

# Prediction of Nonelective Central Venous Catheter Removal in Medically Complex Neonates

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## ABSTRACT

**Introduction:** Central venous catheters (CVCs) are essential to neonatal care but associated with significant morbidity. Nonelective CVC removal (NER) is an inadequately studied outcome associated with increased morbidity, infant and family stress, and cost. This study describes prevalence and predictors of NER in infants admitted to a level IV neonatal intensive care unit and NER variation between peripherally inserted central catheters (PICCs), cutdown PICCs, and surgical CVCs. **Methods:** In this study, we include patient and catheter data for infants admitted to a level IV neonatal intensive care unit (2010–2015). Demographic and clinical characteristics were compared using 1-way analysis of variance (ANOVA), Kruskal-Wallis, and chi-square tests for continuous, non-normally distributed continuous, and categorical variables, respectively. The association between NER due to complication and infant and catheter characteristics was assessed using generalized linear mixed models. **Results:** Patient and catheter characteristics vary significantly by catheter type. The overall rate of NER is 15% (17% PICCs, 13% cutdown PICCs, and 19% surgical CVCs). The most common indications for NER are catheter breakage, blood stream infection (BSI)/central line-associated blood stream infection (CLABSI), catheter malposition, mechanical obstruction, and extravasation. Birth weight, patient diagnosis, catheter dwell time, and concurrent catheters are associated with increased odds of NER. **Conclusions:** Patient risk factors and potentially modifiable catheter characteristics, including catheter dwell time and concurrent catheters, are associated with increased NER. As NER is associated with a broad spectrum of adverse outcomes, we propose a quality improvement strategy to risk stratify patients and reduce exposure to high-risk, modifiable catheter characteristics. (*Pediatr Qual Saf* 2019;4:4:e179; doi: 10.1097/pq9.000000000000179; Published online August 5, 2019.)

## INTRODUCTION

In use since the 1970s, central venous catheters (CVCs) are a critical, life-sustaining component of neonatal care traditionally utilized when peripheral intravenous access is difficult or prolonged venous access is indicated to provide nutrition, hydration, or medication.<sup>1,2</sup> Catheters may be placed percutaneously as a peripherally inserted central catheter (PICC), via neonatologist-performed bedside cutdown PICC (cd-PICC), or as a surgical CVC (sCVC),

depending on the indication, urgency, and ease of line placement. Insertion and routine use of such catheters are not without risk as CVC placement may lead to complications including bloodstream infection, thrombosis, pericardial tamponade, and mechanical complications. Such complications result in not only serious acute and long-term sequelae, but also importantly, nonelective CVC removal (NER).<sup>3–5</sup>

Complications resulting in NER may lead to a delay in therapy, increased infant and family stress, additional sedation medications, and increased cost.<sup>5</sup> Conflicting literature exists describing the role of modifiable factors such as catheter type, size, tip location, dwell time, and insertion site in the development of CVC-associated complications in neonates. Furthermore, there are limited data regarding NER.<sup>2,6–12</sup> The preponderance of these data is in the preterm population, with minimal literature including full-term, critically ill infants, such as those admitted to a level IV neonatal intensive care unit (NICU). As such, insufficient data exist in this high-risk population to analyze the incidence of NER and relative rate of NER between different CVC types or to identify specific risk factors that predict NER.<sup>5,13</sup>

Understanding the incidence and predictors of NER in this complex population may lead to the identification of modifiable clinical variables and, thus, targets for improvement in clinical care and patient outcomes. Thus, this study aims to examine (1) the incidence of NCR,

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Supplemental digital content is available for this article. Clickable URL citations appear in the text.

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To cite: Beard L, Levek C, Hwang S, Grover T. Prediction of nonelective central venous catheter removal in medically complex neonates. *Pediatr Qual Saf* 2019;4:e179.

Received for publication January 19, 2019; Accepted April 30, 2019.

Published online August 5, 2019.

DOI: 10.1097/pq9.000000000000179



comparing relative rates between PICC, cd-PICC, and sCVCs, (2) identify factors associated with NER in a high-risk level IV NICU population, and (3) propose a quality improvement initiative to risk stratify patients and reduce exposure to high-risk, modifiable catheter characteristics.

## METHODS

### *Design*

This report is of a retrospective cohort study utilizing clinical data from infants receiving a PICC, cd-PICC, or sCVC between January 1, 2010, and December 31, 2015, in the level IV regional referral NICU at Children's Hospital Colorado. PICCs are placed by neonatal nurse practitioners or specialized PICC nurses at the bedside, and sCVCs are inserted by pediatric surgeons in the operating room utilizing the open technique by published standards.<sup>14,15</sup> Local practice also utilizes bedside cd-PICCs placed by a neonatologist via an incision in the antecubital fossa or anterior to the medial malleolus. The vein is isolated, catheter tunneled, venotomy performed, and a catheter inserted directly into the vessel.

### *Data Source*

We abstracted single-center data from the Children's Hospital Neonatal Database in addition to a review of individual patient electronic medical records (Epic). Children's Hospital Neonatal Database is a national repository of prospective, clinical data collected from 34 participating regional NICUs, and detailed data abstraction practices have been previously published.<sup>16</sup> Perinatal, neonatal, and catheter-specific data was collected for all eligible infants who received a PICC, cd-PICC, or sCVC during their NICU admission. Data were identified at the patient and catheter level, to isolate consecutive catheters (catheters placed in succession, no overlap in catheter days) and concurrent catheters (catheters with an overlap in catheter days). Additional catheter data included dwell time, French size (Fr), lumen number, insertion site, and removal indication. Perinatal characteristics included maternal demographic and referral data, whereas neonatal characteristics encompassed gestational age, birth weight, primary diagnosis, markers of illness severity, anthropometric data, and length of stay. The Colorado Multiple Institutional Review Board approved this study (COMIRB 16–0583).

### *Patient Population*

The study included all infants who received a PICC, cd-PICC, or sCVC following admission during the study period. We excluded umbilical venous catheters, as they are limited to the immediate postnatal period. CVCs placed before admission or after transfer to another unit are also excluded ( $n = 14$ ), as are catheters with insufficient data for analysis ( $n = 6$ ) and duplicate catheter entries ( $n = 5$ ).

## *Outcomes*

The primary outcome of interest is the incidence of NER, with time to NER as a secondary outcome. Time to NER was defined as the time in days to any complication resulting in NCR, in which deaths were censored.

### *Data Analysis*

Demographic and clinical characteristics were compared using 1-way ANOVA, Kruskal-Wallis, and chi-square tests for continuous, non-normally distributed continuous, and categorical variables, respectively. Variables were visually assessed for normality using histograms. Subject and catheter variables were analyzed separately. It was possible for subjects to receive multiple catheters of the same type and/or all 3 types of catheters: PICC, cd-PICC, and sCVC. In the case of multiple catheters per subject, subject postmenstrual age (PMA) at catheter placement was considered at the first catheter placement. We considered catheters from the same subject as independent observations for the analysis of catheter characteristics.

A Kaplan-Meier plot was used to assess time-to-NER curves for the 3 catheter types and a log-rank test used for comparison. Catheters removed for other indications were censored at the time of removal or death. The association between NER due to complication and demographic and clinical characteristics was assessed using chi-square tests and generalized linear mixed models with a random intercept for the subject. Catheters removed due to death are excluded. Multivariable models for catheter and patient characteristics were created based on variables that were significant at the 0.05 level in univariate analysis. A final multivariable model was created using significant variables from these 2 characteristic models (R version 3.1.1 software; R Foundation for Statistical Computing, Vienna, Austria).

## RESULTS

A total of 1,278 catheters placed in 915 infants were eligible for analysis. Approximately 126 (13.8%) patients received more than 1 catheter and/or catheter type during their hospitalization (Fig. 1) and dwell time for CVCs ranged from 1 to 364 days. We stratified maternal and infant demographic and clinical characteristics by catheter type and summarized in Table 1. Gestational age, birth weight, and PMA at first catheter placement varied between groups, with infants receiving a PICC in isolation or combination with other catheter types demonstrating a lower mean gestational age, birth weight, and PMA at first catheter placement when compared with infants receiving cd-PICCs or sCVCs.

No standardized, composite severity of illness score was available for analysis. As surrogate markers of illness severity, 15% of the study population had a 5-minute Apgar <5 and 44% required vasopressor therapy for hypotension during their admission, with rates varying

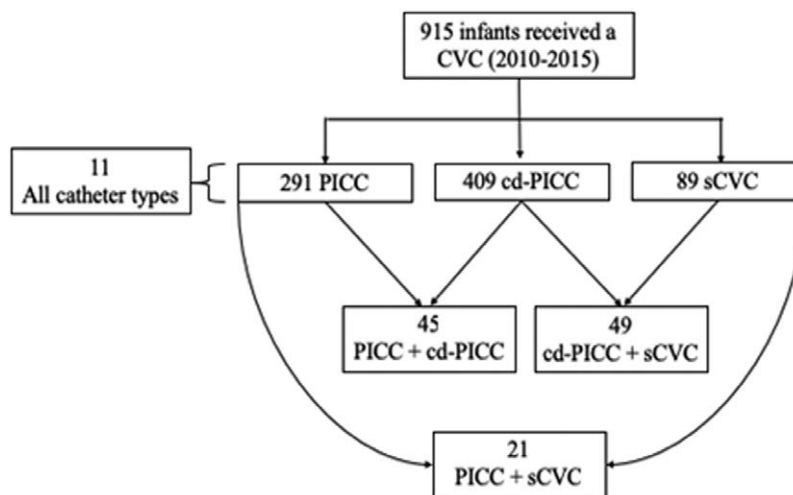


Fig. 1. CVC type inserted during level IV NICU admission for the 915 eligible infants.

Table 1. Maternal and Infant Demographic and Clinical Characteristics\*

Variable	All (n = 915)	PICC (n = 291)	cd-PICC (n = 409)	sCVC (n = 89)	PICC + cd-PICC (n = 45)	PICC + sCVC (n = 21)	cd-PICC + sCVC (n = 49)	All CVC Types (n = 11)
Maternal race								
White	510 (58%)	160 (58%)	240 (61%)	56 (64%)	17 (40%)	9 (45%)	25 (53%)	3 (27%)
Black	44 (5%)	21 (8%)	14 (4%)	2 (2%)	1 (2%)	1 (5%)	4 (9%)	1 (9%)
Hispanic	263 (30%)	81 (29%)	110 (28%)	27 (31%)	18 (43%)	8 (40%)	14 (30%)	5 (45%)
Other	58 (7%)	14 (5%)	27 (7%)	3 (3%)	6 (14%)	2 (10%)	4 (9%)	2 (18%)
Public insurance	184 (64%)	225 (56%)	46 (52%)	28 (62%)	15 (71%)	26 (53%)	6 (55%)	184 (64%)
Inborn	96 (11%)	32 (11%)	47 (12%)	3 (3%)	3 (7%)	3 (14%)	6 (12%)	2 (18%)
Sex (female)	399 (57%)	125 (43%)	175 (43%)	45 (51%)	20 (44%)	10 (48%)	20 (41%)	1 (9%)
GA (wk)	34±5	33±5	36±4	35±5	33±6	33±5	33±5	32±6
BW (kg)	2.36±1	2.03±1.05	2.70±0.95	2.37±1	1.94±1.04	2.01±0.82	2.08±1	1.72±1.09
PMA (wk)	37±7	36±8	39±6	40±8	34±6	36±8	39±7	37±8
Multiple gestation	95 (10%)	38 (13%)	33 (8%)	9 (10%)	7 (16%)	5 (24%)	3 (6%)	0 (0%)
SGA/IUGR	126 (14%)	46 (16%)	43 (11%)	13 (15%)	8 (18%)	6 (29%)	7 (14%)	3 (27%)
5-minute APGAR <5	117 (13%)	32 (13%)	62 (18%)	7 (9%)	6 (15%)	1 (5%)	7 (18%)	2 (18%)
Hypotension	403 (44%)	89 (31%)	240 (59%)	13 (15%)	24 (53%)	9 (43%)	23 (47%)	5 (45%)
Mechanical ventilation	792 (87%)	227 (78%)	361 (89%)	84 (94%)	43 (96%)	20 (95%)	46 (94%)	11 (100%)
Duration mechanical ventilation† (d)	6 (3–16)	5 (2–13)	7 (4–13)	4 (0–9)	14 (6–42)	8 (2–18)	22 (6–86)	33 (14–56)
ECMO	47 (5%)	1 (0%)	36 (9%)	1 (1%)	5 (11%)	0 (0%)	4 (8%)	0 (0%)
LOS (d)	47±56	45±42	33±43	53±66	63±55	92±74	114±104	115±67
Consecutive catheters	151 (17%)	22 (8%)	25 (6%)	9 (10%)	37 (82%)	15 (71%)	33 (67%)	10 (91%)
Concurrent catheters	129 (14%)	4 (1%)	70 (17%)	2 (2%)	14 (31%)	7 (33%)	29 (59%)	3 (27%)

BW indicates birth weight; GA, gestational age; SGA, small for gestational age; IUGR, intrauterine growth restriction; LOS, length of stay.

\*Only data from the first admission was used for subjects that had more than 1 admission.

†Presented values are medians and interquartile ranges (IQRs).

between catheter groups. Extracorporeal membrane oxygenation (ECMO) was performed in 5% of infants, most frequently in the PICC/cd-PICC group (11%). For individual catheter groups, infants receiving a PICC have the lowest birth weight and the fewest number of concurrent catheters, whereas those receiving an sCVC had the most consecutive catheters and longest length of stay.

We further analyzed catheter type concerning by primary patient diagnosis. The most common diagnoses within the study population are surgical, respiratory, infection, cardiac, prematurity, neurologic, genetic/metabolic, and “other.” Catheter type varied markedly between infants when stratified by primary diagnosis. PICCs are most frequently placed in infants due to prematurity (21%) or a surgical diagnosis (31%), whereas neonatologists place

cd-PICCs commonly for surgical (26%), respiratory (23%), or neurologic (17%) diagnoses. sCVCs most frequently are placed for a surgical diagnosis (63%).

Analysis of catheter level characteristics (Table 2) revealed significant differences between all catheter types when comparing insertion site, lumen number, catheter size (Fr), age at catheter placement, and catheter dwell time ( $P < 0.001$ ). PICCs and sCVCs are more likely to be single lumen (70% and 76%, respectively), whereas 75% of cd-PICCs have a double lumen. cd-PICCs are placed earlier (median, day of life (DOL) 6 when compared with DOL 9 and 33 for PICCs and sCVCs, respectively) and have the shortest dwell time (median, 10 days versus 12 and 22 days, respectively).

For the primary outcome (Fig. 2), NER was cause for removal in 15% of all catheters, with relative rates by

Table 2. Catheter Level Characteristics for PICC, cd-PICC, and sCVCs

Variable	PICC (n = 291)	cd-PICC (n = 409)	sCVC (n = 89)	P
Insertion site				
Arm	285 (69%)	487 (73%)	0 (0%)	<0.0001
Leg	123 (30%)	169 (25%)	43 (21%)	
Head/neck/chest	3 (1%)	0 (0%)	123 (61%)	
Femoral	2 (0%)	7 (1%)	36 (18%)	
Lumens				<0.0001
Single	290 (70%)	163 (25%)	153 (76%)	
Double	123 (30%)	500 (75%)	49 (24%)	
Catheter size (Fr)				<0.0001
1–1.1	80 (20%)	15 (2%)	0 (0%)	
1.9–2	236 (58%)	371 (57%)	1 (1%)	
2.6–2.8	71 (18%)	14 (2%)	76 (38%)	
3–5.5	17 (4%)	252 (39%)	121 (61%)	
DOL at catheter placement*	9 (4–30)	6 (2–26)	33 (6–94)	<0.0001
Dwell time (d)*	12 (8–18)	10 (7–18)	22 (8–56)	<0.0001

\*Presented values are medians and IQRs (thus representing values between the 25% and 75%).

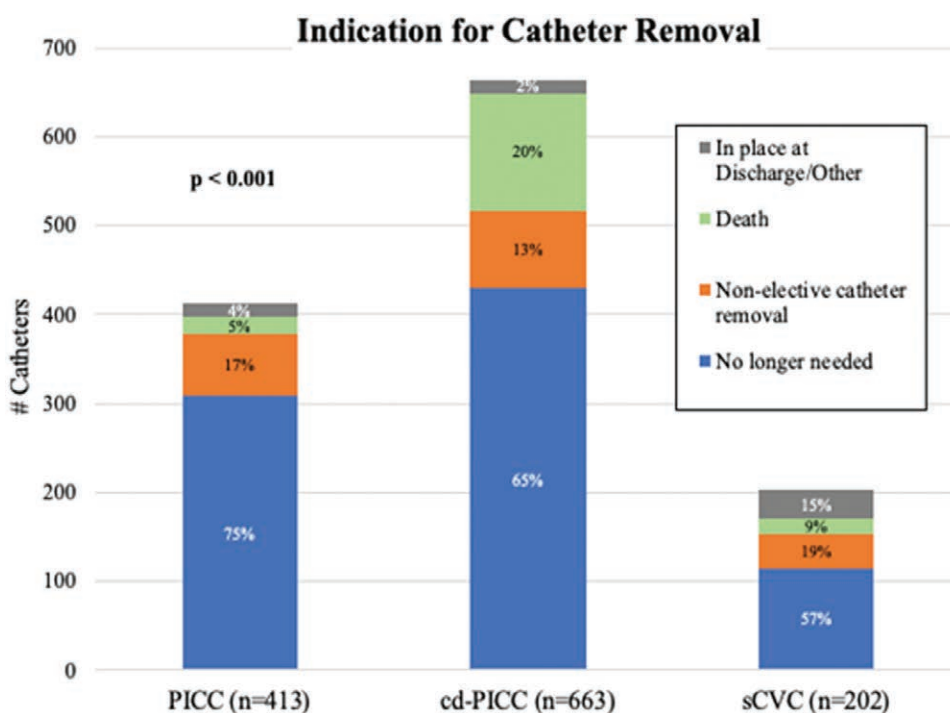


Fig. 2. Indication for catheter removal with the incidence of NER as stratified by catheter type.

catheter type of 17% for PICCs, 13% for cd-PICCs, and 19% for sCVCs ( $P < 0.001$ ). Common indications for NER are catheter breakage, BSI/CLABSI, catheter malposition, mechanical obstruction, extravasation, and unplanned removal (Supplementary Table 1, <http://links.lww.com/PQ9/A99>). Thrombosis, pericardial effusion, and pleural effusion were infrequent. Kaplan-Meier plot (Supplementary Figure 1, <http://links.lww.com/PQ9/A102>) demonstrated a significant difference in time to NER between catheter types with median time for PICCs 48 days (95% confidence interval, 34, inestimable), cd-PICCs 63 days (44–73 days), and sCVCs 139 days (117–168 days) ( $P < 0.0001$ ).

In bivariate analysis, we examined the association between infant and catheter characteristics and NER (Supplementary Table 2, <http://links.lww.com/PQ9/>

A100). Gestational age ( $P < 0.001$ ), catheter dwell time, ( $P < 0.001$ ), primary diagnosis ( $P = 0.002$ ), and both consecutive and concurrent catheters ( $P < 0.01$ ) are significantly associated with NER.

Univariate models reveal patient characteristics such as gestational age, birth weight, cardiac and neurologic diagnoses, and age at catheter placement as associated with NCR. None of the markers of increased illness severity were significantly associated with increased odds of NER (Supplementary Table 3, <http://links.lww.com/PQ9/A101>). Catheter dwell time of 8–59 days has lower odds of NER relative to younger than 8 or older than 59 days, whereas concurrent catheters demonstrate increased odds of NER ( $P < 0.005$ ). In the final multivariable model (Table 3), lower birth weight, a cardiac diagnosis, the day



**Table 3. Multivariate Model for Predictors of NER**

Variable	OR (95% CI)	P
Birth weight (kg)	0.78 (0.64–0.95)	0.0162
DOL at catheter placement (wk)	1.03 (1–1.05)	0.038
Concurrent catheter	2.22 (1.27–3.86)	0.0049*
Dwell time (d, reference <8)		
9–59	0.29 (0.18–0.45)	<0.0001
>59	0.99 (0.37–2.64)	0.9821
Cardiac diagnosis	2.32 (1.35–3.98)	0.0022

OR indicates odds ratio; CI, confidence interval; DOL, day of life.

\*After adjusting for birth weight (kg), day of life at catheter placement, dwell time, and cardiac diagnosis concurrent catheter was significantly associated with NER due to complication;  $P = 0.0049$ . The odds of NER were 122% (27%–286%) higher for concurrent catheters compared with catheters that were not placed concurrently.

of life at catheter placement, concurrent catheters, and catheter dwell time of younger than 8 days or older than 59 days are associated with increased odds of NER. In this adjusted model, the odds of NER are 122% (27%–286%) higher for concurrent catheters compared with catheters not placed concurrently.

## DISCUSSION

In this study, we examine NER in a complex, critically ill, level IV NICU cohort and demonstrate several findings of note. We report that patient characteristics, catheter characteristics, and the indication for NER varied significantly by catheter type in a previously understudied patient population and observed NER in 15% of study patients. Additionally, we demonstrate that time to NER varies significantly by catheter type, with sCVCs having the longest time to NER in this population. Cardiac and neurologic diagnoses, lower birth weight/gestational age, catheter dwell time of younger than 8 days or older than 59 days, and concurrent catheters are all associated with increased odds of NER.

No previous comparative studies between these 3 catheter types have been published, nor has the differential incidence, indication, or predictors of NER. One previous study reported similar overall rates of complication and infection between PICC and sCVCs in a very low birth weight (VLBW) patient population.<sup>17</sup> We found similar risk of NER when stratified by catheter type, despite differences in illness severity within catheter groups, as local practice utilizes cd-PICC placement for rapid central venous access in the highest acuity patients. Although minimal data have been published on neonatologist placed cd-PICCs, our study suggests that the complication rate for cd-PICCs is similar to PICCs and sCVCs and thus cd-PICCs may be a potentially safe alternative for central venous access.

Our composite NER rate of 15% is significantly lower than previous studies evaluating this outcome, with previously reported rates ranging from 31% to 46%.<sup>5,10,18,19</sup> Potential explanations for this difference include unique patient populations encompassing distinct mean gestational ages and birth weights. Additionally, high acuity

may increase the frequency of patients in our study with concurrent catheters which are often used for acute resuscitation, and as such, 1 catheter may be removed more quickly and electively.

NER was seen least frequently for a catheter dwell time of 8–59 days. Association between longer dwell time and complications such as bloodstream infections has been reported for PICCs and sCVCs, though with somewhat conflicting results regarding timing and magnitude of risk.<sup>10,20,21</sup> Our results indicate NER is most likely in the first week after catheter placement, likely related to local/mechanical complications, followed by a period of relative stability in NER risk. For those catheters that do not experience an early complication, prolonged use beyond 2 months appears to increase NER.

Finally, the presence of concurrent catheters is significantly associated with NER. Data from Milstone et al<sup>20</sup> suggest increased infection risk with concurrent catheters (adjusted incidence rate ratio (aIRR), 2.04; 95% confidence interval, 1.12–3.71), which is 1 plausible explanation for this finding. Another explanation is that infants with greater illness severity are more likely to have concurrent catheters and catheter-associated complications, thus a potential source of confounding. However, even after attempting to control for markers of illness severity and excluding death in the model, the use of concurrent catheters was associated with NER. Similar to Costa et al,<sup>5</sup> we found an association between consecutive catheters and the primary outcome in univariate analysis. However, this finding did not persist in multivariable models for NER.

NER is an important outcome of the study in the neonatal population and one for which a better understanding of modifiable predictors could lead to improved outcomes.<sup>5</sup> Also, whereas mechanical causes of NER may have only short-term sequelae, complications such as infection and thrombosis may have significant long-term implications. Bloodstream infection was the second most frequent indication for NER in our population, and neonatal catheter-associated infection increases morbidity and mortality including longer mechanical ventilation, prolongs hospitalization, increases the rate of prematurity complications, and worsens neurologic outcomes.<sup>22–26</sup> We identified modifiable risk factors such as dwell time and concurrent catheter use to be variables associated with NER. As such, strong consideration of catheter removal by 2 months and reduction in the use of concurrent catheters when clinically feasible may decrease catheter-associated complications and improve neonatal outcomes.

Utilizing the findings of our retrospective cohort analysis, we propose a quality improvement initiative to address identifiable and modifiable risk factors (Fig. 3). The next steps for this project will include interventions to prospectively identify high-risk diagnoses, reduce concurrent catheter use and catheter dwell time, and prevent complications leading to NER such as malposition, extravasation, and bloodstream infection.

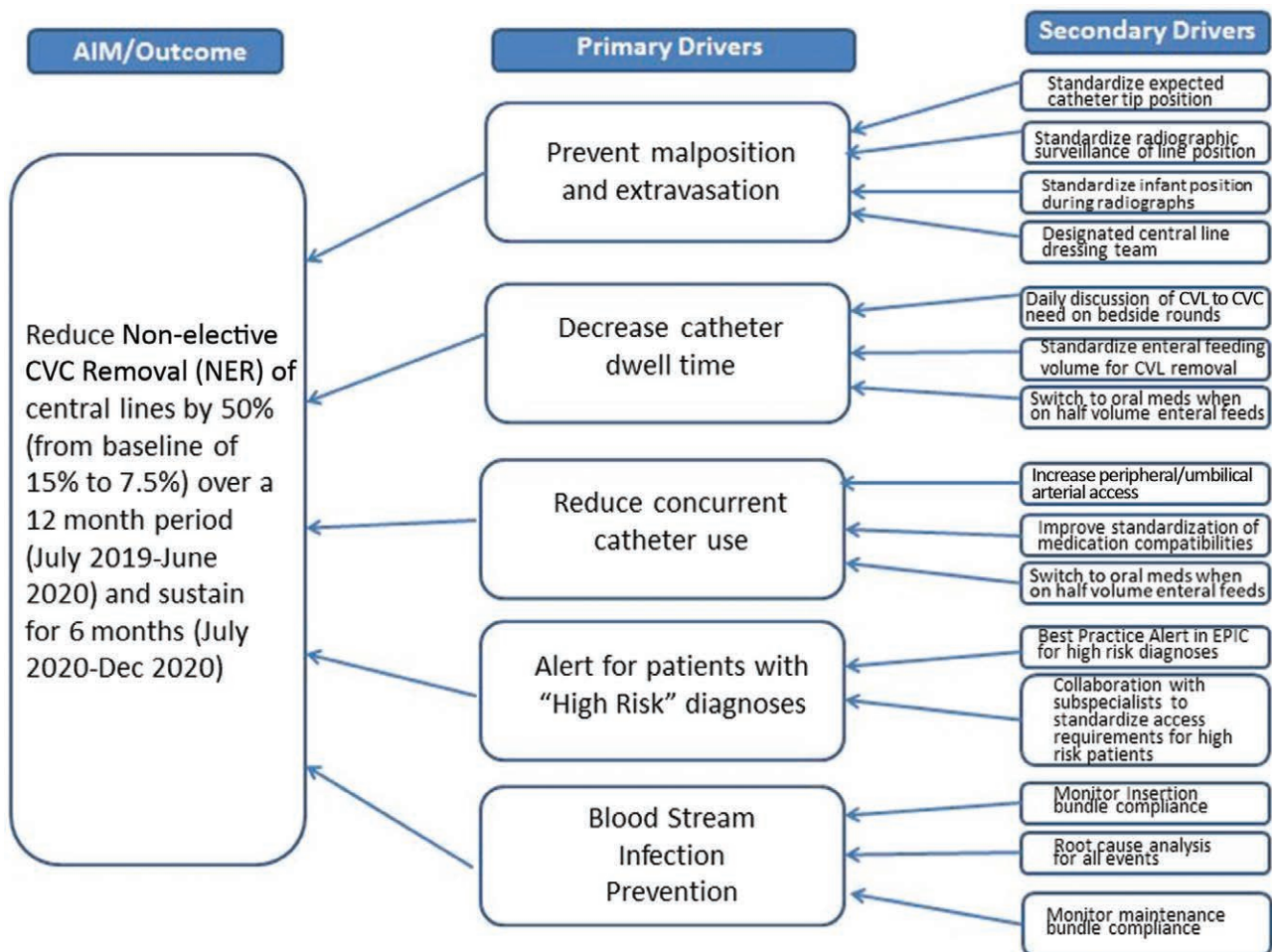


Fig. 3. Proposed Quality Improvement initiative utilizing the study outcomes.

**Strengths and Limitations**

This study is notable for a large, high-acuity, and heterogeneous patient cohort, as well as its focus on NER, for which limited neonatal literature exists. This challenging neonatal population is increasingly found in contemporary level IV NICUs across the country, is progressively complex, and is likely to be unique compared with the traditionally studied preterm population. As increased acuity and medical complexity arguably increase the risk for catheter-associated complications, this is a vital study population. Importantly, we describe patient and catheter characteristics associated with the use of different catheter types, as well as the relative rates and indications for NER as analyzed by catheter type. Although PICCs and sCVCs are relatively standard in the NICU, neonatologist placed cd-PICCs have not been well described in the medical literature. This study supplements existing surgical and neonatal literature on cd-PICCs and serves to further describe their use, characteristics, and safety in neonates.

Limitations include the retrospective and single-center nature of the study. Also, although efforts were made to control for confounding by severity of illness, this was limited by the lack of prospective illness severity scoring

and inability to retrospectively assign a validated severity of illness score. Selection of illness severity variables included those likely to coincide with CVC use (APGAR score, ECMO, and vasopressor use), but they were not stratified by time of occurrence and thus may have been present following catheter removal. As the level of illness distinctly influences the selection of catheter type, this effect may persist despite controlling for variables associated with increased illness severity. Additionally, we only analyzed the effect of birth weight on NER rather than age at the time of catheter insertion, which may also affect NER. Finally, the catheter tip position within a central vessel is associated with lower rates of catheter-associated complications.<sup>13</sup> In this study, the majority of catheters were in central location upon placement (>90%). However, we did not perform routine surveillance of tip position, so tip migration cannot be excluded as a contributing factor in some cases of NER.

**CONCLUSIONS**

In conclusion, NER is an important outcome of interest in neonatal care and occurred in 15% of CVCs in this study.

Specific patient and catheter characteristics associated with NER include patient diagnosis, lower gestational age/birth weight, longer dwell time, and concurrently placed catheters. These data provide the groundwork for a planned quality improvement initiative which will include a risk stratification strategy for high-risk neonatal patient populations and limiting the use of catheters beyond 59 days and concurrent catheters when feasible. Additional prospective studies may allow for further control of confounding by illness severity and provide evidence to develop a more extensive risk stratification model.

## DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

## REFERENCES

- Shah PS, Shah VS. Continuous heparin infusion to prevent thrombosis and catheter occlusion in neonates with peripherally placed percutaneous central venous catheters. *Cochrane Database Syst Rev*. 2008;2:CD002772.
- Hoang V, Sills J, Chandler M, et al. Percutaneously inserted central catheter for total parenteral nutrition in neonates: complications rates related to upper versus lower extremity insertion. *Pediatrics*. 2008;121:e1152–e1159.
- Colacchio K, Deng Y, Northrup V, et al. Complications associated with central and non-central venous catheters in a neonatal intensive care unit. *J Perinatol*. 2012;32:941–946.
- Liu H, Han T, Zheng Y, et al. Analysis of complication rates and reasons for nonelective removal of PICCs in neonatal intensive care unit preterm infants. *J Infus Nurs*. 2009;32:336–340.
- Costa P, Kimura AF, Brandon DH, et al. Predictors of nonelective removal of peripherally inserted central catheters in infants. *Biol Res Nurs*. 2016;18:173–180.
- Hsu JF, Tsai MH, Huang HR, et al. Risk factors of catheter-related bloodstream infection with percutaneously inserted central venous catheters in very low birth weight infants: a center's experience in Taiwan. *Pediatr Neonatol*. 2010;51:336–342.
- Panagiotounakou P, Antonogeorgos G, Gounari E, et al. Peripherally inserted central venous catheters: frequency of complications in premature newborn depends on the insertion site. *J Perinatol*. 2014;34:461–463.
- Wrightson DD. Peripherally inserted central catheter complications in neonates with upper versus lower extremity insertion sites. *Adv Neonatal Care*. 2013;13:198–204.
- Jain A, Deshpande P, Shah P. Peripherally inserted central catheter tip position and risk of associated complications in neonates. *J Perinatol*. 2013;33:307–312.
- Erhard DM, Nguyen S, Guy KJ, et al. Dwell times and risk of non-elective removal of 1-French peripherally inserted central catheters according to catheter tip position in very preterm infants. *Eur J Pediatr*. 2017;176:407–411.
- Isemann B, Sorrels R, Akinbi H. Effect of heparin and other factors associated with complications of peripherally inserted central venous catheters in neonates. *J Perinatol*. 2012;32:856–860.
- Gray BW, Gonzalez R, Warriar KS, et al. Characterization of central venous catheter-associated deep venous thrombosis in infants. *J Pediatr Surg*. 2012;47:1159–1166.
- Costa P, Bueno M, Alves AM, et al. Incidence of nonelective removal of percutaneously inserted central catheters according to tip position in neonates. *J Obstet Gynecol Neonatal Nurs*. 2013;42:348–356.
- Vierboom L, Darani A, Langusch C, et al. Tunnelled central venous access devices in small children: a comparison of open vs. ultrasound-guided percutaneous insertion in children weighing ten kilograms or less. *J Pediatr Surg*. 2018;53:1832–1838.
- Sharpe E, Pettit J, Ellsbury DL. A national survey of neonatal peripherally inserted central catheter (PICC) practices. *Adv Neonatal Care*. 2013;13:55–74.
- Murthy K, Dykes, FD, Padula MA, et al. The Children's Hospitals Neonatal Database: an overview of patient complexity, outcomes, and variation in care. *J Perinatol*. 2014; 34(8): 582–586.
- Foo R, Fujii A, Harris JA, et al. Complications in tunneled CVL versus PICC lines in very low birth weight infants. *J Perinatol*. 2001;21:525–530.
- Paiva ED, Costa P, Kimura AF, et al. Reasons for non-elective removal of epicutaneous catheters in neonates. *Rev Esc Enferm USP*. 2013;47(6):1279–1284.
- Bulbul A, Okan F, Nuhoglu A. Percutaneously inserted central catheters in the newborns: a center's experience in Turkey. *J Matern Fetal Neonatal Med*. 2010;23:529–535.
- Milstone AM, Reich NG, Advani S, et al. Catheter dwell time and CLABSIs in neonates with PICCs: a multicenter cohort study. *Pediatrics*. 2013;132:e1609–e1615.
- Sanderson E, Yeo KT, Wang AY, et al; NICUS Network. Dwell time and risk of central-line-associated bloodstream infection in neonates. *J Hosp Infect*. 2017;97:267–274.
- Payne NR, Carpenter JH, Badger GJ, et al. Marginal increase in cost and excess length of stay associated with nosocomial bloodstream infections in surviving very low birth weight infants. *Pediatrics*. 2004;114:348–355.
- Stoll BJ, Hansen NI, Adams-Chapman I, et al; National Institute of Child Health and Human Development Neonatal Research Network. Neurodevelopmental and growth impairment among extremely low-birth-weight infants with neonatal infection. *JAMA*. 2004;292:2357–2365.
- McMullan RL, Gordon A. Antibiotics at the time of removal of central venous catheter to reduce morbidity and mortality in newborn infants. *Cochrane Database Syst Rev*. 2018;3:CD012181.
- Makhoul IR, Sujov P, Smolkin T, et al; Israel Neonatal Network. Pathogen-specific early mortality in very low birth weight infants with late-onset sepsis: a national survey. *Clin Infect Dis*. 2005;40:218–224.
- Alshaikh B, Yee W, Lodha A, et al. Coagulase-negative staphylococcus sepsis in preterm infants and long-term neurodevelopmental outcome. *J Perinatol*. 2014;34:125–129.