Guideline for Infection Prevention in NICU Patients: Workgroup Update

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Overview

- Draft Recommendations
  - CLABSI
- Updates
  - *S. aureus*
  - Respiratory Illness

Methods: GRADE

Confidence in the Evidence

- RCTs start high
- Non-randomized studies start low

- Factors lower the quality of evidence
  - Risk of Bias, Inconsistency, Indirectness, Imprecision, and Publication bias
- Factors can increase the quality of evidence
  - Large magnitude of effect, Dose-Response, and Confounding

Methods: Updated Recommendation Categories

Recommendation

- Benefits clearly exceed the harms (or vice versa)
- Confidence in supporting evidence:
  - High to moderate
  - Low, very low, or expert opinion if high-quality evidence is impossible to obtain
- Federal regulation

Conditional Recommendation

- Benefits likely to exceed the harms (or vice versa)
- Confidence in supporting evidence is low, moderate, or high when:
  - High quality evidence exists, but benefit/ harm balance is not clearly in one direction
  - Weak evidence and the recommendation may not consistently lead to benefit
  - Indirect high quality evidence (e.g. benefit is seen in other populations & settings)
  - Evidence of benefit (or harm) is in the context of simultaneously implemented interventions
  - The evidence base is likely to change
  - Benefit is most likely if intervention is implemented as a supplemental measure

No Recommendation

- Lack of evidence
- Unclear balance of benefits and harms

Draft Recommendations

1. *Statement* **(Recommendation; Conditional Recommendation; No Recommendation)**

Supporting Evidence:

Level of confidence in evidence:

Benefits:

Harms:

Resource use:

Balance of benefits and harms:

Value judgments

Intentional vagueness:

Exceptions:

CLABSI: What are effective strategies to prevent CLABSI in neonatal intensive care unit patients?

Literature Search

- 134 studies selected for inclusion
  - 71 studies included from 2012
  - 63 studies included from 2012-2018

CLABSI Topics

- Updated Recommendations
  - Umbilical Catheters: Optimal Duration
  - Optimal Central Line Type & Insertion Site
- New Recommendations
  - PICC Dwell Time
  - Number of Catheter Lumens
  - Systemic Anticoagulant Prophylaxis
  - Systemic Antibiotic Prophylaxis

CLABSI Updated Draft Recommendation: *Catheter Type and Insertion Site*

HICPAC May 2019 Feedback

- **Merge & streamline recommendations for optimal catheter type and insertion site**
- **While catheter type is determined by the needs of the patient, choice of insertion site may be influenced by numerous factors**

Draft CLABSI Updated Recommendation:
Catheter Type and Insertion Site Draft Recommendation

1. Choose the central line type (e.g., umbilical venous catheter (UVC), percutaneously inserted central catheter (PICC), tunneled catheter, etc.) based on the clinical needs of the NICU patient. **Recommendation**

2. The choice of central line type to insert in a NICU patient should not be based solely on CLABSI prevention. **Recommendation**

- Supporting Evidence: Nine observational studies. (Arnts, Sanderson, Shalabi, Bhandari, Chien, de Brito, Geldenhuys, Greenberg, Soares).
- Level of confidence in evidence: The level of confidence in this evidence is very low because observational studies are considered at higher risk of bias than randomized controlled trials, and each study compared different interventions and reported different infectious outcome measures resulting in a loss of confidence due to imprecision. Three studies compared umbilical venous catheters to percutaneously inserted central venous catheters (Arnts, Sanderson, Shalabi). Six studies compared various catheter types that included umbilical arterial catheters, umbilical venous catheters, percutaneous arterial catheters, percutaneous venous catheters, peripherally inserted central catheters, intracath, phlebotomy catheters, and tunneled catheters. Only two studies were conducted after robust implementation of insertion and maintenance bundles in 2010.

Draft CLABSI Updated Recommendation:
Catheter Type and Insertion Site Draft Recommendation

1. Choose the central line type (e.g., umbilical venous catheter (UVC), percutaneously inserted central catheter (PICC), tunneled catheter, etc.) based on the clinical needs of the NICU patient. **Recommendation**

2. The choice of central line type to insert in a NICU patient should not be based solely on CLABSI prevention. **Recommendation**

- Benefits: The evidence did not suggest a clear benefit of one catheter type over another; however, studies evaluated different patient populations with varying clinical indications for central venous access and this was likely reflected in the evidence. The variation in dwell time according to catheter type was a confounding factor in interpreting the results seen in the evidence.
- Harms: One study suggested the risk of infiltration was higher with PICCs than with other catheters.
- Balance of benefits and harms: The balance of benefits vs harms was unclear in the 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.

Draft CLABSI Updated Recommendation:
Catheter Type and Insertion Site Draft Recommendation

1. Choose the central line type (e.g., umbilical venous catheter (UVC), percutaneously inserted central catheter (PICC), tunneled catheter, etc.) based on the clinical needs of the NICU patient. Recommendation

2. The choice of central line type to insert in a NICU patient should not be based solely on CLABSI prevention. Recommendation

- Resource use: 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 centers.
- Value judgments: Value judgements 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.

Draft CLABSI Updated Recommendation:
Catheter Type and Insertion Site Draft Recommendation

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

- Supporting Evidence: Seven observational studies (Bashir, Hoang, Wrightson, Breschan, Vegunta, Tsai 2011, Tsai 2009)
- Level of confidence in evidence: The level of confidence in this evidence was very low because observational studies are at higher risk of bias compared to randomized controlled trials, and studies reported heterogeneous outcome measures for infection, resulting in a loss of confidence due to imprecision. The two studies evaluating femoral lines vs. non-femoral lines were conducted in the same NICU with overlapping study periods (Tsai 2011, Tsai 2009). All studies were conducted prior to the robust implementation of insertion and maintenance bundles in 2010.
- Benefits: The evidence was either limited (percutaneous and tunneled catheters) or did not suggest a benefit to use one insertion site over another (PICCs).
- Harms: Association between adverse events and an insertion site was limited and inconsistent, but data suggested adverse events were associated with upper extremities, and non-femoral sites.
- Balance of benefits and harms: There was no benefit to one catheter over another, and the suggestion of adverse events associated with upper extremities and non-femoral sites, however hits evidence was limited and inconsistent in the data.

Draft CLABSI Updated Recommendation:
Catheter Type and Insertion Site Draft Recommendation

Supporting Evidence: Seven 3. Choose the insertion site appropriate to the central line type to be inserted in a NICU patient (e.g., UVC, PICC, etc.) based on the clinical needs of the patient. Recommendation

- Resource use: The literature search did not retrieve studies comparing resource utilization associated with different insertion sites for tunneled catheters or PICCs. Theoretically, there would be no difference in human or materials costs to place a catheter in one site over another 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, this could increase both human and material costs.
- Balance of benefits and harms: There was unclear benefit associated with different insertion sites. There are limited data to suggest an increase in adverse events associated with upper extremity site and non-femoral sites with PICCs. The choice of catheter insertion site is often limited by the availability of venous access sites in the neonate.
- Value judgments: Value judgements 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 to maintaining femoral catheters in diapered children.
- Intentional vagueness: There is no intentional vagueness in this recommendation.
- Exceptions: There are no exceptions to this recommendation.

Questions?

CLABSI *Optimal Dwell Time: Umbilical Catheters*

BSI Guideline 2011 Umbilical Catheter Recommendations.

7. Remove umbilical catheters as soon as possible when no longer needed or when any sign of vascular insufficiency to the lower extremities is observed. Optimally, umbilical artery catheters should not be left in place >5 days [145, 154]. *Category II*

8. Umbilical venous catheters should be removed as soon as possible when no longer needed, but can be used up to 14 days if managed aseptically [155, 156]. *Category II*

9. An umbilical catheter may be replaced if it is malfunctioning, and there is no other indication for catheter removal, and the total duration of catheterization has not exceeded 5 days for an umbilical artery catheter or 14 days for an umbilical vein catheter. *Category II*

CLABSI *Optimal Dwell Time: Umbilical Catheters*

May 2015 Draft Umbilical Catheter Recommendation:

Remove umbilical venous and umbilical arterial catheters as soon as possible and when no longer needed due to the concern for increasing risk of CLABSI associated with increasing dwell time. Recommendation

HICPAC May 2019 Feedback

- **While an optimal dwell time or inflection point for prevention of CLABSI may not be found in the data, the workgroup was urged to determine a total duration for removal**

CLABSI *Optimal Dwell Time: Umbilical Catheters*

Evidence: Umbilical Artery Catheter Removal

1 observational study

- Bhandari 1997, n = 2,091 infants
  - Risk factor analysis for vascular catheter types n=1699 UACs the incidence of sepsis was higher in umbilical artery catheters in situ for ≥8 days when compared with those in situ for ≤7 days. (13.6% vs. 1.3%; $p<0.0001$)

CLABSI *Optimal Dwell Time: Umbilical Catheters*

Evidence: Umbilical Venous Catheter Removal

3 observational studies

- Sanderson 2017, n =1392 removed UVCs
  - Days 4-5 vs. 6-7 = >5 times the risk of CLABSI on days 6-7 (not reported as statistically significant.)
- Vachharajani 2017, n = 201 infants >1000g and <1500g
  - Dwell time increased from 5 days to 7 days prior to PICC insertion
  - No increase in UVC-associated CLABSI (IRR 1.13 (95% confidence interval 0.469–2.332); p = 0.92)
  - 37.5% reduction in replacement with PICCs.
- Bhandari 1997, n=617 UVCs
  - for 1-3 days vs. 4-7 days = increase in the incidence of sepsis (too small for valid statistical analysis.)

CLABSI *Optimal Dwell Time: Umbilical Catheters*

Evidence: UVC Replacement with Long Term Catheter

1 RCT, 3 observational studies

- Butler O'Hara 2006
  - UVC for 7-10 days and replaced by PCVC vs. UVC for up to 28 days: increase in odds of infection, but not statistically significant
  - (OR: 1.66 (95% CI: 0.79 – 3.48); p=0.18)
- Sanderson 2017, and n=1176 UVCs replaced by PICCs
  - CLABSI Hazard Ratio increased beyond 3-4 days of dwell time, and the risk doubled every 2 days thereafter if UVC was followed by PICC insertion.
- Butler O'Hara 2012
  - Increase in the odds of developing a CLABSI for UVCs in situ >7 days
  - OR: 5.48 (95% CI: 1.18-25.50); p=0.03
- Vachharajani 2017, n = 201 infants >1000g and <1500g
  - No increase in UVC-associated CLABSI from 5 to 7 days (IRR 1.13 (95% confidence interval 0.469–2.332); p = 0.92) ; 37.5% reduction in replacement with PICCs.

CLABSI *Optimal Dwell Time: Umbilical Catheters*

Evidence: Adverse events for UVCs replaced by PCVCs compared with long term UVCs

1 Observational study

- Butler O'Hara 2006
  - No difference in thrombosis, mortality, arrhythmia, embolus, hemorrhage, and pleural effusion between UVCs left in place up to 28 days and UVCs left in place 7-10 days

Draft CLABSI *Optimal Dwell Time: Umbilical Catheters*

1. Remove umbilical venous and umbilical arterial catheters as soon as possible and when no longer needed due to the concern for increasing risk of CLABSI associated with each day of increasing dwell time. Recommendation

- Supporting Evidence: One randomized controlled trial (Butler O'Hara, 2006) and four observational studies (Bhandari, Butler O'Hara 2012, Sanderson, Vachharajani).
- Level of confidence in evidence: The level of confidence in this evidence is very low because observational studies are considered at higher risk of bias than randomized controlled trials and there was a loss of confidence due to imprecision. Only one study was conducted in the current standard of care (Vachharajani).
- Benefits: The evidence reported increasing risk of infection 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 (Sanderson) or 7 days (Butler O'Hara 2012); however, neither study used data collected since 2010, after which there was widespread implementation of central line insertion and maintenance bundles. The only study to be conducted in this era (Vachharajani) noted no difference in CLABSI when UVC duration was extended from 5 to 7 days as a part of a QI initiative.
- 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.

Draft CLABSI *Optimal Dwell Time: Umbilical Catheters*

1. Remove umbilical venous and umbilical arterial catheters as soon as possible and when no longer needed due to the concern for increasing risk of CLABSI associated with each day of increasing dwell time. Recommendation

- Balance of Benefits and Harms: The evidence suggested a decreased risk of infection with decreasing dwell time and no harms were reported in association with dwell time. Each study assessed different durations of risk for infection and none of the studies were able to control for how infection risk may vary over time, precluding unjustified confidence in an optimal catheter day for PICC removal to prevent CLABSI.
- Resource use: Reducing PICC dwell time would theoretically reduce material and human resource costs.
- Value judgments: Value judgements 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.

Draft CLABSI *Optimal Dwell Time: Umbilical Catheters*

1. Remove umbilical venous and umbilical arterial catheters as soon as possible and when no longer needed due to the concern for increasing risk of CLABSI associated with each day of increasing dwell time. Recommendation

- Resource use: The literature search did not retrieve evidence on resource use. Theoretically, reducing UVC dwell time could reduce material and human resource costs.
- Balance of benefits and harms: 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. If a patient requires longer-term care, the PICC can be inserted earlier.
- Value judgments: The values 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 the patient characteristics.
- Exceptions: There are no exceptions to this recommendation.

Draft CLABSI *Optimal Dwell Time: Umbilical Catheters*

2. Consider removal of umbilical artery catheters at or before 7 days of dwell time in neonatal intensive care unit patients. Conditional recommendation

- Supporting Evidence: One observational study (Bhandari).
- Level of confidence in evidence: The level of confidence in this evidence is very low because observational studies are considered at higher risk of bias than randomized controlled trials and there was a loss of confidence due to imprecision. This study was not conducted in the current standard of care.
- Benefits: The evidence reported increasing risk of infection with increasing UAC dwell time, suggesting a benefit to removing UACs at the earliest opportunity. One study suggested the risk of sepsis was higher in umbilical artery catheters in situ for ≥8 days when compared with those in situ for ≤7 days.
- Harms: The evidence suggested that increasing dwell time for UACs resulted in an increase in the risk of infections. No other adverse events were reported.
- Resource use: The literature search did not retrieve evidence on resource use. Theoretically, reducing UAC dwell time could reduce material and human resource costs.

Draft CLABSI *Optimal Dwell Time: Umbilical Catheters*

2. Consider removal of umbilical artery catheters at or before 7 days of dwell time in neonatal intensive care unit patients. Conditional recommendation

- Balance of benefits and harms: 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: The values 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.

Draft CLABSI *Optimal Dwell Time: Umbilical Catheters*

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

- Supporting Evidence: Three observational studies (Bhandari, Sanderson, Vachharajani).
- Level of confidence in evidence: The level of confidence in this evidence is very low because observational studies are considered at higher risk of bias than randomized controlled trials and there was a loss of confidence due to imprecision and inconsistency across studies. Only one study was conducted in the current standard of care (Vachharajani).
- Benefits: The evidence reported increasing risk of infection 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 (Sanderson); however, this study used data collected before 2010, after which there was widespread implementation of central line insertion and maintenance bundles. The only study to be conducted in this era (Vachharajani) noted no difference in CLABSI when UVC duration was extended from 5 to 7 days as a part of a QI initiative.
- 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.

Draft CLABSI *Optimal Dwell Time: Umbilical Catheters*

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

- Resource use: The literature search did not retrieve evidence on resource use. Theoretically, reducing UVC dwell time could reduce material and human resource costs.
- Balance of benefits and harms: While the evidence did not provide 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: The values 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 the patient characteristics.
- Exceptions: There are no exceptions to this recommendation.

Draft CLABSI *Optimal Dwell Time: Umbilical Catheters*

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

- Supporting Evidence: One randomized controlled trial (Butler O'Hara, 2006) and three observational studies (Butler O'Hara 2012, Sanderson, Vachharajani).
- Level of confidence in evidence: The level of confidence in this evidence is low because observational studies are considered at higher risk of bias than randomized controlled trials and there was a loss of confidence due to imprecision. Only one study was conducted in the current standard of care (Vachharajani).
- Benefits: The evidence reported increasing risk of infection 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 (Sanderson) or 7 days (Butler O'Hara 2012); however, neither study used data collected since 2010, after which there was widespread implementation of central line insertion and maintenance bundles. The only study to be conducted in this era (Vachharajani) noted no difference in CLABSI when UVC duration was extended from 5 to 7 days as a part of a QI initiative.

Draft CLABSI *Optimal Dwell Time: Umbilical Catheters*

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

- 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 literature search did not retrieve evidence on resource use. Theoretically, reducing UVC dwell time could reduce material and human resource costs.
- Balance of benefits and harms: While the evidence did not provide an optimal day by which to replace a UVC with a longer term catheter to prevent CLABSI, the benefits of replacement with a long-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. If the patient requires longer-term care, the PICC can be inserted earlier.

Draft CLABSI *Optimal Dwell Time: Umbilical Catheters*

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

- Value judgments: The values 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 the patient characteristics.
- Exceptions: There are no exceptions to this recommendation.

Questions?

CLABSI *Optimal Dwell Time: PICCs*

Evidence:

CLABSI risk: 4 Observational Studies

- Sanderson, 2017 (N= 3,332 PICCs)
  - Increasing dwell time was associated with increased risk of CLABSI for PICCs,
  - No clear optimal day for PICC removal or replacement.
- Greenberg, 2015 (N=14,451 PICCs)
  - Increased risk of CLABSI was associated with week 1. No other week was associated with increased risk of CLABSI for PICCs. no clear optimal PICC dwell time to reduce CLABSI risk
- Milstone, 2013 (N=4,797 PICCs)
  - Risk of CLABSIs increased during the 2 weeks after PICC insertion and then remained elevated until PICC removal.
  - No clear inflection point beyond which infection increases
- Sengupta, 2010 (N=683 patients)
  - Increase in CLABSI risk of 14% per day between catheter days 1-18, and of 33% per day from days 35 through 60.

CLABSI *Optimal Dwell Time: PICCs*

Evidence:

CLABSI risk:

Greenberg, 2015
(N=14,451 PICCs)

TABLE 2 Effect of Dwell Time on CLABSI

Week of Dwell Time	PICCs, *N*	CLABSI, *N* (%)	PICCs, HR[a] (95% CI)	Tunneled Catheters, *N*	CLABSI, *N* (%)	Tunneled Catheters, HR[a] (95% CI)
1	14 451	82 (0.6)	Reference	1116	5 (0.4)	Reference
2	8250	56 (0.7)	1.2 (0.9–1.7)	969	5 (0.5)	1.3 (0.4–4.4)
3	4061	31 (0.8)	1.3 (0.8–1.9)	748	3 (0.4)	1.0 (0.2–4.4)
4	2209	5 (0.2)	0.4 (0.1–0.9)	580	2 (0.3)	0.9 (0.2–4.7)
5	1290	7 (0.5)	0.9 (0.4–1.9)	452	3 (0.7)	1.8 (0.4–7.6)
6	765	7 (0.9)	1.5 (0.7–3.2)	355	4 (1.1)	3.2 (0.8–12.0)
7	453	4 (0.9)	1.4 (0.5–4.0)	280	4 (1.4)	4.0 (1.1–15.4)
8	278	3 (1.1)	1.6 (0.5–5.2)	228	1 (0.4)	1.3 (0.1–11.4)
9	183	2 (1.1)	1.5 (0.4–6.3)	178	3 (1.7)	4.7 (1.1–20.3)
10	125	0		151	1 (0.7)	2.0 (0.2–17.7)

CI, confidence interval; HR, hazard ratio.

[a] HRs are adjusted for PMA, year of catheter insertion, and site.

CLABSI *Optimal Dwell Time: PICCs*

Evidence:

CLABSI risk:

Milstone, 2013 (N=4,797 PICCs)

TABLE 4 Unadjusted and Adjusted Risk Factors for CLABSIs in Neonates With PICCs

Variable	CLABSI, *n* = 149, *n* (%)	No CLABSI, *n* = 4648, *n* (%)	Unadjusted IRR (95% CI)	*P* Value	aIRR[a] (95% CI)	*P* Value
Age at line insertion, d			1.00 (0.99–1.00)	.19	1.00 (0.99–1.00)	.31
Birth weight, 100 g			0.98 (0.96–0.99)	.006	0.97 (0.95–0.99)	.006
Concurrent PICCs						
No	134 (89.9)	4413 (94.9)	1.0 (reference)		1.0 (reference)	
Yes	15 (10.1)	235 (5.1)	1.66 (0.97–2.84)	.06	2.04 (1.12–3.71)	.019
CLABSI from previous PICC						
No	143 (96.0)	4577 (98.5)	1.0 (reference)		1.0 (reference)	
Yes	6 (4.0)	71 (1.5)	2.21 (1.00–4.90)	.05	1.66 (0.69–3.98)	.25
Catheter dwell time						
≤7 d	25 (16.6)	1071 (23.0)	1.0 (reference)		—	
8–13 d	32 (21.2)	1257 (27.1)	2.02 (1.21–3.38)	.007	—	
14–22 d	39 (25.8)	1090 (23.5)	3.27 (2.04–5.24)	<.001	—	
≥23 d	55 (36.4)	1228 (26.4)	2.71 (1.71–4.27)	<.001	—	

—, categorical variable not included in aIRR model. Restricted cubic splines used instead.

[a] Adjusted for PICC dwell time by using restricted cubic splines, hospital, and for patient-level clustering.

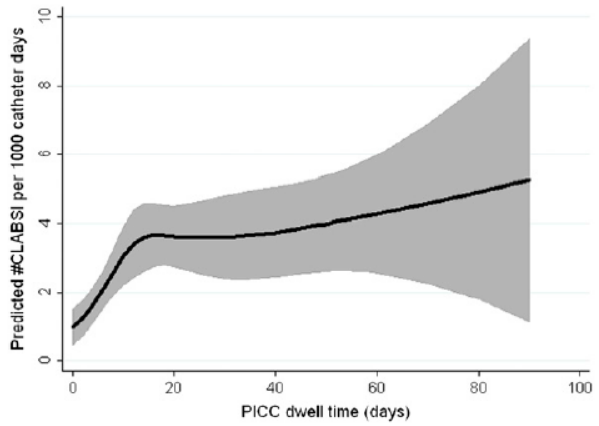

FIGURE 3

criteria for CLABSI.[28] This variability has not been associated with catheter dwell time and should not affect the interpretation of these data.

CONCLUSIONS

PICCs are essential to the care of hospitalized neonates, and CLABSIs are a potentially devastating complication. Our data confirm that the risk of CLABSIs in PICCs increases over the first 2 weeks after insertion and then remains elevated. Health care workers should con-

CLABSI *Optimal Dwell Time: PICCs*

Evidence:

CLABSI risk: Sengupta, 2010 (N=683 patients)

TABLE 3 Incidence of CLA-BSIs Over 10-Day Time Intervals Since PICC Insertion

	Days 1–10	Days 11–20	Days 21–30	Days 31–40	Days 41–50	Days 51–60
No. of events	6	8	4	0	1	2
No. of catheters[a]	315	192	85	50	25	16
No. of catheter-days[b]	5563	2883	1480	810	437	257
Incidence rate per 1000 catheter-days	1.08	2.77	2.7	0	2.29	7.78

[a] Number of catheters at the end of the time bin.

[b] Catheter-days for catheters extending beyond 60 days are included.

CLABSI *Optimal Dwell Time: PICCs*

Evidence:

CRBSI risk: 3 Observational Studies – one suggested an association of CRBSI with increasing dwell time, two did not.

- Rangel, 2014 (N=63 PICCs)
  - No difference in the mean dwell time between infected and non-infected patients. (p=0.6064)
- Ohki , 2013 (N= 946 PICCs)
  - For each week of PICC duration, the trend was for an increasing rate over time, however, this did not reach significance (p=0.09)
  - Dwell time was not a predictor of the odds of developing CR-BSI. (OR: 1.19 (0.91–1.57); p=0.212).
  - Almost all PICCs in this study were removed within 2 weeks after insertion.
- Hsu, 2010 (N=412 PICCs in VLBWI)
  - Increasing dwell time was a significant factor for the odds of developing CRBSI (p<0.01)
  - Optimal timing for removal of a PICC could not be determined.

CLABSI *Optimal Dwell Time: PICCs*

Evidence:

Catheter Related Sepsis : 1 Observational Study

Njere, 2011 (N= 294 PICCs)

- The odds of developing CRS was 3 times higher if the catheter was in place for ≥9 days (OR: 3.1 (95%CI: 1.64-5.87); p<0.01)

CLABSI *Optimal Dwell Time: PICCs*

Evidence:

Studies conducted in the era of insertion and maintenance bundles

Greenberg, 2015 (N=14,451 PICCs)

- Increased risk of CLABSI was associated with week 1. No other week was associated with increased risk of CLABSI for PICCs. no clear optimal PICC dwell time to reduce CLABSI risk

- Rangel, 2014 (N=63 PICCs)
  - No difference in the mean dwell time between patients with CRBSI and non-infected patients. (p=0.6064)

Draft CLABSI *Optimal Dwell Time: PICCs*

1. Remove peripherally inserted central catheters (PICCs) as soon as possible, and when no longer needed due to the concern for increasing risk of CLABSI associated with increasing dwell time. Recommendation
2. For neonates with ongoing need for central venous access, whether to remove and replace a PICC that has been in place for a prolonged period of time to reduce CLABSIs in NICU patients remains an unresolved issue. No Recommendation

- Supporting Evidence: Eight observational studies. (Greenberg, Milstone, Sanderson, Ohki, Rangel, Hsu, Njere, Sengupta)
- Level of confidence in evidence: The level of confidence in the evidence is very low because observational studies are considered at higher risk of bias than randomized controlled trials. There was a loss of precision from heterogeneous outcome definitions and methodology employed across studies.
- Benefits: The evidence suggested a decreased risk of infection with decreasing PICC dwell time. In some patients the risk in the first two weeks, than last two weeks. But there is not clear per day increase in risk that represents an inflection point.
- Harms: The evidence reported an increasing risk of infection with an increasing PICC dwell time. But no specific inflection point was determined that would suggest that infection risk would increase at a specific time. Other PICC-related harms were not reported in relation to dwell time.

Draft CLABSI *Optimal Dwell Time: PICCs*

1. Remove peripherally inserted central catheters (PICCs) as soon as possible, and when no longer needed due to the concern for increasing risk of CLABSI associated with increasing dwell time. Recommendation
2. For neonates with ongoing need for central venous access, whether to remove and replace a PICC that has been in place for a prolonged period of time to reduce CLABSIs in NICU patients remains an unresolved issue. No Recommendation

- Balance of Benefits and Harms: The evidence suggested a increased risk of infection with increasing dwell time, and no harms were reported in association with dwell time. Each study assessed different durations of risk for infection and none of the studies were able to control for how infection risk may vary over time, precluding unjustified confidence in an optimal catheter day for PICC removal to prevent CLABSI.
- Resource use: Reducing PICC dwell time would theoretically reduce material and human resource costs.
- Value judgments: Value judgements 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.

Questions?

CLABSI *Number of UVC Catheter Lumens*

Evidence: 1 RCT

Khilanai, 1991 (N= 43 infants)

- Catheter-associated Sepsis:
  - No infections reported in either group
- Adverse events
  - No difference in leaks around catheter site, occlusion of one lumen, difficulty with insertion, or mechanical problems between groups
- This study may have been underpowered

Draft CLABSI *Number of Catheter Lumens*

1. The choice of single versus double lumen umbilical venous catheter solely for the purpose of preventing CLABSI in neonatal intensive unit care patients remains an unresolved issue. No recommendation.

- Supporting Evidence: One randomized controlled trial. (Khilnani)
- Level of confidence in evidence: The level of confidence in the evidence is low due to imprecision based on low number of events and small sample size.
- Benefits: There was a reduction in the number of additional intravenous catheters required with the use of double lumen-catheters, and there was no difference in the incidence of catheter-related sepsis between single and double lumen catheters.
- Harms: There were no harms reported in the evidence.
- Balance of Benefits and Harms: The benefits outweigh the harms, however the confidence in this evidence is low and future publications may change the strength and direction of this evidence.

Draft CLABSI *Number of Catheter Lumens*

1. The choice of single versus double lumen umbilical venous catheter solely for the purpose of preventing CLABSI in neonatal intensive unit care patients remains an unresolved issue. No recommendation.

- Resource use: The evidence did not report a difference in human resource or material costs associated with the insertion and maintenance of single or double lumen catheters.
- Value judgments: Value judgements 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.

Questions?

CLABSI *Prophylactic Anticoagulant Therapy*

Evidence: 4 RCT

- Birch 2010, n=210 patients
- Kamala 2002, n=66 patients
- Shah 2007, n=201 patients
- Uslu 2010, n=239 patients

- All compared Heparin + TPN or dextrose vs. TPN or dextrose only`

CLABSI *Prophylactic Anticoagulant Therapy*

Evidence: 4 RCT

Catheter-related Sepsis

- All 4 RCTs reported no difference between groups

Definite or Probable Sepsis

- 1 RCT (Birch) reported no difference between groups

Septicemia

- 1 RCT (Uslu) reported no difference between groups

Occlusion

- 2 RCT (Birch, Kamala) reported no difference
- 2 RCT (Uslu, Kamala) reported heparin was associated with reduced occlusion

Intraventricular hemorrhage

- 3 RCT (Birch, Kamala, Shah) reported no difference

Draft CLABSI *Prophylactic Anticoagulant Therapy*

1. Do not use prophylactic anticoagulant infusions solely for the purposes of preventing CLABSI in neonatal intensive care unit patients. Recommendation

- Supporting Evidence: 4 randomized controlled trials. (Birch, Kamala, Shah, Uslu)
- Level of Confidence in Evidence: The level of confidence in the evidence is moderate due inconsistent results across studies, and heterogeneous outcome measures and heterogeneous heparin preparations used across studies. None of the 4 studies was published since 2010 and the era of rigorous implementation of central line insertion and maintenance bundles.
- Benefits: The evidence reported no reduction in catheter related sepsis associated with the use of prophylactic anticoagulants. A reduction in occlusion was inconsistent across studies.
- 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.
- Balance of Benefits and Harms: There are no benefits and there is concern that the harms are under reported. There are reasons other than the prevention of CLABSI to administer prophylactic anticoagulants.

Draft CLABSI *Prophylactic Anticoagulant Therapy*

1. Do not use prophylactic anticoagulant infusions solely for the purposes of preventing CLABSI in neonatal intensive care unit patients. Recommendation

- Resource use: While resource use data was not retrieved by this literature search, it is anticipated that the implementation of prophylactic heparin would likely increase human and material costs.
- Value judgments: Value judgements considered in the formulation of this recommendation include patient safety and economic and human resource costs.
- Intentional vagueness: There may be other clinical reasons than the prevention of CLABSI to use prophylactic heparin. There anticoagulant agent is left intentionally vague in this recommendation.
- Exceptions: There are no exceptions to this recommendation

Questions?

CLABSI *Prophylactic Antimicrobial Therapy*

Evidence: 1 RCT, 3 Observational Studies

- Harms 1995 (RCT), n=148 patients
  - Prophylactic amoxicillin
- Spafford 1994, 70 patients
  - Prophylactic vancomycin
- Elhassan 2004, 294 patients
  - Prophylactic vancomycin
- Ocete 1998, 146 patients
  - Prophylactic vancomycin

CLABSI *Prophylactic Antimicrobial Therapy*

Evidence: 1 RCT, 3 Observational Studies

Proven or Suspected Septicemia

- 1 RCT (Harms) reported no difference between groups for both outcomes with the use of prophylactic amoxicillin

Laboratory Confirmed BSI

- 1 observational study (Elhassan) reported no difference between groups with the use of prophylactic vancomycin

CONS Catheter-related Sepsis, Gram-positive infections, Gram-negative infections

- 2 observational studies (Spafford, Ocete) reported a reduction in infections with the use of prophylactic vancomycin

CLABSI *Prophylactic Antimicrobial Therapy*

Evidence: 1 RCT, 3 Observational Studies

Thrombotic Complications

- 1 RCT (Harms) reported an increase in the incidence of thrombotic complications with the use of prophylactic amoxicillin (9% vs. 3%)

Antimicrobial Resistance

- 1 RCT (Harms) reported 1 incidence of amoxicillin-resistant *S. epidermis* in the control group, and no decrease in amoxicillin susceptibility
- Two studies (Spafford, Ocete) reported no incidence of vancomycin resistant strains during the study period, however one study (Ocete) reported 4 cases of Vancomycin-resistant CONS two years following the study period

Draft CLABSI *Prophylactic Antimicrobial Therapy*

1. Do not use prophylactic antimicrobial infusions routinely to decrease the rate of bacterial CLABSIs. Recommendation.

- Supporting Evidence: One randomized controlled trial (Harms) and 3 observational studies (Spafford, Elhassan, Ocete).
- Level of Confidence in Evidence: The level of confidence in this evidence is very low because one study was considered at high risk of bias, and different definitions of outcome measures across studies resulted in a loss of confidence due to imprecision. All of the studies were published prior to 2004 and the widespread implementation of insertion and maintenance bundles.
- Benefits: Prophylactic amoxicillin did not result in a reduction of infections; however, the use of vancomycin prophylaxis did result in a reduction in coagulase-negative staphylococci (CoNS)-related infections.
- Harms: There was an increase in the incidence of thrombotic events associated with the administration of prophylactic amoxicillin. The long term impact of prophylaxis on the development of antimicrobial resistance and the neonatal microbiome were not adequately assessed in these studies.

Draft CLABSI *Prophylactic Antimicrobial Therapy*

1. Do not use prophylactic antimicrobial infusions routinely to decrease the rate of bacterial CLABSIs. Recommendation.

- 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.
- Balance of benefits and harms: The benefits do not clearly outweigh the harms given the theoretical 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 times 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.

Questions?

CLABSI: What are effective strategies to prevent CLABSI in neonatal intensive care unit patients?

Remaining Interventions:

- Catheter manipulations
- Insertion & Maintenance bundles: 15 studies
- Skin Antisepsis: 8 studies
- Chlorhexidine Bathing: 6 studies
- Line maintenance: 2 studies (e.g., catheter hub antisepsis)
- Other: 4 studies (e.g., compliance measures; probiotic use)

CLABSI: What are effective strategies to prevent CLABSI in neonatal intensive care unit patients?

Next Steps

- Review and update remaining interventions
- GRADE
- Draft Recommendations & Narrative

Respiratory Illness: What are effective strategies to prevent respiratory illness in NICU patients?

Progress

- 2012 extraction tables updated
  - 23 studies included
- Literature search update:
  - 557 studies retrieved for title and abstract screening
  - 112 studies selected for full text review
  - 18 studies included

Respiratory Illness: What are effective strategies to prevent respiratory illness in NICU patients?

Next Steps

- Review Relevant Questions
- Review & Aggregate Applicable Evidence
- Draft Systematic Review

S. aureus

Next Steps

- Public Comment
- Present Public Comments to HICPAC
- Finalize

Workgroup members and support

Workgroup members

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- Alexis Elward
- Loretta Fauerbach (HICPAC)
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Thank you!

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.