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Risk Factors for Peripherally Inserted Central Venous Catheter Complications in Children

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Abstract

Objective(s)—To characterize the epidemiology and identify risk factors for complications necessitating removal of peripherally inserted central venous catheters (PICCs) in children.

Design—Cohort study

Setting—The Johns Hopkins Children’s Center, Baltimore, Maryland.

Participants—Hospitalized children who had a PICC inserted outside of the neonatal ICU between January 1, 2003 and December 1, 2009.

Main Exposures—Age, PICC dwell time, PICC insertion site, PICC tip location, pediatric ICU exposure, indication for PICC insertion

Outcome Measures—Complications necessitating PICC removal as recorded by the PICC Team.

Results—During the study period, 2574 PICCs were placed in 1807 children. Complications necessitating catheter removal occurred in 20.8% of PICCs during 46,021 catheter days (11.6 complications per 1,000 catheter days). These included accidental dislodgement (4.6%), infection (4.3%), occlusion (3.6%), local infiltration (3.0%), leakage (1.5%), breaks (1.4%), phlebitis (1.2%) and thrombosis (0.5%). From 2003 to 2009 complications decreased by 15% per year (IRR 0.85; 95% CI 0.81-0.89). In adjusted analysis, all non-central PICC tip locations - midline (IRR

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4.59, 95% CI 3.69-5.69), mid-clavicular (IRR 2.15, 95% CI 1.54-2.98), and other (IRR 3.26 95% CI 1.72-6.15) - compared to central tip location were associated with an increased risk of complications. Pediatric ICU exposure and age less than one year old were independently associated with complications necessitating PICC removal.

Conclusion(s)—Non-central PICC tip locations, younger age, and pediatric ICU exposure were independent risk factors for complications necessitating PICC removal. Despite reductions in PICC complications, further efforts are needed to prevent PICC-associated complications in children.

Keywords

Catheter-Related infection; Pediatrics; Catheters; Epidemiology

BACKGROUND

Central venous catheters (CVCs) provide secure vascular access to facilitate delivery of medications and nutrition to hospitalized children.¹ Peripherally inserted central venous catheters (PICCs) can be conveniently inserted at the bedside without the need for surgical intervention and are commonly used in pediatrics. Despite these advantages, PICCs are prone to infectious, thrombotic and mechanical complications. These complications are associated with morbidity, so data are needed to inform quality improvement efforts.

Previous studies have identified risk factors for complications of PICCs in children including young age, severity of illness, catheter dwell time, catheter tip location, and catheter insertion site.¹⁻³ Identifying modifiable risk factors of complications is especially important as clinicians work to prevent catheter complications. Previous studies evaluating modifiable risk factors such as catheter dwell time, catheter insertion site, and catheter tip location have had inconsistent results.²⁻¹⁵ Our objective was to determine the association between patient and catheter characteristics and the risk of complications necessitating PICC removal in children.

MATERIALS AND METHODS

PATIENTS AND SETTING

A cohort was compiled of 1819 children who were admitted to the 175-bed Johns Hopkins Children's Center and had a PICC inserted between January 2003 and December 2009. Children admitted to the 30-bed Pediatric Intensive Care Unit (ICU) and the medical/surgical wards were included, but patients in the neonatal ICU were excluded. The pediatric PICC team placed all PICCs, and as previously described² maintained a database of all children with PICCs. The database contains indications for PICC insertion. Members of the PICC team, who were not blinded to patient characteristics, prospectively documented complications necessitating PICC removal, including infectious complications and non infectious complications (see eTable 1) and reviewed hospital records and contacted home care companies or healthcare providers to determine PICC disposition and complications following discharge.

DATA COLLECTION

The PICC team prospectively collected age, sex, race, ethnicity, indication for catheter insertion, and other catheter characteristics. Medical records were queried to validate the PICC database. An administrative claims database was queried to extract information regarding ICU admissions, ICD-9 codes, and length of hospital stay. PICCs were defined as peripherally inserted central venous catheters that were inserted with the intention of

terminating at or close to the heart or in one of the great vessels. Exposures were determined prospectively by the PICC team. PICCs were defined as central at time of placement if they resided in the superior vena cava (SVC), right atrial junction (RAJ), or high inferior vena cava (IVC) or above the level of the diaphragm for lower extremity catheters, and as non-central if located elsewhere.¹⁶ For PICCs placed in the arm, non-central tip locations were further categorized as 'midline' if catheter tip extended no further than axilla, as 'midclavicular' if the catheter tip extended to the middle of the clavicle on x-ray, and as 'other tip location' if the tip extended beyond the middle of the clavicle on x-ray but not into the SVC, or were scalp catheters with tips above the level of the clavicle or lower extremity PICCs with tips below the IVC.

Catheters were removed after completion of therapy or due to a complication. The primary outcome, complications necessitating PICC removal, was defined as outlined in eTable 1 and was divided into secondary outcomes of infectious and non-infectious complications necessitating PICC removal recognizing that risk factors may vary for different complications. The time at risk for complication was the PICC dwell time, calculated as the number of days between PICC insertion and PICC removal.

After exploratory data analysis, variables were categorized for analysis. Age was not evenly distributed and was categorized into quartiles. ICD9 codes were collected for each patient's hospitalization and categorized into underlying complex chronic medical conditions.^{2, 17} To account for severity of illness, patients were categorized as those requiring intensive care in the pediatric ICU (PICU) (referred to as having "PICU exposure") and those not requiring intensive care or having "no PICU exposure". PICC insertion sites were categorized into upper extremity, lower extremity, and head and neck.

STATISTICAL ANALYSIS

Descriptive analyses were performed to characterize the patients and catheter characteristics. We report median values along with the 25th and 75th percentiles for age, PICC duration and length of stay. Patients whose PICCs were removed in the hospital, but who did not have a documented reason for PICC removal in the PICC database or the medical record (n=12, <1%) were not included in the analysis. Patients transferred to another facility for which outcome data were not available were censored at time of hospital discharge.

Independent predictors of any complication necessitating PICC removal were assessed in bivariate and multivariable analyses using Poisson regression models to estimate incidence rate ratios (IRR). Covariates determined a priori to be independent predictors of complications and those with P < 0.10 in bivariate analysis were included. Variables were retained in the final model if they were deemed clinically relevant or if they were observed to have a confounding effect on the association between another predictor and risk of complication. A confounding effect was defined as a change in a model coefficient by >10% after removal of a single variable from the model. After exploring the initial data, cubic spline terms were introduced for modeling PICC dwell time to account for a non-linear association of complications over time.^{18, 19} Similar multivariable models were used to identify risk factors for infectious complications and non-infectious complications as outcomes. An interaction between catheter dwell time and tip location was explored by (1) including interaction terms explicitly in the full model and by (2) evaluating a graph of the model-estimated complication rates across catheter dwell time for a given catheter tip location, age group, PICU and antibiotic exposure status, site of PICC insertion, and year. The interaction term was not included in the final model as it did not improve model fit based on Bayesian Information Criterion (BIC) (results not shown).²⁰ Bootstrapping techniques with 1000 replications were used to assess the internal validity of the final model.^{21, 22} Model fit was confirmed by using Pearson's goodness-of-fit test.

This study was approved by Johns Hopkins University School of Medicine Institutional Review Board with waiver of informed consent. Data were maintained in Microsoft Access and were analyzed using Stata version 11.0 and R version 2.12.²³

RESULTS

During the study period, 2574 PICCs were placed in 1807 children. Over half of the children were male (55.6%). Fifty six percent of children were Caucasian, 32% were African American, and the median age was 5 years old (see Table 1). Median PICC dwell time was 13 days, and median length of hospitalization was 12 days. PICCs were inserted for indications such as administration of antibiotics (1352, 52.5%), total parenteral nutrition (200, 7.8%), chemotherapy (252, 9.8%) or for intravenous access (770, 29.9%). The majority of PICCs (1961, 76.4%) were inserted in the upper extremity. In this cohort, 2152 (83.9%) catheters had a central tip location, while 414 (16.1%) had a non-central tip location. Children with non-central PICCs were younger than those with central PICCs (median age 2 years vs. 7 years, $p < 0.001$).

Most PICCs (1901, 73.8%) were removed electively on completion of therapy, and 139 (5.4%) remained in place at time of patient transfer to an outside facility (see Table 2). Five hundred and thirty four PICCs (20.8%) were removed due to a complication during 46,021 catheter days (incidence rate 11.6 per 1000 catheter days), including 422 PICCs removed secondary to non-infectious complications and 112 PICCs removed for infectious complications. Of those removed for infectious complications, 66 (55.4%) met the National Healthcare Safety Network's criteria as a central line-associated bloodstream infections (CLABSI).²⁴

The incidence of complications declined from 17.2 per 1000 catheter days in the year 2003 to 5.5 per 1000 catheter days in 2009 (see Table 3). In parallel, the use of non-central PICCs declined from 14% in 2003 to 2.8% in 2009. Non-central PICCs were more likely to have complications necessitating removal than central catheters (46% vs. 17.6%; $P < .001$).

Bivariable analyses of potential risk factors for complications necessitating PICC removal are shown in Table 4. All non-central PICC tip locations - midline (IRR 5.57, 95% CI 4.54-6.83), mid-clavicular (IRR 3.62, 95% CI 2.65-4.95) and other (IRR: 4.12, 95% CI 2.20-7.72) compared to central tip location were associated with an increased risk of complications. Compared to children less than one year old, children in older age categories had lower risks of developing complications, with the most significant reduction in risk in those >13 years (IRR 0.35, 95% CI 0.27-0.44). PICU exposure was also associated with a significantly increased risk for complications leading to PICC removal (IRR 1.71, 95% CI 1.44-2.03).

After adjusting for other variables including catheter dwell time, age, insertion site, PICU exposure, indication for PICC insertion, and year of PICC insertion, non-central tip locations were associated with an increased risk of complications compared to central locations (all non-central tip locations - IRR 3.58; 95% CI 2.94-4.34; midline tip location - IRR 4.59, 95% CI 3.69-5.69; mid-clavicular tip location - IRR 2.15, 95% CI 1.54-2.98, and other tip locations - IRR 3.26 95% CI 1.72-6.15) (Table 4). Compared to age group less than 1 year, all age groups remained important risk factors for complications. After adjusting for other variables, children who had PICU exposure during their hospitalization were at 24% increased risk for developing a complication that necessitated PICC removal (IRR: 1.24, 95% CI 1.03-1.52). However, site of PICC insertion and clinical indication for PICC insertion were no longer associated with complications in adjusted analyses.

Recognizing that there may be different risk factors for infectious and non-infectious complications necessitating catheter removal, we performed a sub-analysis to look at variables associated with each outcome (Table 5). After adjusting for catheter dwell time, age, insertion site, tip location, indication for PICC insertion, and year of PICC insertion, ICU exposure was a risk factor for infectious complications, but not non-infectious complications. A non-central tip location was strongly associated with non-infectious complications but not with infectious complications (IRR 4.56 95% CI 3.67-5.61 and IRR 0.75 95% CI 0.34-1.50, respectively).

Figure 1 illustrates the complex and non-linear interaction of catheter dwell time and risk of complication in PICCs with central and non-central locations. PICCs with non-central locations have a consistently higher risk of non-infectious complication regardless of catheter duration, but this association is not seen for infectious complications.

DISCUSSION

We report results from a large cohort of hospitalized children with PICCs that will help clinicians provide anticipatory guidance to families when discussing PICC complications, and that identifies a target for future quality improvement efforts. Although PICCs with a non-central catheter tip location represented a small percentage (16.1%) of inserted PICCs, these catheters were more than three times as likely to be removed secondary to a complication compared with PICCs with a central tip location. Younger children and those with pediatric ICU exposure during the current hospitalization were at increased risk of complications. At our institution, PICC complication rates in children decreased from 17.2 per 1000 catheter days in 2003 to 5.5 per 1000 catheter days in 2009, but further efforts are needed to prevent infectious and non-infectious complications of PICCs in children.

Our data represent the largest study of children with PICCs to report complications necessitating PICC removal. Our study reports similar complication rates to prior studies that have reported rates ranging from 17% to 50%.^{2, 3, 12, 15, 25-28} This large variation in complication rates may be in part explained by differences in types of complications reported (infectious, non-infectious, or both combined), and different populations studied (e.g. oncology or ICU). Additionally, ascertainment of complications can vary by study, for example, our study was unique in that our PICC team followed children to determine PICC disposition after hospital discharge. This approach identified that 25% of complications necessitating removal occurred after hospital discharge.

The association of catheter-tip location and PICC complications remains unclear from conflicting studies in children. Some pediatric studies have found that PICCs placed in non-central veins provided safe and reliable intravenous access^{13, 15}, while others suggested that PICCs terminating in non-central venous locations have higher complication risks.^{10, 14} These studies are difficult to compare in part because of inconsistent definitions of central veins. For example, many authors and clinicians define a PICC to terminate in a central vein if the tip is located in the IVC, SVC, or RAJ.^{9, 14} Other authors, clinicians, and the Centers for Disease Control and Prevention include the subclavian veins as central veins.^{15, 24, 29} Given the size of our cohort, these are the first pediatric data to compare PICCs with distal tip locations in the IVC, SVC and RAJ with PICCs in the subclavian veins and other non-central sites. After adjusting for other important predictors of PICC complications including age, catheter dwell time, PICC insertion site, PICU exposure, and indication for PICC insertion, our data confirmed previous findings that non-central catheter tip location are associated with increased complication rates.^{10, 14} Additionally, we found that PICCs terminating in any site outside the IVC, SVC, or RAJ, including subclavian veins, had an increased risk of complications necessitating removal. A previous study that found no

difference in complication rates between central and non-central PICCs classified 46% of PICCs terminating in the subclavian vein as central which may explain our differing results.¹⁵

Increased complication rates, especially mechanical complications in non-central PICCs may result from a combination of factors including turbulence, vessel size, blood flow rate and endothelial injury.¹⁴ Our data suggest that non-central catheters were an independent risk factor for non-infectious complications. When a central venous catheter is positioned in the SVC, the tip lies parallel to the vessel wall, so infused solutions dilute rapidly. PICCs cannot always be advanced to the SVC due to venospasm, venous valves, and vessel tortuosity.¹⁰ When the catheter tip lies in a non-central location, the tip may contact the vessel, irritate and disrupt the endothelial cell layer, expose the basement membrane, and trigger coagulation.³⁰ We observed a parallel in the reduction in PICC complication rates and the declining use of non-central PICCs from 2003 to 2009. Therefore, non-centrally located PICCs should be used with caution due to their increased risk of complication necessitating catheter removal.

Catheter dwell time has also been suggested as a risk factor for PICC complications with some studies finding longer dwell times associated with complications^{2, 18, 19, 31} and others finding shorter dwell times associated with complications.³ We illustrated the complex interaction of catheter dwell time and risk of complication in PICCs. For example the risk of infectious complications seemed to increase over the first few weeks then plateau, where the risk of non-infectious complications seemed to decrease over the first few weeks then plateau. We also showed that PICCs with non-central locations were prone to a consistently higher risk of non-infectious complication regardless of catheter duration, but were not prone to higher risk of non-infectious complications. These results may explain differences in associations between catheter dwell time and risk of complications in previous studies. Given that non-infectious complications were three times more common than infectious complications, ensuring a central tip location at the RAJ, IVC, or SVC is an appropriate step to prevent PICC complications. However, given the complex association of catheter dwell time with complications, these data do not support the hypothesis that prolonged catheter dwell times are associated with increased PICC complications.

Our data found that younger children were at increased risk of complications requiring PICC removal. Children older than 13 years were at lowest risk for complications, while those less than 1 year were at highest risk, consistent with previous findings that older age may protect against CVC-associated complications.³² Older children have structurally larger and more stable vessels that may tolerate catheters better. Therefore, age may confound the association between tip location and PICC complication, because advancing PICCs in younger children may be more challenging and this may lead to more unintended non-central PICCs in this age group. However, after adjusting for age, we still found an increased risk of complication in those PICCs with a non-central tip location.

Previous studies have identified insertion site as a risk factor for catheter-associated infection^{2, 5, 7}; however these findings have not been supported by other studies.^{4, 6, 33} In unadjusted analysis of our cohort, PICCs placed in the head and neck and lower extremities were associated with an increased risk for complications necessitating removal, however, after adjusting for other important variables including age, catheter dwell time, ICU exposure, indication for PICC insertion, and tip location, insertion site was no longer a significant risk factor for complications. Younger children were more likely to have complications and were more likely to have PICCs placed in the head and neck and lower extremities (data not shown), which may confound this perceived association.

Several limitations should be considered when interpreting our findings. First, a small percentage of patients (5%) were lost to follow up, mostly due to transfer to other healthcare facilities. However, for most catheters, prospective follow up by our PICC team reduced missing data and captured entire PICC dwell time including time after discharge. Secondly, we could only document complications that necessitated line removal; hence we likely underestimated the risk of complications, such as occlusion requiring tissue plasminogen activator (TPA) administration. Additionally, some catheter infections may have been treated with antibiotics while the PICC remained in place, a complication that was not captured. Finally, despite this large cohort, because this is a single-institution study, our findings may not be generalizable to other institutions.

CONCLUSION

Our large cohort and robust adjusted analyses identified non-central catheter tip location as a modifiable risk factor for complications necessitating PICC removal. Clinicians should be cautious in weighing the risks and benefits of maintaining a non-central PICC. Quality improvement initiatives should reinforce the importance of inserting PICCs to terminate in the RAJ, IVC, or SVC to reduce risk of complications. National efforts have dramatically reduced the risk of bloodstream insertions complicating central-venous catheters³⁴, but further efforts are needed to prevent all complications that lead to additional procedures, patient morbidity, and increased healthcare costs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

CVCs	Central venous catheters
PICCs	Peripherally inserted central venous catheters
CLABSI	Central Line–Associated Bloodstream Infection
RAJ	right atrial junction
SVC	superior vena cava
IVC	inferior vena cava
PICU	Pediatric Intensive Care Unit
BIC	Bayesian Information Criterion
IRR	Incidence Rate ratio
TPA	tissue plasminogen activator

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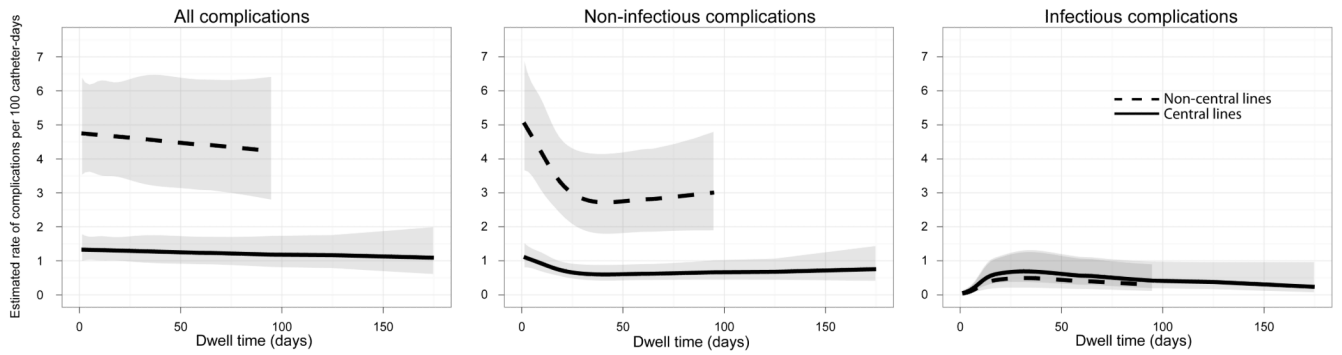


Figure 1. Predicted complication rates over catheter dwell time for a given catheter tip location, age group, PICU and antibiotic exposure status, site, and year. Rates for all complications, non-infectious complications, and infectious complications are stratified for PICCs with a central tip location (solid line) and a non-central tip location (dashed line) with 95% confidence intervals (shading).

Table 1
Characteristics of Hospitalized Children with Peripherally Inserted Central Venous Catheters (PICCs)

Age in years, Median (IQR)	5 (0.83-13)
Sex, n (%)	
Male	1005 (55.6)
Female	802 (44.4)
Race and Ethnicity, n (%)	
Caucasian	1017 (56.3)
African American	575 (31.8)
Asian	161 (8.9)
Hispanic	43 (2.4)
Other	11 (0.6)
PICC Duration in days, Median (IQR)	13 (7-21)
Length of hospital stay, Median (IQR)	12 (6-27)
Indication for PICC insertion, n (%)	
Antibiotics	1352 (52.5)
Total Parenteral Nutrition	200 (7.8)
Chemotherapy	252 (9.8)
Intravenous access	770 (29.9)
Complex chronic conditions, n (%) *	
Neuromuscular	270 (14.9)
Cardiovascular	767 (42.4)
Respiratory	263 (14.5)
Renal	107 (5.9)
Gastrointestinal	121 (6.7)
Hematologic and Immunodeficiencies	57 (3.2)
Metabolic	71 (3.9)
Congenital & Genetic	101 (5.6)
Malignancy	198 (11)
None	455(25.2)
Site of PICC Insertion, n (%)	
Upper Extremity (Basilic, Cephalic, Brachial)	1961 (76.4)
Lower extremity (Saphenous)	132 (5.6)
Head and Neck (Facial, Post Auricular, Ext Jugular)	464 (18.1)
Catheter Tip Location	
Central	2152(83.9)
Midline	262 (10.2)
Mid-Clavicular	121 (4.7)
Other	31(1.2)
Total Number of children hospitalized over study period, n	1807

* All conditions do not add up to a 100% as many chronic conditions overlap.

** 3.32% patients were transferred outside the hospital, and their lines were removed elsewhere

Table 2
Disposition of Peripherally Inserted Central Venous Catheters (PICCs)

Catheter Disposition	Total number (%)
Removed - no longer needed	1901(73.8)
Removed - infectious complications	112 (4.3)
Infection involving PICC	103 (4.0)
Suspected infection involving PICC	9 (0.3)
Removed -non infectious complications	422 (16.4)
Phlebitis	32 (1.2)
Local Infiltration	77 (3.0)
Thrombosis	14 (0.5)
Leakage	38 (1.5)
Occlusion	94 (3.6)
Dislodgement	119 (4.6)
Breakage	36 (1.4)
Other	12 (0.5)
Transferred *	139 (5.4)

* Transferred to another health-care facility with PICC, no further information is available on these patient

Table 3

Incidence Rate of complications by Year

Year	Incidence Rate of complications (per 1000 catheters days)	Incidence Rate of Infections complications (per 1000 catheters days)	Incidence Rate of Non-infectious complications (per 1000 catheters days)	Number of PICCs placed	Number of Non-central PICCs placed
2003	17.2	2.7	14.5	323	45 (14%)
2004	17.9	4.1	13.9	380	42 (11%)
2005	17.9	2.6	15.4	356	34 (9.6%)
2006	10.4	1.6	8.9	326	35 (10.7%)
2007	9.2	2.2	7.0	380	38 (10%)
2008	7.2	2.1	5.2	441	29 (6.6%)
2009	5.5	1.9	3.7	352	10 (2.8%)

Table 4
Adjusted and Unadjusted Risk Factors for Peripherally Inserted Central Venous Catheter (PICC) Complications

Variable	No Complication Number (%)	Complication Number (%)	IRR (95% CI)	p value	Adjusted IRR* (95% CI)	p value
Age						
<1 year	585 (28.7)	255 (47.8)	1		1	
1 to 7 years	401 (19.7)	103 (19.3)	0.58 (0.47-0.71)	<0.001	0.75 (0.60-0.94)	0.01
>7 to 13 years	560 (27.5)	77 (14.4)	0.28 (0.21-0.37)	<0.001	0.44 (0.33-0.60)	<0.001
>13 years	494 (24.2)	99 (18.5)	0.35 (0.27-0.44)	<0.001	0.45 (0.35-0.59)	<0.001
Sex						
Male	1073 (52.6)	301 (56.4)	1		1	
Female	967 (47.4)	233 (43.63)	0.85(0.72-1.01)	0.07	0.99 (0.83-1.18)	0.94
Site of PICC Insertion**						
Upper Extremity	1592 (78.2)	369 (69.3)	1		1	
Lower extremity	91 (4.5)	52 (9.8)	2.34 (1.75-3.13)	<0.001	1.08 (0.79-1.48)	0.64
Head and neck	353 (17.3)	111 (20.9)	1.34(1.09-1.67)	0.006	1.11 (0.89-1.39)	0.37
Clinical Indication for PICC insertion						
Intravenous Access	547 (26.8)	223 (41.7)	1		1	
Antibiotics	158 (7.8)	42 (7.9)	0.62 (0.51-0.76)	<0.001	0.86 (0.69-1.06)	0.15
Total Parenteral Nutrition	183 (9.0)	69 (13.0)	0.89 (0.64-1.24)	0.50	1.21 (0.86-1.69)	0.27
Chemotherapy	1152 (56.4)	200 (37.4)	1.08 (0.82-1.42)	0.58	0.95 (0.71-1.28)	0.74
Catheter Tip Location						
Central	1803 (88.6)	349 (65.8)	1		1	
Non-Central						
Midline	136 (6.7)	126 (23.8)	5.57 (4.54-6.83)	<0.001	4.59 (3.69-5.69)	<0.001
Mid-Clavicular	76 (3.7)	23 (8.5)	3.62 (2.65-4.95)	<0.001	2.15 (1.54-2.98)	<0.001
Other	21 (1.0)	10 (1.9)	4.12 (2.20-7.72)	<0.001	3.26 (1.72-6.15)	<0.001
PICU Exposure						
No	1236 (60.6)	221 (41.4)	1		1	
Yes	804 (39.4)	313 (58.6)	1.71 (1.44-2.03)	<0.001	1.24 (1.03-1.52)	0.03
Line Year	-	-	0.81 (0.78-0.85)	<0.001	0.85 (0.81-0.89)	<0.001

Abbreviations: CI, confidence interval; IRR, incidence rate ratio; PICU, pediatric intensive care unit.

* Adjusted for catheter dwell time using cubic spline terms

** Insertion sites for PICCs were classified as upper extremity, lower extremity and head and neck based on where the PICC was inserted

Table 5
Adjusted Risk Factors for Infectious Complications and Non-Infectious Complications

Variable	Infectious Complications		Non-Infectious Complications	
	Adjusted IRR* (95% CI)	<i>p</i> value	Adjusted IRR* (95% CI)	<i>p</i> value
Age categories				
<1 year	1		1	
1 to 7 years	0.89(0.54-1.48)	0.66	0.75(0.59-0.97)	0.03
>7 to 13 years	0.56(0.30-1.56)	0.07	0.43(0.30-0.59)	<0.001
>13 years	0.56(0.32-0.98)	0.04	0.47(0.35-0.63)	<0.001
Site of PICC Insertion **				
Upper Extremity	1		1	
Lower extremity	0.71(0.32-1.56)	0.41	1.21(0.85-1.70)	0.29
Head and neck	0.45(0.24-0.83)	0.01	1.26(0.99-1.61)	0.06
Tip Location				
Central	1		1	
Non-Central ***	0.75(0.34-1.50)	0.38	4.56(3.67-5.61)	<0.001
PICU Exposure				
No	1		1	
Yes	2.23(1.43-3.48)	<0.001	1.11(0.89-1.38)	0.35
Line Year	0.86(0.78-0.95)	0.003	0.86(0.82-0.91)	<0.001

Abbreviations: CI, confidence interval; IRR, incidence rate ratio; PICU, pediatric intensive care unit.

* Adjusted for catheter dwell time using cubic spline terms, sex, and indication for catheter insertion

** Insertion sites for PICCs were classified as upper extremity, lower extremity and head and neck based on where the PICC was placed

*** Catheter tip locations were categorized as non-central if they did not reside in the superior vena cava, right atrium, or high inferior vena cava or above the level of the diaphragm for lower extremity catheters.