

Infection Control



Summary of Recommendations

Recommendations for Prevention and Control of Infections in NICU Patients: CLABSI

AT A GLANCE

Summary of Recommendations from the Recommendations for Prevention and Control of Infections in NICU Patients: CLABSI guideline.

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Summary of Recommendations

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1.

The use of non-sterile gloves after hand hygiene, but before all patient contact, compared with hand hygiene alone, to reduce central line-associated bloodstream infection (CLABSI) in neonatal intensive care unit (NICU) patients, remains an unresolved issue.

Recommendation 1. details.

No Recommendation

2.a.

Choose the central line type (e.g., umbilical venous catheter (UVC), peripherally inserted central catheter (PICC), tunneled catheter, etc.) based on the clinical needs of the neonatal intensive care unit (NICU) patient.

Recommendation 2.a. details.

Recommendation

2.b.

The choice of central line type to insert in a neonatal intensive care unit (NICU) patient should not be based solely on central line-associated blood stream infection (CLABSI) prevention.

Recommendation 2.b. details.

Recommendation

3.a.

Choose the insertion site appropriate to the central line type to be inserted in a neonatal intensive care unit (NICU) patient (e.g., UVC, PICC, etc.) based on the clinical needs of the patient.

Recommendation 3.a. details.

Recommendation

3.b.

The choice of insertion site in a neonatal intensive care unit (NICU) patient should not be based solely on central line associated blood stream infection (CLABSI) prevention.

Recommendation 3.b. details.

Recommendation

| Consider choosing the fewest number of lumens based on the clinical needs of the neonatal intensive care unit patient. |
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| 5. |
| Consider the use of alcohol-containing chlorhexidine for skin antisepsis to prevent central line-associated blood stream infection (CLABSI) in neonatal intensive care unit (NICU) patients in whom the benefits are judged to outweigh the potential risks. Gestational age, chronologic age, and skin maturity should be considered when assessing risks and benefits of chlorhexidine-containing agents in determining eligible patients. |
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| Consider use of chlorhexidine bathing to prevent central line-associated blood stream infection (CLABSI) in neonatal intensive care unit (NICU) patients in whom the benefits are judged to outweigh the potential risks. |
| Recommendation 6.a. details. |
| Conditional recommendation |
| 6.b. |
| The identification of neonatal intensive care unit (NICU) patients who might benefit from chlorhexidine bathing remains an unresolved issue. |
| Recommendation 6.b. details. |
| No recommendation |
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| If undertaken, the frequency of chlorhexidine bathing for neonatal intensive care unit (NICU) patients remains an unresolved issue. |

Recommendation 6.c. details.

| No recommendation |
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| 7. |
| Minimize the number of times central line hubs are accessed and minimize blood sampling through central lines to decrease the risk for central line-associated blood stream infection (CLABSI) in neonatal intensive care unit (NICU) patients. |
| Recommendation 7. details. |
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| Consider central line antimicrobial locks for neonatal intensive care unit (NICU) patients in addition to core infection prevention and control strategies when a unit is experiencing ongoing central line-associated blood stream infection (CLABSIs). |
| Recommendation 8. details. |
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| 9.a. |
| Remove umbilical venous and umbilical arterial catheters in neonatal intensive care unit (NICU) patients as soon as possible and when no longer needed due to the concern for increasing risk of central line-associated blood stream infection (CLABSI) associated with each day of increasing dwell time. |
| Recommendation 9.a. details. |
| Recommendation |
| 9.b. |
| Consider removal of umbilical artery catheters at or before 7 days of dwell time in neonatal intensive care unit (NICU) patients. |
| Recommendation 9.b. details. |
| Conditional Recommendation |
| 9.c. |
| Consider removal of umbilical venous catheters at or before 7 days of dwell time in neonatal intensive care unit (NICU) patients. |

Recommendation 9.c. details.

| Conditional Recommendation |
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| 9.d. |
| Consider removal of umbilical venous catheters and inserting a peripherally inserted central catheter (PICC) or other long-term central venous catheter at or before 7 days of umbilical venous catheter dwell time for neonatal intensive care unit (NICU) patients requiring long term central venous access. |
| Recommendation 9.d. details. |
| Conditional Recommendation |
| 10.a. |
| For neonatal intensive care unit (NICU) patients, remove peripherally inserted central catheters (PICCs) as soon as possible and when no longer needed due to the concern for increasing risk of central line-associated blood stream infection (CLABSI) associated with increasing dwell time. |
| Recommendation 10.a. details. |
| Recommendation |
| 10.b. |
| For neonates with ongoing need for central venous access, whether to remove and replace a peripherally inserted central catheter (PICC) that has been in place for a prolonged period of time to reduce central line-associated blood stream infection (CLABSIs) in neonatal intensive care unit (NICU) patients remains an unresolved issue. |
| Recommendation 10.b. details. |
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| Consider implementing a dedicated catheter care team to prevent central line-associated blood stream infection (CLABSI) in neonatal intensive care unit (NICU) patients. |
| Recommendation 11. details. |
| Conditional Recommendation |

Use "bundled" interventions for central line insertion and maintenance as part of a single or multiple intervention quality improvement effort to reduce rates of central line-associated blood stream infection (CLABSI) in neonatal intensive care unit (NICU) patients. Elements of insertion and maintenance bundles for all patients have been recommended by the Centers for Disease Control and Prevention.

Recommendation 12. details.

Recommendation

13.

Do not use prophylactic antimicrobial infusions routinely to decrease the risk of bacterial central line-associated blood stream infection (CLABSI) in neonatal intensive care unit (NICU) patients.

Recommendation 13. details.

Recommendation

14.

Do not use prophylactic anticoagulant infusions for the purposes of preventing central line-associated blood stream infection (CLABSI) in neonatal intensive care unit (NICU) patients.

Recommendation 14. details.

Recommendation

Recommendation 1

The use of non-sterile gloves after hand hygiene, but before all patient contact, compared with hand hygiene alone, to reduce central line-associated bloodstream infection (CLABSI) in neonatal intensive care unit (NICU) patients, remains an unresolved issue. (No Recommendation)

- Supporting Evidence: One randomized, non-blinded, controlled trial.[3]
- Level of Confidence in the Evidence: The level of confidence in this evidence is moderate due to imprecision.
- *Benefits:* The evidence suggested a benefit to using non-sterile gloves after hand hygiene and prior to all patient contact to decrease possible CLABSI and gram-positive bloodstream infections (BSIs) in a subset of preterm infants (for infants <1000 g or <29 weeks gestational age and <8 days old) admitted into a single facility. Definitive CLABSI diagnosed using the 2008 National Healthcare Safety Network (NHSN) definition were not reduced.[4]
- Risks and Harms: Harms were not assessed in this study.
- Resource Use: Implementing glove use after hand hygiene could likely result in an increase in material cost, but it is anticipated that this cost could be offset by the decrease in costs associated with CLABSI.
- Benefit-Harm Assessment: Even though harms were not assessed, the evidence suggested a potential benefit to implementing glove use after hand hygiene practices as a part of infection prevention and control practices with the potential to decrease possible CLABSI and grampositive BSI in preterm infants.
- Value Judgments: Value judgments considered in the formulation of this recommendation include the age of the study compared to the current standard of care, and patient safety.

- *Intentional Vagueness:* The standard of care for hand hygiene in a given NICU may be different from the control in this study (alcohol hand rub or use of an antimicrobial soap, e.g., 2% chlorhexidine gluconate). Hand hygiene compliance reported in this study was 79%. It is unknown if similar outcomes would have been reported with higher compliance.
- Exceptions: There are no exceptions to this recommendation.

Recommendation 2.a.

Choose the central line type (e.g., umbilical venous catheter (UVC), peripherally inserted central catheter (PICC), tunneled catheter, etc.) based on the clinical needs of the neonatal intensive care unit (NICU) patient. (Recommendation)

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Recommendation 2.b.

The choice of central line type to insert in a neonatal intensive care unit (NICU) patient should not be based solely on central line-associated blood stream infection (CLABSI) prevention. (Recommendation)

- Supporting Evidence: Eleven observational studies.[5-15]
- Level of Confidence in the Evidence: The level of confidence in this evidence is very low due to imprecision: each study compared different interventions and reported heterogeneous outcome measures for infection. Three studies compared UVCs to PICCs. Six studies compared various catheter types that included umbilical arterial catheters (UACs), UVCs, percutaneous arterial catheters, percutaneous venous catheters, peripherally inserted central catheters, phlebotomy catheters, extended dwell peripheral intravenous catheters (EPIV), and tunneled catheters. Four of these studies were conducted after the widespread implementation of central line insertion and maintenance bundles in 2010.
- **Benefits:** This evidence did not suggest clear benefit of one catheter type over another; however, the studies evaluated different patient populations with varying clinical indications for central venous access, which was likely reflected in the evidence. The variations in dwell time according to catheter type confounded interpretation of the results.
- *Risks and Harms:* One study suggested that the risk of infiltration was higher with PICCs than with other catheter types, and another suggested that the risk of infiltration was higher in EPIVs.
- Resource Use: One study reported that use of EPIVs is more cost effective than PICCs, however this study did not incorporate line success or the cost of hyaluronidase to treat EPIV infiltration into their assessment. Other than this study, the literature search did not retrieve data on the comparative material costs of different catheter types. It is likely that material and human resource costs for insertion and maintenance of each catheter type will vary from facility to facility. Insertion of some catheter types (i.e., tunneled catheters) requires technical expertise that may not be available in all facilities.
- Benefit-Harm Assessment: The balance of benefits and harms was unclear in this evidence. Factors that influence catheter type selection include, but are not limited to, the chronologic and gestational age of the patient, patient size, the presence or absence of congenital abnormalities, prior device utilization, and the projected duration of central venous catheterization. CLABSI prevention is not the primary consideration when choosing which catheter type to insert in a NICU patient.
- Value Judgments: Value judgments considered in the formulation of these recommendations include patient safety and economic and human resource costs.
- Intentional Vagueness: There is no intentional vagueness in these recommendations.
- *Exceptions:* There are no exceptions to these recommendations.

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Recommendation 3.a.

Choose the insertion site appropriate to the central line type to be inserted in a neonatal intensive care unit (NICU) patient (e.g., UVC, PICC, etc.) based on the clinical needs of the patient. (Recommendation)

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Recommendation 3.b.

The choice of insertion site in a neonatal intensive care unit (NICU) patient should not be based solely on central line associated blood stream infection (CLABSI) prevention. (Recommendation)

- Supporting Evidence: Ten observational studies.[16-25]
- Level of Confidence in the Evidence: The level of confidence in this evidence was low due to inconsistent results or no difference. The studies reported heterogeneous outcome measures for infection. The two studies evaluating femoral lines vs. non-femoral lines were conducted in the same NICU with overlapping study periods.[19, .20] All studies were conducted prior to the widespread implementation of central line insertion and maintenance bundles in 2010.
- *Benefits:* The evidence was limited regarding the benefit of one insertion site versus another for percutaneous and tunneled catheters. No benefit of one site versus another was suggested for PICCs.
- *Risks and Harms:* Associations between adverse events and insertion sites were limited and inconsistent, but data suggested that adverse events were associated with upper extremities and non-femoral sites.
- Resource Use: The literature search did not retrieve studies comparing resource utilization associated with different insertion sites for tunneled catheters or PICCs. No difference in human or materials costs to place a catheter in one site or another are anticipated, but in two studies, the femoral insertion site was chosen only if insertion in other sites failed. If placement in the first insertion site chosen is technically more challenging and results in multiple attempts, both human and material costs could increase.
- Benefit-Harm Assessment: The benefit associated with different insertion sites was unclear. Limited data suggest an increase in adverse events associated with inserting PICCs in upper extremity sites and non-femoral sites. The choice of catheter insertion site is often limited by the availability of venous access sites in NICU patients.
- Value Judgments: Value judgments considered in the formulation of this recommendation include patient safety and economic and human resource costs, as well as practical considerations. There may be logistical challenges associated with maintaining femoral catheters in diapered children.
- Intentional Vagueness: There is no intentional vagueness in this recommendation.
- *Exceptions:* There are no exceptions to this recommendation.

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Recommendation 4.

Consider choosing the fewest number of lumens based on the clinical needs of the neonatal intensive care unit patient. (Conditional recommendation)

- Supporting Evidence: One randomized controlled trial[26], and two observational studies[24], [27]
- Level of Confidence in the Evidence: The level of confidence in this evidence is low due to imprecision.
- *Benefits:* Two observational studies[24], [27] reported an increase in the adjusted risk or odds of CLABSI with the use of double lumen catheters, compared with single lumen catheters, however there is concern for confounding by indication in these studies. The RCT[26] was small and reported no infections; however, a reduction was found in the number of additional intravenous catheters required with the use of double-lumen catheters.[27]

- *Risks and Harms:* One observational study reported a non-significant increase in complications with double lumens compared with single lumens, however limited conclusions can be drawn from this because this increase also included CLABSI.[27] The RCT[26] reported no difference in adverse events. Notably, increasing number of lumens in other types of catheters has been associated with an increased risk of infection in adults.[28]
- **Resource Use:** No difference in human or material costs associated with the insertion and maintenance of single- versus double-lumen catheters was reported.
- Benefit-Harm Assessment: The balance of benefits or harms was inconsistent across studies; however, the confidence in this evidence is low because patients requiring more care will likely have more CVC inserted or more lumens in their CVCs. Thus, it is likely these studies are subject to confounding by indication. Future publications may change the strength and direction of this evidence. Increasing the number of lumens has been associated with increased risk of thrombotic and other infectious complications in adult populations.
- Value Judgments: Value judgments considered in the formulation of this recommendation include patient safety and economic and human resource costs.
- Intentional Vagueness: There is no intentional vagueness in this recommendation.
- Exceptions: There are no exceptions to this recommendation.

Recommendation 5.

Consider the use of alcohol-containing chlorhexidine for skin antisepsis to prevent central line-associated blood stream infection (CLABSI) in neonatal intensive care unit (NICU) patients in whom the benefits are judged to outweigh the potential risks. Gestational age, chronologic age, and skin maturity should be considered when assessing risks and benefits of chlorhexidine-containing agents in determining eligible patients. (Conditional Recommendation)

- Supporting Evidence: One randomized controlled trial.[29]
- Level of Confidence in the Evidence: The level of confidence in this evidence is very low due to indirectness and imprecision.
- **Benefits:** Alcoholic chlorhexidine gluconate (CHG) for skin preparation for central line insertion and maintenance for CLABSI prevention has demonstrated efficacy in other populations, compared to povidone iodine (PI). In NICU patients, a single study (Garland) reported no reduction in infections when using either alcoholic CHG or PI with an unspecified base for catheter insertion or maintenance.
- *Risks and Harms:* One study reported an increased incidence of CHG absorption after single use for skin preparation; no significant systemic side effects were observed. The clinical impact of this level of systemic CHG absorption on neonatal health and microbiome is unknown. Garland reported no increased risk of contact dermatitis, although the trial enrolled a select group of NICU patients (those weighing >1500 gm and >7 days of age). Harms were not assessed in smaller or younger infants.
- **Resource Use:** There is no additional resource use as skin preparation for central line insertion and maintenance is standard of care. Minimal differences in human, education, and material costs between alcoholic CHG and alcoholic PI are anticipated.
- Benefit-Harm Assessment: The use of CHG for skin preparation is associated with both potential benefits and potential harms. The balance of benefits and harms may vary based on individual patient characteristics (e.g., gestational age, chronologic age, skin maturity).
- Value Judgments: Value judgments considered in the formulation of this recommendation include the age of the studies and the applicability of the evidence base, the current standard of care, and patient safety.
- Intentional Vagueness: The NICU populations for whom CHG skin antisepsis is most appropriate are not clearly defined.
- Exceptions: Alcoholic chlorhexidine will not be appropriate for all NICU patients.

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Recommendation 6.a

Consider use of chlorhexidine bathing to prevent central line-associated blood stream infection (CLABSI) in neonatal intensive care unit (NICU) patients in whom the benefits are judged to outweigh the potential risks. (Conditional Recommendation)

- Supporting Evidence: One randomized controlled trial[30] and 3 observational studies.[31–33]
- Level of Confidence in the Evidence: The level of confidence in this evidence is low due to imprecision. One of the studies was published prior to the widespread implementation of central line insertion and maintenance bundles in 2010.
- **Benefits:** The efficacy of CHG bathing to prevent CLABSI has been demonstrated in other populations. This evidence suggested a benefit to routine CHG bathing for NICU patients in facilities with high baseline rates despite implementation of, and adherence to, insertion and maintenance bundles and infection prevention and control practices. The evidence suggested no benefit to a single CHG bath.
- *Risks and Harms:* Hypothermia was not observed when using CHG washcloths for a single bath.[30] All three studies reported no skin reaction associated with CHG bathing with washcloths or solutions. CHG resistance was not assessed in any of the studies, nor was systemic absorption or effects on the microbiome.
- Resource Use: Implementing CHG bathing could result in an increase in human, education, and material cost, but it is anticipated that this cost could be offset by the decrease in costs associated with CLABSI.
- **Benefit-Harm Assessment:** The evidence suggested a benefit to routine CHG bathing in facilities with high baseline CLABSI rates despite implementation of, and adherence to, insertion and maintenance bundles and infection prevention and control practices. Other adverse events were not reported in association with CHG bathing. The long-term impact of CHG bathing on the development of resistance and cross-resistance was not adequately assessed in the evidence.
- Value Judgments: Value judgments considered in the formulation of these recommendations include the age of the studies compared to the current standard of care, and patient safety.
- *Intentional Vagueness:* The delivery method for CHG bathing (impregnated bath wipes vs traditional bath), the frequency of bathing, and the target population are left intentionally vague in these recommendations.
- Exceptions: CHG bathing will not be appropriate for all NICU patients.

Recommendation 6.b

The identification of neonatal intensive care unit (NICU) patients who might benefit from chlorhexidine bathing remains an unresolved issue. (No recommendation)

- Supporting Evidence: One randomized controlled trial[30] and 3 observational studies.[31–33]
- Level of Confidence in the Evidence: The level of confidence in this evidence is low due to imprecision. One of the studies was published prior to the widespread implementation of central line insertion and maintenance bundles in 2010.
- **Benefits:** The efficacy of CHG bathing to prevent CLABSI has been demonstrated in other populations. This evidence suggested a benefit to routine CHG bathing for NICU patients in facilities with high baseline rates despite implementation of, and adherence to, insertion and maintenance bundles and infection prevention and control practices. The evidence suggested no benefit to a single CHG bath.
- *Risks and Harms:* Hypothermia was not observed when using CHG washcloths for a single bath.[30] All three studies reported no skin reaction associated with CHG bathing with washcloths or solutions. CHG resistance was not assessed in any of the studies, nor was systemic absorption or effects on the microbiome.
- Resource Use: Implementing CHG bathing could result in an increase in human, education, and material cost, but it is anticipated that this cost could be offset by the decrease in costs associated with CLABSI.
- **Benefit-Harm Assessment:** The evidence suggested a benefit to routine CHG bathing in facilities with high baseline CLABSI rates despite implementation of, and adherence to, insertion and maintenance bundles and infection prevention and control practices. Other adverse events were not reported in association with CHG bathing. The long-term impact of CHG bathing on the development of resistance and cross-resistance was not adequately assessed in the evidence.

- Value Judgments: Value judgments considered in the formulation of these recommendations include the age of the studies compared to the current standard of care, and patient safety.
- *Intentional Vagueness:* The delivery method for CHG bathing (impregnated bath wipes vs traditional bath), the frequency of bathing, and the target population are left intentionally vague in these recommendations.
- Exceptions: CHG bathing will not be appropriate for all NICU patients.

Recommendation 6.c

If undertaken, the frequency of chlorhexidine bathing for neonatal intensive care unit (NICU) patients remains an unresolved issue. (No recommendation)

- Supporting Evidence: One randomized controlled trial[30] and 3 observational studies.[31–33]
- Level of Confidence in the Evidence: The level of confidence in this evidence is low due to imprecision. One of the studies was published prior to the widespread implementation of central line insertion and maintenance bundles in 2010.
- **Benefits:** The efficacy of CHG bathing to prevent CLABSI has been demonstrated in other populations. This evidence suggested a benefit to routine CHG bathing for NICU patients in facilities with high baseline rates despite implementation of, and adherence to, insertion and maintenance bundles and infection prevention and control practices. The evidence suggested no benefit to a single CHG bath.
- *Risks and Harms:* Hypothermia was not observed when using CHG washcloths for a single bath.[30] All three studies reported no skin reaction associated with CHG bathing with washcloths or solutions. CHG resistance was not assessed in any of the studies, nor was systemic absorption or effects on the microbiome.
- Resource Use: Implementing CHG bathing could result in an increase in human, education, and material cost, but it is anticipated that this cost could be offset by the decrease in costs associated with CLABSI.
- Benefit-Harm Assessment: The evidence suggested a benefit to routine CHG bathing in facilities with high baseline CLABSI rates despite implementation of, and adherence to, insertion and maintenance bundles and infection prevention and control practices. Other adverse events were not reported in association with CHG bathing. The long-term impact of CHG bathing on the development of resistance and cross-resistance was not adequately assessed in the evidence.
- Value Judgments: Value judgments considered in the formulation of these recommendations include the age of the studies compared to the current standard of care, and patient safety.
- Intentional Vagueness: The delivery method for CHG bathing (impregnated bath wipes vs traditional bath), the frequency of bathing, and the target population are left intentionally vague in these recommendations.
- Exceptions: CHG bathing will not be appropriate for all NICU patients.

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Recommendation 7

Minimize the number of times central line hubs are accessed and minimize blood sampling through central lines to decrease the risk for central line-associated blood stream infection (CLABSI) in neonatal intensive care unit (NICU) patients. (Recommendation)

- Supporting Evidence: One observational study.[34]
- Level of Confidence in the Evidence: The level of confidence in this evidence is very low due to imprecision.
- **Benefits:** The evidence suggested an association between increased catheter manipulations and an increase in catheter-associated bloodstream infections.
- Risks and Harms: Potential harms associated with reduced catheter manipulations were not reported.

- Resource Use: Reducing the number of times catheters are physically accessed could reduce human and material costs because supplies are needed every time the line is accessed; however, thoughtful planning and coordination of multiple access needs is required to achieve this reduction.
- Benefit-Harm Assessment: The evidence suggests benefit to reducing catheter hub manipulations. Reducing the number of times central line hubs are accessed is considered standard of care, and it is unlikely that future research will be conducted in this area.
- Value Judgments: Value judgments considered in the formulation of this recommendation include patient safety and economic and human resource costs.
- *Intentional Vagueness:* "Central line hub access" is left intentionally vague to capture the range of possible manipulations to the hub (e.g., disinfection, access). Strategies to decrease catheter hub manipulation were not assessed.
- Exceptions: There are no exceptions to this recommendation.

Recommendation 8

Consider central line antimicrobial locks for neonatal intensive care unit (NICU) patients in addition to core infection prevention and control strategies when a unit is experiencing ongoing central line-associated blood stream infection (CLABSIs). (Conditional Recommendation)

- Supporting Evidence: Three randomized controlled trials.[35–37]
- Level of Confidence in the Evidence: The level of confidence in this evidence is high because randomized controlled trials are considered at low risk of bias; however, the level of confidence could decrease due to indirectness, as the studies were not conducted in the current standard of care.
- **Benefits:** A reduction in definite catheter-related blood stream infection (CRBSI) was seen in all three studies. No benefit was seen in the outcomes of suspected or probable CRBSI, or BSI without a source.
- Risks and Harms: Harms that could result from this recommendation include hypoglycemia, adverse product-related events, and the development of antimicrobial resistance to the agent used. The presence of a lock results in the interruption of fluid to the neonate: asymptomatic hypoglycemia occurred in greater than 10% of infants during use of the locks, whether the lock contained antibiotics-heparin or saline-heparin. In one study, antibiotic levels were not detected in the majority of NICU infants' blood, and when antibiotics were detected, they were at very low levels.
- Benefit-Harm Assessment: The benefits of CRBSI reduction are balanced with the potential harms of hypoglycemia and the development of antimicrobial resistance. However, all three studies reported high baseline CRBSI rates, which may confound the benefit, as the implementation of evidence-based insertion and maintenance practices has resulted in baseline CRBSI rates that are much lower than the baseline rates at the time of the studies. In the context of high baseline rates, these benefits may outweigh the harms.
- **Resource Use:** The use of antimicrobial lock prophylaxis will result in increased human and material cost; however, in the context of high baseline rates, it is anticipated that this cost could be offset by the decrease in costs associated with reduced infections.
- Value Judgments: Value judgments considered in the formulation of this recommendation include patient safety, facility infection rates, economic and human resource use, and the development of antimicrobial resistance.
- Intentional Vagueness: The antimicrobial agent is not specified in this recommendation. Facilities with ongoing CLABSIs can review their antibiograms and the causal bacteria when determining the optimal antibiotic agent. Not all catheters may be compatible with all antimicrobial agents.
- Exceptions: Some NICU patients require continuous infusions that cannot be interrupted.

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Recommendation 9.a

Remove umbilical venous and umbilical arterial catheters in neonatal intensive care unit (NICU) patients as soon as possible and when no longer needed due to the concern for increasing risk of central line-associated blood stream infection (CLABSI) associated with each day of increasing dwell time. (Recommendation)

- Supporting Evidence: One randomized controlled trial [38] and five observational studies. [6], [11], [39], [40], [27]
- Level of Confidence in the Evidence: The level of confidence in this evidence is very low due to imprecision. Two studies were conducted in the current standard of care. [27], [40]
- Benefits: Increasing risk of infection was reported with increasing UVC dwell time, suggesting a benefit to removing UVCs at the earliest opportunity. Three studies suggested the risk of CLABSI was notably different at either 4 days[11] or 7 days;[39] however, two studies used data collected after the widespread implementation of central line insertion and maintenance bundles in 2010. One of the two studies to be conducted in this era[27], [40] suggested a slight increase in risk at 7 days of dwell time, but the more substantial increases in risk occurred at 14 days of use. The other study noted no difference in CLABSI when UVC duration was extended from 5 to 7 days as a part of a quality improvement (QI) initiative.
- *Risks and Harms:* The evidence suggested that increasing dwell time for UVCs resulted in an increase in the risk of infections, with no difference in other adverse events.
- Resource Use: The impacts of reducing UVC dwell time on material and human resource costs is unknown.
- Benefit-Harm Assessment: While the evidence did not indicate an optimal day by which to remove a UVC to prevent CLABSI, the benefits of removing UVCs at the earliest opportunity outweigh the harms. It is important to note that UVC dwell time and the risk of CLABSI is only one consideration to balance in the clinical needs of a patient.
- Value Judgments: Value judgments considered in the formulation of this recommendation include patient safety and economic and human resource costs.
- Intentional Vagueness: Facilities can determine the need for longer-term access based on patient characteristics.
- *Exceptions:* There are no exceptions to this recommendation.

Recommendation 9.b

Consider removal of umbilical artery catheters at or before 7 days of dwell time in neonatal intensive care unit (NICU) patients. (Conditional Recommendation)

- Supporting Evidence: Two observational studies.[6], [27]
- Level of Confidence in the Evidence: The level of confidence in this evidence is low because observational studies start at low quality evidence in the GRADE methodology. One study[6] was not conducted in the current standard of care.
- *Benefits:* Increasing risk of infection was reported with increasing UAC dwell time in one study[6], suggesting a benefit to removing UACs at the earliest opportunity. The study suggested the risk of sepsis was higher in UACs in situ for ≥8 days when compared with those in situ for ≤7 days. The other study[27] reported two CLABSI, and limited conclusions can be drawn on the impact of UAC dwell time on the risk of CLABSI in this population.
- *Risks and Harms:* The evidence suggested that increasing dwell time for UACs was associated with a higher proportion of infections including occlusion and thrombosis.
- Resource Use: The impact of reducing UAC dwell time on material and human resource costs is unknown.
- **Benefit-Harm Assessment:** While the evidence suggested the optimal duration for UACs may be up to 7 days, the data did not provide certainty regarding the optimal day for UAC removal to prevent CLABSI. It is important to note that UAC dwell time and the risk of CLABSI is only one consideration to balance in the clinical needs of a patient.
- Value Judgments: Value judgments considered in the formulation of this recommendation include patient safety and economic and human resource costs.
- Intentional Vagueness: Facilities can determine the need for longer-term access based on patient characteristics.

• Exceptions: There are no exceptions to this recommendation.

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Recommendation 9.c

Consider removal of umbilical venous catheters at or before 7 days of dwell time in neonatal intensive care unit (NICU) patients. (Conditional Recommendation)

- Supporting Evidence: Four observational studies.[6], [11], [27], [40]
- Level of Confidence in the Evidence: The level of confidence in this evidence is very low due to imprecision and inconsistency across studies.

 Only one study was conducted in the current standard of care.[40]
- Benefits: Increasing risk of infection was reported in association with increasing UVC dwell time, suggesting a benefit to removing UVCs at the earliest opportunity. One study suggested the risk of CLABSI was significantly different at 4 days;[11] however, this study used data collected before the widespread implementation of central line insertion and maintenance bundles in 2010. Two studies were conducted in this era[27], [40] and noted no difference in CLABSI when UVC duration was extended from 5 to 7 days as a part of a quality improvement (QI) initiative. The other reported an increase in risk at 7 days followed by a three-fold increase in risk at 14 days.
- *Risks and Harms:* The evidence suggested that increasing dwell time for UVCs resulted in an increase in the risk of infections, and one of the two studies[27], [40] suggested adverse events such as occlusion were associated with increasing dwell time.
- Resource Use: The impact of reducing UVC dwell time on material and human resource costs is unknown.
- Benefit-Harm Assessment: While the evidence did not suggest an optimal day by which to remove a UVC to prevent CLABSI, the benefits of removal of UVCs at the earliest opportunity outweigh the harms. The data also did not support extending UVC dwell time past 7 days. It is important to note that UVC dwell time and the risk of CLABSI is only one consideration to balance in the clinical needs of a patient.
- Value Judgments: Value judgments considered in the formulation of this recommendation include patient safety and economic and human resource costs.
- Intentional Vagueness: Facilities can determine the need for longer-term access based on patient characteristics.
- *Exceptions:* There are no exceptions to this recommendation.

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Recommendation 9.d

Consider removal of umbilical venous catheters and inserting a peripherally inserted central catheter (PICC) or other long-term central venous catheter at or before 7 days of umbilical venous catheter dwell time for neonatal intensive care unit (NICU) patients requiring long-term central venous access. (Conditional Recommendation)

- Supporting Evidence: One randomized controlled trial [38] and three observational studies. [11], [39], [40]
- Level of Confidence in the Evidence: The level of confidence in this evidence is low due to imprecision. Only one study was conducted in the current standard of care.[40]
- **Benefits:** Increasing risk of infection was reported with increasing UVC dwell time, suggesting a benefit to removing UVCs at the earliest opportunity. Two studies suggested the risk of CLABSI was significantly different at either 4 days[11] or 7 days;[39] however, neither study used data collected after the widespread implementation of central line insertion and maintenance bundles in 2010. The only study to be conducted in this era[40] noted no difference in CLABSI when UVC duration was extended from 5 to 7 days as a part of a quality improvement (QI) initiative.
- *Risks and Harms:* The evidence suggested that increasing dwell time for UVCs resulted in an increase in infection risk, with no difference in other adverse events.
- Resource Use: The impact of reducing UVC dwell time on material and human resource costs is unknown.

- Benefit-Harm Assessment: While the evidence did not suggest an optimal day by which to replace a UVC with a longer-term catheter to prevent CLABSI, the benefits of replacement with a longer-term catheter at the earliest opportunity outweigh the harms. The data also did not support extending UVC dwell time past 7 days. It is important to note that UVC dwell time and the risk of CLABSI is only one consideration to balance in the clinical needs of a patient.
- Value Judgments: Value judgments considered in the formulation of this recommendation include patient safety and economic and human resource costs.
- Intentional Vagueness: Facilities can determine the need for longer term access based on patient characteristics.
- Exceptions: There are no exceptions to this recommendation.

Recommendation 10.a

For neonatal intensive care unit (NICU) patients, remove peripherally inserted central catheters (PICCs) as soon as possible and when no longer needed due to the concern for increasing risk of central line-associated blood stream infection (CLABSI) associated with increasing dwell time. (Recommendation)

- Supporting Evidence: Eight observational studies.[10], [11], [41–46]
- Level of Confidence in the Evidence: The level of confidence in this evidence is very low due to imprecision from heterogeneous outcome definitions and methodologies across studies.
- **Benefits:** The evidence suggested a decreased risk of infection with decreasing PICC dwell time. In some patients, risk is higher in the first two weeks than in the last two weeks; however, there is not clear per-day increase in risk that represents an "inflection point."
- *Risks and Harms:* An increasing risk of infection with an increasing PICC dwell time was reported, but no specific inflection point was determined to suggest that infection risk increases at a specific time. Other PICC-related harms were not reported in relation to dwell time.
- Resource Use: The impact of reducing PICC dwell time on material and human resource costs is unknown.
- Benefit-Harm Assessment: The evidence suggested a decreased risk of infection with decreasing dwell time, and no harms were reported in association with decreased dwell time. Each study assessed different durations of risk for infection, and none of the studies was able to control for how infection risk may vary over time, precluding confidence in an optimal catheter day for PICC removal to prevent CLABSI.
- Value Judgments: Value judgments considered in the formulation of this recommendation include patient safety and economic and human resource costs.
- Intentional Vagueness: There is no intentional vagueness in this recommendation.
- *Exceptions:* There are no exceptions to this recommendation.

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Recommendation 10.b

For neonates with ongoing need for central venous access, whether to remove and replace a peripherally inserted central catheter (PICC) that has been in place for a prolonged period of time to reduce central line-associated blood stream infection (CLABSIs) in neonatal intensive care unit (NICU) patients remains an unresolved issue. (No Recommendation)

- Supporting Evidence: Eight observational studies.[10], [11], [41–46]
- Level of Confidence in the Evidence: The level of confidence in this evidence is very low due to imprecision from heterogeneous outcome definitions and methodologies across studies.
- *Benefits:* The evidence suggested a decreased risk of infection with decreasing PICC dwell time. In some patients, risk is higher in the first two weeks than in the last two weeks; however, there is not clear per-day increase in risk that represents an "inflection point."

- *Risks and Harms:* An increasing risk of infection with an increasing PICC dwell time was reported, but no specific inflection point was determined to suggest that infection risk increases at a specific time. Other PICC-related harms were not reported in relation to dwell time.
- Resource Use: The impact of reducing PICC dwell time on material and human resource costs is unknown.
- Benefit-Harm Assessment: The evidence suggested a decreased risk of infection with decreasing dwell time, and no harms were reported in association with decreased dwell time. Each study assessed different durations of risk for infection, and none of the studies was able to control for how infection risk may vary over time, precluding confidence in an optimal catheter day for PICC removal to prevent CLABSI.
- Value Judgments: Value judgments considered in the formulation of this recommendation include patient safety and economic and human resource costs.
- Intentional Vagueness: There is no intentional vagueness in this recommendation.
- Exceptions: There are no exceptions to this recommendation.

Recommendation 11

Consider implementing a dedicated catheter care team to prevent central line-associated blood stream infection (CLABSI) in neonatal intensive care unit (NICU) patients. (Conditional recommendation)

- Supporting Evidence: Two observational studies.[47], [48]
- Level of Confidence in the Evidence: The level of confidence in this evidence is very low due to imprecision.
- *Benefits:* The evidence consisted of two studies, one reported the clinical outcome of CRBSI and the other reported the surveillance outcome of CLABSI, and both suggested a decrease in risk of infection with the use of a catheter care team in NICU patients. One study suggested CRBSI reductions when patients were stratified by duration of catheter use: patients with an indwelling central line ≥30 days had a 50% lower risk of CRBSIs, while there was no difference in risk of CRBSI for patients with an indwelling catheter <30 days. Another study reported a decrease in CLABSI rate, regardless of birthweight when a catheter care team was implemented.
- Risks and Harms: Harms attributable to the catheter care team were not reported.
- Resource Use: Implementing a catheter care team could result in an increase in human resource cost, but it is anticipated that this cost could be offset by the decrease in costs associated with CLABSI.
- Benefit-Harm Assessment: The benefits outweighed the harms.
- Value Judgments: Value judgments considered in the formulation of this recommendation include the age of the studies compared to the current standard of care, and patient safety.
- Intentional Vagueness: The composition of the catheter care team and assigned duties are not specified.
- Exceptions: Exceptions do not apply to an unresolved issue.

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Recommendation 12

Use "bundled" interventions for central line insertion and maintenance as part of a single or multiple intervention quality improvement effort to reduce rates of central line-associated blood stream infection (CLABSI) in neonatal intensive care unit (NICU) patients. Elements of insertion and maintenance bundles for all patients have been recommended by the Centers for Disease Control and Prevention. (Recommendation)

- Supporting Evidence: Three observational studies.[50–52]
- Level of Confidence in the Evidence: The level of confidence in this evidence is low.

- *Benefits:* The evidence suggested a benefit to using insertion and maintenance bundles to decrease CLABSI. The evidence did not suggest a benefit to one bundle element or a specific combination of bundle elements over another.
- Risks and Harms: Harms of neither specific, nor bundled, interventions were assessed in the studies.
- Resource Use: Implementing insertion and maintenance checklists or bundles could result in an increase in material and human resource cost, but it is anticipated that this cost could be offset by the decrease in costs associated with CLABSI.
- Benefit-Harm Assessment: Even though harms were not assessed, the evidence suggested a benefit to implementing insertion and maintenance bundles as part of infection prevention and control practices with the potential to decrease CLABSI.
- Value Judgments: Value judgments considered in the formulation of this recommendation include the age of the studies compared to the current standard of care, and patient safety. Use of insertion and maintenance bundles has become the standard of care in patients with central lines, including NICU patients.
- *Intentional Vagueness:* The components of insertion and maintenance bundles studied in NICU patients vary, and no study has compared the effectiveness of one bundle versus another in this population. The optimal components of NICU-specific bundles, above and beyond the standard measures recommended by CDC, cannot be determined from the available evidence.
- *Exceptions:* There are no exceptions to this recommendation.

Recommendation 13

Do not use prophylactic antimicrobial infusions routinely to decrease the risk of bacterial central line-associated blood stream infection (CLABSI) in neonatal intensive care unit (NICU) patients. (Recommendation)

- Supporting Evidence: One randomized controlled trial[53] and 3 observational studies.[54–56]
- Level of Confidence in the Evidence: The level of confidence in this evidence is very low due to imprecision resulting from different definitions of outcome measures across studies. One study was considered at high risk of bias. All of the studies were published prior to the widespread implementation of central line insertion and maintenance bundles in 2010.
- *Benefits:* Prophylactic amoxicillin did not result in a reduction of infections. The use of vancomycin prophylaxis did result in a reduction in coagulase-negative staphylococci (CoNS)-related bloodstream infections.
- *Risks and Harms:* An increase in the incidence of thrombotic events was associated with the administration of prophylactic amoxicillin. The long-term impacts of prophylaxis on the development of antimicrobial resistance and the neonatal microbiome were not adequately assessed in these studies.
- Resource Use: One study reported that prophylactic vancomycin resulted in a reduction in overall administration of vancomycin when compared to treatment only with vancomycin; however, this study was small, and its results may not be applicable in every environment.
- **Benefit-Harm Assessment:** The benefits do not clearly outweigh the harms given concerns for the development of antimicrobial resistance. All of the studies were published prior to 2004, and the impact of the use of prophylactic antimicrobials in the current standard of care is unknown.
- Value Judgments: Value judgments considered in the formulation of this recommendation include the time since publication of the studies, patient safety, resource use, and the development of antimicrobial resistance.
- Intentional Vagueness: There is no intentional vagueness in this recommendation.
- Exceptions: There are no exceptions to this recommendation.

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Recommendation 14

Do not use prophylactic anticoagulant infusions for the purposes of preventing central line-associated blood stream infection (CLABSI) in neonatal intensive care unit (NICU) patients. (Recommendation)

- Supporting Evidence: Four randomized controlled trials.[57–60]
- Level of Confidence in the Evidence: The level of confidence in this evidence is moderate due to inconsistent results across studies, heterogeneous outcome measures, and heterogeneous heparin preparations used across studies. All of the studies were published before the widespread implementation of central line insertion and maintenance bundles in 2010.
- **Benefits:** No reduction in catheter-related sepsis associated with the use of prophylactic anticoagulants was reported. Reduction in occlusion was inconsistent across studies.
- *Risks and Harms:* Administering anticoagulant comes with the risk of harm; however, the evidence reported no increase in intravascular hemorrhaging associated with the use of prophylactic anticoagulants.
- **Resource Use:** While resource use data were not retrieved by this literature search, theoretically the implementation of prophylactic heparin could likely increase human and material costs.
- Benefit-Harm Assessment: No benefits were reported, and there is concern that harms are under-reported. There are reasons other than the prevention of CLABSI to administer prophylactic anticoagulants.
- Value Judgments: Value judgments considered in the formulation of this recommendation include patient safety and economic and human resource costs.
- *Intentional Vagueness:* There may be clinical reasons other than the prevention of CLABSI to use prophylactic heparin. The specific anticoagulant agent is left intentionally vague in this recommendation.
- Exceptions: There are no exceptions to this recommendation.

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