosenthal VD, Guzman S, Safdar N. Reduction in nosocomial infection with improved hand hygiene in intensive care units of a tertiary care hospital in Argentina. Am J Infect Control 2005;33:392-7.
31. van der Kooi T, Sax H, Pittet D, et al. Prevention of hospital infections by intervention and training (PROHIBIT): results of a pan-European cluster-randomized multicentre study to reduce central venous catheter-related bloodstream infections. Intensive Care Med 2018;44:48-60.
32. Capretti MG, Sandri F, Tridapalli E, Galletti S, Petracci E, Faldella G. Impact of a standardized hand hygiene program on the incidence of nosocomial infection in very low birth weight infants. Am J Infect Control 2008;36:430-5.
33. Kampf G, Löffler H, Gastmeier P. Hand hygiene for the prevention of nosocomial infections. Dtsch Arztebl Int 2009;106:649-55.
34. Hu KK, Lipsky BA, Veenstra DL, Saint S. Using maximal sterile barriers to prevent central venous catheter-related infection: a systematic evidence-based review. Am J Infect Control 2004;32:142-6.
35. Masuyama T, Yasuda H, Sanui M, Lefor AK. Effect of skin antiseptic solutions on the incidence of catheter-related bloodstream infection: a systematic review and network meta-analysis. J Hosp Infect 2021;110:156-64.
36. Yasuda H, Sanui M, Abe T, et al. Comparison of the efficacy of three topical antiseptic solutions for the prevention of catheter colonization: a multicenter randomized controlled study. Crit Care 2017;21:320.
37. Lai NM, Lai NA, O'Riordan E, Chaiyakunapruk N, Taylor JE, Tan K. Skin antisepsis for reducing central venous catheter-related infections. Cochrane Database Syst Rev 2016;7:CD010140.
38. Chaiyakunapruk N, Veenstra DL, Lipsky BA, Saint S. Chlorhexidine compared with povidone-iodine solution for vascular catheter-site care: a meta-analysis. Ann Intern Med 2002;136:792-801.
39. 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.
40. 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;286:700-7.
41. Arvaniti K, Lathyris D, Blot S, Apostolidou-Kiouti F, Koulenti D, Haidich AB. Cumulative evidence of randomized controlled and observational studies on catheter-related infection risk of central venous catheter insertion site in ICU patients: a pairwise and network meta-analysis. Crit Care Med 2017;45(4):e437-e448.
42. Adwaney A, Lim C, Blakey S, Duncan N, Ashby DR. Central venous stenosis, access outcome and survival in patients undergoing maintenance hemodialysis. Clin J Am Soc Nephrol 2019;14:378-84.
43. Timsit J-F, 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;186:1272-8.
44. Timsit J-F, 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;301:1231-41.
45. Puig-Asensio M, Marra AR, Childs CA, Kukla ME, Perencevich EN, Schweizer ML. Effectiveness of chlorhexidine dressings to prevent catheter-related bloodstream infections: does one size fit all? A systematic literature review and meta-analysis. Infect Control Hosp Epidemiol 2020;41:1388-95.
46. Safdar N, O'Horo JC, Ghufran A, et al. Chlorhexidine-impregnated dressing for prevention of catheter-related bloodstream infection: a meta-analysis. Crit Care Med 2014;42:1703-13.
47. Righetti M, Palmieri N, Bracchi O, et al. Tegaderm CHG dressing significantly improves catheter-related infection rate in hemodialysis patients. J Vasc Access 2016;17:417-22.
48. Apata IW, Hanfelt J, Bailey JL, Niyyar VD. Chlorhexidine-impregnated transparent dressings decrease catheter-related infections in hemodialysis patients: a quality improvement project. J Vasc Access 2017;18:103-8.
49. Climo MW, Yokoe DS, Warren DK, et al. Effect of daily chlorhexidine bathing on hospital-acquired infection. N Engl J Med 2013;368:533-42.
50. Afonso E, Blot K, Blot S. Prevention of hospital-acquired bloodstream infections through chlorhexidine gluconate-impregnated washcloth bathing in intensive care units: a systematic review and meta-analysis of randomised crossover trials. Euro Surveill 2016;21:30400.
51. Milstone AM, Elward A, Song X, et al. Daily chlorhexidine bathing to reduce bacteraemia in critically ill children: a multicentre, cluster-randomised, crossover trial. Lancet 2013;381:1099-106.
52. Huang SS, Septimus E, Kleinman K, et al. Chlorhexidine versus routine bathing to prevent multidrug-resistant organisms and all-cause bloodstream infections in general medical and surgical units (ABATE Infection trial): a cluster-randomised trial. Lancet 2019;393:1205-15.
53. Tien K-L, Sheng W-H, Shieh S-C, et al. Chlorhexidine bathing to prevent central line-associated bloodstream infections in

hematology units: a prospective, controlled cohort study. Clin Infect Dis 2020;71:556-63.
54. Zerr DM, Milstone AM, Dvorak CC, et al. Chlorhexidine gluconate bathing in children with cancer or those undergoing hematopoietic stem cell transplantation: a double-blinded randomized controlled trial from the Children's Oncology Group. Cancer 2021;127:56-66.
55. Raad I, Darouiche R, Dupuis J, et al. Central venous catheters coated with minocycline and rifampin for the prevention of catheter-related colonization and bloodstream infections: a randomized, double-blind trial. Ann Intern Med 1997;127:267-74.
56. Rupp ME, Lisco SJ, Lipsett PA, et al. Effect of a second-generation venous catheter impregnated with chlorhexidine and silver sulfadiazine on central catheter-related infections: a randomized, controlled trial. Ann Intern Med 2005;143:570-80.
57. Chong HY, Lai NM, Apisarnthanarak A, Chaiyakunapruk N. Comparative efficacy of antimicrobial central venous catheters in reducing catheter-related bloodstream infections in adults: abridged Cochrane systematic review and network meta-analysis. Clin Infect Dis 2017;64:Suppl 2:S131-S140.
58. Gilbert RE, Mok Q, Dwan K, et al. Impregnated central venous catheters for prevention of bloodstream infection in children (the CATCH trial): a randomised controlled trial. Lancet 2016;387:1732-42.
59. Voor In 't Holt AF, Helder OK, Vos MC, et al. Antiseptic barrier cap effective in reducing central line-associated bloodstream infections: a systematic review and meta-analysis. Int J Nurs Stud 2017;69:34-40.
60. Ullman AJ, Paterson RS, Schults JA, et al. Do antimicrobial and antithrombogenic peripherally inserted central catheter (PICC) materials prevent catheter complications? An analysis of 42,562 hospitalized medical patients. Infect Control Hosp Epidemiol 2022;43:427-34.
61. Free online toolkit supports CLABSI prevention. Jt Comm Perspect 2014;34:1, 3.
62. Flynn JM, Larsen EN, Keogh S, Ullman AJ, Rickard CM. Methods for microbial needleless connector decontamination: a systematic review and meta-analysis. Am J Infect Control 2019;47:956-62.
63. Brunelli SM, Van Wyck DB, Njord L, Ziebol RJ, Lynch LE, Killion DP. Cluster-randomized trial of devices to prevent catheter-related bloodstream infection. J Am Soc Nephrol 2018;29:1336-43.
64. Loftus RW, Brindeiro BS, Kispert DP, et al. Reduction in intraoperative bacterial contamination of peripheral intravenous tubing through the use of a passive catheter care system. Anesth Analg 2012;115:1315-23.
65. Wright M-O, Tropp J, Schora DM, et al. Continuous passive disinfection of catheter hubs prevents contamination and bloodstream infection. Am J Infect Control 2013;41:33-8.
66. Sweet MA, Cumpston A, Briggs F, Craig M, Hamadani M. 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;40:931-4.
67. Hymes JL, Mooney A, Van Zandt C, Lynch L, Ziebol R, Killion D. Dialysis catheter-related bloodstream infections: a cluster-randomized trial of the ClearGuard HD Antimicrobial Barrier Cap. Am J Kidney Dis 2017;69:220-7.
68. Oto J, Imanaka H, Konno M, Nakataki E, Nishimura M. A prospective clinical trial on prevention of catheter contamination using the hub protection cap for needleless injection device. Am J Infect Control 2011;39:309-13.
69. Calderwood MS, Kawai AT, Jin R, Lee GM. Centers for Medicare and Medicaid Services hospital-acquired conditions policy for central line-associated bloodstream infection (CLABSI) and catheter-associated urinary tract infection (CAUTI) shows minimal impact on hospital reimbursement. Infect Control Hosp Epidemiol 2018;39:897-901.
70. Lee GM, Kleinman K, Soumerai SB, et al. Effect of nonpayment for preventable infections in U.S. hospitals. N Engl J Med 2012;367:1428-37.
71. Waters TM, Daniels MJ, Bazzoli GJ, et al. Effect of Medicare's nonpayment for hospital-acquired conditions: lessons for future policy. JAMA Intern Med 2015;175:347-54.
72. Mayer J, Greene T, Howell J, et al. Agreement in classifying bloodstream infections among multiple reviewers conducting surveillance. Clin Infect Dis 2012;55:364-70.
73. Tomlinson D, Mermel LA, Ethier M-C, Matlow A, Gillmeister B, Sung L. Defining bloodstream infections related to central venous catheters in patients with cancer: a systematic review. Clin Infect Dis 2011;53:697-710.
74. Gaur AH, Miller MR, Gao C, et al. Evaluating application of the National Healthcare Safety Network central line-associated bloodstream infection surveillance definition: a survey of pediatric intensive care and hematology/oncology units. Infect Control Hosp Epidemiol 2013;34:663-70.
75. de Grooth HJ, Timsit J-F, Mermel L, et al. Validity of surrogate endpoints assessing central venous catheter-related infection: evidence from individual- and study-level analyses. Clin Microbiol Infect 2020;26:563-71.
76. Niedner MF, 2008 National Association of Children's Hospitals and Related Institutions Pediatric Intensive Care Unit Patient Care FOCUS Group. The harder you look, the more you find: catheter-associated bloodstream infection surveillance variability. Am J Infect Control 2010;38:585-95.
77. Kato Y, Hagihara M, Kurumiya A, et al. Impact of mucosal barrier injury laboratory-confirmed bloodstream infection (MBI-LCBI) on central line-associated bloodstream infections (CLABSIs) in department of hematology at single university hospital in Japan. J Infect Chemother 2018;24:31-5.
78. Metzger KE, Rucker Y, Callaghan M, et al. The burden of mucosal barrier injury laboratory-confirmed bloodstream infection among hematology, oncology, and stem cell transplant patients. Infect Control Hosp Epidemiol 2015;36:119-24.
79. Torres D, González ML, Loera A, et al. The Centers for Disease Control and Prevention definition of mucosal barrier injury-associated bloodstream infection improves accurate detection of preventable bacteremia rates at a pediatric cancer center in a low- to middle-income country. Am J Infect Control 2016;44:432-7.
80. Birkmeyer JD, Barnato A, Birkmeyer N, Bessler R, Skinner J. The impact of the COVID-19 pandemic on hospital admissions in the United States. Health Aff (Millwood) 2020;39:2010-7.
81. LeRose J, Sandhu A, Polistico J, et al. The impact of coronavirus disease 2019 (COVID-19) response on central-line-associated bloodstream infections and blood culture contamination rates at a tertiary-care center in the greater Detroit area. Infect Control Hosp Epidemiol 2021;42:997-1000.
82. Pérez-Granda MJ, Carrillo CS, Rabadán PM, et al. Increase in the frequency of catheter-related bloodstream infections during the COVID-19 pandemic: a plea for control. J Hosp Infect 2022;119:149-54.
83. McMullen KM, Smith BA, Rebmann T. Impact of SARS-CoV-2 on hospital acquired infection rates in the United States: predictions and early results. Am J Infect Control 2020;48:1409-11.
84. O'Horo JC, Maki DG, Krupp AE, Safdar N. Arterial catheters as a source of bloodstream infection: a systematic review and meta-analysis. Crit Care Med 2014;42:1334-9.
85. Mermel LA. Short-term peripheral venous catheter-related bloodstream infections: a systematic review. Clin Infect Dis 2017;65:1757-62.