Catheter Dwell Time and CLABSI in Neonates With PICCs: A Multicenter Cohort Study

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KEY WORDS

infection, catheter-related infections, NICU, central venous catheters, peripheral venous catheterization

ABBREVIATIONS

aIRR—adjusted incidence rate ratio
CI—confidence interval
CLABSI—central line–associated bloodstream infection
IP—infection preventionist
IRR—incidence rate ratio
NHSN—National Healthcare Safety Network
PICC—peripherally inserted central catheter

Dr Milstone conceptualized and designed the study, oversaw data collection at 1 site, participated in the analyses, and drafted the initial manuscript; Dr Reich designed and oversaw the analyses, and reviewed and revised the manuscript; Dr Advani coordinated data collection, participated in the analyses, and reviewed and revised the manuscript; Mr Yuan performed the primary data analyses and critically reviewed the manuscript; Drs Bryant, Coffin, Huskins, Livingston, Saiman, Smith, and Song supervised data collection at 1 site and critically reviewed the manuscript; and all authors approved the final manuscript as submitted.

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WHAT'S KNOWN ON THIS SUBJECT: Peripherally inserted central catheters (PICCs) are essential to deliver life-saving treatment to neonates. Longer PICC dwell times may increase the risk of central line–associated bloodstream infections (CLABSI) in neonates, but previous studies have yielded inconsistent results, likely due to different study designs, analytic methods, and small sample sizes.

WHAT THIS STUDY ADDS: The risk of CLABSI increases during the 2 weeks after PICC insertion and remains elevated for the catheter duration. These data support daily review of PICC necessity, optimization of catheter maintenance practices, and consideration of novel strategies to prevent CLABSI.

abstract

OBJECTIVE: To determine whether the daily risk of central line–associated bloodstream infections (CLABSI) increases over the dwell time of peripherally inserted central catheters (PICCs) in high-risk neonates.

METHODS: Multicenter retrospective cohort including NICU patients with a PICC inserted between January 2005 and June 2010. We calculated incidence rates and used Poisson regression models to assess the risk of developing CLABSI as a function of PICC dwell time.

RESULTS: A total of 4797 PICCs placed in 3967 neonates were included; 149 CLABSI occurred over 89 946 catheter-days (incidence rate 1.66 per 1000 catheter-days). In unadjusted analysis, PICCs with a dwell time of 8 to 13 days, 14 to 22 days, and ≥ 23 days each had an increased risk of infection compared with PICCs in place for ≤ 7 days ($P < .05$). In adjusted analysis, the average predicted daily risk of CLABSI after PICC insertion increased during the first 2 weeks after PICC insertion and remained elevated for the dwell time of the catheter. There was an increased risk of CLABSI in neonates with concurrent PICCs (adjusted incidence rate ratio 2.04, 1.12–3.71). The incidence of Gram-negative CLABSI was greater in PICCs with dwell times > 50 days (incidence rate ratio 5.26, 2.40–10.66).

CONCLUSIONS: The risk of CLABSI increased during the 2 weeks after PICC insertion and then remained elevated until PICC removal. Clinicians should review PICC necessity daily, optimize catheter maintenance practices, and investigate novel CLABSI prevention strategies in PICCs with prolonged dwell times. *Pediatrics* 2013;132:e1609–e1615

Intravenous access is essential to provide fluids, medications, and nutrition to many hospitalized patients. Peripherally inserted central catheters (PICCs) are frequently used to provide life-saving intravenous access for neonates. PICCs can be placed at the bedside without general anesthesia and can remain in place for days to weeks. However, infectious and noninfectious complications occur, including central line-associated bloodstream infections (CLABSI).^{1,2}

In the NICU, CLABSI are the most common health care-associated infection and are a significant cause of morbidity and mortality in high-risk neonates.^{3–5} National campaigns and collaborative efforts have reduced CLABSI in NICUs, but infection rates have not fallen to zero.^{6–9} These successes have in large part relied on a widespread awareness that catheter maintenance practices are essential to prevent CLABSI, especially as catheters often remain in place for prolonged periods.

Many studies have suggested that the longer a catheter remains in place, the greater the risk of a catheter complication, including CLABSI.^{1,2,10–14} The cumulative risk of CLABSI increases the longer a PICC remains in place, but it is unknown whether the daily risk of CLABSI increases over the dwell time of the catheter.¹⁵ A recent study of neonates suggested that for PICCs that remained indwelling for >35 days, the risk of CLABSI increased by 33% per additional day the catheter was in place.¹¹ These findings are plausible, because intra-luminal catheter colonization and biofilm formation are associated with CLABSI, and both are associated with increased catheter dwell time.¹⁶ If confirmed, these data could challenge the common practice of keeping PICCs in place until signs or symptoms of a complication necessitate their removal. Our objective was to

perform a multicenter study to determine if the risk of CLABSI in neonates with PICCs increases over catheter dwell time and identify a threshold beyond which time the daily risk of CLABSI increases.

METHODS

Setting and Participants

We performed a multicenter retrospective cohort study of neonates who had a PICC inserted in the NICU. Institutions were recruited to participate if they had access to an electronic medical record or other electronic database that contained catheter insertion and removal dates and catheter type. Mayo Eugenio Litta Children's Hospital (Rochester, MN), Children's Hospital of Philadelphia (Philadelphia, PA), Duke University Medical Center (Durham, NC), Morgan Stanley Children's Hospital of New York-Presbyterian at Columbia University Medical Center (New York City, NY), Children's National Medical Center (Washington, DC), Kosair Children's Hospital (Louisville, KY), Children's Mercy Hospital and Clinics (Kansas City, MO), and Johns Hopkins Children's Center (Baltimore, MD) provided data. A child was included if he or she had a PICC inserted between January 1, 2005, and June 30, 2010. Not all sites provided data for the entire study period. This study was approved by each site's institutional review board with a waiver of informed consent.

Data Collection

Each institution collected data on patient demographics, catheter characteristics, and positive blood cultures by querying administrative and laboratory databases. Race, ethnicity, gender, date of birth, date of hospital admission, date of hospital discharge, date of NICU admission, date of NICU discharge, gestational age, and birth weight were extracted from hospital databases and

medical records when available. Collected catheter characteristics included catheter insertion and removal dates, insertion location, and number of lumens when available. The primary exposure was PICC dwell time, defined as days from PICC insertion until either PICC removal or the date of CLABSI, whichever was earlier.

The outcome of interest was PICC-associated CLABSI. Each participating institution had trained infection preventionists (IPs) who performed prospective surveillance to monitor positive blood cultures in patients with indwelling catheters, by using laboratory databases and infection surveillance support systems. CLABSI were identified prospectively by IPs at each site and defined using criteria from the Centers for Disease Control and Prevention's National Healthcare Safety Network's (NHSN) surveillance definitions.¹⁷ A list of all CLABSI in the NICU of participating hospitals was obtained from the site's IP. The NHSN CLABSI definition changed in 2008 to include "two or more blood cultures drawn on separate occasions" for common skin commensal bacteria (ie, coagulase-negative staphylococci)¹⁷; therefore, additional microbiology data were collected and reviewed by study investigators for CLABSI occurring before 2008. Ten (21%) of 49 CLABSI occurring before 2008 were not included because they did not meet the NHSN criteria of having ≥ 2 blood cultures drawn on separate occasions. A PICC-associated CLABSI was defined as a CLABSI in a patient with a PICC.^{1,11}

Statistical Analysis

Descriptive analyses were performed to characterize the patient population with reporting of median values, quartiles, and percentages. Because some sites were not able to obtain gestational age, number of catheter lumens, and PICC insertion site, these

variables were not included in the analysis. The unit of analysis was a PICC. We excluded from the analysis PICCs that were placed and removed on the same day. For patients with multiple PICCs placed during their NICU hospitalization, all PICCs were included. For patients with >1 PICC in place at the same time (concurrent PICCs), both PICCs were included while accounting for correlated observations at the patient level by using a robust variance estimator. One site was not reliably able to capture PICC insertion and removal dates, so data from that site were not included. Data for concurrent non-PICC central catheters (ie, tunneled-catheters, umbilical catheters) were not available. For patients who had a CLABSI and simultaneous PICCs (3 patients), the CLABSI was randomly attributed to 1 of the 2 PICCs and a sensitivity analysis was performed and found no change in the results when these CLABSIs were attributed to the other PICC. If multiple CLABSIs were associated with the same PICC, only the first CLABSI was included and at-risk time was censored at the time of the first CLABSI. Subsequent CLABSIs in the same patient with a different PICC were included.

The risk of CLABSI over PICC dwell time was estimated by calculating incidence rates per 10-day intervals from PICC insertion and by using Poisson regression models to estimate unadjusted and adjusted incidence rate ratios (IRRs and aIRRs). Catheter dwell time was categorized into quartiles for the unadjusted models, but an adjusted Poisson regression model with restricted cubic splines was developed to account for the nonlinear risk of CLABSIs over PICC dwell time.² We included covariates determined a priori to be independent predictors of CLABSIs, including presence of a simultaneous PICC, having a CLABSI attributed to a previous PICC, age at time of line

insertion, and birth weight. We included hospital as a fixed effect and accounted for patient-level clustering with a robust variance estimator. Sensitivity analyses included omitting the site with highest rates, including calendar year of PICC placement, only including the first PICC for each child, using a hierarchical model to account for patient-level clustering, and using a robust variance estimator to account for hospital-level clustering. Data were maintained in Microsoft Excel 2007 (Bellevue, WA) and analyzed by using Stata 11.0 (Stata Corp, College Station, TX). Restricted cubic splines and the predicted model graphic were generated by using the *postcrspline* package for Stata.¹⁸

RESULTS

Of the 4899 identified PICCs, 4797 PICCs were eligible for analysis. Seventy-three PICCs were excluded because they were inserted and removed on the same day, 22 had missing insertion or removal dates, and 7 were duplicate entries. Of the 3967 neonates who had ≥ 1 PICCs, the median birth weight was 2000 g (quartiles 1030, 2991) and the median age at time of PICC insertion was 5 days (quartiles 2, 13) (Table 1). Most patients were boys (57.1%) and Caucasian (53.4%).

The total observation time was 89 946 catheter days. The median PICC dwell time was 14 days (quartiles 7, 23), and 25% of PICCs remained in place for ≥ 23 days. The distribution of PICC dwell time is shown in Fig 1. The distribution of PICC dwell time was similar at each site (Supplemental Fig 4).

There were 149 CLABSIs from 4797 PICCs (3.1%). Of the 143 neonates with a CLABSI, 54% were boys, 54% were Caucasian, and the median birth weight was 1032 g. The median time from PICC insertion to CLABSI was 18 days (range 1–166 days). The incidence of PICC-associated CLABSIs was 1.66 per 1000

TABLE 1 Characteristics of 3967 Neonates With 4797 PICCs

Age at line insertion, median (quartiles), d	5 (2–13)
Birth weight, median (quartiles), g	2000 (1030–2991)
Sex, n (% female) ^a	1681 (42.9)
Race, n (%) ^a	
White	2119 (53.4)
Black	1146 (28.9)
Other	448 (11.3)
Year of study, n (%)	
2005	305 (6.4)
2006	590 (12.3)
2007	787 (16.4)
2008	1029 (21.5)
2009	1394 (29.0)
2010	692 (14.4)
Study site, n (%)	
Johns Hopkins	925 (19.3)
Children's Center	
Children's Mercy	1630 (34.0)
Hospital and Clinics	
Kosair Children's Hospital	528 (11.0)
Children's Hospital of Philadelphia	586 (12.2)
Children's National	591 (12.3)
Medical Center	
Duke University	491 (10.2)
Medical Center	
Mayo Clinic	46 (1.0)
PICC dwell times, n (%)	
≤ 7 d	1096 (22.9)
8–13 d	1289 (26.8)
14–22 d	1129 (23.6)
≥ 23 d	1283 (26.7)

^a Denominator does not add up to 3967 because of missing data.

catheter-days (95% confidence interval [CI] 1.40–1.94). The highest incidence of CLABSIs was observed in PICCs with dwell times >50 days (Table 2 and Supplemental Table 5). The most commonly identified organisms were coagulase-negative staphylococci (32.2%) and *Staphylococcus aureus* (20.1%), as shown in Table 3. Gram-positive organisms were most commonly recovered in the first 40 days after catheter insertion (Fig 2). There was an increase in the incidence of Gram-negative CLABSIs in PICCs with dwell times >50 days compared with PICCs with dwell times ≤ 50 days (IRR 5.26, 95% CI 2.40–10.66).

In unadjusted analyses, neonates with higher birth weight were at reduced risk for CLABSIs (Table 4). There was not

FIGURE 1

Distribution of PICC dwell time. PICCs were grouped into 5-day time bins based on their dwell time. PICCs with dwell times of >90 days ($n = 35$) are not shown.

a statistically significant difference in the risk of CLABSIs in neonates with or without concurrent PICCs ($P = .06$) or those with or without a CLABSI from a previous PICC ($P = .05$). PICCs with a dwell time of 8 to 13 days, 14 to 22 days, and ≥ 23 days each had an increased risk of infection compared with PICCs in place for ≤ 7 days ($P < .05$). In multivariable analyses, for every 100-g increase in birth weight there was a 3% reduction in the risk of CLABSIs (aIRR 0.97, 0.95–0.99). Neonates with a concurrent PICC were twice as likely to develop a CLABSI (aIRR 2.04, 1.12–3.71). There was not an increased risk of CLABSIs in neonates with a CLABSI from a previous PICC (aIRR 1.66, 95% CI 0.69–3.98).

Figure 3 illustrates the complex and nonlinear relationship between catheter dwell time and risk of CLABSIs in neonates with PICCs. We found evidence that the predicted risk of CLABSIs increases steadily until ~ 2 weeks after PICC insertion and then remains elevated until catheter removal. Beyond

a 50-day dwell time, limited data and widening CIs make it difficult to predict the trajectory of the risk of CLABSIs, and there is no clear inflection point after which the daily risk of CLABSIs increases. To account for a change in catheter care practices over time, we performed a secondary analysis to include calendar year in our regression model and observed the same association between the predicted daily risk of infection and PICC dwell time.

Based on the observation from Fig 3 that the predicted risk of CLABSIs remains elevated beyond 14 days after PICC insertion, we sought to estimate the number of catheter days that would need to be eliminated to prevent 1 CLABSI. The observed incidence of CLABSIs in PICCs indwelling for >2 weeks was 2.43 per 1000 catheter-days among catheter days that occurred beyond 14 days from insertion (95% CI 1.96–2.98). To prevent 1 CLABSI, 412 catheter days (95% CI 335–510) that occur >14 days after PICC insertion would need to be eliminated.

DISCUSSION

These data confirm that the daily risk of infection is higher in PICCs that have been in place for >2 weeks as compared with those that have been in place for <2 weeks. However, we found no evidence that the daily risk of infection changes after the 2-week time point. CLABSIs are the most common health care–associated infection in NICUs.⁴ Many studies have identified risk factors for CLABSIs in neonates, but this is the first multicenter study to examine the association between PICC dwell time and CLABSIs. Frequently, PICCs remain in place for prolonged periods in the NICU. The decision about whether to remove a functioning PICC must take into account the ongoing daily risk of infection and potential complications associated with PICC replacement.

This study is a major advance over previous single-center studies that have evaluated the relationship between catheter dwell time and CLABSIs.^{1,2,10–13} Previous studies have treated time as a categorical^{19,20} or continuous^{21,22} variable to assess risk of CLABSIs over catheter dwell time and have found differing results. Our data demonstrate a nonlinear association of catheter dwell time with CLABSIs and explain differences reported in the literature. Our large sample size enabled a more robust estimate of the risk of CLABSIs over the entire catheter dwell time.

Sengupta et al¹¹ accounted for the nonlinear association of PICC dwell time and CLABSIs and suggested that for lines in place for >35 days, the daily risk of CLABSIs increased by 33%

TABLE 2 Incidence Rate of CLABSIs During 10-Day Time Intervals After PICC Insertion

	1–10 d	11–20 d	21–30 d	31–40 d	41–50 d	51–60 d	>60 d
No. of CLABSIs	44	44	23	15	6	6	11
No. of catheters ^a	4797	2989	1478	782	440	253	150
No. of catheter days ^b	41 739	22 186	11 106	6079	3472	2037	3327
Incidence rate per 1000 catheter days (95% CI)	1.05 (0.77–1.41)	1.98 (1.44–2.66)	2.07 (1.31–3.11)	2.47 (1.38–4.07)	1.73 (0.63–3.76)	2.95 (1.08–6.41)	3.31 (1.65–5.92)

^a Number of catheters at the start of the time bin.

^b Catheter days in each time bin.

TABLE 3 Pathogens Causing CLABSI in Neonates With PICCs

	n (%)
Coagulase-negative staphylococci	48 (32.2)
<i>Staphylococcus aureus</i> ^a	30 (20.1)
<i>Candida</i> spp	13 (8.7)
<i>Enterococcus</i> spp	12 (8.1)
<i>Klebsiella</i> spp	12 (8.1)
<i>Enterobacter</i> spp	8 (5.4)
<i>Pseudomonas aeruginosa</i>	8 (5.4)
<i>Escherichia coli</i>	6 (4.0)
Other organisms	5 (3.3)
<i>Serratia</i> spp	4 (2.7)
<i>Streptococcus</i> spp	3 (2.0)

^a Five isolates were methicillin-resistant *Staphylococcus aureus*.

per day. This study reported 21 events, only 3 of which occurred in PICCs with dwell times >40 days. In the current study, 23 CLABSI (15%) occurred in PICCs with dwell times >40 days. Despite the larger sample size, the widening 95% CIs in Fig 3 illustrate the uncertainty in the predicted daily risk of CLABSI in PICCs with a prolonged dwell time. Given this uncertainty, making any definitive projections about the risk over prolonged dwell times remains challenging. These data explain and confirm previous studies that have found an increased risk of CLABSI in PICCs with longer dwell time. Although these data did not identify a second phase during which the daily risk of infection again increases, possibly due to being underpowered, the findings do verify that the risk of CLABSI remains elevated in PICCs that remain in place for >2 weeks. There-

fore, clinicians should continue to review the need for a PICC on a daily basis, consider removal, and optimize practices to maintain the catheter to prevent infection. In addition, future studies are needed to determine if additional interventions, such as antibiotic or antiseptic locks, should be considered in neonates with prolonged PICC dwell times to further reduce the risk of infection.

In neonates and children, central line insertion and maintenance care practices can be optimized to prevent CLABSI.^{6–9} Compliance with maintenance practices may be especially important in children with prolonged catheter dwell times. A previous study in neonates demonstrated that most catheter-related bloodstream infections are caused by intraluminal catheter contamination.¹⁶ Catheter maintenance practices, including hand hygiene before contact with the catheter and thorough scrubbing of the catheter hub, may help to prevent intraluminal catheter contamination and subsequent infection. Ensuring compliance with basic PICC insertion and maintenance practices should be the first step in a program to reduce and prevent CLABSI.^{23–26} In addition to PICC maintenance practices, clinicians should actively discuss the ongoing need for a catheter, recognizing the significant daily risk of infection. Our data suggest that 1 CLABSI can be prevented by

eliminating 412 catheter days in PICCs that remain in place for >14 days. That number may seem high, but if 200 neonates on a unit have a PICC in place for >14 days each year, reducing PICC duration by 2 days per patient would prevent 1 CLABSI. Such targets are important for quality improvement initiatives aimed at reducing CLABSI in the NICU.

Our study confirms previous observations that the organisms causing CLABSI and bacteremia may change over catheter dwell time.^{11,22} Smith et al²² found that median time to develop Gram-positive bacteremia was 8 days after catheter insertion, whereas the median time to develop Gram-negative bacteria was 13.5 days after catheter insertion. Sengupta et al¹¹ found that coagulase-negative staphylococci were the predominant organism (55.6%) within the first 2 weeks after PICC insertion, whereas Gram-negative bacteria were the dominant pathogens (58.3%) after the first 2 weeks. Our data showed a 3.5-fold increase in the incidence of Gram-negative CLABSI in PICCs with a dwell time >50 days.

Several considerations should be made when interpreting our findings. This was a retrospective study that relied on available databases from multiple centers. Because of unique data resources at each site, we were unable to capture and adjust for known confounders of CLABSI, including receipt of parenteral nutrition, gestational age, and severity of illness. Follow-up data were limited to a neonate's hospital or NICU stay, so an event that occurred after NICU discharge would not have been captured; however, we previously found that >90% of children had their PICCs removed before NICU discharge.¹¹ We captured and adjusted for simultaneous PICCs, but did not collect data on other types of concurrent central lines, a known risk factor for CLABSI, so residual confounding

FIGURE 2

Incidence of CLABSI during 10-day time intervals after PICC insertion for Gram-positive bacteria, Gram-negative bacteria, and *Candida* spp.

TABLE 4 Unadjusted and Adjusted Risk Factors for CLABSI 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

Predicted CLABSI rate (solid line) with 95% CIs (shading) over catheter dwell time for a given hospital, age, birth weight, CLABSI from previous PICC, and concurrent PICC. For a neonate with different characteristics, the predicted risk of CLABSI could be higher or lower, but the shape of the line would remain the same.

remains possible.²⁷ Each site had and implemented different infection prevention practices during the course of the study. We accounted for these temporal and hospital characteristics in our statistical models, which may have affected the power to detect a change in daily CLABSI risk beyond 14 days of PICC dwell time. Because not all sites provided data for the entire study period, we were not able to assess change

in risk of CLABSI over time, but the association between daily CLABSI risk and PICC dwell time remained after adjusting for temporal trends. As practices have changed over time and as national collaboratives have shown reductions in rates, our findings are informative but should be confirmed with contemporary data. Finally, previous research has identified variability in how different practitioners apply NHSN

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 CLABSI are a potentially devastating complication. Our data confirm that the risk of CLABSI in PICCs increases over the first 2 weeks after insertion and then remains elevated. Health care workers should continue to review the need for a PICC on a daily basis, remove if possible, and optimize practices to maintain the catheter to prevent infection. Future studies are needed to determine if additional interventions are warranted in neonates with prolonged PICC dwell times to further reduce the risk of infection.

ACKNOWLEDGMENTS

We thank Priya Prasad, Juyan Julia Zhou, Darian C. Younger, and the Infection Prevention Departments at each site for their support of this study.

REFERENCES

1. Advani S, Reich NG, Sengupta A, Gosey L, Milstone AM. Central line-associated bloodstream infection in hospitalized children with peripherally inserted central venous catheters: extending risk analyses outside the intensive care unit. *Clin Infect Dis*. 2011; 52(9):1108–1115.
2. Jumani K, Advani S, Reich NG, Gosey L, Milstone AM. Risk factors for peripherally inserted central venous catheter complications in children. *JAMA Pediatr*. 2013;167(5):429–435.
3. Sohn AH, Garrett DO, Sinkowitz-Cochran RL, et al; Pediatric Prevention Network. Prevalence of nosocomial infections in neonatal

- intensive care unit patients: results from the first national point-prevalence survey. *J Pediatr*. 2001;139(6):821–827
4. Hovecar SN, Edwards JR, Horan TC, Morrell GC, Iwamoto M, Lessa FC. Device-associated infections among neonatal intensive care unit patients: incidence and associated pathogens reported to the National Healthcare Safety Network, 2006–2008. *Infect Control Hosp Epidemiol*. 2012;33(12):1200–1206
 5. Stoll BJ, Hansen N, Fanaroff AA, et al. Late-onset sepsis in very low birth weight neonates: the experience of the NICHD Neonatal Research Network. *Pediatrics*. 2002;110(2 pt 1):285–291
 6. Bizzarro MJ, Sabo B, Noonan M, Bonfiglio MP, Northrup V, Diefenbach K; Central Venous Catheter Initiative Committee. A quality improvement initiative to reduce central line-associated bloodstream infections in a neonatal intensive care unit. *Infect Control Hosp Epidemiol*. 2010;31(3):241–248
 7. Kaplan HC, Lannon C, Walsh MC, Donovan EF; Ohio Perinatal Quality Collaborative. Ohio statewide quality-improvement collaborative to reduce late-onset sepsis in preterm infants. *Pediatrics*. 2011;127(3):427–435
 8. Schulman J, Stricof R, Stevens TP, et al; New York State Regional Perinatal Care Centers. Statewide NICU central-line-associated bloodstream infection rates decline after bundles and checklists. *Pediatrics*. 2011;127(3):436–444
 9. Wirtschafter DD, Powers RJ, Pettit JS, et al. Nosocomial infection reduction in VLBW infants with a statewide quality-improvement model. *Pediatrics*. 2011;127(3):419–426
 10. McLaws ML, Berry G. Nonuniform risk of bloodstream infection with increasing central venous catheter-days. *Infect Control Hosp Epidemiol*. 2005;26(8):715–719
 11. Sengupta A, Lehmann C, Diener-West M, Perl TM, Milstone AM. Catheter duration and risk of CLA-BSI in neonates with PICCs. *Pediatrics*. 2010;125(4):648–653
 12. Timsit JF. Scheduled replacement of central venous catheters is not necessary. *Infect Control Hosp Epidemiol*. 2000;21(6):371–374
 13. García-Teresa MA, Casado-Flores J, Delgado Domínguez MA, et al; Spanish Central Venous Catheter Pediatric Study Group. Infectious complications of percutaneous central venous catheterization in pediatric patients: a Spanish multicenter study. *Intensive Care Med*. 2007;33(3):466–476
 14. Ohki Y, Maruyama K, Harigaya A, Kohno M, Arakawa H. Complications of peripherally inserted central venous catheter in Japanese NICU. *Pediatr Int*. 2013;55(2):185–189
 15. Milstone AM, Sengupta A. Do prolonged peripherally inserted central venous catheter dwell times increase the risk of bloodstream infection? *Infect Control Hosp Epidemiol*. 2010;31(11):1184–1187
 16. Garland JS, Alex CP, Sevallius JM, et al. Cohort study of the pathogenesis and molecular epidemiology of catheter-related bloodstream infection in neonates with peripherally inserted central venous catheters. *Infect Control Hosp Epidemiol*. 2008;29(3):243–249
 17. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control*. 2008;36(5):309–332
 18. Hardin JW, Hilbe JM. *Generalized Linear Models and Extensions*. 2nd ed. College Station, TX: Stata Press; 2001
 19. Chathas MK, Paton JB, Fisher DE. Percutaneous central venous catheterization. Three years' experience in a neonatal intensive care unit. *Am J Dis Child*. 1990;144(11):1246–1250
 20. Mahieu LM, De Mynck AO, Ieven MM, De Dooy JJ, Goossens HJ, Van Reempts PJ. Risk factors for central vascular catheter-associated bloodstream infections among patients in a neonatal intensive care unit. *J Hosp Infect*. 2001;48(2):108–116
 21. Stenzel JP, Green TP, Fuhrman BP, Carlson PE, Marchessault RP. Percutaneous central venous catheterization in a pediatric intensive care unit: a survival analysis of complications. *Crit Care Med*. 1989;17(10):984–988
 22. Smith PB, Benjamin DK Jr, Cotten CM, et al. Is an increased dwell time of a peripherally inserted catheter associated with an increased risk of bloodstream infection in infants? *Infect Control Hosp Epidemiol*. 2008;29(8):749–753
 23. Powers RJ, Wirtschafter DW. Decreasing central line associated bloodstream infection in neonatal intensive care. *Clin Perinatol*. 2010;37(1):247–272
 24. Richter JM, Brilli RJ. It's all about dwell time—reduce it and infection rates decrease? *Pediatrics*. 2010;125(4):820–821
 25. Marschall J, Mermel LA, Classen D, et al. Strategies to prevent central line-associated bloodstream infections in acute care hospitals. *Infect Control Hosp Epidemiol*. 2008;29(suppl 1):S22–S30
 26. O'Grady NP, Alexander M, Burns LA, et al; Healthcare Infection Control Practices Advisory Committee (HICPAC). Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis*. 2011;52(9):e162–e193
 27. Elward AM, Fraser VJ. Risk factors for nosocomial primary bloodstream infection in pediatric intensive care unit patients: a 2-year prospective cohort study. *Infect Control Hosp Epidemiol*. 2006;27(6):553–560
 28. Gaur AH, Miller MR, Gao C, et al. Evaluating application of the national healthcare safety network central line-associated bloodstream infection surveillance definition: a survey of pediatric intensive care and hematology/oncology units. *Infect Control Hosp Epidemiol*. 2013;34(7):663–670

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www.pediatrics.org/cgi/doi/10.1542/peds.2013-1645

doi:10.1542/peds.2013-1645

Accepted for publication Sep 16, 2013

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Supported by the National Institute for Nursing Research, National Institutes of Health (1R03NR012558 to Dr Milstone). Funded by the National Institutes of Health (NIH).

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.