INTERNATIONAL SOCIETY FOR INFECTIOUS DISEASES

GUIDE TO INFECTION CONTROL IN THE HEALTHCARE SETTING

Recommendations for The Prevention of Central Line-Associated Bloodstream Infections

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Topic Outline

DEFINITION

This document intends to review the available evidence and provide a more international spectrum, including specific recommendations to address situations that are particularly concerning in low- and middle-income countries (LMIC). It highlights practical recommendations in a concise format designed to assist acute-care hospitals in implementing and prioritizing their central line-associated bloodstream infection (CLABSI) prevention efforts in LMICs as well as in high-income countries. We acknowledge recommendations from several previous guidelines, such as those of the Infusion Nurses Society, 2021 Infusion Therapy Standards of Practice Update[1], and SHEA/IDSA/APIC, Practice Recommendation Strategies to prevent CLABSIs in acute-care hospitals: 2022 Update[2]. This expert guidance document, sponsored by the International Society of Infectious Diseases, updates the previous position paper published in 2019[3].

KEY ISSUES

- The CLABSI rates reported by the World Health Organization, through a systematic review and meta-analysis of published data, identified that in high-income countries, the CLABSI rate was 3.5 CLABSI per 1,000 CL-days, while in LMICs, it was 12.2[4].
- CLABSI rates in the USA, as reported by the CDC National Healthcare Safety Network (NHSN), show a median CLABSI rate of 0.8/1,000 central line (CL)-days in medical-surgical intensive care units (ICUs)[5].
- Over the last two decades, the International Nosocomial Infection Control Consortium (INICC) has been conducting prospective active surveillance of CLABSI rates, obtained primary data, and consistently observed higher CLABSI rates in LMICs compared to high-income countries. However, there were positive changes. The INICC report from 2002 to 2005 indicated a CLABSI rate of 12.5/1,000 CL-days[6], gradually reducing to 4.5 in the report covering data from 2015 to 2020[7].
- Costs associated with CLABSI vary globally, with reported costs in the USA, of $36,000 in 2009[8]. Italy reported $9,034 in 2010[9] and China, $3,528, in 2018[10].
- Associated length of stay (LOS): Pooling 630 ICUs from 2015 to 2020 of 45 LMICs, from Africa, Asia, Eastern Europe, Latin America, and the Middle East, with data from 204,770 patients, 1,480,620 patient-days, 936,976 CL-days, and 4,270 CLABSIs, LOS was as follows: 6.57 days for patients without healthcare-associated infections (HAIs), 23.17 days for those with CLABSI. Patients with two simultaneous HAIs experienced LOS ranging from 29.13 to 32.01 days, while those with all three types of HAIs (CLABSI + ventilator-associated pneumonia [VAP] + catheter-associated urinary tract infection [CAUTI]) had a LOS of 33.53 days[7].
- Associated mortality. CLABSIs have a significant impact on healthcare, leading to increased mortality rates,[7] with CLABSIs associated with a 12% to 25% increase in mortality.[11] Pooling 630 ICUs from 2015 to 2020 of 45 LMICs, the mortality rates were as follows: 14.06% for patients without HAI, and 39.81% for those with CLABSI. Patients with two simultaneous HAIs experienced mortality rates ranging from 38.79% to 43.32%, while those with all three types of HAIs (CLABSI + VAP + CAUTI) had a mortality rate of 46.56%[7].
- Risk factors for mortality: Studies have documented that CLABSI is an independent significant risk factor for mortality. In a multicenter, multinational, multicontinental study involving 786 ICUs across 312 hospitals in 147 cities spanning 37 countries between 1998 and 2022, a total of 300,827 patients were followed for 2,167,397 patient-days, with 21,371 HAIs. Multiple logistic regression identified the following mortality risk factors: CLABSIs ($p<0.0001$), LOS with a risk increase of 1% per day ($p<0.0001$), CL-days with a risk increase of 2% per day ($p<0.0001$), VAP ($p<0.0001$), CAUTI ($p<0.0001$), medical hospitalization ($p<0.0001$), female sex ($p<0.0001$), age ($p<0.0001$), and mechanical ventilator (MV)-utilization ratio ($p<0.0001$)[12].

- Hospital-onset bacteremia and fungemia (HOB):
    - CLABSIs require intensive surveillance and review. All-cause HOB may be a simpler reporting metric, correlates with CLABSI, and is viewed positively by HAI experts. *HOB is defined as the growth of a recognized bacterial or fungal pathogen from a blood culture specimen collected on or after the third calendar day of admission*[13].
    - A retrospective observational study was conducted on patients in 41 acute-care hospitals. CLABSI cases were defined according to the criteria reported to the NHSN. The cross-sectional analysis revealed that among 1,977 total HOB cases, 403 (20.38%) were classified as NHSN-reportable CLABSIs, while 1,574 (79.61%) were categorized as non-CLABSI HOB[14].
    - Efforts to reinstate well-established, evidence-based infection prevention practices, particularly for CLABSI, have intensified. Enhancing these efforts will also help prepare hospitals for upcoming broader surveillance and intervention activities aimed at reducing HOB associated with all types of vascular access devices[15].

KNOWN FACTS

Risk factors for CLABSI

- Individuals susceptible to acquiring a CLABSI in acute-care facilities are those with a CL in place. The likelihood of CLABSI is elevated among ICU patients, attributed to the frequent insertion of multiple catheters[16], and the utilization of particular catheter types, which carry significant risks (e.g., pulmonary artery catheters with catheter introducers). Additionally, emergency circumstances often necessitate catheter placement, leading to repeated daily access and prolonged usage[17]. Efforts in infection prevention and control should encompass additional vulnerable populations, including individuals undergoing hemodialysis through catheters[18], post-surgical patients[19], and cancer patients[20],
- Factors that have been identified as independent risks for CLASBI in high-income countries include: extended LOS before catheterization, prolonged catheterization duration, high microbial colonization at the insertion site, substantial microbial colonization of the catheter hub, multi-lumen catheters, simultaneous use of multiple catheters, neutropenia, Body Mass Index exceeding 40, premature birth, the reduced nurse-to-patient ratio in the ICU, patient cared for by a float nurse, parenteral nutrition, inadequate catheter care, blood product transfusion (in children), femoral site of insertion, and presence of internal jugular site and simultaneous tracheostomy[2].
- Despite the predominant emphasis on the ICU setting in the past two decades, it is noteworthy that the majority of CLABSIs occur in hospital units beyond the ICU or among outpatient cases[21]. Apart from CLs, there is also an elevated risk of infection associated with short-term peripheral catheters, as demonstrated in 727 ICUs of 42 LMICs[22]. At risk are also peripherally inserted central venous catheters (PICCs), midline catheters, and peripheral arterial catheters[17].
- From 1998 to 2022, a multinational multicenter prospective cohort study, encompassing 728 ICUs within 286 hospitals situated in 147 cities across 41 African, Asian, Eastern European, Latin American, and Middle Eastern countries, utilizing an online standardized surveillance system and unified forms, identified factors independently associated with CLABSI, including a 3% daily risk increase in CLABSI with prolonged LOS (p<0.0001), a 4% risk increase per CL-day (p<0.0001), surgical hospitalization (p<0.0001), tracheostomy use (p<0.0001), hospitalization at a publicly owned facility (p<0.0001) or at a teaching hospital (p<0.0001), and hospitalization in a middle-income country (p<0.0001); with the highest CLABSI risk observed in adult oncology (p<0.0001), followed by pediatric oncology (p<0.0001), and PICU (p<0.0001), while the highest CLABSI risk was associated

with internal-jugular (p<0.0001), followed by femoral (p<0.0001), and the lowest CLABSI risk was found with PICCs (p=0.04)[23].

SUGGESTED PRACTICE

Necessary prerequisites

Establishments and implementation of CLABSI prevention interventions should possess the following components:

- Assets for delivering suitable education and training[2].
- A sufficiently staffed infection prevention program is responsible for identifying patients who meet the surveillance definition for CLABSI[2].
- An Infection Prevention program with information technology support is crucial for gathering and computing CL-days as a denominator in CLABSI rate calculations[2].
- Patient days are essential for determining CL device utilization. It is advisable to validate CL-days obtained from information systems by comparing them to a manual method, with an acceptable margin of error not exceeding ±5%[24].
- Effective laboratory support is crucial for the timely processing of specimens and reporting results, adhering to the instructions provided by the supervisor of the surveillance program[2].

Implementation of CLABSI prevention strategies

- **Four Es "Engage, Educate, Execute, and Evaluate".** Preventing CLABSI relies on integrating best practices, and one example involves the Four Es—engage, educate, execute, and evaluate[25].

  a. This approach emphasizes the incorporation of a culture supporting implementation, addressing both technical and socio-adaptive components of CLABSI prevention, including formal health care professionals (HCP) training on indications, placement, and device maintenance, along with regular competency assessments[26].

- **Multidimensional approach.** Numerous national, multinational, and multicontinental studies, employing a multidimensional approach, have been conducted, achieving a significant reduction in rates of CLABSI and mortality. All of them include six components: (a) bundle, (b) education, (c) surveillance of CLABSI, (d) monitoring compliance with recommendations to prevent CLABSI, (e) internal reports of CLABSI rates, and (f) performance feedback[27-39].

1. **Bundles:**

- Care "bundles" in infection prevention and safety are simple sets of evidence-based practices that, when implemented collectively, improve the reliability of their delivery and improve patient outcomes.[40] In 2014, Blot et al. conducted a systematic review and meta-analysis regarding the prevention of CLABSIs through quality improvement interventions. Forty-one before-after studies were identified, revealing a decrease in infection rates (p<0.001). This effect was more pronounced for trials implementing a bundle or checklist approach (p=0.03)[41].
- Berenholtz, S. M., et al. at The Johns Hopkins Hospital conducted a study from 1998 through 2002. The aim was to determine whether a multifaceted systems intervention could eliminate CLABSIs. The bundle included the implementation of five interventions: educating the staff; creating a catheter insertion cart; asking providers daily whether catheters could be removed; implementing a checklist to ensure adherence to evidence-based guidelines for preventing CLABSIs; and empowering nurses to stop the catheter insertion procedure if a violation of the guidelines was observed. Before the intervention, it was found that physicians followed infection control guidelines during 62% of the

procedures. The CLABSI rate in the study ICU decreased from 11.3/1,000 CL-days to 0/1,000 CL-days[42].

- Pronovost, P., et al., published a study in 2006 on a collaborative cohort study in 103 ICUs in Michigan. A bundle with 5 components was implemented (hand hygiene, maximal barriers, skin antisepsis with chlorhexidine, avoiding the femoral vein, and removing the catheter as soon as possible). The median rate of CLABSIs per 1000 CL-days decreased from 2.7 CLABSI/1,000 CL-days at baseline to 0 at 3 months, and the mean rate per 1000 CL-days decreased from 7.7 at baseline to 1.4 at 16 to 18 months of follow-up ($p<0.002$)[43].
- The INICC utilizes a bundle as part of its approach to reduce CLABSI rates and was effective in Africa, Asia, Latin America, Eastern Europe, and the Middle East, resulting in a CLABSI rate reduction from 15.34/1,000 CL-days to 2.23 over a follow-up period of 29 months[38].

2. **Education:**

HCPs, patients, and caregivers participating in the care of a CL should receive training and demonstrate competence, commensurate with their roles, in understanding the suitable indications for insertion, recommendations to prevent CLABSI, and conducting daily assessments to determine the ongoing necessity of the device[44].

3. **Surveillance of CLABSI.**

- **CLABSI.** Employ uniform surveillance methods and definitions to facilitate the comparison of data with benchmark standards as published by the CDC/NHSN[45].
    - Calculate the CLABSI rate using CDC/NHSN definitions by dividing the number of CLABSIs in each unit by the total number of CL-days, then multiply the result by 1,000 to express the measure as the number of CLABSIs/1,000 CL-days[45].
    - Risk adjustment: Stratify CLABSI rates based on the type of patient-care unit and provide comparisons using both historical data, CDC/NHSN data[5], and INICC data[7].
    - Device utilization ratio (DUR): DUR can be monitored longitudinally to identify any variations, allowing for comparisons at both hospital and unit levels, and serving as a surrogate for assessing patient exposure risk[46]. The DUR, a CDC/NHSN[5], and INICC measure[7], considers facility- and location-level factors influencing device use, calculated as the observed device days divided by observed patient days.
- **Surveillance of other types of catheters**[47]. Most surveillance systems typically exclude peripheral arterial catheters, short-term peripheral venous catheters, and midline catheters, despite their association with infection risk. Future surveillance systems should encompass these catheter types and may contemplate extending their surveillance programs to cover all catheter types to accurately assess the scope of the issue. Several studies from LMICs demonstrated that short-term peripheral venous catheter-associated bloodstream infections are a significant challenge [22].

4. **Internal reporting of CLABSI rates.**

- These measures are crafted to enhance internal hospital quality improvement initiatives, and it is important to convey these measures to senior hospital leadership, nursing leadership, and clinicians engaged in the care of patients at risk for CLABSI[48].
- When providing internal reporting as a benchmark, compare the CLABSI rates of the given hospital against data from the CDC/NHSN[5], and the INICC[7].

5. **Monitoring Compliance with Recommendations to Prevent CLABSI.**

- Assess compliance with CL insertion and maintenance guidelines by employing a documented insertion paper or online checklist across all hospital settings, assigning knowledgeable HCP to this task[38].

- This checklist could be a paper form or an online form. Documenting compliance using the checklist ensures adherence to proper procedural steps, identifies and addresses any gaps, with the Institute for Health Improvement (IHI) offering a CL checklist as an example[49].
- Document CL insertion procedures, encompassing all relevant measures.
- Calculate compliance by dividing the compliance of each recommendation by the total number of CL insertions, then multiply by 100 for a percentage expression. As one example, evaluate compliance with the documentation of daily assessments for the necessity of continuing CL access by measuring the percentage of patients with a CL where daily assessment documentation is present.

6. **Performance feedback.**

- For the performance feedback, IPPs present charts, showcasing data related to attending HCPs' monthly degree of compliance with infection prevention practices[38].
- The infection control tool plays a crucial role, enabling attending HCPs to identify areas for improvement in cases of low degree of compliance with infection prevention practices. Leveraging the "observer effects" on HCPs' behavior, this method's strength lies in influencing their practices to enhance efficiency[50].
- This approach aimed to shape behaviors for more effective implementation[51].

Main approaches

Before insertion

- **Mandated education and competency assessments for HCPs engaged in the insertion, care, and maintenance of CL with a focus on CLABSI prevention**. (Quality of Evidence: MODERATE)[52].
  - Incorporate information on indications for catheter use, proper insertion and maintenance practices, the risk of CLABSI, and general infection prevention strategies into the education and competency assessments for HCPs involved in CL procedures[2].
  - Guarantee that all HCPs engaged in catheter insertion and maintenance undergo an educational program covering crucial practices to prevent CLABSI before undertaking these responsibilities[53].
  - Conduct periodic assessments of HCP's knowledge and adherence to preventive measures[2].
  - Mandate that all HCPs involved in CL insertion undergo a credentialing process, as determined by the healthcare institution, to verify their competence. This process should ensure their ability to independently insert a CL and maintain an aseptic technique throughout the procedure and subsequent access and maintenance of the CL[2].
  - Provide additional education when an institution modifies components of the infusion system, necessitating a corresponding change in practice. For instance, if a shift to a new needleless connector occurs, re-education should be conducted to align with the updated nursing practices[2].
  - If accessible, incorporate simulation training for accurate catheter insertion and maintenance procedures[54].

- **Administer a daily chlorhexidine preparation bath to ICU patients aged over two months**. (Quality of Evidence: HIGH)[55]
  - In long-term acute-care hospitals, contemplating daily chlorhexidine bathing is an option to be considered for preventive measures[56].
  - The effectiveness of chlorhexidine bathing in non-ICU patients is still uncertain[57]. In a cluster-randomized study, a notable decrease in device-associated bacteremia was observed with chlorhexidine bathing in this patient population. However, it is important to note that some of these patients also underwent methicillin-resistant Staphylococcus aureus (MRSA) decolonization, complicating the ability to definitively attribute the observed effects solely to chlorhexidine

bathing[57]. Multiple studies have indicated potential benefits for adult hematology-oncology patients; nevertheless, a comparable reduction was not observed in pediatric patients with similar conditions[58]. Thus, it is crucial to carefully weigh the potential benefits and risks, including concerns about resistance and cost implications.

- The safety and effectiveness of routinely employing chlorhexidine bathing in infants under two months of age after birth are not established[59]. While life-threatening skin injuries resulting from chlorhexidine have been reported in very young or extremely preterm infants, such incidents typically occur in infants with a birth weight below 1,000 grams who are less than 7 days postnatal age. Such occurrences appear to be rare in older infants[60].
- The extensive use of chlorhexidine may lead to a decrease in its effectiveness as an antiseptic, although the clinical significance of this observation is not clearly defined[61].

At insertion

- **In both ICU and non-ICU settings, it is recommended for facilities to implement a process, such as a *checklist,* to ensure strict adherence to infection prevention practices during the insertion of CL.** (Quality of Evidence: MODERATE)[62].
  - Guarantee and document the adherence to aseptic technique[2].
  - Utilizing checklists to ensure optimal insertion practices is recommended. In such cases, documentation should be completed by an individual other than the inserter[2].
  - Observation of CL insertion should be conducted by a nurse, physician, or another HCP who has undergone suitable education (as mentioned above) to ensure the maintenance of aseptic technique[2].
  - HCPs should be authorized to halt the procedure if any lapses in aseptic technique are identified[2].
- **Use an *all-inclusive catheter cart or kit*** (Quality of Evidence: MODERATE)[42].
  - Ensure that all units where CLs are inserted have readily accessible catheter carts or kits containing all essential components for aseptic catheter insertion[2].
- **Perform *hand hygiene* before catheter insertion or manipulation** (Quality of Evidence: MODERATE)[63].
  - Utilize either an alcohol-based waterless product or soap and water[2].
  - Wearing gloves does not eliminate the need for hand hygiene[2].
- **Adopt *maximum sterile barrier* precautions during CL insertion**. (Quality of Evidence: MODERATE)[64]
  - Employ maximum sterile barrier precautions by ensuring that all HCP involved in the catheter insertion procedure wear a mask, cap, sterile gown, and sterile gloves. Additionally, cover the patient with a large ("full-body") sterile drape during catheter insertion, and adhere to these measures as well as when exchanging a catheter over a guidewire[64].
  - Despite a prospective, randomized study in surgical patients showing no additional benefit for maximum sterile barrier precautions, the majority of available evidence suggests a risk reduction with this intervention[65].
- **Utilize an alcoholic *chlorhexidine antiseptic for skin* preparation**. (Quality of Evidence: HIGH)[66]
  - Before catheter insertion, apply an alcoholic chlorhexidine solution containing a minimum of 2% chlorhexidine to the insertion site, allowing the antiseptic solution to dry before making the skin puncture. Consider the use of alcoholic chlorhexidine for skin antisepsis to prevent CLABSI in Neonatal Intensive Care Unit (NICU) patients based on a risk-benefit assessment, ensuring that the benefits outweigh potential risks[2].
- **In the ICU setting, *avoid using the femoral site* to minimize infectious complications when placing the catheter**. (Quality of Evidence: HIGH)[67]

- According to several studies, the femoral site of insertion increases the risk of CLABSI[68].
  - In an ICU setting, according to three recent large, prospective multicenter, multinational, and multicontinental research studies that utilized multiple logistic regression analyses, PICCs demonstrate a lower risk of CLABSI compared to other types of central lines. This suggests that employing a PICC could be a strategy to decrease the risk of CLABSI[69]. Previous studies showed a similar risk of CLABSI compared PICC with other types of CLs[70].
  - In non-ICU settings, the risk of infection among different catheter insertion sites is not definitively established. Particularly in emergent situations, the priority may be to secure life-saving vascular access as quickly as possible, which could influence the choice of access site.[2]
  - For children and infants, femoral vein catheterization may be contemplated if upper body sites are contraindicated[71]. The use of tunneled femoral vein catheters, positioned with an exit site outside the diaper area on the mid-thigh, could be safer and offer an additional level of risk reduction[72].
  - The evaluation of risk and benefit for different insertion sites must be conducted on an individual basis, taking into account both infectious and noninfectious complications.[73] This consideration is particularly relevant for patients currently undergoing or anticipated to require hemodialysis, where the subclavian site is avoided due to the associated risk of stenosis.
  - Midline catheters are increasingly chosen as an alternative to CLs for short-term vascular access. Certain observational studies indicate a potential decrease in CLABSI risk with midline catheters compared to PICCs[74], and versus CLs[75], respectively. There is a need for randomized controlled trials to compare the risk of CLABSIs and other complications associated with these devices.
- **Incorporate *ultrasound* guidance for catheter insertion.** (Quality of Evidence: HIGH)[76]
  - Utilizing ultrasound guidance for internal jugular and femoral vein catheterization has been shown to reduce the risk of noninfectious complications associated with CL placement[76], However, it is crucial to acknowledge that the use of ultrasound may introduce challenges in maintaining aseptic technique.
  - The impact of ultrasound-guided subclavian vein insertion on the reduction of infectious complications is not established[77].

After insertion

- **Maintain an appropriate *nurse-to-patient ratio* and restrict the use of float nurses in ICUs.** (Quality of Evidence: HIGH)[2,78]
  - Observational studies indicate the importance of maintaining an adequate nurse-to-patient ratio in ICUs, especially when nurses are handling patients with CLs. Additionally, these studies suggest that the presence of float nurses in the ICU environment should be minimized[2].
- **Apply *dressings containing chlorhexidine* for CLs in patients over two months of age.** (Quality of Evidence: HIGH)[79]
  - The impact of using a chlorhexidine dressing on the reduction of infectious complications is unclear for long-term catheters, such as hemodialysis catheters, in well-healed access sites[80].
  - The use of chlorhexidine dressings for children under two months of age, especially in very preterm or low birth weight infants, is not clearly defined[81].
  - A matched-pair analysis published in 2023 evaluated the effectiveness of chlorhexidine gluconate (CHG)-coated gel pad dressings in preventing CLABSIs in patients with hematologic malignancies. A total of 2070 CLs were assessed, and there was no statistically significant difference in the incidence of CRBSI (2.0 vs. 3.2/1000 CL-days) between patients with and without CHG gel dressings. The use of CHG gel dressings did not result in a reduction in CRBSI rates among patients with hematologic malignancies[82].

- **For non-tunneled CLs in both adults and children, it is recommended to *replace transparent dressings and conduct site care using a chlorhexidine-based antiseptic at least every 7 days*. If the dressing becomes soiled, loose, or damp, immediate replacement is advised. Gauze dressings should be changed every 2 days or earlier if they become soiled, loose, or damp**. (Quality of Evidence: MODERATE)[83]
    - For NICU patients or those at a high risk of serious complications from catheter dislodgement, less frequent dressing changes, based on clinical indications, may be considered[84].
    - If there is considerable bleeding or drainage from the catheter exit site, choose gauze dressings instead of transparent dressings until the drainage resolves[2].

- **Before accessing the catheter, *disinfect the catheter hubs, needleless connectors, and injection ports*.** (Quality of Evidence: MODERATE)[85]
    - Before accessing catheter hubs, needleless connectors (NCs), or injection ports, thoroughly apply mechanical friction using an alcoholic chlorhexidine preparation or 70% alcohol. Alcoholic chlorhexidine is preferred as it may offer additional residual activity compared to alcohol for this purpose[86].
    - Ensure mechanical friction is applied for at least 5 seconds to effectively reduce contamination[87]. The applicability of this disinfection duration to NCs that were not assessed in these studies remains uncertain.
    - Regularly monitor compliance with hub-connector-port disinfection protocols, as approximately half of such catheter components may become colonized under standard practice conditions[88].
- ***Remove catheters that are not essential.*** (Quality of Evidence: MODERATE)[63]
    - Evaluate the necessity for ongoing intravascular access daily during multidisciplinary rounds. Remove catheters that are not essential for patient care. Reducing CL utilization contributes to a decrease in the risk of CLABSIs[63].
    - Conducting audits to assess whether CLs are consistently removed after their intended use can be beneficial[89]. Both simple and multifaceted interventions have proven effective in reducing the unnecessary use of CLs[90].
- **It is acceptable to *routinely replace administration sets not used for blood, blood products, or lipid formulations at intervals of up to 7 days*.** (Quality of Evidence: HIGH)[91]
    - The most effective schedule for replacing intermittently used administration sets is still undetermined.
- **Conduct *surveillance for CLABSI* in both ICU and non-ICU settings.** (Quality of Evidence: HIGH)[92]
    - Quantify the unit-specific incidence of CLABSI, such as CLABSI per 1,000 CL-days, and regularly communicate this data to the respective units, physician and nursing leadership, as well as hospital administrators overseeing the units[2].
    - Compare the occurrence of CLABSI with historical data specific to individual units and with national, CDC/NHSN[5], and INICC rates[7].
    - Conduct periodic audits of surveillance as needed to reduce variation in interobserver reliability[93].

Supplementary interventions

These additional measures are recommended for implementation in hospital areas or among populations experiencing unacceptably high CLABSI rates, even after applying essential CLABSI prevention strategies outlined earlier, or individuals who possess restricted venous entry and a background of recurring CLABSI.

- **Utilize CLs that are impregnated with antiseptic or antimicrobial agents.** (Quality of Evidence: HIGH in adult patients[94], and MODERATE in pediatric patients)[95]
    - The risk of CLABSI is diminished with certain currently available antiseptic-impregnated (e.g., chlorhexidine-silver sulfadiazine) catheters and antimicrobial-impregnated (e.g., minocycline-rifampin) catheters. Some evidence indicates that such interventions may not provide extra advantages in patient care units that have already achieved a low incidence of CLABSI[96].
    - Clinical evidence supporting the risk reduction linked to the routine use of silver-coated catheter connectors or other antimicrobial catheter connectors is currently limited.
    - Keep a vigilant watch on patients for adverse effects, including the possibility of anaphylaxis[97].
- **Implement antimicrobial lock therapy for long-term CLs.** (Quality of Evidence: HIGH)[98]
    - Filling the catheter lumen with a supratherapeutic concentration of an antibacterial or antiseptic solution and maintaining it until catheter hub re-access is known as an anti-infective lock. This method has shown potential in reducing the risk of CLABSI. Ongoing research is focusing on determining the optimal antimicrobial agent or combination, their concentration, and the duration of lock therapy. Due to concerns about potential resistance emergence in exposed organisms, consider employing antimicrobial locks as a preventive strategy for patients with long-term hemodialysis catheters who have a history of recurrent CLABSI[99]. This preventive measure can be considered for patients at an elevated risk of severe consequences from CLABSI, such as those with recently implanted intravascular devices like a prosthetic heart valve or aortic graft.
    - To reduce the risk of systemic toxicity, aspirate the antimicrobial lock solution after the designated dwell time instead of flushing it[100].
    - Before utilizing ethanol locks, it is essential to thoroughly assess the potential for adverse effects[101].
    - A meta-analysis published in 2023 investigated ethanol lock therapy (ELT) in pediatric patients with CLs to prevent CLABSI. The post-ELT treatment significantly reduced mean CLABSI rates compared to pre-treatment without ELT ($p<0.001$). However, the risks of thrombosis and catheter issues increased. ELT proves effective in preventing CLABSIs, but further research is needed to establish optimal protocols and assess adverse events[102].
- **Administer recombinant tissue plasminogen activator (rt-PA) once weekly following hemodialysis in patients using a CL for hemodialysis.** (Quality of Evidence: HIGH)[103]
- **Leverage infusion or vascular access teams to decrease rates of CLABSI.** (Quality of Evidence: LOW)[104,105]
    - Research indicates that the implementation of an infusion/vascular access team, tasked with the insertion and maintenance of peripheral intravenous catheters, effectively lowers the risk of BSIs[104].
    - Nevertheless, there is a scarcity of studies examining the influence of intravenous therapy teams on rates of CLABSI[105].
- **Apply antimicrobial ointments to the insertion sites of hemodialysis catheters.** (Quality of Evidence: HIGH)[106]
    - Use polysporin "triple" or povidone-iodine ointment for hemodialysis catheter insertion, provided it is compatible with the catheter material. Exercise caution regarding potential interactions between ointment ingredients and the chemical composition of certain catheters. Ensure the selected ointment is compatible with the catheter material before application to the insertion/exit site, considering that ointments containing glycol should not be used on insertion/exit sites of polyurethane catheters. Avoid applying Mupirocin ointment to the catheter insertion site due to the associated risks of fostering mupirocin resistance and potential harm to polyurethane catheters[2].

- **Employ an antiseptic-containing hub/connector cap/port protector to cover connectors.** (Quality of Evidence: MODERATE)[107]
    - The effectiveness of routinely disinfecting hub connectors and ports while utilizing antiseptic-containing hub/connector cap/port protectors is currently uncertain.

Not Advisable Interventions to Prevent CLABSI

- Avoid employing antimicrobial prophylaxis for short-term or tunneled catheter insertion or while catheters are in place. (Quality of Evidence: HIGH)[108].
- Avoid the routine replacement of CL or arterial catheters. (Quality of Evidence: HIGH)[109].

Interventions Pending Resolution

- **The utilization of silver-coated catheter connectors may be linked to decreased intraluminal contamination in ex vivo catheters and a potential reduction in CLABSI**[110]
    - There is limited clinical evidence available regarding the risk reduction associated with the routine use of silver-coated catheter connectors or the use of other antimicrobial catheter connectors.
- **The relationship between the use of standard, nonantimicrobial transparent dressings and the risk of CLABSI.**
    - An unresolved issue has arisen from a meta-analysis that identified a connection between CLABSI and the usage of transparent dressings[111].
- **The influence of employing chlorhexidine-based products on the development of bacterial resistance to chlorhexidine.**
    - Standardized testing for chlorhexidine susceptibility is lacking, and the clinical implications of reduced chlorhexidine susceptibility remain uncertain[112].
- **Suture-less securement**
    - The effectiveness of suture-less securement devices in reducing CLABSI is currently uncertain[113].
- **The impact of silver zeolite-impregnated umbilical catheters on preterm infants, especially in areas where approval for pediatric use has been authorized**[114]
    - A randomized study indicates that antimicrobial-impregnated umbilical catheters seem to be both safe and effective in NICU patients[114].
- **The requirement for mechanically disinfecting a catheter hub, needleless connector, and injection port before catheter access when utilizing antiseptic-containing caps**.
    - The efficacy of employing an antiseptic-containing cap in preventing CLABSI, compared to the traditional method of manual disinfection during application and removal, remains uncertain.
    - According to a meta-analysis published in 2022, a total of 391 CLABSIs in 273,993 CL-days occurred in the intervention group versus 620 CLABSIs in 284,912 days in the standard care group, resulting in a risk ratio of 0.65 (p<0.00001). While available evidence suggests that ABCs are effective, safe, easy to use, and cost-effective, however, due to the poor methodological quality of most available studies, more robust data should justify their use at this point[115].

SUGGESTED PRACTICE IN UNDER-RESOURCED SETTINGS

The use of outdated technology has been observed, prompting a recommendation to adopt new device designs:

- **It was found that the routine use of collapsible closed-system intravenous fluid containers is an effective strategy for preventing CLABSI.** (Quality of Evidence: MODERATE)[116]
    - Open-system semi-rigid or rigid IV fluid containers increase the risk of CLABSI compared with closed-system collapsible IV fluid containers, as demonstrated in prospective studies, and a metanalysis[116].

- **It was found that the routine use of needleless connectors is an effective strategy for preventing CLABSI.** (Quality of Evidence: MODERATE)[117,118]. Three-way stopcocks increase the risk of catheter infections compared with needless connectors (NCs), as demonstrated in randomized clinical trials,[118] a systematic review [119], and a meta-analysis[117]. Multiple devices are currently available, but the optimal design for preventing infections remains unresolved.
    - A study evaluated eight design factors of NC for their impact on bacterial transfer and biofilm formation, based on the following characteristics: the mechanism of access, access portal, flow path, fluid displacement, hydrodynamics, seal length, flow path surface area and volume, and neutral displacement. The NC designs associated with the least bacterial transfer and biofilm formation were: split septum, minimal seal length, internal cannula, low flow path surface area and volume, simple hydrodynamics, and neutral displacement[120].
    - A secondary analysis of a national US database of CLABSI and manufacturer customer database found that the use of the NC characterized by a split septum, minimal seal length, internal cannula, low flow path surface area and volume, simple hydrodynamics and minimal (neutral) or zero displacement is an effective risk reduction strategy for CLABSI prevention, reduced mortality, and substantial cost savings compared to other types of NCs[121].
    - It is crucial to note that studies published from 2006 to 2009, conducted at the inception of these devices' market launch, revealed an elevated rate of CLABSI, employing a time series before-after analysis methodology rather than randomized clinical trials; it is plausible that the observed rise in CLABSI rates was attributable to the improper utilization of these devices[122].

- **There has been evidence of the need to educate and train HCWs in LMICs.**
    - **Compliance with recommendations to prevent CLABSI in the Middle East:** In their 2018 study, Aloush et al. aimed to assess compliance with the CLABSI prevention guidelines. Using a prospective design, observations were conducted over three months in the intensive care units of 58 hospitals across three Middle Eastern countries. Results revealed considerable variability in compliance levels. Lower bed numbers and patient-nurse ratios were associated with higher compliance. Reducing patient-nurse ratios and the number of beds in ICUs could enhance compliance efforts[123].
    - **Compliance with recommendations to prevent CLABSI in Jordan:** In their 2022 study, Matlab et al. aimed to evaluate knowledge and compliance regarding the prevention of CLABSIs among registered nurses in Jordan. Using a cross-sectional correlational design, the study selected a sample of 114 registered nurses from three hospitals in Jordan. Significant differences in nurses' compliance with the CVC care bundle were noted across hospitals and nurse-to-patient ratios. Nurse-to-patient ratio was identified as the single significant predictor of nurse compliance with the CVC care bundle. It highlights the importance of programs aimed at enhancing nurses' knowledge about CLABSI prevention and their compliance with CVC care, taking into account factors such as age and workplace circumstances, particularly the nurse-to-patient ratio[124].

- **Bundle Approach:** According to published research studies implemented by INICC[27-39], a bundle with the following eleven components was effective in significantly reducing CLABSI rates in LMICs:

1. Strict adherence to hand hygiene before CL insertion or manipulation;
2. Implementation of maximum sterile barrier precautions during CL insertion;
3. Utilization of alcoholic chlorhexidine antiseptic for skin preparation;
4. A preference for avoiding the femoral site;
5. Reduction of CL-days by eliminating nonessential CLs;
6. Maintenance of proper insertion site dressing, changing it when it becomes loose, wet, dirty, or bloody;
7. Minimization of the length of stay by promptly discharging eligible patients;
8. Daily chlorhexidine preparation bathing for ICU patients aged over 2 months;
9. Prioritization of NC connectors over three-way stopcocks;
10. A preference for collapsible closed IV fluid systems over semi-rigid open systems;
11. A focus on single-use flushing over manual admixture.

- **Multidimensional Approach**: Numerous national, multinational, and multicontinental studies, employing a multidimensional approach, have been conducted in LMICs, achieving a significant reduction in rates of CLABSI and mortality. All of them include six components: (a) bundle, (b) education, (c) surveillance of CLABSI, (d) monitoring compliance with recommendations to prevent CLABSI, (e) internal reports of CLABSI rates, and (f) performance feedback. The following 13 studies were conducted applying this specific intervention:

1. Conducted in Argentina in 2003. Following the intervention, the CLABSI rate was significantly reduced (46.63 vs 11.10 CLABSI/1,000 CL-days [RR= 0.25; 95% CI= 0.17-0.36; *p*<0.0001])[27].
2. Conducted in Mexico in 2005. Following the intervention, the CLABSI rate was significantly reduced (46.3 vs 19.5 CLABSI/1,000 CL-day [RR= 0.42; 95% CI= 0.27-0.66; *p*=0.0001]). Additionally, crude unadjusted mortality rates significantly decreased from baseline (48.5% vs. 32.8% per 100 discharges [RR= 0.68; 95% CI= 0.50-0.31; *p*=0.01])[28].
3. Applying this strategy, a study was conducted in adult ICUs in 15 LMICs in 2010. Following the intervention, the CLABSI rate was significantly reduced (14.5 vs 7.4 CLABSIs per 1,000 central line days [RR, 0.46, 95% CI, 0.33-0.63; *p*<0.001]). The number of deaths in CLABSI patients decreased by 58%[29].
4. Conducted in pediatric intensive care units across five LMICs in 2012. Following the intervention, the CLABSI rate was significantly reduced (10.7 vs 5.2 CLABSI/1,000 CL-days ([RR 0.48, 95% CI 0.29-0.94, *p*=0.02])[30].
5. Conducted in 16 adult intensive care units (ICUs) across 11 hospitals in India in 2013. Following the intervention, the CLABSI rate was significantly reduced (6.4 vs 3.9 CLABSI/1,000 CL-days [incidence rate ratio 0.47, 95% CI 0.31-0.70; *p*=0.0001])[31].
6. Conducted in eight cities in Turkey in 2013. Following the intervention, the CLABSI rate was significantly reduced (22.7 vs 12.0 CLABSI/1,000 CL-days [incidence rate ratio [IRR] 0.613; 95% CI 0.43 - 0.87; p=.007]).[32]
7. Conducted in neonatal intensive care units (NICUs) across four LMICs in 2013. Following the intervention, the CLABSI rate was significantly reduced (21.4 vs 9.7 CLABSI/1,000 CL-days [rate ratio, 0.45 [95% CI, 0.33-0.63], *p*<0.001)[33].
8. Conducted in Colombia in 2016. Following the intervention, the CLABSI rate was significantly reduced (12.9 vs 3.5 CLABSI/1,000 CL-days [RR, 0.27; 95% CI, 0.14-0.52; *p*=0.002])[34].
9. Conducted in five cities in Saudi Arabia in 2017. Following the intervention, the CLABSI rate was significantly reduced (6.9 vs 3.1 CLABSI/1,000 CL-days [incidence-density rate, 0.44; 95% CI, 0.28-0.72; *p*=0.001])[35].
10. Conducted in 14 intensive care units (ICUs) across 11 hospitals in 5 cities in Argentina in 2018. Following the intervention, the CLABSI rate was significantly reduced (9.6 vs 4.1 CLABSI/1,000 CL-days [incidence density rate: 0.43; 95% CI, 0.34-0.6; *p*<0.001])[36].

11. Conducted in Bahrain in 2020. Following the intervention, the CLABSI rate was significantly reduced (10.4 vs 1.2 CLABSI/1,000 CL-days [incidence density rate, 0.11; 95% CI 0.1-0.3; *p*= 0.001])[37].
12. Conducted in 316 ICUs in 30 low- and middle-income countries in 2023. Throughout 283,087 patients, hospitalized during 1,837,750 patient days, 1,218,882 CL-days were utilized. Following the intervention, the CLABSI rate was significantly reduced (15.34 vs 2.23 CLABSI/1,000 CL-days in the 17 to 29 months (RR= 0.15; 95% CI= 0.13-0.17; *p*<0.001). The in-ICU all-cause mortality rate decreased from 16.17% to 13.68% (*p*=0.0013) at 17 to 29 months[38].
13. Conducted in 122 ICUs in 9 Asian countries in 2024. Throughout 124,946 patients, hospitalized during 717,270 patients days, 238,595CL-days were utilized. Following the intervention, the CLABSI rate was significantly reduced (16.64 vs 2.18 CLABSI/1,000 CL-days in the 17 to 29 months (RR= 0.13; 95% CI= 0.11-0.15; *p*<0.001). The in-ICU all-cause mortality rate decreased from 13.23% to 10.96% (p=.0001)[39].

SUMMARY

The empirical evidence delineated in this review incontrovertibly establishes that CLABSI rates in LMICs persist at a magnitude exceeding fivefold that observed in high-income countries. The review systematically presents scientific insights regarding the efficacy of diverse interventions across all settings, distinguishing between proven effective measures, those demonstrated to be ineffective, and the prescription of supplementary measures specifically advocated for adoption in LMICs.

REFERENCES

1. Gorski LA, Hadaway L, Hagle ME, et al. Infusion Therapy Standards of Practice, 8th Edition. *J Infus Nurs* 2021; **44**(1S Suppl 1): S1-S224.
2. 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: 1-17.
3. Lutwick L, Al-Maani AS, Mehtar S, et al. Managing and preventing vascular catheter infections: A position paper of the international society for infectious diseases. *Int J Infect Dis* 2019; **84**: 22-9.
4. Allegranzi B, Bagheri Nejad S, Combescure C, et al. Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis. *Lancet* 2011; **377**(9761): 228-41.
5. Dudeck MA, Edwards JR, Allen-Bridson K, et al. National Healthcare Safety Network report, data summary for 2013, Device-associated Module. *Am J Infect Control* 2015; **43**(3): 206-21.
6. Rosenthal VD, Maki DG, Salomao R, et al. Device-associated nosocomial infections in 55 intensive care units of 8 developing countries. *Ann Intern Med* 2006; **145**(8): 582-91.
7. Rosenthal VD, Yin R, Nercelles P, et al. International Nosocomial Infection Control Consortium (INICC) report of health care associated infections, data summary of 45 countries for 2015 to 2020, adult and pediatric units, device-associated module. *Am J Infect Control* 2024.
8. Stone PW. Economic burden of healthcare-associated infections: an American perspective. *Expert Rev Pharmacoecon Outcomes Res* 2009; **9**(5): 417-22.

9. Tarricone R, Torbica A, Franzetti F, Rosenthal VD. Hospital costs of central line-associated bloodstream infections and cost-effectiveness of closed vs. open infusion containers. The case of Intensive Care Units in Italy. *Cost Eff Resour Alloc* 2010; **8**: 8.
10. Cai Y, Zhu M, Sun W, Cao X, Wu H. Study on the cost attributable to central venous catheter-related bloodstream infection and its influencing factors in a tertiary hospital in China. *Health Qual Life Outcomes* 2018; **16**(1): 198.
11. Centers for Disease C, Prevention. Vital signs: central line-associated blood stream infections--United States, 2001, 2008, and 2009. *MMWR Morb Mortal Wkly Rep* 2011; **60**(8): 243-8.
12. Rosenthal VD, Yin R, Lu Y, et al. The impact of healthcare-associated infections on mortality in ICU: A prospective study in Asia, Africa, Eastern Europe, Latin America, and the Middle East. *Am J Infect Control* 2023; **51**(6): 675-82.
13. Stack MA, Dbeibo L, Fadel W, Kelley K, Sadowski J, Beeler C. Etiology and utility of hospital-onset bacteremia as a safety metric for targeted harm reduction. *Am J Infect Control* 2024; **52**(2): 195-9.
14. Yu KC, Jung M, Ai C. Characteristics, costs, and outcomes associated with central-line-associated bloodstream infection and hospital-onset bacteremia and fungemia in US hospitals. *Infect Control Hosp Epidemiol* 2023; **44**(12): 1920-6.
15. Garcia R, Septimus EJ, LeDonne J, et al. Prevention of Vascular Access Device-Associated Hospital Onset Bacteremia and Fungemia: A Review of Emerging Perspectives and Synthesis of Technical Aspects. *Clin Infect Dis* 2024.
16. Mermel LA. How Should Surveillance Systems Account for Concurrent Intravascular Catheters? *JAMA Netw Open* 2020; **3**(3): e200400.
17. 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.
18. Nguyen DB, Shugart A, Lines C, et al. National Healthcare Safety Network (NHSN) Dialysis Event Surveillance Report for 2014. *Clin J Am Soc Nephrol* 2017; **12**(7): 1139-46.
19. Loftus RW, Brown JR, Koff MD, et al. Multiple reservoirs contribute to intraoperative bacterial transmission. *Anesth Analg* 2012; **114**(6): 1236-48.
20. Zakhour R, Chaftari AM, Raad, II. Catheter-related infections in patients with haematological malignancies: novel preventive and therapeutic strategies. *Lancet Infect Dis* 2016; **16**(11): e241-e50.
21. Rhee Y, Heung M, Chen B, Chenoweth CE. Central line-associated bloodstream infections in non-ICU inpatient wards: a 2-year analysis. *Infect Control Hosp Epidemiol* 2015; **36**(4): 424-30.
22. Rosenthal VD, Bat-Erdene I, Gupta D, et al. Six-year multicenter study on short-term peripheral venous catheters-related bloodstream infection rates in 727 intensive care units of 268 hospitals in 141 cities of 42 countries of Africa, the Americas, Eastern Mediterranean, Europe, South East Asia, and Western Pacific Regions: International Nosocomial Infection Control Consortium (INICC) findings. *Infect Control Hosp Epidemiol* 2020; **41**(5): 553-63.
23. Rosenthal VD, Yin R, Myatra SN, et al. Multinational prospective study of incidence and risk factors for central-line-associated bloodstream infections in 728 intensive care units of 41 Asian, African, Eastern European, Latin American, and Middle Eastern countries over 24 years. *Infect Control Hosp Epidemiol* 2023: 1-11.

24. Tejedor SC, Garrett G, Jacob JT, et al. Electronic documentation of central venous catheter-days: validation is essential. *Infect Control Hosp Epidemiol* 2013; **34**(9): 900-7.
25. Owings A, Graves J, Johnson S, Gilliam C, Gipson M, Hakim H. Leadership line care rounds: Application of the engage, educate, execute, and evaluate improvement model for the prevention of central line-associated bloodstream infections in children with cancer. *Am J Infect Control* 2018; **46**(2): 229-31.
26. Chopra V, Flanders SA, Saint S, et al. The Michigan Appropriateness Guide for Intravenous Catheters (MAGIC): Results From a Multispecialty Panel Using the RAND/UCLA Appropriateness Method. *Ann Intern Med* 2015; **163**(6 Suppl): S1-40.
27. Rosenthal VD, Guzman S, Pezzotto SM, Crnich CJ. Effect of an infection control program using education and performance feedback on rates of intravascular device-associated bloodstream infections in intensive care units in Argentina. *Am J Infect Control* 2003; **31**(7): 405-9.
28. Higuera F, Rosenthal VD, Duarte P, Ruiz J, Franco G, Safdar N. The effect of process control on the incidence of central venous catheter-associated bloodstream infections and mortality in intensive care units in Mexico. *Crit Care Med* 2005; **33**(9): 2022-7.
29. Rosenthal VD, Maki DG, Rodrigues C, et al. Impact of International Nosocomial Infection Control Consortium (INICC) strategy on central line-associated bloodstream infection rates in the intensive care units of 15 developing countries. *Infect Control Hosp Epidemiol* 2010; **31**(12): 1264-72.
30. Rosenthal VD, Ramachandran B, Villamil-Gomez W, et al. Impact of a multidimensional infection control strategy on central line-associated bloodstream infection rates in pediatric intensive care units of five developing countries: findings of the International Nosocomial Infection Control Consortium (INICC). *Infection* 2012; **40**(4): 415-23.
31. Jaggi N, Rodrigues C, Rosenthal VD, et al. Impact of an international nosocomial infection control consortium multidimensional approach on central line-associated bloodstream infection rates in adult intensive care units in eight cities in India. *Int J Infect Dis* 2013; **17**(12): e1218-24.
32. Leblebicioglu H, Ozturk R, Rosenthal VD, et al. Impact of a multidimensional infection control approach on central line-associated bloodstream infections rates in adult intensive care units of 8 cities of Turkey: findings of the International Nosocomial Infection Control Consortium (INICC). *Ann Clin Microbiol Antimicrob* 2013; **12**: 10.
33. Rosenthal VD, Duenas L, Sobreyra-Oropeza M, et al. Findings of the International Nosocomial Infection Control Consortium (INICC), part III: effectiveness of a multidimensional infection control approach to reduce central line-associated bloodstream infections in the neonatal intensive care units of 4 developing countries. *Infect Control Hosp Epidemiol* 2013; **34**(3): 229-37.
34. Alvarez-Moreno CA, Valderrama-Beltran SL, Rosenthal VD, et al. Multicenter study in Colombia: Impact of a multidimensional International Nosocomial Infection Control Consortium (INICC) approach on central line-associated bloodstream infection rates. *Am J Infect Control* 2016; **44**(11): e235-e41.
35. Al-Abdely HM, Alshehri AD, Rosenthal VD, et al. Prospective multicentre study in intensive care units in five cities from the Kingdom of Saudi Arabia: Impact of the International Nosocomial Infection Control Consortium (INICC) multidimensional approach on rates of central line-associated bloodstream infection. *J Infect Prev* 2017; **18**(1): 25-34.

36. Rosenthal VD, Desse J, Maurizi DM, et al. Impact of the International Nosocomial Infection Control Consortium (INICC)'s Multidimensional Approach on Rates of Central Line-Associated Bloodstream Infection in 14 Intensive Care Units in 11 Hospitals of 5 Cities in Argentina. *Infect Control Hosp Epidemiol* 2018; **39**(4): 445-51.
37. Alkhawaja S, Saeed NK, Rosenthal VD, et al. Impact of International Nosocomial Infection Control Consortium's multidimensional approach on central line-associated bloodstream infection rates in Bahrain. *J Vasc Access* 2020; **21**(4): 481-9.
38. Rosenthal VD, Jin Z, Brown EC, et al. Decreasing central line-associated bloodstream infections rates in intensive care units in 30 low- and middle-income countries: An INICC approach. *Am J Infect Control* 2023.
39. Rosenthal VD, Yin R, Myatra SN, et al. Evaluating the outcome of a bundle with 11 components and the INICC multidimensional approach in decreasing rates of central line-associated bloodstream infections across nine Asian countries. *J Vasc Access* 2024: 11297298241242163.
40. Evidence-Based Care Bundles. Institute for Healthcare Improvement (IHI). http://www.ihi.org/Topics/Bundles/Pages/default.aspx (accessed November 23rd 2021.
41. Blot K, Bergs J, Vogelaers D, Blot S, Vandijck D. 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.
42. 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.
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. Safdar N, Abad C. Educational interventions for prevention of healthcare-associated infection: a systematic review. *Crit Care Med* 2008; **36**(3): 933-40.
45. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control* 2008; **36**(5): 309-32.
46. Fakih MG, Gould CV, Trautner BW, et al. Beyond Infection: Device Utilization Ratio as a Performance Measure for Urinary Catheter Harm. *Infect Control Hosp Epidemiol* 2016; **37**(3): 327-33.
47. Rosenthal VD, Gupta D, Rajhans P, et al. Six-year multicenter study on short-term peripheral venous catheters-related bloodstream infection rates in 204 intensive care units of 57 hospitals in 19 cities of India: International Nosocomial Infection Control Consortium (INICC) findings. *Am J Infect Control* 2020; **48**(9): 1001-8.
48. Sawyer M, Weeks K, Goeschel CA, et al. Using evidence, rigorous measurement, and collaboration to eliminate central catheter-associated bloodstream infections. *Crit Care Med* 2010; **38**(8 Suppl): S292-8.
49. Central-line insertion checklist: Virginia Mason Medical Center example. Institute for Healthcare Improvement website. http://www.ihi.org/resources/Pages/Tools/CentralLineInsertionChecklist.aspx. Accessed February 5, 2024.
50. Monahan T, Fisher JA. Benefits of "Observer Effects": Lessons from the Field. *Qual Res* 2010; **10**(3): 357-76.

51. Rosenthal VD. International Nosocomial Infection Control Consortium (INICC) resources: INICC multidimensional approach and INICC surveillance online system. *Am J Infect Control* 2016; **44**(6): e81-90.
52. 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.
53. Cherry MG, Brown JM, Neal T, Ben Shaw N. What features of educational interventions lead to competence in aseptic insertion and maintenance of CV catheters in acute care? BEME Guide No. 15. *Med Teach* 2010; **32**(3): 198-218.
54. Cartier V, Inan C, Zingg W, Delhumeau C, Walder B, Savoldelli GL. Simulation-based medical education training improves short and long-term competency in, and knowledge of central venous catheter insertion: A before and after intervention study. *Eur J Anaesthesiol* 2016; **33**(8): 568-74.
55. 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.
56. Munoz-Price LS, Hota B, Stemer A, Weinstein RA. Prevention of bloodstream infections by use of daily chlorhexidine baths for patients at a long-term acute care hospital. *Infect Control Hosp Epidemiol* 2009; **30**(11): 1031-5.
57. 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**(10177): 1205-15.
58. 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**(1): 56-66.
59. Milstone AM, Bamford P, Aucott SW, Tang N, White KR, Bearer CF. Chlorhexidine inhibits L1 cell adhesion molecule-mediated neurite outgrowth in vitro. *Pediatr Res* 2014; **75**(1-1): 8-13.
60. Chandonnet CJ, Toole C, Young V, et al. Safety of Biweekly Chlorhexidine Gluconate Bathing in Infants 36 To 48 Weeks' Postmenstrual Age. *Am J Crit Care* 2019; **28**(6): 451-9.
61. Kampf G. Acquired resistance to chlorhexidine - is it time to establish an 'antiseptic stewardship' initiative? *J Hosp Infect* 2016; **94**(3): 213-27.
62. 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**(1): 267.
63. 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**(1): 48-60.
64. Lee DH, Jung KY, Choi YH. Use of maximal sterile barrier precautions and/or antimicrobial-coated catheters to reduce the risk of central venous catheter-related bloodstream infection. *Infect Control Hosp Epidemiol* 2008; **29**(10): 947-50.
65. 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.

66. 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.
67. Parienti JJ. Catheter-Related Bloodstream Infection in Jugular Versus Subclavian Central Catheterization. *Crit Care Med* 2017; **45**(7): e734-e5.
68. Rosenthal VD, Jin Z, Valderrama-Beltran SL, et al. Multinational prospective cohort study of incidence and risk factors for central line-associated bloodstream infections in ICUs of 8 Latin American countries. *Am J Infect Control* 2023; **51**(10): 1114-9.
69. Rosenthal VD, Yin R, Rodrigues C, et al. Multinational prospective cohort study of incidence and risk factors for central line-associated bloodstream infections over 18 years in 281 ICUs of 9 Asian countries. *J Vasc Access* 2023: 11297298231169542.
70. Chopra V, O'Horo JC, Rogers MA, Maki DG, Safdar N. The risk of bloodstream infection associated with peripherally inserted central catheters compared with central venous catheters in adults: a systematic review and meta-analysis. *Infect Control Hosp Epidemiol* 2013; **34**(9): 908-18.
71. Ullman AJ, Bernstein SJ, Brown E, et al. The Michigan Appropriateness Guide for Intravenous Catheters in Pediatrics: miniMAGIC. *Pediatrics* 2020; **145**(Suppl 3): S269-S84.
72. Chau A, Hernandez JA, Pimpalwar S, Ashton D, Kukreja K. Equivalent success and complication rates of tunneled common femoral venous catheter placed in the interventional suite vs. at patient bedside. *Pediatr Radiol* 2018; **48**(6): 889-94.
73. 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.
74. Swaminathan L, Flanders S, Horowitz J, Zhang Q, O'Malley M, Chopra V. Safety and Outcomes of Midline Catheters vs Peripherally Inserted Central Catheters for Patients With Short-term Indications: A Multicenter Study. *JAMA Intern Med* 2022; **182**(1): 50-8.
75. Mushtaq A, Navalkele B, Kaur M, et al. Comparison of complications in midlines versus central venous catheters: Are midlines safer than central venous lines? *Am J Infect Control* 2018; **46**(7): 788-92.
76. Hind D, Calvert N, McWilliams R, et al. Ultrasonic locating devices for central venous cannulation: meta-analysis. *BMJ* 2003; **327**(7411): 361.
77. Buetti N, Mimoz O, Mermel L, et al. Ultrasound Guidance and Risk for Central Venous Catheter-Related Infections in the Intensive Care Unit: A Post Hoc Analysis of Individual Data of 3 Multicenter Randomized Trials. *Clin Infect Dis* 2021; **73**(5): e1054-e61.
78. Cimiotti JP, Haas J, Saiman L, Larson EL. Impact of staffing on bloodstream infections in the neonatal intensive care unit. *Arch Pediatr Adolesc Med* 2006; **160**(8): 832-6.
79. 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**(12): 1388-95.
80. 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**(2): 103-8.
81. Neri I, Ravaioli GM, Faldella G, Capretti MG, Arcuri S, Patrizi A. Chlorhexidine-Induced Chemical Burns in Very Low Birth Weight Infants. *J Pediatr* 2017; **191**: 262-5 e2.
82. Teschner D, Berisha M, Panse J, et al. Chlorhexidine gluconate-coated gel pad dressings for prevention of central venous catheter-related bloodstream infections in patients with

hematologic diseases or autologous stem cell transplantation: A registry-based matched-pair analysis. *Eur J Haematol* 2023; **111**(6): 914-21.
83. Gavin NC, Webster J, Chan RJ, Rickard CM. Frequency of dressing changes for central venous access devices on catheter-related infections. *Cochrane Database Syst Rev* 2016; **2**(2): CD009213.
84. Short KL. Implementation of a Central Line Maintenance Bundle for Dislodgement and Infection Prevention in the NICU. *Adv Neonatal Care* 2019; **19**(2): 145-50.
85. Munoz-Price LS, Dezfulian C, Wyckoff M, et al. Effectiveness of stepwise interventions targeted to decrease central catheter-associated bloodstream infections. *Crit Care Med* 2012; **40**(5): 1464-9.
86. Hong H, Morrow DF, Sandora TJ, Priebe GP. Disinfection of needleless connectors with chlorhexidine-alcohol provides long-lasting residual disinfectant activity. *Am J Infect Control* 2013; **41**(8): e77-9.
87. 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.
88. Hankins R, Majorant OD, Rupp ME, et al. Microbial colonization of intravascular catheter connectors in hospitalized patients. *Am J Infect Control* 2019; **47**(12): 1489-92.
89. Rotz S, Sopirala MM. Assessment beyond central line bundle: audits for line necessity in infected central lines in a surgical intensive care unit. *Am J Infect Control* 2012; **40**(1): 88-9.
90. Faruqi A, Medefindt J, Dutta G, Philip SA, Tompkins D, Carey J. Effect of a multidisciplinary intervention on central line utilization in an acute care hospital. *Am J Infect Control* 2012; **40**(6): e211-5.
91. Rickard CM, Marsh NM, Larsen EN, et al. Effect of infusion set replacement intervals on catheter-related bloodstream infections (RSVP): a randomised, controlled, equivalence (central venous access device)-non-inferiority (peripheral arterial catheter) trial. *Lancet* 2021; **397**(10283): 1447-58.
92. Zingg W, Sax H, Inan C, et al. Hospital-wide surveillance of catheter-related bloodstream infection: from the expected to the unexpected. *J Hosp Infect* 2009; **73**(1): 41-6.
93. Niedner MF, National Association of Children's H, Related Institutions Pediatric Intensive Care Unit Patient Care FG. The harder you look, the more you find: Catheter-associated bloodstream infection surveillance variability. *Am J Infect Control* 2010; **38**(8): 585-95.
94. Wang H, Tong H, Liu H, et al. Effectiveness of antimicrobial-coated central venous catheters for preventing catheter-related blood-stream infections with the implementation of bundles: a systematic review and network meta-analysis. *Ann Intensive Care* 2018; **8**(1): 71.
95. Lai L, Yue X. Efficacy of Antimicrobial-Impregnated Catheters for Prevention of Bloodstream Infections in Pediatric Patients: A Meta-Analysis. *Front Pediatr* 2021; **9**: 632308.
96. 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**(4): 427-34.
97. Guleri A, Kumar A, Morgan RJ, Hartley M, Roberts DH. Anaphylaxis to chlorhexidine-coated central venous catheters: a case series and review of the literature. *Surg Infect (Larchmt)* 2012; **13**(3): 171-4.

98. Sheng KX, Zhang P, Li JW, et al. Comparative efficacy and safety of lock solutions for the prevention of catheter-related complications including infectious and bleeding events in adult haemodialysis patients: a systematic review and network meta-analysis. *Clin Microbiol Infect* 2020; **26**(5): 545-52.
99. Arechabala MC, Catoni MI, Claro JC, et al. Antimicrobial lock solutions for preventing catheter-related infections in haemodialysis. *Cochrane Database Syst Rev* 2018; **4**(4): CD010597.
100. Heng AE, Abdelkader MH, Diaconita M, et al. Impact of short term use of interdialytic 60% ethanol lock solution on tunneled silicone catheter dysfunction. *Clin Nephrol* 2011; **75**(6): 534-41.
101. Wolf J, Connell TG, Allison KJ, et al. Treatment and secondary prophylaxis with ethanol lock therapy for central line-associated bloodstream infection in paediatric cancer: a randomised, double-blind, controlled trial. *Lancet Infect Dis* 2018; **18**(8): 854-63.
102. Sierra CM, Rodriquez C, Bahjri K. Ethanol Lock for Prevention of CVC-Related Bloodstream Infection in Pediatric Patients: A Systematic Review and Meta-Analysis. *J Pediatr Pharmacol Ther* 2023; **28**(5): 386-96.
103. 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.
104. Soifer NE, Borzak S, Edlin BR, Weinstein RA. Prevention of peripheral venous catheter complications with an intravenous therapy team: a randomized controlled trial. *Arch Intern Med* 1998; **158**(5): 473-7.
105. Carr PJ, Higgins NS, Cooke ML, Mihala G, Rickard CM. Vascular access specialist teams for device insertion and prevention of failure. *Cochrane Database Syst Rev* 2018; **3**(3): CD011429.
106. Battistella M, Bhola 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.
107. 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**(8): 956-62.
108. van de Wetering MD, van Woensel JB, Lawrie TA. Prophylactic antibiotics for preventing Gram positive infections associated with long-term central venous catheters in oncology patients. *Cochrane Database Syst Rev* 2013; **2013**(11): CD003295.
109. Cook D, Randolph A, Kernerman P, et al. Central venous catheter replacement strategies: a systematic review of the literature. *Crit Care Med* 1997; **25**(8): 1417-24.
110. 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.
111. Webster J, Gillies D, O'Riordan E, Sherriff KL, Rickard CM. Gauze and tape and transparent polyurethane dressings for central venous catheters. *Cochrane Database Syst Rev* 2011; (11): CD003827.
112. Batra R, Cooper BS, Whiteley C, Patel AK, Wyncoll D, Edgeworth JD. Efficacy and limitation of a chlorhexidine-based decolonization strategy in preventing transmission of methicillin-resistant Staphylococcus aureus in an intensive care unit. *Clin Infect Dis* 2010; **50**(2): 210-7.

113. Karpanen TJ, Casey AL, Whitehouse T, et al. A clinical evaluation of two central venous catheter stabilization systems. *Ann Intensive Care* 2019; **9**(1): 49.
114. Bertini G, Elia S, Ceciarini F, Dani C. Reduction of catheter-related bloodstream infections in preterm infants by the use of catheters with the AgION antimicrobial system. *Early Hum Dev* 2013; **89**(1): 21-5.
115. Gillis V, van Es MJ, Wouters Y, Wanten GJA. Antiseptic barrier caps to prevent central line-associated bloodstream infections: A systematic review and meta-analysis. *Am J Infect Control* 2023; **51**(7): 827-35.
116. Maki DG, Rosenthal VD, Salomao R, Franzetti F, Rangel-Frausto MS. Impact of switching from an open to a closed infusion system on rates of central line-associated bloodstream infection: a meta-analysis of time-sequence cohort studies in 4 countries. *Infect Control Hosp Epidemiol* 2011; **32**(1): 50-8.
117. Rosenthal VD. Impact of needle-free connectors compared with 3-way stopcocks on catheter-related bloodstream infection rates: A meta-analysis. *Am J Infect Control* 2020; **48**(3): 281-4.
118. Rosenthal VD, Udwadia FE, Kumar S, et al. Clinical impact and cost-effectiveness of split-septum and single-use prefilled flushing device vs 3-way stopcock on central line-associated bloodstream infection rates in India: a randomized clinical trial conducted by the International Nosocomial Infection Control Consortium (INICC). *Am J Infect Control* 2015; **43**(10): 1040-5.
119. Rosenthal VD. Clinical impact of needle-free connector design: A systematic review of literature. *J Vasc Access* 2020; **21**(6): 847-53.
120. Ryder M, deLancey-Pulcini E, Parker AE, James GA. Bacterial transfer and biofilm formation in needleless connectors in a clinically simulated in vitro catheter model. *Infect Control Hosp Epidemiol* 2023; **44**(11): 1760-8.
121. Ryder M, Battle J. Choice of needleless connector technology as a risk reduction strategy for catheter-related bloodstream infection, mortality, and cost: a secondary data analysis. Journal of Vascular Access. June 2024. Accepted and in Press.
122. Maragakis LL, Bradley KL, Song X, et al. Increased catheter-related bloodstream infection rates after the introduction of a new mechanical valve intravenous access port. *Infect Control Hosp Epidemiol* 2006; **27**(1): 67-70.
123. Aloush SM, Al-Sayaghi K, Tubaishat A, et al. Compliance of Middle Eastern hospitals with the central line associated bloodstream infection prevention guidelines. *Appl Nurs Res* 2018; **43**: 56-60.
124. Matlab AA, Al-Hussami MO, Alkaid Albqoor M. Knowledge and compliance to prevention of central line-associated blood stream infections among registered nurses in Jordan. *J Infect Prev* 2022; **23**(4): 133-41.