CDC and HICPAC Guideline for Infection Prevention in the NICU

Meeting of the Healthcare Infection Control Practices Advisory Committee
March 14, 2013

Disclaimer: The findings and conclusions are draft and have not been formally disseminated by the Centers for Disease Control and Prevention and should not be construed to represent any agency determination or policy.
Guideline Development

GUIDELINE SEARCH

DEVELOPMENT OF KEY QUESTIONS
Review of relevant guidelines to inform key questions

LITERATURE SEARCH
Databases identified; search strategy developed; references stored; duplicates resolved

ABSTRACT AND FULL-TEXT SCREENING
To identify studies which were a) relevant to one or more key questions b) primary analytic research, systematic review or meta-analysis and c) written in English

DATA EXTRACTION AND SYNTHESIS
Data abstracted into evidence tables; study quality assessed

DRAFT RECOMMENDATIONS
Quality of evidence graded; summaries and recommendations drafted

FINALIZE RECOMMENDATIONS
Recommendations and their strength finalized; guideline published
Accomplishments since October

• Evidence and GRADE tables finalized
• Respiratory pathogen, and MRSA narrative summaries revised to incorporate HICPAC feedback
• Narrative summary drafted for CLABSI section and sent to expert review panel
• Discussion with SHEA for implementation guidance companion document
Guideline Team

• Core Writing Group
  – Alex Kallen
  – Martha Iwamoto
  – Jason Newland
  – Alexis Elward
  – Craig Umscheid
  – Brian Leas
  – Gretchen Kuntz
  – Michael Brady
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• Expert Reviewers
Key Questions

I. Respiratory Infection
II. Methicillin resistant *Staphylococcus aureus* (MRSA)
III. *Clostridium difficile* (C difficile)
IV. Central line associated bloodstream infection (CLABSI)
V. Fungal infections
Grading the Evidence

<table>
<thead>
<tr>
<th>Type of evidence</th>
<th>Initial grade</th>
<th>Criteria to decrease grade</th>
<th>Criteria to increase grade</th>
<th>Overall quality grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT</td>
<td>High</td>
<td>Study quality limitations&lt;br&gt;Serious (-1) or very serious (-2) study quality limitations</td>
<td>Strength of Association&lt;br&gt;Strong (+1) or very strong evidence of association (+2)</td>
<td>High</td>
</tr>
<tr>
<td>Observational study</td>
<td>Low</td>
<td>Inconsistency&lt;br&gt;Important inconsistency (-1)</td>
<td>Dose-Response&lt;br&gt;Evidence of a dose-response gradient (+1)</td>
<td>Moderate</td>
</tr>
<tr>
<td>Any other evidence</td>
<td>Very low</td>
<td>Indirectness&lt;br&gt;Some (-1) or major (-2) uncertainty about directness</td>
<td>Confounding&lt;br&gt;Inclusion of unmeasured confounders increases the magnitude of effect (+1)</td>
<td>Low</td>
</tr>
<tr>
<td>(e.g. expert opinion)</td>
<td></td>
<td>Imprecision&lt;br&gt;Imprecise or sparse data (-1)</td>
<td></td>
<td>Very Low</td>
</tr>
</tbody>
</table>
Overall Quality Grades

- **High**
  - Further research is *very unlikely* to change confidence in the estimate of effect

- **Moderate**
  - Further research is *likely* to impact confidence in the estimate of effect and *may change* the estimate

- **Low**
  - Further research is *very likely* to impact confidence in the estimate of effect and is *likely to change* the estimate

- **Very low**
  - Any estimate of effect is uncertain
Formulating Recommendations

• Three key inputs:
  – Values and preferences used to determine the “critical” outcomes
  – Overall GRADE of the evidence for the “critical” outcomes
  – Net benefits, net harms, or trade-offs that result from weighing the "critical" outcomes

• Recommendations
  – For or against (direction)
  – Strong or weak (strength)
CDC and HICPAC -Updated Categorization Scheme for Recommendations

Category IA
A strong recommendation supported by high to moderate quality evidence suggesting net clinical benefits or harms.

Category IB
A strong recommendation supported by low-quality evidence suggesting net clinical benefits or harms, or an accepted practice (e.g., aseptic technique) supported by low to very low-quality evidence.

Category IC
A strong recommendation required by state or federal regulation

Category II
A weak recommendation supported by any quality evidence suggesting a tradeoff between clinical benefits and harms.

No Recommendation
An unresolved issue for which there is low to very low-quality evidence with uncertain tradeoffs between benefits and harms.

Respiratory Pathogen Revisions

• Categories of Isolation used rather than specific components of personal protective equipment
• Discussion regarding aerosol generating procedures and N95s removed
  – Discussed in other guidance
  – Ongoing topic of scientific investigation
• Staff Cohorting changed to Category II recommendation
• “Rapid” and “early” detection changed to antigen and PCR testing
Respiratory Pathogen Revisions

I.A.2. Personal protective equipment

Recommendations for personal protective equipment that are applicable to all healthcare settings (e.g., ICU, SICU) are specified in the 2007 CDC and HICPAC Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings. The following recommendations are based on our evidence review and are consistent with the 2007 recommendations.

a) Contact precautions
   i. Contact precautions before direct contact with patients or surfaces and articles in close proximity to a NICU patient with any respiratory infection, including Rhinovirus, human metapneumovirus, Bocavirus, undifferentiated suspected viral illness, influenza, parainfluenza, adenovirus infection, pertussis, and varicella. **(Category IB)**
I.A.2. Personal protective equipment

a) Contact precautions (continued)

ii. Wear a gown whenever anticipating that clothing will have direct contact with the infected patient or potentially contaminated environmental surfaces or equipment. *(Category IB)*

iii. Remove gown and gloves and observe hand hygiene before leaving the patient-care environment. *(Category IB)*

iv. Maintain isolation precautions for the duration of illness (Category IB)
I.A.2. Personal protective equipment (continued)
b) Droplet precautions
   i. Wear a facemask upon entry into the room or cubicle of patients known or suspected to be infected with pathogens transmitted by respiratory droplets (influenza, parainfluenza, adenovirus, and pertussis) that are generated by a patient who is coughing or sneezing. (Category IB)
   ii. Further research is needed on the benefit of routinely wearing eye protection, in addition to facemask, for close contact with patients with respiratory infection. (No recommendation/unresolved issue)
Respiratory Pathogen Revisions

I.A.4. Cohorting of healthcare personnel

During outbreaks, assign dedicated healthcare personnel to care for one patient cohort and not move between patient cohorts (e.g., restrict personnel who give care to infected or exposed patients from giving care to uninfected or unexposed patients). (Category II)

In an nonoutbreak setting, assign dedicated healthcare personnel based primary in the NICU to care for one patient cohort and not move between patient cohorts when feasible assessing the risks and benefits (e.g., restrict personnel who give care to infected or exposed patients from giving care to uninfected or unexposed patients). (Category II)
I.A.5. Active detection

Perform antigen detection or molecularly based diagnostic laboratory tests for RSV, influenza, parainfluenza, and pertussis on NICU patients who have symptoms of illness or who have been exposed to the particular respiratory pathogen. Promptly implement appropriate isolation precautions prior to testing for symptomatic or exposed patients. Isolation precautions should be maintained for the duration of symptoms even if laboratory testing is negative. (Category IB)
Respiratory Pathogen Revisions

Evidence Review Table I.C. What is the most effective diagnostic approach to identifying respiratory pathogen outbreaks in the NICU?

I.C.1. Promptly perform PCR assay or antigen detection laboratory testing on patients who are suspected to be infected or who have been exposed to persons with RSV infection. *(Category IB)*
Evidence Review Table I.C. What is the most effective diagnostic approach to identifying respiratory pathogen outbreaks in the NICU? (continued)

I.C.2. Promptly perform PCR assay or antigen detection laboratory testing on patients who are suspected to be infected or who have been exposed to persons with adenovirus infection. (Category IB)

I.C.3. Promptly perform PCR assay if available on patients suspected to be infected with or who have been exposed to persons with pertussis infection. Do not use serology (Category IB).
MRSA revisions

- Categories of isolation used rather than components of PPE
- Tier I and II language used to differentiate between outbreak and nonoutbreak settings
- Education recommended for families in addition to healthcare personnel
QIII.A. What are the risk factors for MRSA colonization or infection in NICU patients?

*Draft recommendation:*

Minimize central line duration, mechanical ventilation use and duration and antibiotic use in all NICU patients, particularly those at higher risk for MRSA infection such as low birth weight, younger gestational age, multiple gestation or those colonized with MRSA *(Category IB)*
Q III.C.8 What are the most effective measures to prevent hospital-acquired infection or colonization with MRSA?

*Draft recommendation*

III.C.8. Education of healthcare personnel
Educate all healthcare personnel and families on preventing transmission of MRSA, including medical, nursing, laboratory, and maintenance personnel, students, volunteer staff, visitors and families. *(Category IB)*
CENTRAL LINE-ASSOCIATED BLOODSTREAM INFECTION (CLABSI) SECTION
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Intervention Bundles

*Narrative evidence summary*

- Ten studies evaluated the use of bundled interventions to prevent central line-associated bloodstream infections (CLABSI) among neonates. Low quality evidence from these ten studies suggested a benefit to the bundled interventions.

- This was based on a reduction, in all ten studies, in a bloodstream infection (BSI)-related outcome such as the CLABSI rate, the proportion of patients with a late-onset nosocomial infection, or the proportion of patients with a catheter–related BSI infection (CRBSI).
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Draft recommendation:

Use “bundled” interventions for central line insertion and maintenance as part of a single or multiple facility quality improvement effort to reduce rates of CLABSIs. Bundled interventions should include staff education and efforts to promote adherence to recommended practices (e.g., checklist). Category IB
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Hand Hygiene Promotion

**Narrative evidence summary**

• Two studies evaluated the effect of hand hygiene promotion on the incidence of CLABSI in neonatal intensive care units (NICUs). Low quality evidence suggested a benefit to hand hygiene promotional efforts to increase hand hygiene adherence and to decrease healthcare-associated infections.

• This was based on a reduction in both studies in healthcare–associated infections although determining the effect on CLABSI alone was not part of either evaluation. Both studies also identified a significant increase in adherence to hand hygiene.
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

*Draft recommendation:*

Promote adherence to hand hygiene to prevent healthcare-associated infections. Hand hygiene adherence programs should include education of healthcare personnel about the importance of hand hygiene for infection prevention, reminders, and adherence surveillance with feedback of results to frontline providers. *Category IB*
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Number of Umbilical Venous Catheter Lumens

**Narrative evidence summary**

- One randomized trial evaluated the difference in sepsis risk for short-term catheter-related sepsis between single- and double-lumen umbilical venous catheters. Low quality evidence suggested that there was no difference in the proportion of neonates with single- or double-lumen umbilical venous catheters that developed catheter-related sepsis.
- This was based on finding no infections in patients randomly assigned to receive either umbilical catheter. Of note, neonates in this study had catheters only for about 3 days.
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

*Draft recommendation:*

When using umbilical venous catheters, consider using single- or double-lumen catheters as needed. *Category II*
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Central Line Site 1

**Narrative evidence summary**

- Two studies compared the risk for catheter-associated BSIs between percutaneous central catheters placed in the femoral vein versus peripheral veins. Low quality evidence suggested an increase in BSIs in neonates with a percutaneous central catheter placed directly into the femoral vein compared to those placed peripherally (non-femoral).
- This was based on two studies which found that a significantly higher proportion of neonates with a percutaneous central catheter placed at a femoral site developed a BSI or that neonates with a percutaneous central catheter placed at a femoral site had an increase in the adjusted odds ratio for a BSI. The findings in both of these studies might have been biased by the fact that peripheral sites were chosen first and femoral sites were used only if attempts to place a percutaneous central catheter in a peripheral site were unsuccessful.
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

*Draft recommendation:*

When inserting a percutaneous central catheter, consider placement in a peripheral vein instead of placement directly into the femoral vein. **Category II**
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Central Line Site 2

**Narrative evidence summary**

- One study (observational) evaluated the risk of a BSI for percutaneous central catheters placed in the lower extremity peripheral sites (generally saphenous veins) versus upper extremity peripheral sites (antecubital). Very low quality evidence suggested the incidence of BSIs did not differ between percutaneous central catheters placed in upper extremity vs. lower extremity veins.
- This was based on one small study that found the proportion of neonates who developed a CRBSI did not significantly differ between those in whom the percutaneous central catheter was placed in a lower extremity vein compared to those in whom the catheter was placed in an upper extremity vein.
- Cholestasis was higher and time to first complication was shorter for those placed into the upper extremity.
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

*Draft recommendation:*

No recommendation can be made about whether or not percutaneous central catheter placement in upper extremity peripheral veins or lower extremity peripheral veins is preferred. **Unresolved issue**
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Central Line Site 3

Narrative evidence summary

• Two studies evaluated the risk of a BSI for surgically-implanted central lines in neonates placed in either the femoral, subclavian, or jugular site. Very low quality evidence suggested that the risk for BSIs might be highest for the internal jugular site.

• One study evaluated the risk for BSIs among neonates with tunneled central lines placed in femoral sites (via the saphenous veins) compared to those placed in other sites (jugular or subclavian – 67% jugular) and suggested a benefit to central lines placed in a femoral site. The other study evaluated the risk for catheter-associated infections among patients with surgically implanted central lines placed in the internal jugular vein compared to the subclavian vein and suggested a benefit associated with central lines placed in the subclavian vein.
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

*Draft recommendation:*

For long-term surgically-implanted central lines, consider using the subclavian or femoral sites rather than the internal jugular due to an increase in the risk for CLABSIs. **Category II**
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Closed Medication Systems

**Narrative evidence summary**

- Two studies evaluated the effect of closed medication systems on catheter-associated BSIs among neonates. Very low quality evidence did not suggest a clear benefit to closed medication systems for preventing catheter-associated BSIs possibly related to use of different definitions of a closed medication system.
- This was based on conflicting results from the two studies. One study found a decrease in catheter-associated BSIs when closed medication systems were added to several interventions in a single NICU. The second study did not find a significant difference in catheter-associated BSIs between a NICU that implemented a closed system compared to one that did not.
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

*Draft recommendation:*

More research using standardized definitions is needed to define the role of closed medication systems for preventing CLABSIs.

*Unresolved issue*
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Central Line Types

**Narrative evidence summary**

• Four studies evaluated the differential risk of BSIs among neonates with different central line types. Very low quality evidence did not allow for a clear determination about the BSI risk among neonates with different central line types.

• This was based on inconsistent results from the four studies. One study found a significantly higher sepsis rates among neonates with a central venous “Broviac” catheter than those with a percutaneous central catheter. The second study found a significantly higher central venous catheter-associated BSI rate in patients with a peripherally-inserted central line compared to other central lines. The third study was the only study that attempted to adjust rates for patient characteristics and found the relative risk of a BSI for percutaneous central lines and “Broviac” catheters appeared to be significantly higher than that found for umbilical venous catheters; this study did not appear to adjust for the time the catheter was placed, which was shorter for umbilical venous catheters. The fourth study found higher rates of CLABSI among percutaneous central catheters compared to “Broviac” catheters and both were higher than umbilical venous catheters, but no test was applied to determine if these differences were statistically significant.
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

*Draft recommendation:*

More research is needed to determine if specific central line types are associated with different rates of CLABSI among comparable patient types. **Unresolved issue**
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Peripherally-Inserted Central Catheter Replaced at Same Site vs. New Site

**Narrative evidence summary**

- One study evaluated the risk of BSIs for peripherally-inserted central catheters replaced at a new site compared to those replaced over the previous peripherally-inserted central catheter at the same site. Very low quality evidence suggested that BSI rates were higher for peripherally-inserted central catheters placed using an introducer that is placed over the peripherally-inserted central catheter being replaced.
- This was based on significantly higher odds of a CLABSI in the week following replacement in the group in whom the central line was placed over the existing peripherally-inserted central catheter compared to those in whom the central line was placed at a new site.
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

*Draft recommendation:*

Consider placing peripherally-inserted central catheters at a new site rather than through an introducer placed over a peripherally-inserted central catheter that is being replaced. *Category II*
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

In-Line Filters

**Narrative evidence summary**

• Two studies evaluated the use of in-line filters to decrease the incidence of sepsis (1847,3049). Moderate quality evidence suggested no benefit to the routine use of in-line filters to prevent sepsis episodes.

• This was based on two studies that did not find a significant difference in the proportion of neonates who developed sepsis between those with and without in-line filters (1847,3049).
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

*Draft recommendation:*

Do not use in-line filters solely for the prevention of CLABSIs. *Category IA*
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Catheter Care Education

**Narrative evidence summary**

- One study evaluated the effect of an educational program on catheter sepsis rates. Very low quality evidence suggested a benefit to an ongoing, multifaceted staff educational program on preventing catheter sepsis.
- This is based on one study that found a reduction in the proportion of primarily neonates that developed catheter sepsis following the institution of a regular educational-based intervention that highlighted proper catheter care and proper technique when changing parenteral nutrition.
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Draft recommendation:
Conduct regular ongoing education for staff that care for central lines that highlight proper catheter care to prevent CLABSI.s.

Category IB (accepted practice)
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Dedicated Percutaneous Central Line Care Team

**Narrative evidence summary**

• Three studies evaluated the effect of a percutaneous central catheter care team on BSIs. Low quality evidence suggested the use of teams for central line care resulted in lower number of BSIs.

• This is based on two studies that found a reduction in the catheter-associated BSI rate or risk following institution of a percutaneous central catheter care team; however, in one of the studies the significant benefit was only found in the group with a percutaneous central catheter for 30 or more days. In the third study, a significant correlation was found between the number of days the percutaneous central catheter care team did not provide care and the monthly CLABSI rate.
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

*Draft recommendation:*

Allow only trained personnel to insert and care for central lines. **Category 1A**

Use specialized central line care teams that are responsible for dressing changes and exit site care for patients with percutaneously-inserted central catheters. **Category 1B**
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Silver Alginate Dressing

Narrative evidence summary

• Two studies evaluated the effect of silver alginate dressings on BSIs. Moderate quality evidence did not suggest a benefit to the use of silver alginate dressings compared to standard care.

• This was based on two small pilot studies, both of which found a decrease that was not statistically significant in BSIs in neonates using a silver alginate dressing. No adverse skin reactions were identified in either study; one study found a statistically significant increase in serum silver levels but the authors suggest that the levels identified were below that expected to cause toxicity.
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

*Draft recommendation:*

No recommendation can be made about the use of silver alginate dressings for the purpose of reducing CLABSIs. **Unresolved issue**
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Chlohexidine-impregnated Dressing

**Narrative evidence summary**

- Two studies evaluated the effect of chlorhexidine-impregnated dressings on rates of BSIs and catheter colonization. Moderate quality evidence did not suggest a substantial benefit to the use of a chlorhexidine-impregnated disc compared to standard care and also suggested possible use-limiting toxicity in a subgroup of neonates.

- This was based on one study that found that rates of CRBSIs did not differ among neonates receiving central line exit site care with a chlorhexidine-impregnated disc under a polyurethane dressing following skin antisepsis with 70% isopropyl alcohol compared to standard care with 10% povidone-iodine and a polyurethane dressing. A second study of pediatric patients (mean age 21 to 31 months) randomized to a chlorhexidine-impregnated disc under a transparent polyurethane dressing or just a transparent polyurethane dressing found no difference in catheter-associated BSIs. Both studies found lower rates of catheter colonization in the intervention groups.

- Toxicities were evaluated in both studies. In one study, local redness was found in one control patient and in four patients in the chlorhexidine-impregnated dressing group. In the second study in the chlorhexidine-impregnated dressing arm, contact dermatitis developed in 15% of neonates < 1,000 grams and in 1.5% of neonates 1,000 grams or greater.
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

*Draft recommendation:*
Consider using chlorhexidine-impregnated sponge dressings with caution in neonates ≤ 1000 grams due to high rates of cutaneous reactions (about 15% required discontinuation) especially within the first two weeks of life.

*Category II*
No recommendation can be made about the use of chlorhexidine-impregnated sponge dressings in neonates >1,000 grams. *Unresolved issue*
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Catheter Manipulations/Blood Draws

Narrative evidence summary

*One study evaluated the effect of catheter hub manipulations and blood draws through the catheter on catheter-associated BSIs. Very low quality evidence suggested that more frequent central line hub manipulations requiring disinfection (e.g., disconnection of the infusion set from a central line) or drawing blood through a central line increases the risk of catheter-associated BSIs.

*Both of these findings were based on an increase in the odds of catheter-associated BSI in a multivariate model.
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

*Draft recommendation:*

Minimize the number of times central line hubs are accessed and minimize blood sampling through central lines to decrease the risk for CLABSI. **Category IB**
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Chlorhexidine with Alcohol for Hub Antisepsis

**Narrative evidence summary**

- One study evaluated the effect of 2% chlorhexidine with 70% alcohol compared to 70% alcohol for antisepsis of the catheter hub. Very low quality evidence suggested a benefit to the use of chlorhexidine with alcohol compared to alcohol alone.
- This was based on a reduction in the incidence rate ratio for positive blood cultures and for clinically suspected sepsis among surgical infants on total parenteral nutrition (TPN) treated with chlorhexidine with alcohol compared to those receiving alcohol alone.
- Of note, the incidence of clinically suspected sepsis (71% of infants) and positive blood cultures (32% of infants) were very high in this study. No data on adverse events were included.
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

*Draft recommendation:*

Consider the use of chlorhexidine with alcohol (2% with 70% alcohol) over 70% alcohol alone for central line hub antisepsis when rates of CLABSIs are high and not responding to initial prevention measures.

*Category II*
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Prophylactic Antimicrobials

*Narrative evidence summary*

- Four studies evaluated the effect of prophylactic antibiotics on BSIs among patients with central lines. Moderate quality evidence did not suggest a clear net benefit to prophylactic antibiotics for preventing total BSIs although prophylactic vancomycin did appear to result in a decrease in BSIs due to coagulase-negative Staphylococci.
- This was based on three studies that evaluated the use of prophylactic vancomycin and one that evaluated prophylactic amoxicillin (3680). Three found a decrease in Gram-positive BSIs with vancomycin and the study of amoxicillin showed no difference in proven or suspected septicemia.
- The development of antimicrobial resistance was not adequately evaluated in any of these studies.
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Draft recommendation:

Do not use prophylactic antimicrobial infusions routinely to decrease the rate of bacterial CLABSIs. Category IB
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Heparin to Prevent CLABSIs

Narrative evidence summary

- Four studies evaluated the effect of heparin infusions on BSI-related outcomes. Moderate quality evidence suggested that continuous infusions of heparin did not result in significant reductions in catheter-related sepsis.

- This was based on one study that showed no decreases in catheter-related sepsis or suspected catheter-related sepsis among neonates with peripherally-inserted central catheters receiving 0.5 to 1 ml/hour infusions of heparin. No adverse events related to heparin were identified.

- Moderate quality evidence suggested that heparin added to or infused with TPN did not result in reductions in catheter-related sepsis.

- This was based on heterogeneous results from three randomized-controlled trials studies, two of which showed no significant decrease in catheter-related sepsis or septicemia and one that showed a significant risk reduction in a combined outcome of definite, probable, or possible catheter-related sepsis.
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

*Draft recommendation:*

Do not use heparin infusions solely for the purpose of preventing CLABSIs. **Category IA**
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Central Line Antimicrobial Locks

**Narrative evidence summary**

- Three studies of neonates evaluated the effect of central line antimicrobial locks on catheter-related BSIs. There was high quality evidence that the use of catheter locks prevented catheter-related BSIs.
- This was based on studies of three different antimicrobial locks that were used at least once per day that demonstrated a decrease in definite and total CRBSIs.
- The development of antimicrobial resistance over the short term was evaluated in two of the studies and was not found to be higher in the antimicrobial lock group. Of note, rates of catheter-related BSIs were very high in the non-intervention groups (17.8 to 20.4 per 1,000 catheter days).
Draft recommendation:

Consider central line antimicrobial locks as a strategy to decrease high rates of CLABSI when other recommended strategies have failed. The long term effect of locks that use antibiotics on antimicrobial resistance is not known. Category II
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Catheter Dwell Times (Percutaneous Central Catheters)

**Narrative evidence summary**

- Four studies evaluated the risk of a BSI over time for percutaneous central catheters (10757, 10407, 10394, 10410). Low quality evidence suggested that the longer a percutaneous central catheter was in place, the higher the odds or risk of CLABSI, CRBSIs, or catheter-related sepsis.

- This was based on significantly higher rates of sepsis for catheters in place for longer periods of time although the risks and time periods varied.
Draft recommendation:

Discontinue percutaneous central catheters as soon as they are no longer needed.

Category IB
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Catheter Dwell Times (Umbilical Catheters)

**Narrative evidence summary**

- Four studies evaluated the risk of a BSI outcome for patients with umbilical catheters (3 venous, 1 arterial). Very low quality evidence suggested the longer an umbilical arterial or venous catheter was in place the higher the odds or risk of a BSI-related outcome; however, the time periods evaluated varied between studies.

- One suggested a significant 20% increase in the odds of a BSI for each day that an umbilical venous catheter was in place, one found a significant increase in the risk of a CLABSI in patient with a umbilical venous catheter for more than 10 days compared to those with a catheter for \( \leq 7 \) days, and the third study found increases in the incidence of sepsis in patients with umbilical venous catheters but did not evaluate how likely these changes were due to chance. One study showed a significant increase in sepsis for patients with an umbilical artery catheter for more than seven days compared to those with a catheter for \( \leq 7 \) days. The fourth study, a randomized-controlled trial, evaluated the effect of routinely removing umbilical venous catheters and replacing them with a percutaneous central catheter after seven to ten days. There was no significant differences in the two study arms between time to catheter-related infection, the overall incidence of catheter sepsis, and the duration of catheter use before infection.
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

*Draft recommendation:*

Discontinue functioning umbilical catheters as soon as they are no longer needed.

*Category IB*

No recommendation can be made about the duration a functioning umbilical catheter can remain in place. *Unresolved issue*
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Central Line Tip Placement for Lower Extremity Peripherally-Inserted Central Catheter

_Narrative evidence summary_

• One study evaluated the effect of different catheter tip locations in catheters inserted in the lower extremities (3512). Very low quality evidence suggested that there were no differences in catheter complications between catheters that terminated in the upper vena cava (T8-T10) compared to those that terminated in the lower vena cava (around L2).
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

*Draft recommendation:*

Consider allowing peripherally-inserted central catheters inserted into the lower extremity veins to terminate in the either the upper or lower vena cava. *Category II*
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Skin Antiseptics

Narrative evidence summary

- Four studies addressed the effect of or toxicities associated with skin antiseptic use for catheter insertion and/or catheter maintenance. Moderate quality evidence suggested that there was no difference between 2% chlorhexidine and 10% povidone iodine used at catheter insertion and during dressing changes to prevent BSIs or catheter tip colonization but that both chlorhexidine and povidone-iodine might be associated with toxicity.

- The efficacy evaluation was based on one small randomized controlled trial which showed no difference between 10% povidone-iodine and 2% chlorhexidine in any BSI, presumed BSI, and in catheter tip colonization (3015). This study was likely underpowered.
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Skin Antiseptics

**Narrative evidence summary**

- Toxicity associated with the use of povidone-iodine alone or compared to chlorhexidine was evaluated in four studies.
- Thyroid toxicities were evaluated in three studies. Two found elevated thyroid stimulating hormone (TSH) levels among 20% to 25% of exposed neonates exposed to 1% to 10% povidone-iodine. Both of these studies were in neonates ≤1500 to 2000 grams.
- Cutaneous toxicities were evaluated in one study. This study found no difference in severe contact dermatitis among neonates ≥1500 grams treated with either 10% povidone-iodine or 2% chlorhexidine gluconate for catheter site cares; seven of ten chlorhexidine-treated infants developed measurable serum chlorhexidine levels, but there is no mention of the clinical significance of this finding.
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

Skin Antiseptics

*Narrative evidence summary*

- Toxicities associated with use of chlorhexidine were also evaluated using eleven studies that reported adverse events associated with the use of a chlorhexidine bath in newborns. Low quality evidence suggested that there were rarely adverse events associated with one-time chlorhexidine bathing of newborns, although several studies found measurable levels of chlorhexidine in blood or feces.

- This determination was based on eight studies that found either no increase in skin reactions or a low incidence of minor rashes following exposure to chlorhexidine varying from 0.25% to 2%, and four studies that found measurable blood levels of chlorhexidine following one to three chlorhexidine baths (9877, 9718, 9639, 10337). None of the studies that found measurable blood levels noted adverse reactions related to these blood levels.
Question 2A: What are the most effective strategies to prevent central line-associated bloodstream infection in the neonatal intensive care unit?

*Draft recommendation:*

No recommendation can be made about the preferred antiseptic for catheter insertion and exit site care. *Unresolved issue*
IMPLEMENTATION DOCUMENT
Topics for Implementation Document: Respiratory Pathogens

• Isolette distance for patients on isolation if no private room available
• Cohorting of undifferentiated suspected viral illness
• Specific agents for post exposure prophylaxis
• Pertussis Serology
Topics for Implementation Document for MRSA

• Active surveillance testing
  – Patient population
  – Interval
  – Anatomic sites

• Discordant multiples
Next Steps

• Incorporate HICPAC feedback into draft summaries and recommendations
• Submit draft to CDC clearance
• Federal Register for Public Comment
• Review public comments and potential changes at subsequent HICPAC meeting
• Finalize guideline
• CDC clearance
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