

#### **SHEA White Paper**

# SHEA Neonatal Intensive Care Unit (NICU) White Paper Series: Practical approaches for the prevention of central-line-associated bloodstream infections

Martha Muller MD<sup>1,2</sup>, Kristina A. Bryant MD<sup>3,4</sup>, Claudia Espinosa MD, MSC<sup>5</sup>, Jill A. Jones MS, APRN, NNP-BC<sup>6</sup>, Caroline Quach MD, MSc, FRCPC<sup>7,8</sup>, Jessica R. Rindels MBA, BSN, RN, CIC<sup>9</sup>, Dan L. Stewart MD<sup>10,11</sup>, Kenneth M. Zangwill MD<sup>12</sup> and Pablo J. Sánchez MD<sup>13,14</sup>

<sup>1</sup>Pediatric Infectious Disease, University of New Mexico School of Medicine, Albuquerque, New Mexico, United States, <sup>2</sup>UNM Health Sciences, Albuquerque, New Mexico, United States, <sup>3</sup>Pediatric Infectious Diseases, University of Louisville, Louisville, Kentucky, United States, <sup>4</sup>Norton Children's Hospital, Louisville, Kentucky, United States, <sup>5</sup>Pediatric Infectious Diseases, University of South Florida Morsani College of Medicine, Tampa, Florida, United States, <sup>6</sup>Nationwide Children's Hospital, Columbus, Ohio, United States, <sup>7</sup>Departments of Microbiology, Infectious Diseases and Immunology and Pediatrics, University of Montreal, Montreal, Québec, Canada, <sup>8</sup>Clinical Department of Laboratory Medicine, CHU Sainte-Justine, Québec, Canada, <sup>9</sup>Children's Mercy Hospital, Kansas City, Missouri, United States, <sup>10</sup>Norton Children's Hospital, Louisville, Kentucky, United States, <sup>11</sup>University of Louisville School of Medicine, Louisville, Kentucky, United States, <sup>12</sup>Division of Pediatric Infectious Diseases and Department of Infection Prevention and Control, Harbor-UCLA Medical Center, Torrance, California, United States, <sup>13</sup>Divisions of Neonatology and Pediatric Infectious Diseases, Department of Pediatrics, Nationwide Children's Hospital, Columbus, Ohio, United States and <sup>14</sup>Center for Perinatal Research, Abigail Wexner Research Institute at Nationwide Children's Hospital, The Ohio State University College of Medicine, Columbus, Ohio, United States

#### Abstract

This document is part of the "SHEA Neonatal Intensive Care Unit (NICU) White Paper Series." It is intended to provide practical, expert opinion, and/or evidence-based answers to frequently asked questions about CLABSI detection and prevention in the NICU. This document serves as a companion to the CDC Healthcare Infection Control Practices Advisory Committee (HICPAC) Guideline for Prevention of Infections in Neonatal Intensive Care Unit Patients. Central line-associated bloodstream infections (CLABSIs) are among the most frequent invasive infections among infants in the NICU and contribute to substantial morbidity and mortality. Infants who survive CLABSIs have prolonged hospitalization resulting in increased healthcare costs and suffer greater comorbidities including worse neurodevelopmental and growth outcomes. A bundled approach to central line care practices in the NICU has reduced CLABSI rates, but challenges remain. This document was authored by pediatric infectious diseases specialists, neonatologists, advanced practice nurse practitioners, infection preventionists, members of the HICPAC guideline-writing panel, and members of the SHEA Pediatric Leadership Council. For the selected topic areas, the authors provide practical approaches in question-and-answer format, with answers based on consensus expert opinion within the context of the literature search conducted for the companion HICPAC document and supplemented by other published information retrieved by the authors. Two documents in the series precede this one: "Practical approaches to *Clostridioides difficile* prevention" published in August 2018 and "Practical approaches to *Staphylococcus aureus* prevention," published in September 2020.

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Central-line-associated bloodstream infections (CLABSIs) are among the most frequent invasive infections among infants in the NICU, and they contribute to substantial morbidity and mortality. Infants who develop CLABSIs have prolonged hospitalizations, resulting in increased healthcare costs; these infants also suffer greater comorbidities, including worse neurodevelopmental and growth outcomes. <sup>1-3</sup> A bundled approach to central-line care practices in the NICU has reduced CLABSI rates significantly, <sup>4-6</sup> but challenges remain. A cross-sectional study using 2013–2018 Centers for Disease Control and Prevention (CDC) surveillance

Corresponding author: Kristina A. Bryant, MD, E-mail: kristina.bryant@louisville.edu
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data from 132 NICUs that report to the National Healthcare Safety Network (NHSN) suggested that previous improvements in CLABSI rates have plateaued.<sup>7</sup> During the study period, CLABSI rates remained stable, with mean rates of 1.56 CLABSIs per 1,000 central venous catheter (CVC) days in NICU patients with birth weights ≤1,500 grams and 0.72 CLABSIs per 1,000 CVC days for those with birth weights >1,500 grams. Infants in the NICU have certain unmodifiable risk factors for infection (eg, an immature immune system), and they require life-sustaining invasive procedures (eg, endotracheal intubation and umbilical, central venous and arterial catheterization) that are essential for respiratory and nutritional support. Importantly, these infants often suffer from disruption in skin and intestinal integrity that may contribute to translocation of pathogens resulting in a diagnosis of CLABSI. Nevertheless, adherence to proper insertion

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techniques and management of the CVC can reduce CLABSI rates, even among the highest-risk infants. The CDC has recommended elements of insertion and maintenance bundles for all patients, although the nuances of care for NICU patients are not included (Table 3).<sup>8</sup> This white paper provides clinicians with practical guidance on the implementation of strategies to prevent CLABSIs in NICU patients, including those strategies above and beyond the elements suggested by CDC.

#### Intended use

The Society for Healthcare Epidemiology of America (SHEA) intends for this document to serve as a companion to the CDC Healthcare Infection Control Practices Advisory Committee (HICPAC) *Guideline for Prevention of Infections in Neonatal Intensive Care Unit Patients*, and to provide practical, expert opinions, and/or evidence-based answers to frequently asked questions about CLABSI detection and prevention in the NICU. This document is not a comprehensive compilation of infection prevention strategies recommended for NICUs. Hand hygiene, environmental cleaning and disinfection, infection prevention education for family members and caregivers, and other core practices recommended by the CDC for all healthcare settings are essential to CLABSI prevention and are detailed elsewhere https://www.cdc.gov/hicpac/recommendations/core-practices.html.

The published literature related to the questions presented herein is not sufficient to meet Grading of Recommendations Assessment, Development and Evaluation (GRADE) standards<sup>9,10</sup>; therefore, the authors provide no evidence grading, and answers incorporate experts' clinical experience. No guideline, expert guidance, or white paper can anticipate all situations. This document is meant to serve as an adjunct to individual judgment by qualified professionals. In general, these recommendations apply to nonoutbreak settings. Healthcare personnel (HCP) may implement additional measures during an outbreak or other special clinical scenarios.

#### **Methods**

This document has been developed by pediatric infectious diseases specialists, neonatologists, advanced practice nurse practitioners, infection preventionists, and members of the HICPAC guideline-writing panel, as well as members of the SHEA Pediatric Leadership Council, to identify and address practical questions anticipated from practitioners and infection prevention professionals. This document is part of the "SHEA Neonatal Intensive Care Unit (NICU) White Paper Series." Two documents in the series precede this one: "Practical approaches to *Clostridioides difficile* prevention" published in August 2018<sup>11</sup> and "Practical approaches to *Staphylococcus aureus* prevention," published in September 2020.<sup>12</sup>

Unlike the SHEA expert guidance format, this document is not based on a systematic literature search. Instead, for the selected topic areas, the authors provide practical approaches in question-and-answer format, with answers based on consensus expert opinion within the context of the literature search conducted for the companion HICPAC document and supplemented by other published information retrieved by the authors.

The full white paper series is overseen by a group of experts in pediatrics, including pediatric infectious diseases specialists,

Table 1. Abbreviations

| Table 1. Abbreviations |   |  |
|------------------------|---|--|
| AAP                    | American Academy of Pediatrics                                      |  |
| AAP/<br>SOID           | American Academy of Pediatrics Section on Infectious Diseases       |  |
| AHA                    | American Hospital Association                                       |  |
| APIC                   | Association for Professionals in Infection Control and Epidemiology |  |
| CDC                    | US Centers for Disease Control and Prevention                       |  |
| CHG                    | Chlorhexidine gluconate   |  |
| CI                     | Confidence Interval   |  |
| CLABSI                 | Central-line-associated bloodstream infection                       |  |
| CVC                    | Central venous catheter   |  |
| EBM                    | Evidence-based medicine   |  |
| FDA                    | US Food and Drug Administration                                     |  |
| НСР                    | Healthcare personnel  |  |
| IDSA                   | Infectious Diseases Society of America                              |  |
| kg                     | Kilogram  |  |
| mg                     | Milligram   |  |
| mL                     | Milliliter  |  |
| NANN                   | National Association of Neonatal Nurses                             |  |
| NICU                   | Neonatal intensive care unit  |  |
| NS                     | Normal saline   |  |
| OR                     | Odds Ratio  |  |
| PICC                   | Peripherally inserted central catheter                              |  |
| PIDS                   | Pediatric Infectious Diseases Society                               |  |
| SHEA                   | Society for Healthcare Epidemiology of America                      |  |
| TPN                    | Total parenteral nutrition  |  |
| VAT                    | Vascular access team  |  |
| VON                    | Vermont Oxford Network  |  |
|                        |   |  |

neonatologists, advanced practice nurse practitioners, and infection preventionists, convened by SHEA, called the NICU Advisory Panel (see the Acknowledgments). The NICU Advisory Panel members serve as representatives for the following organizations: the American Hospital Association (AHA), the American Academy of Pediatrics (AAP), the Association for Professionals in Infection Control and Epidemiology (APIC), the Infectious Diseases Society of America (IDSA), The Joint Commission, the National Association of Neonatal Nurses (NANN), the Pediatric Infectious Diseases Society (PIDS), and the Vermont Oxford Network (VON). This document was reviewed by the NICU Advisory Panel member organizations, the SHEA Guidelines Committee, and the SHEA Publications Committee.

This white paper has been endorsed by SHEA, AHA, APIC, IDSA, The Joint Commission, NANN, and PIDS.

A list of abbreviations, including organization acronyms, is provided in Table 1.

#### **Authors**

The authors include current and past members of the SHEA Guidelines Committee and the SHEA Pediatric Leadership Council, and representation from AAP and APIC. All authors

Table 2. Questions and Recommendations

| # | Question   | Answer  |
|---|--|---|
| 1 | Which NICU patients are likely to benefit from use of chlorhexidine (CHG) skin antisepsis for CVC insertion and maintenance?                                   | <ul> <li>Skin antisepsis should occur for all infants in the NICU and optimally should be performed with a CHG-containing product.</li> <li>For infants ≥8 weeks of age 2% CHG in 70% alcohol should be used.</li> <li>For infants &lt;8 weeks of age, the authors' clinical experience shows that a CHG-containing product may be used safely. Additionally, FDA has stated that CHG may be "[used] with care in premature infants or infants under 2 months of age."<sup>13</sup></li> <li>For infants born at &lt;28 weeks gestation, especially ≤7 days of age, NICUs may consider use of aqueous 2% CHG for skin antisepsis.</li> </ul>  |
| 2 | How often should CVC dressings be changed in NICU infants?   | <ul> <li>To reduce skin barrier breakdown and the risk for dislodgement of the CVC, CVC dressings should be changed only if soiled, damp, or loose, regardless of gestational age (and not according to a specific interval of time, eg, every 7 days).</li> <li>The integrity of the CVC dressing should be inspected by designated HCP at least daily.</li> </ul>   |
| 3 | In which NICU patients should CHG-impregnated sponges or other CHG-impregnated dressings be used?  | <ul> <li>CHG-impregnated dressings are associated with an increased risk of contact dermatitis in NICU infants. Benefits have not been demonstrated in NICU infants and these products are not recommended by the authors.<sup>25</sup></li> <li>If other interventions have failed to reduce CLABSI in an infant in the NICU, or if there is an increase in the NICU's baseline CLABSI rates, CHG-impregnated dressings may be considered in infants ≥28 weeks gestation and ≥7 days of age.</li> </ul>  |
| 4 | Should alcohol disinfectant caps be used in the NICU?  | <ul> <li>NICUs may consider use of disinfectant caps as an additional intervention to<br/>reduce CLABSI rates when other interventions have failed.</li> </ul>  |
| 5 | In which NICU patients are the benefits of CHG bathing likely to outweigh the risks?   | <ul> <li>Routine CHG bathing is not recommended for all NICU infants.</li> <li>In NICUs that have high CLABSI rates (see Question 10), despite implementation of other evidence-based strategies, CHG bathing may be used in the NICU for infants with CVCs. The optimal frequency of CHG-bathing has not been established and depends on chronological age and gestational age: <ul> <li>o CHG bathing in term infants (≥37 weeks): may be performed from birth.</li> <li>o CHG bathing in preterm infants (&lt;37 weeks gestation) may be considered beginning at 4 weeks of chronological age, recognizing the potential for skin irritation and systemic absorption (the latter being of unknown clinical significance).</li> <li>o CHG bathing in preterm infants (&lt;37 weeks gestation) and &lt;4 weeks of age is not recommended due to potential adverse local and systemic effects. In these infants, an alternative approach of bathing with sterile water with or without mild soap may help decrease bacterial counts on skin.</li> <li>When CHG bathing is utilized, NICUs should ensure careful surveillance for local and systemic adverse effects, including allergic reactions.</li> </ul> </li> </ul> |
| 6 | What are practical strategies for minimizing central-line entry in NICU patients?  | <ul> <li>NICUs should perform laboratory and diagnostic stewardship (ie, consolidation of necessary tests and elimination of those not clinically relevant).</li> <li>HCP should avoid using the CVC to obtain routine blood tests.</li> <li>Although not a universal recommendation, NICUs may consider the use of closed blood sampling systems.</li> <li>The utility of obtaining blood cultures through an indwelling CVC remains an unresolved issue.</li> </ul>   |
| 7 | When and how should prophylactic antimicrobial lock therapy be implemented in NICU patients?   | <ul> <li>Prophylactic antimicrobial lock therapy as a universal prevention measure is not recommended.</li> <li>Antimicrobial locks may be considered as an additional intervention in NICU infants with recurrent CLABSIs.</li> </ul>  |
| 8 | Should prophylactic antimicrobials be administered to a NICU patient at the time of PICC removal to reduce the incidence of CLABSI or culture-positive sepsis? | <ul> <li>Prophylactic antimicrobials are not recommended at the time of PICC<br/>removal.</li> </ul>  |
| 9 | What are practical considerations for the implementation of a neonatal vascular access team (VAT)?   | <ul> <li>NICUs should consider use of a VAT. Such teams have demonstrated effectiveness in reducing catheter-related complications and are cost-effective. <sup>22,81-83</sup></li> <li>VAT proceduralists should receive education and clinical training, and upon completion, demonstrate knowledge and proficiency in PICC insertion, care, and removal, and a commitment to the team-based approach.</li> <li>VAT proceduralists should successfully insert a predefined number of PICCs as defined by the local facility's delineation of privileges.</li> <li>The team should monitor relevant quality measures (see Table 7).</li> </ul>   |

(Continued)

Table 2. (Continued)

| #  | Question  | Answer   |
|----|---|--|
| 10 | What threshold should prompt a NICU to consider implementing additional preventive measures?  | <ul> <li>Zero CLABSIs is the aspirational and potentially achievable goal.</li> <li>Although there is no nationally endorsed threshold above which additional CLABSI prevention measures should be implemented, a variety of quantitative or qualitative metrics may be utilized to identify CLABSI prevention success over time and determine when additional intervention is necessary.</li> <li>A decision to identify a threshold for action in an individual NICU should assess a variety of factors including: <ul> <li>A AN SIR or rate of CLABSI that is above goal or increasing despite the consistent implementation of current organizational interventions</li> <li>Local interest in setting a specific lower target with input from Infection Prevention and Control (infection preventionists, healthcare epidemiologist)</li> <li>Patient mix and clinical acuity, which may predict general likelihood of CLABSI</li> <li>Resource and personnel capacity for initiation and/or maintenance of specific interventions and practice processes.</li> </ul> </li> <li>Any quantitative or qualitative metric that is defined should be developed and accepted by all stakeholders.</li> </ul> |
| 11 | What preventive bundle elements, above and beyond those recommended by CDC, could be considered by a NICU experiencing ongoing CLABSIs? | <ul> <li>Additional practices that lack robust evidence may be effective. NICUs may consider many different products, technologies, and processes, some of which are described below.</li> <li>Implementation of an expanded NICU central-line care bundle should take into account the risks and benefits of additional measures, as well as the needs, resources, and local expertise at individual institutions.</li> </ul>   |

served as volunteers. At their respective institutions, the authors are directly involved or provide an advisory role in the development of policies pertaining to pediatric and/or neonatal infection prevention in the NICU.

The NICU Advisory Panel (see the Acknowledgments), a collaborative group of pediatric and pathogen-specific experts convened by SHEA, provided oversight and review of the draft document.

#### Practical approaches: Questions and Answers

Questions and recommendations are listed in Table 2.

Question 1: Which NICU patients are likely to benefit from use of chlorhexidine (CHG) skin antisepsis for CVC insertion and maintenance?

#### Answer 1:

- Skin antisepsis should occur for all infants in the NICU and optimally should be performed with a CHG-containing product.
- For infants ≥8 weeks of age or older, 2% CHG in 70% alcohol should be used.
- For infants <8 weeks of age, the authors' clinical experience shows that a CHG-containing product may be used safely. Additionally, the US Food and Drug Administration (FDA) has stated that CHG may be "[used] with care in premature infants or infants under 2 months of age." 13
- For infants born at <28 weeks gestation, especially ≤7 days of age, NICUs may consider use of aqueous 2% CHG for skin antisepsis.

A variety of antiseptics, containing differing amounts of CHG, with and without alcohol (aqueous CHG), are available. The use of a CHG-containing skin antiseptic, in combination with alcohol, for CVC insertion and maintenance is preferred, based on its efficacy in reducing CLABSI in populations outside the NICU. In the NICU, the optimal concentration of CHG-containing agent has

not been determined. Although the FDA has stated that CHG may be "[used] with care in premature infants or infants under 2 months of age,"13 the authors' clinical experience shows that it may be used safely. Figure 1, from the Centre Hospitalier Universitaire (CHU) Sainte-Justine Hospital in Montreal, Canada details how one hospital has operationalized options for antisepsis for various procedures commonly performed in the NICU setting. Although more detailed than the recommendations provided in this document, it could serve as a useful model for NICUs seeking to implement the use of CHG. Infants (>8 weeks of age) may benefit from a higher CHG concentration (ie, 2%) (Fig. 1). 14 For CVC insertion, some centers use 2% aqueous rather than alcohol-based CHG in extremely preterm infants (<28 weeks gestation), but recommend that, once dried, CHG should be rinsed off the skin with sterile water to prevent burns. However, Garland et al<sup>15</sup> showed that the application of 2% CHG in 70% isopropyl alcohol for skin antisepsis before CVC placement and with each weekly dressing change in infants weighing ≥1500 grams and ≥7 days of age was not associated with dermatitis although cutaneous absorption of CHG occurred in 15% of infants. 15

As an alternative to alcohol-based CHG solutions that may potentiate skin irritation and cutaneous CHG absorption, some NICUs use 1% or 2% aqueous CHG for skin antisepsis. In a randomized, blinded, non-inferiority trial of 308 infants who were 26-42 weeks gestation, the use of 1% aqueous CHG for skin antisepsis was comparable to a 2% aqueous CHG solution when assessed by the proportion of negative skin swab cultures after skin antisepsis. 14 Overall, 93% of swabs were sterile in the 1% CHG group compared with 95.6% in the 2% CHG group (risk difference, -2.7%; 95% CI, -6.2 to +0.8%). The lower bound of the 95% CI crossed the prespecified absolute non-inferiority limit of 5%. Mild dermatitis was identified in 2.3% of infants in each group, with the worst being transient slightly pink discoloration of the skin without edema. Percutaneous absorption of chlorhexidine occurred in all 59 sampled infants but did not differ by the concentration of the aqueous preparation with the median CHG concentration at

All Antiseptics

|  | All Antiseptics   |   |                                       |  |
|--|---|---|---------------------------------------|--|
| Minimum contact time                                   | >30 seconds   |   |                                       |  |
| Drying time  | Let all dry completely  |   |                                       |  |
|  |   | All Infants   |                                       |  |
| Vial cap   |   | Alcohol 70% swab  |                                       |  |
| Injections IM, SC, ID, etc.                            |   | Alcohol 70% swab  |                                       |  |
| Injection site, needleless connectors, "scrub the hub" |   | Alcohol 70% swab  |                                       |  |
| Blood procurement                                      | Alcohol 70% swab  |   |                                       |  |
| Age and weight   | <ul> <li>&lt;28 weeks         gestation OR</li> <li>&lt;1000g         AND</li> <li>&lt;4 weeks of life</li> </ul> | Everyone else<br>not included in<br>columns to left or<br>right | Term infant  AND     ≥4 weeks of life |  |
| Location   | • <4 weeks of file  |   | <u> </u>                              |  |
| Blood cultures   | CHG 2% aqueous  | CHG 0.5% +<br>alcohol 70% swab                                  | CHG 2% +<br>alcohol 70% swab          |  |
| Arterial draws   | CHG 2% aqueous  | CHG 0.5% +<br>alcohol 70% swab                                  | CHG 2% +<br>alcohol 70% swab          |  |
| Peripheral IV insertion                                | CHG 2% aqueous  | CHG 0.5% +<br>alcohol 70% swab                                  | CHG 2% +<br>alcohol 70% swab          |  |
| CVC insertion (includes UAC/UVC, PICC)                 | CHG 2% aqueous<br>swabstick   | CHG 0.5% + alcohol 70% swabstick                                |                                       |  |
| CVC insertion site                                     | CHG 2% aqueous<br>swabstick   | CHG 0.5% + alcohol 70% swabstick                                |                                       |  |

<sup>\*</sup>The recommendations in this table are presented as an example of how one hospital implemented CHG use in a NICU and are more detailed than the recommendations presented in the text.

Fig. 1. Use of antiseptics in the NICU at CHU Sainte-Justine Hospital in Montreal, Canada.

24 hours being 19.6 ng/mL and 12.6 ng/mL in the 1% and 2% aqueous CHG group, respectively. 14 Therefore, use of the lower CHG concentration does not offer any substantial safety advantage.

CHG skin antisepsis is commonly used in many NICUs. In 2016, a survey of 58 academic NICUs in the United States found that CHG was used by 86% of centers, mostly for skin antisepsis at the time of CVC insertion, CVC dressing changes, CVC maintenance, and peripheral intravenous catheter insertion. In NICUs where CHG was restricted by age or weight, the most common requirements for CHG use were gestational age >28 weeks and weight >1000 grams. <sup>16</sup>

CHG-based skin antisepsis has demonstrated superiority compared to povidone-iodine in settings outside the NICU.<sup>17</sup> Limited data from clinical trials in the NICU have failed to demonstrate superiority of either product from a safety and efficacy standpoint, although the use of povidone-iodine was associated with an increased risk of high thyroid stimulating hormone level requiring treatment.<sup>15,18</sup> Recent guidelines from CDC for the prevention of CLABSIs in NICU patients advise to "consider the use of alcohol-containing chlorhexidine for skin antisepsis to prevent central-line–associated bloodstream infection (CLABSI) in neonatal intensive care unit (NICU) patients in whom the benefits are judged to outweigh the potential risks." The consensus of the authors is that CHG-based skin antisepsis and not an iodine-based product is

optimal for all infants regardless of gestational age and birth weight.

Frequent inspection of the skin site where CHG has been applied is important to detect and manage cutaneous adverse effects including chemical burns. <sup>19</sup> To decrease their occurrence, only the minimum amount of CHG-containing solution should be used, with removal of any excess solution, as well as any soaked materials or drapes, from the skin. Parents should be informed of the potential for CHG to cause skin irritation at the time consent for CVC placement is obtained. <sup>20</sup> When severe dermatitis or chemical burns occur, temporary use of povidone-iodine or a lower concentration of aqueous CHG may be needed until the skin injury is healed. Consultation with the NICU wound team or other specialists such as burn and plastic surgeons may be necessary.

### Question 2: How often should CVC dressings be changed in NICU infants?

#### Answer 2:

• To reduce skin barrier breakdown and the risk for dislodgement of the CVC, CVC dressings should be changed only if soiled, damp, or loose, regardless of gestational age (and not according to a specific interval of time, eg, every 7 days).

Table 3. Adapted CDC Checklist for Prevention of CLABSI\*8,17

| Insertion   | Maintenance   |
|---|---|
| ☐ Perform hand hygiene before insertion.  | ☐ Perform hand hygiene.   |
| ☐ Adhere to aseptic technique.  | ☐ Bathe ICU patients who are ≥2 months of age with CHG daily.   |
| ☐ Use maximal sterile barrier precautions (i.e., mask, cap, gown, sterile gloves, and sterile full body drape).   | ☐ Use only sterile devices to access catheters.   |
| <ul> <li>☐ Choose the best insertion site to minimize infections and noninfectious complications based on individual patient characteristics.</li> <li>☐ Prepare the insertion site with &gt;0.5% CHG with alcohol* (see Question/Answer 1).</li> </ul>   | ☐ Scrub the access port or hub with friction immediately prior to each use with an appropriate antiseptic (CHG, povidone iodine, an iodophor, or 70% alcohol).  |
| <ul> <li>□ Place a sterile gauze dressing or a sterile, transparent, semipermeable dressing over the insertion.</li> <li>□ For patients ≥18 years of age, use a CHG-impregnated dressing with an FDA cleared label that specifies a clinical indication for reducing CLABSI for short-term non-tunneled catheters unless the facility is demonstrating success at preventing CLABSI with baseline prevention practices*.</li> </ul> | <ul> <li>☐ Immediately replace dressings that are wet, soiled, or dislodged.</li> <li>☐ Perform routine dressing changes using aseptic technique with clean or sterile gloves:</li> <li>☐ Change gauze dressings at least every 2 days.</li> <li>☐ Change semipermeable dressings at least every 7 days.</li> <li>☐ For patients ≥18 years of age, use a chlorhexidine impregnated dressing with an FDA cleared label that specifies a clinical indication for reducing CLABSI for short-term non-tunneled catheters unless the facility is demonstrating success at preventing CLABSI*.</li> </ul> |
|   | <ul> <li>□ Change administrations sets for continuous infusions no more frequently than every 4 days, but at least every 7 days.</li> <li>□ If blood or blood products or fat emulsions are administered, change tubing every 24 hours.</li> <li>□ If propofol is administered, change tubing every 6-12 hours or when the vial is changed.</li> </ul>  |
|   | ☐ Perform daily audits to assess if central line is still needed  |

<sup>\*</sup>This is the complete CDC checklist. Some recommendations are different from those in this paper or are not pertinent because they are specific to older patients. The recommendations in this paper reflect the nuances of care in the NICU.

• The integrity of the CVC dressing should be inspected by designated HCP at least daily.

Transparent CVC dressings have been recommended to be changed every 7 days, and more frequently if soiled, damp, or loose. However, it also is likely that in extremely preterm infants in particular (<28 weeks gestation), each dressing removal may result in skin barrier breakdown leading to an increased risk of CLABSI. Some NICUs will only change a transparent dressing if it is soiled, damp, or loose, and this is the authors' consensus recommendation for all NICU patients regardless of gestational or chronologic age or weight. Although the authors acknowledge that this is different than the CDC recommendation (Table 3), deferring changing dressings of NICU patients if they are intact has been recommended by other experts. Tr. 22, 23 Daily inspection of the dressing's integrity, preferably by a dedicated team or trained bedside nurse, is recommended.

Very limited data suggest that use of cyanoacrylate glue at the CVC insertion site may decrease bleeding and thus increase the time between dressing changes in extremely preterm infants. In one NICU the addition of cyanoacrylate glue to the insertion bundle for percutaneously placed CVCs significantly reduced accidental catheter dislodgement and anecdotally reduced bleeding at the insertion site.<sup>24</sup>

### Question 3: In which NICU patients should CHG-impregnated sponges or other CHG-impregnated dressings be used?

#### Answer 3:

 CHG-impregnated dressings are associated with an increased risk of contact dermatitis in NICU infants. Benefits have not

- been demonstrated in NICU infants, and these products are not recommended by the authors.<sup>25</sup>
- If other interventions have failed to reduce CLABSI in an infant in the NICU, or if there is an increase in the NICU's baseline CLABSI rates, CHG-impregnated dressings may be considered in infants ≥28 weeks gestation and ≥7 days of age.

Several types of dressings incorporate chlorhexidine, including CHG-impregnated sponges, transparent dressings, and films. A CHG-impregnated sponge, also called a patch or disk, is a device composed of sterile polyurethane foam impregnated with CHG. It is intended to be applied at the insertion site of a central line before a sterile, transparent dressing is placed. This device is designed to provide continuous protection from skin recolonization by slowly releasing CHG while also absorbing and drawing fluids away from the site.<sup>26</sup> The use of CHG-impregnated sponges (eg, Biopatch Protective Disk with CHG, Ethicon, Raritan, NJ) has been shown to reduce CLABSIs in adults, but the benefits are less clear in pediatric patients.<sup>27</sup> The National Health Service (NHS UK) recommends that if used, CHG-impregnated sponges should be restricted to infants ≥28 weeks gestation and  $\geq$ 7 days of age and that pressure over the sponge be avoided to prevent skin necrosis.<sup>28</sup> Adverse skin reactions, including dermatitis and cellulitis at the insertion site, may occur and may not be visible under the sponge, and this may be a deterrent to their use in some infants.

Dressings impregnated with antiseptics or antibiotics (ie, antimicrobial dressings) have also been studied in NICU infants. Responsible to Cochrane review evaluated the effectiveness and safety of antimicrobial dressings used at the time of CVC insertion in reducing CLABSIs in the NICU. Compared to polyurethane dressing/

povidone-iodine cleansing, CHG sponges/alcohol cleansing reduced catheter colonization (risk ratio [RR], 0.62; 95% CI, 0.45–0.86) but did not change the important outcomes of bloodstream infection (BSI; RR, 1.18; 95% CI, 0.53–2.65) or sepsis (RR, 1.06; 95% CI, 0.75–1.52).<sup>29</sup> In addition, the use of CHG-impregnated dressings was associated with contact dermatitis in preterm infants (RR, 43.06; 95% CI, 2.61–710.44).<sup>29</sup> The use of a silver-alginate patch appeared safe, but there was insufficient evidence of benefit.

The CDC Checklist for the Prevention of CLABSI does not recommend the use of CHG-impregnated dressings (including sponges) to protect the sites of short-term, nontunneled CVCs for premature infants due to the risk of serious adverse skin reactions. While recent guidance recommends the use of chlorhexidine-containing dressings for patients >2 months of age with CVCs, use of dressings in younger infants, particularly in pre-term or very low birthweight infants, remains an unresolved issue.<sup>17</sup>

Some NICUs utilize CHG dressings for selected infants. Of 50 neonatology training program directors in the United States who responded to a 2014 survey, 10 (20%) reported using impregnated dressings or disks (the survey did not differentiate between the products). A survey of SHEA Pediatric Leadership Council members in April 2014 revealed that 5 (19%) of 26 NICUs used a "CHG dressing" on infants with surgically placed CVCs but the criteria for use were variable and included infants who were >28 weeks gestation and weighing >1,000 grams,  $\geq$ 34 weeks corrected age, or >2 months chronologic age. Only 3 (11%) of 27 NICUs used CHG dressings on similar infants with peripherally inserted central catheters (PICCs, also called percutaneously inserted CVCs). The survey did not differentiate between sponges and impregnated dressings.

#### Question 4: Should alcohol disinfectant caps be used in the NICU?

#### Answer 4:

 NICUs may consider use of disinfectant caps as an additional intervention to reduce CLABSI rates when other interventions have failed.

Access of pathogenic organisms to the bloodstream via a CVC is prevented in part by careful disinfection of the catheter hub. The manual "scrub-the-hub" process is time-consuming; thus, compliance by HCP may be suboptimal. Disinfectant caps containing 70% isopropyl alcohol placed over intravenous needleless connectors act as antiseptic barriers by passive disinfection, decreasing hub colonization.<sup>31</sup> Two in vitro studies found leakage of alcohol through the hub membrane,<sup>32, 33</sup> but the potential clinical significance of this leakage is unknown. Adverse effects resulting from alcohol leakage in a clinical setting have not been identified. In vitro, alcohol leakage can vary by cap manufacturer and may be reduced by allowing the hub membrane to dry for 30 seconds prior to an infusion and limiting the number of days that the cap remains in place (ie, <7 days).

In pediatric patients, disinfectant caps have been used in many hospitals, usually as part of a bundle, with subsequent reduction in CLABSIs. In 2019, the National Institute of Health and Care Excellence (NICE) cited disinfectant caps as a potential intervention to reduce CLABSIs, but due to insufficient evidence, further research to assess their clinical benefit was recommended.<sup>34</sup> A systematic review that included 9 studies comparing the effects of disinfectant caps (Curos<sup>TM</sup> and SwabCap<sup>TM</sup>) with manual

disinfection in multiple US and UK hospital settings (including 1 pediatric hospital) found that disinfectant caps effectively reduced CLABSIs (incidence rate ratio [IRR], 0.59; 95% CI, 0.45–0.77; P < .001) and were cost-saving.<sup>35, 36,</sup> In a prospective, single-center, pre- and post-observational study conducted in pediatric intensive care units (PICUs) and NICUs, CLABSI rates decreased by 22% with the use of disinfectant caps compared to the manual scrub-the-hub method, but the difference was not statistically significant (95% CI, 34%–55%; P = .368).<sup>36</sup> Among ambulatory pediatric oncologic patients, a randomized controlled trial evaluating disinfectant caps did not demonstrate a significant reduction in CLABSI incidence.<sup>37</sup>

Despite the lack of supportive evidence in pediatrics, many NICUs utilize disinfectant caps without reporting clinically significant adverse effects. A survey conducted by the SHEA Pediatric Leadership Council in April 2014 showed that 9 (33%) of 27 participating NICUs used ethanol or alcohol caps on all hubs or ports of the intravenous administration set in all NICU patients.<sup>30</sup>

### Question 5: In which NICU patients are the benefits of CHG bathing likely to outweigh the risks?

#### Answer 5:

- Routine CHG bathing is not recommended for all NICU infants.
- In NICUs that have high CLABSI rates (see Question 10), despite implementation of other evidence-based strategies, CHG bathing may be used in the NICU for infants with CVCs. The optimal frequency of CHG-bathing has not been established and depends on chronological age and gestational age:
  - o CHG bathing in term infants (≥37 weeks): may be performed from birth.
  - o CHG bathing in preterm infants <37 weeks gestation may be considered beginning at 4 weeks of chronological age, recognizing the potential for skin irritation and systemic absorption (the latter being of unknown clinical significance).
  - o CHG bathing in preterm infants (<37 weeks gestation) and <4 weeks of age is not recommended due to potential adverse local and systemic effects. In these infants, an alternative approach of bathing with sterile water with or without mild soap may help decrease bacterial counts on skin.
- When CHG bathing is utilized, NICUs should ensure careful surveillance for local and systemic adverse effects, including allergic reactions.

The use of CHG for skin antisepsis and the use of CHG for bathing are distinct interventions with unique sets of benefits and risks in NICU infants<sup>38</sup>. Daily bathing of ICU patients  $\geq 8$  weeks (ie,  $\geq 2$ months) is now considered to be standard infection prevention practice<sup>17</sup> including patients in the NICU. With the exception of children with cancer or those undergoing hematopoietic stem cell transplantation, daily CHG bathing of children in the PICU who were ≥2 months of age (8 weeks) resulted in decreased bacteremia and CLABSIs.<sup>39</sup> Recommendations for bathing younger infants, especially preterm infants, is more nuanced. Bathing infants with cloths infused with CHG decreases bacterial colony counts on skin transiently. 40,41 Nonrandomized trials in NICU patients suggest a decrease in CLABSI rates in CHG-bathed neonates in the absence of observed adverse events. 42,43 However, safety concerns persist, especially in very preterm infants whose poor skin integrity may predispose them to contact dermatitis, chemical burns, and systemic absorption.44 An additional concern comes from studies

in pediatric and adult patients that have noted higher prevalence of reduced CHG susceptibility in organisms that cause CLABSIs in units that perform daily CHG bathing of patients. <sup>45</sup> In adults, the potential development of cross resistance to other cell-envelope agents such as daptomycin and colistin has raised further concerns. These phenomena have not been evaluated in NICU patients.

For these reasons, CHG bathing has not been used routinely in extremely preterm (<28 weeks gestation) infants with birth weights of ≤1,000 grams who are <4 weeks of age, and alternate bathing methods with sterile water and/or mild soap are advocated. However, based on decreases in CLABSI rates in CHG-bathed neonates as noted above, CHG bathing may be considered in more mature preterm and term infants between 4 and 8 weeks of age if CLABSI rates remain high despite implementation of other evidence-based interventions.

### Question 6: What are practical strategies for minimizing central-line entry in NICU patients?

#### Answer 6:

- NICUs should perform laboratory and diagnostic stewardship (ie, consolidation of necessary tests and elimination of those not clinically relevant).
- HCP should avoid using the CVC to obtain routine blood tests.
- Although not a universal recommendation, NICUs may consider the use of closed blood sampling systems.
- The utility of obtaining blood cultures through an indwelling CVC remains an unresolved issue.

Infants in the NICU require frequent blood draws for clinical monitoring. CDC guidelines for CLABSI prevention in NICU patients recommend minimizing the number of times central-line hubs are accessed, as well as minimizing blood sampling through central lines, even though high-quality data are lacking. 9,46 Only 1 study among infants in the NICU reported an increased risk of CLABSI from procedures involving catheter manipulation such as disinfection of the catheter hub following disconnection of the CVC (OR, 1.2; 95% CI, 1.1-1.3) and blood sampling other than for blood gases (OR, 1.4; 95% CI, 1.1-1.8). 47 The authors reported a cumulative dose-effect of the number of blood samples obtained from the CVC with an odds ratio (OR) of 1.04 for 1-7 blood samples (95% CI, 0.33–3.27;P=0.95) to 8.4 (95% CI, 0-67.1;P=0.036) for >14 blood samples. Obtaining blood samples by other methods may also create risk. In an observational case-control study, there was an increased risk of CLABSI among NICU infants who had at least 3 capillary blood draws by heel punctures within 48 hours before CLABSI onset (OR, 5.36; 95% CI, 2.37-12.15). 48 This retrospective study could not confirm causality, but it is plausible that multiple skin breaks contributed to the development of bacteremia.

The first steps in decreasing the number of central-line system entries are (1) not using CVCs for routine blood draws and (2) performing laboratory and diagnostic stewardship to minimize tests that are not clinically relevant. Reducing laboratory testing is an achievable goal. After implementing a multifaceted quality improvement project that included guideline development, dashboard creation and distribution, electronic medical record optimization, and expansion of noninvasive and point-of-care testing, one NICU achieved a 26.8% decrease in routine laboratory testing per 1,000 patient days over a 24-month period. 49

The utility of obtaining blood cultures through an indwelling CVC remains controversial. In general, catheter-drawn blood cultures have higher rates of contamination (ie, false positives),<sup>50</sup> and

some expert guidance recommends peripheral venipuncture as the preferred method for obtaining blood cultures.<sup>51</sup> The Bright Star Collaborative is a multicenter quality improvement collaborative that includes children's hospitals in 17 states across the United States.<sup>52</sup> The mission of the group is to reduce bacterial culture overuse in critically ill children by implementing diagnostic stewardship interventions. Consensus recommendations from the group for PICU patients advise against obtaining blood cultures from every lumen of a CVC or from a peripheral intravenous catheter. The group did not reach consensus regarding the utility of a blood culture drawn from a CVC, since a positive culture cannot differentiate between catheter colonization or BSI.<sup>53</sup> NICU-specific recommendations do not exist but the issues are likely to be similar.

The clinician must weigh practical considerations when deciding how to obtain blood cultures in a NICU patient. The NHSN surveillance definitions for CLABSI require 2 positive blood cultures, taken at different sites or at different times, when potential commensal bacteria (eg, coagulase-negative staphylococci) are detected to diagnose a true device-associated infection. It may be difficult to obtain 2 separate samples by peripheral venipuncture in NICU infants. A CVC sample may be paired with a peripherally obtained sample to help differentiate between catheter colonization and a true BSI, especially when a commensal organism is isolated. A CVC culture is considered to have higher sensitivity compared to peripheral specimens, at the cost of lower specificity.<sup>54</sup> Finally, HCP also may opt to draw a blood culture from a CVC to minimize painful procedures. A recent study conducted at a level IV NICU compared concurrently drawn peripheral and catheter blood cultures and found that most blood cultures were positive with the same organism from both sites, although a small but important minority of episodes (12%) grew virulent pathogens from either culture site alone. 50 The authors concluded that while dual-site blood-culture practices may be useful, the gain in sensitivity of bacteremia detection should be weighed against additive contamination risk. Even when HCP want to obtain a blood culture from a CVC, it may not be feasible. Catheters with very small lumens may collapse when suction is applied during the blood draw.

Adopting the Bright Star Consensus Recommendations for PICU patients may reduce the total number of blood cultures ordered, as well as the number of samples obtained through the catheter. Before ordering a blood culture, HCP should review the patient's clinical data, including previous cultures, and perform a physical examination, and they should discuss the patient's status with the bedside nurse. If a blood culture needs to be drawn from the CVC, then additional blood draws can be performed at the same time or scheduled with other required laboratory tests to decrease system entry.<sup>53</sup> Because bacteremia occurs before the onset of fever, once the fever has occurred, the timing of the blood culture is not as critical except in situations when obtaining a blood culture before a change in antimicrobial therapy informs antimicrobial stewardship efforts.

Previous studies have shown that closed infusion systems are associated with a decrease in overall CLABSI rates compared to open-infusion systems. Other studies have proposed that closed blood-sampling systems, such as the venous arterial blood management and protection (VAMP<sup>TM</sup>) and KidsKit<sup>TM</sup> systems, decrease system entry, blood waste, and microbial contamination.<sup>55–57</sup> A pediatric study evaluated both systems and compared implementation of the KidsKit system to the conventional 3-way stopcock methods used on umbilical arterial catheters in the PICU and NICU. The authors found a decrease in CLABSIs below the national benchmark.<sup>57</sup> NICUs may consider use of a closed

Table 4. Considerations for Use of Lock Therapies in NICU Patients<sup>96</sup>

| Prophylactic Antimicrobial Lock Therapy   |  |  |  |  |
|---|--|--|--|--|
| Optimal Procedures:   | <ul> <li>Pharmacy-dispensed volume-specific syringes for each lumen</li> <li>Minimum dwell time of 4 hours, without disruption, while all lumens are locked</li> <li>Changing all line lock solutions inserted into ports every 24 hours</li> <li>Routine administration of a thrombolytic drug other than saline or heparin to maintain catheter patency (e.g., alteplase). Each lumen of the catheter should be easy to flush and aspirate</li> <li>VAT evaluation and intervention if unable to withdraw antimicrobial lock from any lumen</li> </ul> |  |  |  |
| Do not use for:   | <ul> <li>Infants with allergy to any component of antimicrobial lock therapy</li> <li>2 French or smaller PICCs, umbilical arterial and venous catheters, arterial lines, midline catheters, and peripheral intravenous catheters</li> <li>Infants who are receiving continuous infusions that require a dedicated lumen line (e.g., amiodarone, heparin, narcotics, pressors, and TPN)</li> <li>Obtaining antimicrobial levels</li> </ul>   |  |  |  |
| Do not use if:  | <ul> <li>Lock is incompatible with catheter being used</li> <li>Patency of line cannot be assessed</li> <li>Logistical challenges of rotating lumens when multiple lumens and/or catheters require antimicrobial lock therapy make use ineffective</li> </ul>  |  |  |  |
| Considerations for Ethano   | Lock Therapy   |  |  |  |
| Ethanol lock therapy has very limited use in the NICU <sup>65, 67, 70</sup>   |  |  |  |  |
| Do not use in:  | A non-silicone central catheter     A peripherally inserted central catheter   |  |  |  |
| Do not use if:  • The catheter has more than 1 lumen • The infant is less than 6 months of age • The infant weighs less than 5 kg • The infant is receiving continuous infusions. Ethanol may precipitate if in contact with TPN and cause catheter of Inability to maintain the lock for a minimum of 4 hours (optimal dwell time) |  |  |  |  |
| Do not mix with heparin   |  |  |  |  |

blood-sampling system as a potential intervention when CLABSI rates remain elevated despite high rates of compliance with insertion and maintenance bundles.

### Question 7: When and how should prophylactic antimicrobial lock therapy be implemented in NICU patients?

#### Answer 7:

- Prophylactic antimicrobial lock therapy as a universal prevention measure is not recommended.
- Antimicrobial locks may be considered as an additional intervention in NICU infants with recurrent CLABSIs.

Antimicrobial locks are solutions used for prophylactic or adjunctive treatment of CLABSI when the catheter cannot be removed in the setting of bacteremia. They contain a solution of highly concentrated antimicrobial agent in combination with an anticoagulant that is inserted into the lumen of a CVC and removed after a specified period (dwell time). Three randomized controlled trials in NICU infants demonstrated that use of prophylactic antimicrobial lock therapy decreased CLABSIs in NICUs with high baseline CLABSI rates. 58-60 These studies, however, were conducted before routine implementation of insertion and maintenance bundles, which have reduced NICU CLABSI rates substantially. We do not, therefore, recommend prophylactic antimicrobial lock therapy as a universal prevention measure, although it may be considered in individual infants who experience recurrent CLABSIs. The authors recommend collaboration with a pediatric infectious diseases specialist and the NICU vascular access team (VAT) before implementation of lock therapy.

NICUs will need to consider practical implementation challenges, including that some catheters are not suitable for antimicrobial locks and that the optimal minimum dwell time for lock therapy is 4 hours (Table 4).

There is no single preferred antimicrobial lock preparation. Several concentrations of antimicrobial agents and ethanol have been studied in combination with heparin and other anticoagulants (Table 5). When used, antimicrobial locks should have activity against common CLABSI pathogens, the ability to penetrate biofilms, compatibility with anticoagulants such as heparin or an alternative ion chelator such as citrate, and prolonged stability.<sup>61</sup> In addition, they should have low risk of toxicity and low potential for inducing antimicrobial resistance. Ampicillin and other  $\beta$ -lactam agents, with and without an extended spectrum, have been studied in combination with heparin and form stable locking solutions. Aminoglycosides and vancomycin have been studied with different additives such as heparin, citrate, and tissue plasminogen activator (TPA).<sup>61</sup> In the NICU population, there is insufficient evidence for the effectiveness and safety of citrate locking solutions, although some institutions use sodium citrate 4% as the anticoagulant in the antimicrobial locks in combination with antimicrobial agents such as cefepime, vancomycin, or gentamicin.<sup>62</sup>

The safety and efficacy of ethanol locks have not been studied in NICU patients, but limited data exist on their use in infants with intestinal failure<sup>63</sup> as young as 0.3 years and who weigh at least 5 kilograms.<sup>64–70</sup> A recent systematic review and meta-analysis concluded that prophylactic ethanol locks in patients with intestinal failure reduced CLABSIs and catheter replacements but were associated with an increased need for catheter repair.<sup>71</sup> The potential for alcohol-related toxicity was also assessed in a pilot study that enrolled 10 infants (mean age, 3.5 months; mean weight, 4.5 kg). Blood-alcohol concentrations were assessed 1 hour after a 0.4 mL dose of ethanol was flushed through the CVC, equivalent to the volume that would be used during ethanol lock therapy.<sup>72</sup> At

Table 5. Examples of Antimicrobial Locks<sup>96</sup>

| Antimicrobial Lock Therapy | Vial Concentration                           | Vol. 1mL | Vol. 2mL | Vol. 3mL | Vol. 5mL | Final Concentration | Stability           |
|----------------------------|--|----------|----------|----------|----------|---------------------|---------------------|
| Vancomycin                 | Vancomycin 50 mg/mL vial                     | 0.2      | 0.4      | 0.6      | 1.0      | 10 mg/mL            | 7 days refrigerated |
| vanconiye                  | 0.9% normal saline (NS)                      | 0.8      | 1.6      | 2.4      | 4.4      |                     | , aayo rogeracca    |
|                            | Vancomycin 5 mg/mL solution (dilute with NS) | 0.5      | 1.0      | 1.5      | 2.5      | 2.5 mg/mL           |                     |
|                            | Heparin 100 units/mL                         | 0.5      | 1.0      | 1.5      | 2.5      | 50 units/mL         |                     |
| Gentamicin                 | Gentamicin 10 mg/mL vial                     | 0.5      | 1.0      | 1.5      | 2.5      | 5 mg/mL             | 7 days refrigerated |
|                            | 0.9% NS                                      | 0.5      | 1.0      | 1.5      | 2.5      |                     |                     |
| Ceftazidime                | Ceftazidime 100 mg/mL vial                   | 0.1      | 0.2      | 0.3      | 0.5      | 10 mg/mL            | 7 days refrigerated |
|                            | Heparin 100 units/mL                         | 0.5      | 1.0      | 1.5      | 2.5      | 50 units/mL         |                     |
|                            | 0.9% NS                                      | 0.4      | 0.8      | 1.2      | 2.0      |                     |                     |
| Amphotericin B*            | Amphotericin B 5 mg/mL vial                  | 0.5      | 1.0      | 1.5      | 2.5      | 2.5 mg/mL           | 7 days refrigerated |
|                            | Heparin 100 units/mL                         | 0.5      | 1.0      | 1.5      | 2.5      | 50 units/mL         |                     |

<sup>\*</sup>Rarely used since removal of catheter is recommended in the setting of fungemia.

5 minutes, 8 patients had undetectable blood alcohol concentrations and 2 patients had alcoholaemia of 0.011%. At 1 hour, blood alcohol concentrations were undetectable in all infants and there was no evidence of hepatic injury. No data are available on the repeated use of ethanol locks in the neonatal population. The cost and general availability of ethanol lock solutions many limit their potential use.

Practical guidance for implementation when the decision is made to use antimicrobial lock therapy is presented in Table 6.

# Question 8: Should prophylactic antimicrobials be administered to a NICU patient at the time of PICC removal to reduce the incidence of CLABSI or culture-positive sepsis?

#### Answer 8:

 Prophylactic antimicrobials are not recommended at the time of PICC removal.

The proposed rationale for prophylactic antimicrobials administered to NICU patients at the time of PICC removal is to mitigate the potential impact of dislodgement of intra- or extra-luminal bacterial biofilm and subsequent bacteremia that elevates the frequency of BSI or culture-positive sepsis in the days following catheter removal. The actual risk of BSI following catheter removal is not well described. One single-center, retrospective, cohort study of 101 preterm infants did not identify an increased risk of catheter-related BSI in the 48 hours following removal of PICCs. A second retrospective cohort study that included 1,002 PICCs in 856 infants did not find a difference in the prevalence of BSIs or culture-negative sepsis when comparing the 72 hours before PICC removal to the 72 hours after removal.<sup>74</sup> However, for infants with birth weight <1,500 grams, the odds for culture-negative sepsis increased 6.3-fold following removal of PICC not used for antimicrobial delivery (95% CI, 1.78–26.86; P < .01).<sup>74</sup> A third retrospective cohort study conducted before the widespread implementation of CVC insertion and maintenance bundles reported a high rate of culture-positive sepsis within 5 days of PICC removal (24 of 345, 7%).<sup>75</sup> The incidence of sepsis was lower in infants who received antimicrobials at the time of catheter removal: 2 (1.5%) of 132 versus 22 (10.3%) of 213 (P = .002).

Subsequent studies have not demonstrated a benefit to prophylactic antimicrobials before PICC removal. One retrospective study identified no difference in clinical or culture-positive sepsis in 137 infants who received a single dose of vancomycin before PICC removal and 64 infants who received no antimicrobial. 76 In a second retrospective cohort study of 216 NICU patients with PICCs, the occurrence of microbiologically proven (n = 6) or clinical sepsis (n = 8) was uncommon within 5 days of catheter removal, and no benefit was identified with antimicrobial use at the time of PICC removal (OR, 0.6; 95% CI, 0.1–2.7; P = .74). A single randomized, unblinded trial enrolled 88 infants who received intravenous cefazolin administered 1 hour before or 12 hours after catheter removal.<sup>78</sup> Although the authors reported a difference in culture-positive sepsis within 48 hours (0% of treated infants vs 11% of controls, P = .021), there were significant methodological issues, and subsequent analyses suggested that this difference was not statistically significant (RR, 0.09; 95% CI, 0.01-1.60).<sup>79,80</sup> No studies have systematically evaluated potential harms of antimicrobial prophylaxis at the time of catheter removal, such as impact on the neonatal microbiome. A 2018 Cochrane review concluded that there is insufficient evidence to assess the efficacy or safety of antimicrobials given at the time of catheter removal.<sup>79</sup>

### Question 9: What are practical considerations for the implementation of a neonatal vascular access team (VAT)?

#### Answer 9:

- NICUs should consider use of a VAT. Such teams have demonstrated effectiveness in reducing catheter-related complications and are cost-effective.<sup>22,81-83</sup>
- VAT proceduralists should receive education and clinical training, and upon completion, demonstrate knowledge and proficiency in PICC insertion, care, and removal, and a commitment to the team-based approach.
- VAT proceduralists should successfully insert a predefined number of PICCs as defined by the local facility's delineation of privileges.
- The team should monitor relevant quality measures (see Table 7).

Table 6. Antimicrobial Lock Implementation

#### Instilling an Antimicrobial Lock

- 1. Order the antimicrobial lock therapy through the electronic medical record system, if used in the facility, to avoid errors
- 2. Obtain pharmacy-dispensed volume-specific syringes for each lumen
- 3. Prepare for:
  - a. 4 hours of dwell time (optimal)
- b. Changing all line locks solutions inserted into ports every 24 hours
- 4. Flush each lumen with 0.9% sodium chloride before instilling the antimicrobial lock
- 5. At the end of the dwell time, withdraw the instilled antimicrobial lock priming volume and discard. Some institutions will withdraw an additional 0.1 mL, or an additional percentage of the total volume
- 6. After removing and discarding the lock, flush the lumen(s) with 0.9% sodium chloride before infusion of other medications or fluids through the line
- 7. If patient is being transferred to a procedure area (line may be accessed), withdraw all lock solutions prior to patient leaving the unit
- 8. Obtain VAT evaluation and intervention if unable to withdraw antimicrobial lock from any lumen

#### Assessing Fill or Priming Volume of Existing CVCs

- 1. Perform hand hygiene
- 2. Disinfect cap/lumen connection with hospital-approved antiseptic
- 3. Clamp the lumen and remove existing needleless access device from the CVC hub of the lumen
- 4. Attach empty 3 mL luer-lock syringe directly to the hub of the lumen
- 5. Aspirate plunger slowly and gently until blood reaches the end of the hub
- 6. Clamp the line
- 7. Remove the syringe: the volume of fluid in the 3 mL syringe is the volume to be used for the lock volume
- 8. Flush the line

Table 7. Neonatal Vascular Access Team (VAT) Training, Evaluation, and Responsibilities 15

| After receiving training, <b>who</b> may be a proceduralist on a Neonatal VAT?                                | Neonatal nurse practitioners, registered nurses (in accordance with State Board of Nursing scope of practice), neonatal fellows with appropriate supervision, neonatologists  |
|---|---|
| What should clinical training and education for proceduralists include?                                       | <ul> <li>Indications and contraindications of PICC placement</li> <li>Increased awareness of pain management</li> <li>Knowledge of the anatomy of venous and arterial systems</li> <li>Maintenance of the sterile insertion bundle</li> </ul>   |
| What <b>knowledge and clinical competencies</b> should a proceduralist be able to demonstrate after training? | <ul> <li>Knowledge of published guidelines and standards of infusion therapy</li> <li>Appropriate catheter care and maintenance</li> <li>Ability to recognize and manage complications</li> <li>Successful placement of at least 5 PICC lines</li> </ul>  |
| <b>How many procedures</b> should a proceduralist perform to maintain competency?                             | Proceduralists should consistently perform a requisite number of procedures, as defined by the local facility's delineation of privileges. At a minimum, a proceduralist should perform 5 successful PICC insertions per year   |
| What are examples of <b>quality measures</b> that a VAT should monitor?                                       | <ul> <li>Success rate of individual proceduralists</li> <li>Rates of complications (CLABSI, thrombus, pericardial and pleural effusions, etc.)</li> <li>Confirmation of final line location via radiographic imaging or point-of-care ultrasound</li> </ul>   |
| What <b>additional responsibilities</b> might a VAT handle?   | <ul> <li>Troubleshooting and managing complications</li> <li>Providing formal and informal staff education related to care and maintenance of central lines</li> <li>Performing catheter site surveillance and dressing changes</li> <li>Discussing removal of PICC line when patient reaches 120 ml/kg/day of enteral intake<sup>97</sup></li> </ul> |

This document defines VAT as any organized group of HCP involved in the management of vascular access. Prevention of CLABSIs benefits from the establishment of a team dedicated to all aspects of intravenous therapy. A recommendation of the Consensus Conference on Prevention of Central-Line–Associated Bloodstream Infections was the establishment of dedicated intravenous therapy teams, citing studies that showed reductions in infections and complications from central and peripheral intravenous catheters.<sup>84</sup> In practice, the duties of VATs toward the catheters they care for vary by institution. The authors suggest that the VAT's responsibilities include catheter insertion, daily inspection, and maintenance, as well as development and education related to policies and

procedures. A dedicated team with expertise in PICC assessment, placement, and care can serve as an invaluable resource for the NICU. The VAT also can provide information to infection preventionists in the form of data collection and identification of trends to inform quality improvement efforts. Including the team members in infection prevention meetings will assist in guiding the focus of prevention during insertion of the PICC. Duties may also include investigation of positive blood cultures, in conjunction with the healthcare epidemiology and infection prevention teams. This places the focus of the team on prevention rather than just job duties. In one medical center, including a VAT as part of a "better bundle" strategy was associated with a significant decrease in CLABSIs. Published guidelines state

that specialized "IV teams," such as the VAT, have shown unequivocal effectiveness in reducing the incidence of catheter-related BSI (CR-BSI), associated complications, and costs.<sup>81</sup>

Proper sterile technique during the placement of CVCs remains paramount for reduction of CLABSIs. Standardization of procedures for long-term maintenance of CVCs helps to reduce the incidence of CLABSIs in intensive-care patients. <sup>86</sup> An identified VAT allows organizations to centralize the responsibility for PICC-related activities with a select group of proceduralists, thus enhancing accountability and ultimately, clinical outcomes. <sup>83</sup> The upfront investment in a VAT results in cost savings from a reduction in the number of CLABSIs and other CVC-related complications. In one NICU, the initiation of a dedicated PICC insertion and maintenance team resulted in a nearly 50% decrease in the risk of CLABSI in patients who required long-term central venous access (ie, >30 days). <sup>87</sup>

Additionally, by developing a VAT, a facility may reduce the resources spent training and retraining proceduralists and ancillary support staff in central-line insertion and maintenance. Regardless, standards for the training of proceduralists vary. A recent national survey showed that most proceduralists attend informal training sessions, with less stringent training requirements for physicians than registered nurses or nurse practitioners. Many of proceduralists have <5 successful placements before being allowed to insert a PICC independently. Table 7 provides a list of recommended education, training, and competencies for members of a neonatal VAT.

### Question 10: What threshold should prompt a NICU to consider implementing additional preventive measures?

#### Answer 10:

- Zero CLABSIs is the aspirational and potentially achievable goal.
   Although there is no nationally endorsed threshold above which additional CLABSI prevention measures should be implemented, a variety of quantitative or qualitative metrics may be utilized to identify CLABSI prevention success over time and determine when additional intervention is necessary.
- A decision to identify a threshold for action in an individual NICU should assess a variety of factors including the following:
  - An SIR or rate of CLABSI that is above goal or increasing despite the consistent implementation of current organizational interventions
  - Local interest in setting a specific lower target with input from Infection Prevention and Control (infection preventionists, healthcare epidemiologist)
  - Patient mix and clinical acuity, which may predict general likelihood of CLABSI
  - Resource and personnel capacity for initiation and/or maintenance of specific interventions and practice processes.
- Any quantitative or qualitative metric that is defined should be developed and accepted by all stakeholders.

CLABSI prevention should be a continuous goal and integrated into usual NICU practices and processes. Successful CLABSI prevention requires attention to the importance of practices related to central-line insertion and maintenance over time and collaboration among a variety of stakeholders, including infection preventionists, nurses, physicians, advanced practice HCP, and educators, among others. The decision to increase infection prevention efforts requires the involvement of NICU leadership or a local champion to ensure that new processes

and education are prioritized within existing workflows. Individual units have achieved very low rates of CLABSIs–even zero CLABSIs–over sustained periods.<sup>6,22</sup>

A variety of quantitative metrics can be used to reveal a lapse in CLABSI prevention success. Quantitative metrics may include total NICU-wide CLABSI incidence over a predefined period, compared to a similar period that allows for adjustment for time-varying confounders (eg, season, census, staff shortages, and turnover). Alternatively, an absolute number of CLABSIs may be deemed "acceptable" in a particular NICU for a given period or a given patient census. Either of these metrics also may be considered for a subset of high-risk infants as a marker for general CLABSI prevention effectiveness (eg, postoperative patients, premature infants, and others). Lastly, a NICU may consider a predefined target standard infection ratio (SIR), a risk-adjusted metric generated by the CDC using NICU-specific surveillance data reported to NHSN (eg, SIR < 1.0). 89

NICUs may also choose to increase CLABSI prevention efforts based upon rigorously evaluated or even anecdotal qualitative observations in the unit. Qualitative observations can be performed actively on an ad hoc basis or via routine mechanisms such as team huddles with checklists or overt comprehensive audits of any or all practices. Real-time perceptions among staff of waning vigilance toward CVC maintenance practices or repeated breaches in protocol for specific practices related to line insertion or maintenance must be taken seriously and properly investigated. Ultimately, any developed target metric that may trigger more intensive CLABSI prevention efforts should be acceptable to all a priori, particularly those involved with CVC use and CLABSI prevention at the bedside.

Before a decision is made to introduce new processes for CLABSI prevention, it is important to assess the adherence to existing prevention practices in the NICU in a systematic fashion, for example, through a quality improvement (QI) program. Such assessments should include direct input from infection preventionists, nurses, advance practice HCP, and physicians. If additional CLABSI measures are deemed necessary, it is helpful to distinguish between those shown to be effective and those that are not proven robustly but may have an impact nonetheless. Known effective evidence-based interventions have been identified by the CDC and other experts (Table 3).<sup>8,17</sup>

If an effort to enhance CLABSI prevention activities is deemed necessary, it must be recognized that staff at various levels of responsibility may have different attitudes or willingness to add tasks to the workflow. Simply having a written policy is insufficient to effect practice change(s) that will lead to fewer CLABSIs. In 2011, a national survey noted that 84%−93% of NICUs had written policies for insertion checklist and for bundle practices, but ≥75% adherence for individual components was achieved only 68%−73% of the time for at least 1 component and only 28% for all monitored processes. Allowance for adaptations (dependent on local workflows and priorities) is important, and quantitative metrics should be used as a guide to effectiveness. 2

## Question 11: What preventive bundle elements, above and beyond those recommended by the CDC, could be considered by a NICU experiencing ongoing CLABSIs?

#### Answer 11:

Additional practices that lack robust evidence may be effective.
 NICUs may consider many different products, technologies, and processes, some of which are described below.

 Implementation of an expanded NICU central-line care bundle should take into account the risks and benefits of additional measures, as well as the needs, resources, and local expertise at individual institutions.

• If implemented, the impact of these practices should be evaluated by a multidisciplinary team.

Evidence-based care bundles effectively reduce CLABSIs in the NICU. A meta-analysis performed by Payne et al<sup>4</sup> reported a 60% decrease in CLABSI rates after the introduction of a care bundle in neonatal units. Additionally, care bundles contribute to a reduction in total central-line use and duration. The CDC has recommended basic insertion and maintenance bundles for all patients with CVCs, including NICU patients (Table 3). Nevertheless, published reports suggest substantial variability in bundles utilized in NICUs and little consensus about what constitutes the optimal bundle. A variety of CLABSI prevention bundles with different individual components have been shown to minimize CLABSIs in NICU settings, although most include hand hygiene, maximal sterile barrier precautions, and effective skin antisepsis. 93 Few studies have compared the effectiveness of different bundles in a way that permits assessment of individual bundle components.

Throughout this document, we have reviewed practices and products that could be added to basic prevention bundles, including CHG bathing, CHG-containing sponges at central-line insertion sites, ethanol disinfectant caps, and prophylactic antimicrobial locks. Additional practices may be effective and have been implemented by some NICUs, but they lack robust evidence and therefore have not been reviewed in detail in these recommendations. Such practices include but are not limited to regular sharing of CLABSI incidence data with NICU staff, the use of nonsterile gloves for all central-line care,94 and a standard process for assessing when to discontinue a central line, such as when the infant is tolerating full enteral feeds and medications can be provided enterally.<sup>22,95</sup> For the assessment of continued need or discontinuation of a CVC, a short checklist in the daily note of the nurse or physician with discussion on multidisciplinary patient rounds may be a useful tool.

Most studies of bundle effectiveness have been conducted in larger, higher level-of-care NICUs. Similar effectiveness is anticipated in community NICUs that care for infants with CVCs.

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The assessment of disclosed relationships for possible conflicts of interest will be based on the relative weight of the financial relationship (ie, monetary amount) and the relevance of the relationship (ie, the degree to which an association might reasonably be interpreted by an independent observer as related to the topic or recommendation of consideration). The reader of this guidance should be mindful of this when the list of disclosures is reviewed

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