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ORIGINAL RESEARCH

Effectiveness of Evidence-Based Continuous Quality Improvement in Reducing Peripherally Inserted Central Catheter Complications Among Premature Infants in China: A Four-Year Retrospective Study

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Purpose: This study evaluated the effectiveness of evidence-based continuous quality improvement strategies in reducing peripherally inserted central catheter complications among premature infants in a tertiary neonatal intensive care unit.

Patients and Methods: A retrospective cohort analysis was conducted on 722 premature infants requiring peripherally inserted central catheter placement from January 2020 to December 2023. The control group (n=154, January-December 2020) received routine bundle care, while a multidisciplinary evidence-based nursing team implemented continuous quality improvement protocols across three intervention periods: first-year implementation (n=147, 2021), second-year refinement (n=201, 2022), and third-year optimization (n=220, 2023). Primary outcomes included total complication rates and unplanned catheter removal. Multivariate logistic regression identified independent risk factors for complications.

Results: Baseline characteristics showed comparable gestational age (31.32±4.05 to 31.98±4.21 weeks, P=0.419) and insertion timing across groups. Total complication rates demonstrated progressive reduction from 46.10% in controls to 32.65% in year 1, 19.90% in year 2, and 15.45% in year 3 (χ^2=51.214, P<0.001), representing a 66.5% overall reduction. Unplanned removal rates decreased from 24.03% to 11.82% (χ^2=13.128, P=0.004). Multivariate logistic regression analysis revealed routine care (adjusted OR=4.707, 95% CI: 2.861–7.742, P<0.001) and first-year implementation (adjusted OR=2.672, 95% CI: 1.595–4.477, P<0.001) as independent risk factors, while higher gestational age was protective (adjusted OR=0.876, 95% CI: 0.837–0.916, P<0.001).

Conclusion: Implementation of evidence-based continuous quality improvement strategies achieved substantial and sustained reductions in peripherally inserted central catheter complications among premature infants, supporting systematic adoption of multidisciplinary approaches to optimize vascular access outcomes in vulnerable neonatal populations.

Keywords: evidence-based practice, quality improvement, infant, premature, central venous catheters, postoperative complications, intensive care, neonatal

Introduction

Premature infants represent one of the most vulnerable patient populations within healthcare systems, characterized by underdeveloped physiological systems and heightened susceptibility to iatrogenic complications.[1,2] The management of vascular access in these infants presents particular challenges, as their survival often depends on prolonged intravenous therapy for nutrition, medications, and other essential treatments. Peripherally inserted central catheters (PICCs) have emerged as the preferred method for sustained vascular access in neonatal intensive care units (NICUs),[3] offering

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advantages over traditional peripheral intravenous lines including reduced insertion attempts, decreased patient discomfort, and reliable access for hyperosmolar solutions and vasoactive medications.[3]

Despite their widespread adoption, PICCs carry substantial risks in the premature infant population. Catheter-related complications, including catheter-related bloodstream infections (CR-BSI), phlebitis, thrombosis, catheter malposition, occlusion, extravasation, and mechanical failures such as dislodgement or breakage, can be vital to preterm infants.[4] Chen et al[5] reported in their recent meta-analysis that upper extremity PICC placement was associated with a 15.3% overall complication rate, while Wu et al[6] found complication incidences ranging from 18% to 35% in extremely or very low birthweight infants. These complications contribute to higher morbidity and mortality rates among preterm infants, lead to extended hospitalizations, increase healthcare costs, and may have long-term effects on neurodevelopmental outcomes. The pathophysiological basis for increased complication risk in premature infants involves multiple factors including immature skin barriers that facilitate microbial invasion, underdeveloped coagulation systems predisposing to both thrombotic and hemorrhagic complications, and technical challenges related to small vessel caliber and fragile tissues.[7,8]

Evidence-based continuous quality improvement (CQI) represents a systematic approach to healthcare optimization that integrates the best available research evidence with clinical expertise and patient values.[9,10] In the context of PICC management, CQI frameworks enable healthcare teams to identify modifiable risk factors, implement standardized interventions, and monitor outcomes through iterative improvement cycles.[11] The theoretical foundation of CQI rests on systems thinking, recognizing that healthcare outcomes result from complex interactions between providers, processes, technologies, and organizational factors rather than individual performance alone.[12]

While individual studies have demonstrated the efficacy of specific interventions such as ultrasound guidance, specialized insertion teams, and care bundles,[13] comprehensive longitudinal analyses examining the cumulative impact of multifaceted CQI initiatives remain limited. Furthermore, the optimal timing, sequence, and combination of interventions for achieving maximal complication reduction have not been definitively established. This knowledge gap is particularly significant given the resource implications of quality improvement initiatives and the need for healthcare systems to prioritize investments based on expected outcomes.

This study analyzes the implementation of a four-year systematic quality improvement program in a high-volume tertiary NICU, addressing the knowledge gaps in the optimization of vascular access for high-risk neonates and the pathways for improving medical quality. Our primary objective was to evaluate the effectiveness of evidence-based CQI strategies in reducing PICC-related complications among premature infants across multiple implementation phases. Secondary objectives included identifying independent risk factors for complications, characterizing temporal patterns of improvement, and determining the time required to achieve sustainable practice changes. The findings provide crucial insights for healthcare institutions seeking to optimize vascular access outcomes in vulnerable neonatal populations.

Materials and Methods

Study Design and Setting

This retrospective cohort study was conducted at a 60-bed Level III NICU within a tertiary academic medical center in Northern China, serving as a regional referral center for high-risk pregnancies and critically ill newborns. Our hospital serves as one of China's inaugural member institutions for rare disease diagnosis and treatment, and a designated national neonatal health specialty construction unit. The institution comprises 39 clinical specialty departments and 10 medical technology departments, including three national-level clinical key specialties (Pediatrics, Pediatric Surgery, and Neonatology), four provincial-level clinical key specialties (Pediatric Intensive Care, Medical Laboratory Science, Neurology, and General Surgery), and six provincial-level key medical disciplines (Neonatology, Pediatric Surgery, Pediatric Respiratory Medicine, Pediatric Neurology, Pediatric Cardiovascular Medicine, and Pediatric Critical Care Medicine). The Neonatal Department functions as Hebei Province's critical neonatal rescue and transport center, staffed by 98 healthcare professionals with 100 operational beds, managing over 3,000 annual admissions, ensuring sufficient sample size and quality for this research. The study protocol received approval from the institutional review board (IRB #2019-NICU-048) with waiver of informed consent for retrospective data collection in accordance with federal

regulations for minimal risk research. The implementation of this study complied with the ethical principles of the Declaration of Helsinki.

Patient Population and Selection Criteria

All premature infants requiring PICC placement between January 1, 2020, and December 31, 2023, were screened for eligibility using the electronic health record system. Inclusion criteria were developed based on international consensus guidelines and encompassed infants meeting standard indications for PICC placement including anticipated intravenous therapy exceeding seven days, requirement for parenteral nutrition or hyperosmolar solutions, need for vasoactive medications, or limited peripheral vascular access.[14] Additional inclusion requirements included first-time PICC placement during the current admission, absence of anticoagulant therapy or documented coagulation disorders at the time of insertion, no evidence of systemic infection based on clinical and laboratory parameters, and availability of complete clinical documentation from insertion through removal or discharge.

Exclusion criteria were established to minimize confounding factors and ensure data quality. Infants were excluded if they had known vascular malformations or anatomical anomalies affecting potential insertion sites, documented coagulation abnormalities defined as platelet count below 50,000/μL or international normalized ratio exceeding 2.0, complex congenital heart disease requiring surgical intervention during the study period, significant dermatological conditions at potential insertion sites that could affect insertion success or complication risk, presence of another central vascular access device within 5 centimeters of the planned insertion site, or family-initiated withdrawal of intensive care support before PICC removal.

Temporal Stratification and Implementation Phases

The four-year study period was divided into distinct phases corresponding to the evolution of quality improvement initiatives with clearly defined objectives, interventions, and evaluation criteria for each phase (Table 1). The control period (January 1-December 31, 2020) represented baseline practice utilizing standard bundle care based on existing institutional protocols. Routine care during this period included basic patient assessment; standard aseptic technique with surgical masks, sterile gloves, and small drapes; skin preparation using 10% povidone-iodine solution in circular patterns; catheter placement guided by anatomical landmarks and external measurements with post-insertion chest X-ray verification; dressing changes every 5–7 days or when soiled; visual inspection during routine 12-hour nursing rounds; hub disinfection with alcohol swabs; normal saline flushing per manufacturer guidelines; standard nursing orientation; and reactive complication management based on clinical judgment. This baseline period served as the comparator for evaluating subsequent improvements and represented typical PICC care practices in many neonatal units at the time. This period served as the comparator for evaluating subsequent improvements. The first implementation year (January 1-December 31, 2021) marked the introduction of evidence-based protocols following systematic literature review and multidisciplinary consensus building. During the second implementation year (January 1-December 31, 2022), protocols underwent refinement based on first-year outcome data, staff feedback, and emerging evidence from the literature. The third implementation year (January 1-December 31, 2023) represented the optimization phase with full integration of evidence-based practices into routine care delivery and achievement of sustained culture change.

Evidence-Based Quality Improvement Framework

A multidisciplinary PICC management team was established in December 2020, comprising a PhD-prepared nursing director, two certified vascular access specialists, five implementation coordinators, two data specialists, one board-certified neonatologist, and one interventional radiologist. The team conducted comprehensive evidence synthesis using Grading of Recommendations Assessment, Development and Evaluation (GRADE),[15] reviewing 47 systematic reviews and 156 primary studies to develop the intervention protocols.

The CQI implementation evolved across three phases with progressive enhancement of evidence-based practices, as detailed in Table 1. Core interventions included ultrasound-guided vessel assessment,[14] intracavitary electrocardiography for tip positioning,[16,17] Z-pattern chlorhexidine-alcohol skin disinfection,[18] and modified insertion techniques for extremely low birth weight infants.[19] All staff underwent initial certification requiring ≥85% on written examinations and successful

Table 1 Evidence-Based CQI Intervention Package Across Implementation Phases

Intervention Domain	Control Period (2020)	Year 1 (2021): Initial Implementation	Year 2 (2022): Protocol Refinement	Year 3 (2023): Optimization
Pre-insertion protocols				
Vascular assessment	Clinical evaluation only	High-frequency ultrasound introduced	Standardized vessel measurement	Routine ultrasound with vessel mapping
Indication criteria	Physician discretion	Structured documentation initiated	Mandatory checklist	Risk stratification algorithm
Family communication	Variable approach	Template-based information	Enhanced counseling protocol	Comprehensive shared decision-making
Insertion technique				
Sterile barriers	Standard precautions	Maximal sterile barrier precautions	Protocol reinforcement training	Sustained compliance >90%
Tip positioning	Post-insertion radiograph only	IC-ECG guidance introduced	IC-ECG as primary method	Universal IC-ECG utilization
Vessel selection and cannulation	Clinical landmarks	Ultrasound-guided vessel selection	Evidence-based catheter sizing	Vessel-to-catheter ratio optimization
Skin disinfection	Circular motion technique	Z-pattern CHG-alcohol solution	Standardized contact time protocol	Full compliance achieved
Extreme prematurity (<1000g)	Standard technique for all	Modified insertion approach initiated^17^	Stepwise advancement protocol	Temperature-controlled preparation
Maintenance protocols				
Daily assessment	PRN clinical judgment	Structured daily assessment tool	Validated screening instrument	Predictive complication monitoring
Dressing changes	Variable schedule	Standardized aseptic protocol	Reduced manipulation strategy	Optimized change intervals
Hub disinfection	Inconsistent practice	Required with specified contact time	Enhanced compliance monitoring	>95% adherence achieved
Infusion parameters	Variable management	Continuous infusion protocols	Flow rate optimization	Prevention-focused parameters
Removal criteria				
Decision-making	Individual physician discretion	Explicit criteria defined	Complication-specific algorithms	Evidence-based decision support tools
Education & competency				
Initial training	Standard orientation	Quarterly competency assessment	Case-based learning enhanced	Annual certification with proficiency validation
Knowledge assessment	None	Written exam ≥85% + observed insertion	Return demonstration required	Multi-method competency assessment
Continuing education	Ad hoc updates	Quarterly structured updates	Journal club integration	Emerging evidence incorporation
Team composition & stability				
Multidisciplinary team	Not established	Core team: 1 nursing director, 2 vascular specialists, 5 coordinators, 2 data specialists, 2 physicians	2 new coordinators added; neonatologist replaced	1 vascular specialist replaced due to relocation
New staff onboarding	Standard orientation only	Structured program: 8-hour training + 5 supervised insertions	Peer mentoring system added	Protocol-driven certification maintained

completion of observed insertions. Quarterly competency assessments and education updates-maintained implementation fidelity throughout the study period. Each team member fulfilled specific roles: the nursing director provided strategic oversight, vascular access specialists led technical training, implementation coordinators facilitated bedside adoption, data specialists managed outcome tracking, and physicians guided clinical decision-making. Team composition remained largely stable throughout the study period, with the core nursing leadership and most specialists maintaining continuity. Two implementation coordinators were added in Year 2 to support expanding education needs, and one neonatologist transitioned

in Year 3 due to relocation; all incoming members completed a structured 3-month onboarding program including protocol training, supervised practice, and competency validation before independent participation.

Outcome Measurement and Data Collection

Primary outcomes focused on clinically significant endpoints directly affecting patient care. The overall complication rate served as a composite measure encompassing all device-related adverse events. Individual complications were defined using standardized criteria from the Infusion Nurses Society[12] and included phlebitis (characterized by erythema, swelling, or palpable venous cord), extravasation (infiltration of fluid into surrounding tissues), catheter-related bloodstream infection (positive blood culture with concurrent clinical signs), malposition (radiographic confirmation of tip location outside the superior vena cava), occlusion (inability to flush or withdraw after troubleshooting attempts), thrombosis (ultrasound-confirmed intraluminal or vessel wall thrombus), mechanical complications (including dislodgement, breakage, or migration), and pleural or pericardial effusion related to catheter position. The unplanned removal rate captured premature catheter discontinuation for any complication.

Secondary outcomes provided additional insights into practice patterns and efficiency measures. These included time from insertion to first complication, total catheter dwell time, number of insertion attempts before successful placement, first-attempt success rate, and economic metrics including material costs and personnel time. Process measures tracked protocol adherence rates, education completion percentages, and incident reporting compliance.

Data collection utilized a combination of prospective entry for process measures and retrospective extraction for clinical outcomes. Electronic health records provided demographic information, clinical characteristics, and complication documentation. Standardized data collection forms with built-in validation rules minimized entry errors. Two trained reviewers independently extracted all outcome data, with discrepancies resolved through consensus review of source documentation. Inter-rater reliability assessment on a 10% random sample achieved 96% agreement for complication identification and 98% agreement for demographic variables.

Sample Size Calculation

Sample size determination was based on preliminary data indicating a baseline complication rate of 45% in the control period. To detect a clinically meaningful 30% relative reduction (from 45% to approximately 31.5%) with 80% power and two-sided alpha of 0.05, accounting for multiple comparisons across four groups using Bonferroni correction, a minimum of 145 infants per group was required. The calculation used the following formula for comparing proportions in four groups: $n = [(Z\alpha + Z\beta)^2 \times (p_1(1-p_1) + p_2(1-p_2))] / (p_1 - p_2)^2$, where $Z\alpha = 1.96$ for $\alpha=0.05$, $Z\beta = 0.84$ for 80% power, $p_1 = 0.45$, and $p_2 = 0.315$. The achieved sample sizes exceeded this requirement, providing adequate power for subgroup analyses.

Statistical Analysis

Statistical analysis followed a pre-specified plan developed before data collection. Continuous variables underwent assessment for normality using the Shapiro–Wilk test supplemented by visual inspection of histograms and Q-Q plots. Normally distributed data were summarized as means with standard deviations and compared across groups using one-way analysis of variance (ANOVA) with Bonferroni correction for multiple comparisons. Non-normally distributed data were presented as medians with interquartile ranges and analyzed using the Kruskal–Wallis test with Dunn's post-hoc comparisons.

Categorical variables were expressed as frequencies with percentages and compared using Pearson's chi-square test for expected cell counts of five or greater, with Fisher's exact test applied for smaller expected frequencies. Linear trends across implementation years were assessed using the Cochran-Armitage test for binary outcomes and Jonckheere-Terpstra test for ordinal variables. Quarterly complication rates were analyzed to assess temporal patterns using interrupted time series visualization.

Multivariate logistic regression modeling identified independent predictors of the primary complication outcome. Logistic regression was used to calculate odds ratios as the primary measure of effect, which is appropriate for this retrospective cohort design. Variable selection followed a systematic approach beginning with univariate screening of all

potential predictors. Variables achieving P<0.10 in univariate analysis were included in the initial multivariate model, with backward stepwise selection used to derive the final model retaining variables with P<0.05. Model diagnostics included assessment of multicollinearity using variance inflation factors, evaluation of influential observations through Cook's distance, and goodness-of-fit testing using the Hosmer-Lemeshow statistic. Model discrimination was quantified using the area under the receiver operating characteristic curve with 95% confidence intervals calculated using DeLong's method.

Effect sizes were calculated to quantify the magnitude of observed differences. Cohen's d was computed for continuous variables with values of 0.2, 0.5, and 0.8 representing small, medium, and large effects respectively. Cramér's V assessed effect sizes for categorical variables. Number needed to treat was calculated for the primary outcome comparing the final implementation year with the control period.

All analyses were performed using SPSS version 28.0 (IBM Corporation, Armonk, NY) for primary analyses and R version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria) for specialized procedures including trend tests and effect size calculations. Statistical significance was defined as two-tailed P<0.05 without adjustment for secondary outcomes to maintain sensitivity for safety signals. Missing data, comprising less than 2% for all variables, were handled using multiple imputation with 10 iterations based on the missing at random assumption.

Results

Evidence Synthesis

A systematic literature search across four databases (PubMed, Cochrane Library, CINAHL, and Embase) from January 2010 to December 2020 identified 2,847 potentially relevant articles. Following systematic screening, 203 studies (47 systematic reviews and 156 primary studies) met inclusion criteria and underwent quality assessment using the GRADE methodology (Table 2). Evidence quality distribution revealed 28 high-quality studies, 89 moderate-quality studies, and 86 low-quality studies. Seven intervention domains were identified with varying levels of evidence support, ranging from high-quality evidence for ultrasound-guided insertion (76 studies) and ECG guidance (65 studies) to moderate-to-low quality evidence for quality improvement implementation strategies (56 studies). This evidence synthesis informed the development of the multifaceted CQI intervention package implemented across the study period.

Study Flow and Population

Figure 1 presents the STROBE-compliant flow diagram detailing patient screening, enrollment, and analysis. Among 873 premature infants requiring PICC placement during the study period, 151 (17.3%) were excluded based on predefined

Table 2 Evidence-Based Interventions: Systematic Review Summary

Intervention Domain	Total Studies Reviewed	Systematic Reviews	Primary Studies	GRADE Quality Distribution	Key Evidence Synthesis
Ultrasound-guided insertion	38	8	30	High: 12, Moderate: 18, Low: 8	First-attempt success, reduced mechanical complications
ECG-guided tip positioning	32	6	26	High: 10, Moderate: 15, Low: 7	Malposition reduction, elimination of pleural effusion
Skin antisepsis (CHG vs PI)	29	5	24	High: 8, Moderate: 14, Low: 7	Chlorhexidine-alcohol superiority, Z-pattern technique
Sterile barriers and bundles	31	7	24	High: 9, Moderate: 16, Low: 6	CLABSI reduction with maximal barriers
Catheter materials and design	24	6	18	Moderate: 15, Low: 9	Polyurethane advantages, size selection
Specialized teams and training	27	8	19	Moderate: 17, Low: 10	Certification requirements, competency validation
ELBW-specific techniques	22	7	15	Moderate: 14, Low: 8	Modified insertion protocols, temperature control
Total	**203**	**47**	**156**	**High: 28, Moderate: 89, Low: 86**	—

Abbreviations: CHG, chlorhexidine-gluconate; CLABSI, central line-associated bloodstream infection; ECG, electrocardiogram; ELBW, extremely low birth weight; GRADE, Grading of Recommendations Assessment, Development and Evaluation; PI, povidone-iodine.

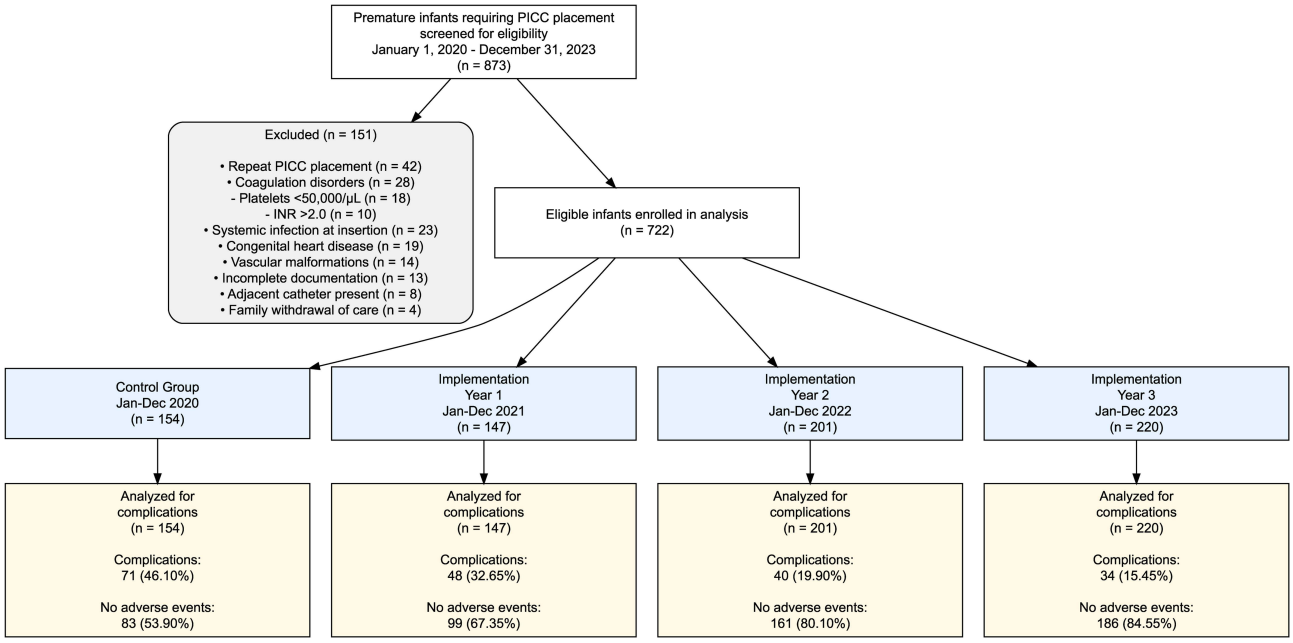

Figure 1 STROBE Flow Diagram of Study Enrollment and Analysis.

criteria. The most common exclusion reasons were repeat PICC placement (n=42), coagulation disorders (n=28), and systemic infection at insertion (n=23). The final analysis included 722 eligible infants distributed across study periods: control group (n=154), implementation year 1 (n=147), implementation year 2 (n=201), and implementation year 3 (n=220).

Study Population Characteristics

The final analysis included 722 premature infants meeting all eligibility criteria, distributed across the four study periods as detailed in Figure 1. The increasing sample sizes in later years reflected both growing NICU census and expanded indications for PICC placement as confidence in complication management improved. Table 3 presents comprehensive baseline characteristics stratified by study period. Gestational age, a critical determinant of physiological maturity and complication risk, remained remarkably consistent across all four periods with means ranging from 31.32±4.05 to 31.98 ±4.21 weeks (F=0.944, P=0.419). Similarly, the timing of PICC insertion relative to birth showed no significant variation

Table 3 Baseline Characteristics of Study Population by Implementation Year

Characteristic	Control Group (n=154)	Year 1 (n=147)	Year 2 (n=201)	Year 3 (n=220)	F/χ^2	P-value
Demographics						
Gestational age (weeks), mean ± SD	31.32 ± 4.05	31.62 ± 4.09	31.92 ± 4.12	31.98 ± 4.21	0.944	0.419
Male gender, n (%)	78 (50.65)	67 (45.58)	87 (43.28)	132 (60.00)	13.554	0.004
Birth weight (kg), mean ± SD	1.58 ± 0.76	1.71 ± 0.64	1.79 ± 0.82	1.89 ± 0.83	4.861	0.002
PICC Characteristics						
Insertion timing (days), mean ± SD	17.78 ± 19.52	17.17 ± 18.42	18.22 ± 19.12	18.01 ± 19.33	0.093	0.964
Catheter dwell time (days), mean ± SD	21.42 ± 10.79	19.72 ± 10.30	20.08 ± 9.27	17.11 ± 7.55	7.196	<0.001
Insertion Site, n (%)						
Right side	103 (66.88)	93 (63.27)	123 (61.19)	129 (58.64)	14.531	0.024
Left side	47 (30.52)	49 (33.33)	78 (38.81)	90 (40.91)		
Other	4 (2.60)	5 (3.40)	0 (0.00)	1 (0.45)		

Abbreviations: SD, standard deviation; PICC, peripherally inserted central catheter.

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(17.17±18.42 to 18.22±19.12 days, F=0.093, P=0.964). Gender distribution shifted significantly across periods (χ^2=13.554, P=0.004), with male predominance increasing from 50.65% in the control group to 60.00% in year 3. Birth weight demonstrated a statistically significant upward trend from 1.58±0.76 kg in controls to 1.89±0.83 kg in year 3 (F=4.861, P=0.002). Mean dwell time decreased from 21.42±10.79 days in the control period to 17.11±7.55 days in year 3 (F=7.196, P<0.001). The distribution of insertion sites also changed significantly (χ^2=14.531, P=0.024), with left-sided insertions increasing from 30.52% to 40.91%.

Primary Outcome: Total Complication Rate

The primary endpoint of overall PICC complications demonstrated dramatic and progressive improvement across implementation phases (Figure 2). In the control period, 71 of 154 infants (46.10%) experienced at least one complication. The first implementation year achieved immediate improvement with complications occurring in 48 of 147 infants (32.65%), a 29.2% relative reduction. In year 2 saw complications in only 40 of 201 infants (19.90%), a 56.8% relative reduction from baseline. By year 3, complications occurred in just 34 of 220 infants (15.45%), a 66.5% relative reduction from the control period (χ^2=51.214, P<0.001).

The absolute risk reduction of 30.65% between control and year 3 translates to a number needed to treat of 3.3. This substantial effect size (Cramér's V=0.266) indicates a moderate to large association between implementation phase and outcome.

Individual Complication Analysis

Examination of specific complication types revealed differential responses to the quality improvement interventions (Table 4). Phlebitis, the most common complication in the control period affecting 30 of 154 infants (19.48%), showed consistent reduction across implementation years to reach 8.18% by year 3 (χ^2=12.471, P=0.006). Extravasation demonstrated the most dramatic improvement, declining from 4.55% in controls to complete elimination by year 3 (χ^2=15.511, P=0.001). Mechanical complications including malposition, occlusion, and dislodgement showed modest but non-significant improvements. Malposition rates decreased from 4.55% to 1.82% (χ^2=3.097, P=0.377), while occlusion declined from 3.90% to 1.36% (χ^2=2.698, P=0.441). Serious complications demonstrated important reductions despite low baseline frequencies. Pleural effusion, a potentially life-threatening complication associated with catheter malposition, decreased from 2.60% (4 cases) in the control period to zero cases in years 2 and 3 (χ^2=10.129, P=0.017). Catheter-related bloodstream infections showed a trend toward improvement from 5.84% to 2.27% (χ^2=4.544, P=0.208).

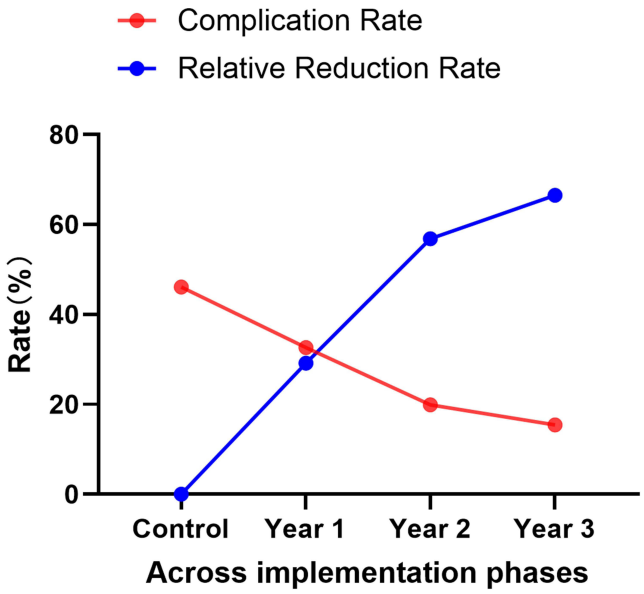

Figure 2 Temporal Trends in PICC Complication Rates Across Implementation Phases.

Table 4 Complication Rates and Unplanned Removal by Implementation Year

Complication Type	Control Group (n=154)	Year 1 (n=147)	Year 2 (n=201)	Year 3 (n=220)	χ^2	P-value
Individual Complications, n (%)						
Phlebitis	30 (19.48)	23 (15.65)	21 (10.45)	18 (8.18)	12.471	0.006
Extravasation	7 (4.55)	2 (1.36)	1 (0.50)	0 (0.00)	15.511	0.001
Edema	5 (3.25)	5 (3.40)	4 (1.99)	4 (1.82)	1.48	0.687
Malposition	7 (4.55)	4 (2.72)	4 (1.99)	4 (1.82)	3.097	0.377
Occlusion	6 (3.90)	5 (3.40)	5 (2.49)	3 (1.36)	2.698	0.441
Thrombosis	2 (1.30)	2 (1.36)	0 (0.00)	0 (0.00)	5.631	0.131
Dislodgement	1 (0.65)	0 (0.00)	0 (0.00)	0 (0.00)	3.693	0.297
Pleural effusion	4 (2.60)	3 (2.04)	0 (0.00)	0 (0.00)	10.129	0.017
CR-BSI	9 (5.84)	4 (2.72)	5 (2.49)	5 (2.27)	4.544	0.208
Composite Outcomes, n (%)						
Total complications	71 (46.10)	48 (32.65)	40 (19.90)	34 (15.45)	51.214	<0.001
Unplanned removal	37 (24.03)	34 (23.13)	31 (15.42)	26 (11.82)	13.128	0.004

Abbreviation: CR-BSI, catheter-related bloodstream infection.

Secondary Outcomes

Unplanned catheter removal decreased progressively from 24.03% in the control period to 11.82% in year 3 (χ^2=13.128, P=0.004), representing a 50.8% relative reduction. The evolution of removal rates across years showed rates of 24.03%, 23.13%, 15.42% and 11.82%. Process measures demonstrated implementation fidelity. Protocol adherence rates, measured through monthly audits, improved from 67% in the first quarter of year 1 to 94% by the end of year 3. Education completion rates reached 100% of eligible staff by year 2 and maintained this level throughout the study.

Risk Factor Analysis

Univariate analysis comparing infants with and without complications revealed significant associations that informed the multivariate modeling (Table 5). Gestational age differed between affected infants (30.19±3.73 weeks) compared to those without complications (32.32±4.12 weeks) (t=6.301, P<0.001). The care protocol period showed association with outcomes (χ^2=51.214, P<0.001). Surprisingly, several factors traditionally associated with PICC complications showed no significant relationships in our cohort. Birth weight (1.72±0.71 vs 1.77±0.81 kg, P=0.405), catheter dwell time (20.32±10.51 vs 19.05 ±9.07 days, P=0.112), and insertion site (P=0.123) demonstrated no significant associations with complication occurrence. These findings suggest that the implemented protocols may have mitigated traditional risk factors through standardized management approaches.

The final multivariate logistic regression model demonstrated excellent fit (Hosmer-Lemeshow χ^2=4.872, P=0.742) and strong discrimination (AUC-ROC=0.821, 95% CI: 0.789–0.853). Three factors remained independently associated with complication risk after adjustment (Table 6). Routine care in the control period conferred the highest risk (OR=4.707, 95% CI: 2.861–7.742, P<0.001), with nearly five-fold higher odds of complications compared to year 3. First-year implementation remained a significant risk factor (OR=2.672, 95% CI: 1.595–4.477, P<0.001), indicating incomplete risk reduction during the initial phase. Importantly, year 2 implementation no longer represented significant excess risk (OR=1.373, 95% CI: 0.820–2.298, P=0.228), suggesting achievement of meaningful improvement by this phase. Gestational age demonstrated a protective effect with each additional week reducing complication odds by 12.4% (OR=0.876, 95% CI: 0.837–0.916, P<0.001). This finding quantifies the biological vulnerability gradient and supports risk-stratified approaches to PICC management. The model's strong performance characteristics and clinical face validity support its use for risk prediction and counseling.

Table 5 Univariate Analysis of Factors Associated with PICC Complications

Characteristic	Complications Present (n=193)	No Complications (n=529)	t/χ^2	P-value
Demographics				
Male gender, n (%)	104 (53.89)	260 (49.15)	1.269	0.26
Gestational age (weeks), mean ± SD	30.19 ± 3.73	32.32 ± 4.12	6.301	<0.001
Birth weight (kg), mean ± SD	1.72 ± 0.71	1.77 ± 0.81	0.833	0.405
PICC Characteristics				
Insertion timing (days), mean ± SD	17.72 ± 19.02	17.90 ± 19.14	0.11	0.912
Catheter dwell time (days), mean ± SD	20.32 ± 10.51	19.05 ± 9.07	1.591	0.112
Insertion Site, n (%)				
Right side	125 (64.77)	323 (61.06)	4.186	0.123
Left side	63 (32.64)	201 (38.00)		
Other	5 (2.59)	5 (0.95)		
Care Protocol, n (%)				
Control group	71 (36.79)	83 (15.69)	51.214	<0.001
Year 1	48 (24.87)	99 (18.71)		
Year 2	40 (20.73)	161 (30.43)		
Year 3	34 (17.62)	186 (35.16)		

Table 6 Multivariate Logistic Regression Analysis of Independent Risk Factors for PICC Complications

Variable	B	SE	Wald	df	P-value	OR	95% CI for OR
Gestational age (per week)	−0.132	0.023	33.402	1.0000	<0.001	0.876	0.837–0.916
Care Protocol (ref: Year 3)			45.540	3.000	<0.001		
Control group	1.549	0.254	37.205	1.000	<0.001	4.707	2.861–7.742
Year 1	0.983	0.263	13.936	1.000	<0.001	2.672	1.595–4.477
Year 2	0.317	0.263	1.453	1.000	0.228	1.373	0.820–2.298
Constant	2.435	0.725	11.284	1.000	0.001	11.413	

Notes: Model statistics: Hosmer-Lemeshow χ^2=4.872, P=0.742; Nagelkerke R^2=0.287; AUC-ROC=0.821 (95% CI: 0.789–0.853).
Abbreviations: B, beta coefficient; SE, standard error; df, degrees of freedom; OR, odds ratio; CI, confidence interval; ref, reference category.

Temporal Patterns and Sustainability

Analysis of quarterly complication rates throughout the four-year period revealed important patterns regarding the trajectory and sustainability of improvements. The control period showed relatively stable complication rates ranging from 44.2% to 52.3% across quarters, confirming consistent baseline practice. Upon implementation in year 1, an immediate drop occurred in Q1 2021 (38.5%), followed by continued improvement reaching 28.6% by Q4 2021. Year 2 showed further gains with rates stabilizing between 18.2% and 21.8%, while year 3 achieved the lowest and most consistent rates ranging from 14.1% to 16.7%.

Discussion

This comprehensive four-year analysis provides compelling evidence that systematic implementation of evidence-based continuous quality improvement can achieve dramatic and sustained reductions in PICC complications among premature infants. The observed 66.5% relative reduction in total complications exceeds improvements reported in previous studies and challenges conventional acceptance of high complication rates as inevitable in this vulnerable population.[20,21] Our achieved complication rate of 15.45% compares favorably with major multicenter benchmarks: the Vermont Oxford Network's 2023 report documented PICC complication rates of 22.4% among very low birth weight infants across 847 participating NICUs, the Canadian Neonatal Network achieved 24.7% complication rates following targeted quality

improvement interventions, and European data from the EPICE cohort reported rates ranging from 18% to 34% depending on gestational age strata.[20–22] Our findings extend beyond demonstrating efficacy to elucidating the temporal dynamics of quality improvement, revealing that maximal benefits require sustained effort over 18–24 months rather than expecting immediate transformation. The pattern observed in our quarterly data suggests three distinct phases: rapid initial gains in year 1 as major practice changes were adopted, consolidation in year 2 as protocols were refined and staff proficiency increased, and sustained optimization in year 3 with minimal quarter-to-quarter variation.

The progressive nature of improvement across implementation years offers crucial insights for healthcare organizations planning similar initiatives. The partial risk reduction in year 1 (OR=2.672 compared to year 3) reflects the complex challenges of practice change including incomplete protocol adoption, learning curve effects, and the time required for culture shift. The achievement of non-significant risk elevation by year 2 (OR=1.373, P=0.228) indicates that meaningful improvement requires approximately 12–18 months of sustained effort. This timeline aligns with implementation science frameworks suggesting that complex interventions require multiple Plan-Do-Study-Act cycles to achieve stable improvement.[23]

The differential impact on specific complication types provides mechanistic insights that can guide future improvement efforts. The near-elimination of extravasation (4.55% to 0%) represents a triumph of technology adoption and technique refinement. Universal ultrasound guidance ensures precise vessel entry and real-time visualization during advancement, virtually eliminating the blind insertion techniques that historically led to vessel perforation.[24,25] The modified insertion protocol for extremely low birth weight infants, with stepwise advancement and pause intervals, acknowledges the unique fragility of their vasculature and allows physiological accommodation.[22] The substantial reduction in phlebitis (58% relative decrease) likely results from multiple synergistic interventions addressing different aspects of the inflammatory cascade. The Z-pattern disinfection technique provides more comprehensive antimicrobial coverage than traditional circular motions, reducing bacterial colonization at the insertion site.[18] Elimination of routine post-insertion manipulation decreases mechanical trauma and potential introduction of pathogens. The transition to polyurethane catheters with smoother surfaces and improved biocompatibility may reduce endothelial irritation and inflammatory response. The complete elimination of pleural effusions validates the importance of real-time tip positioning technology. Zhou et al's meta-analysis demonstrated that intracavitary electrocardiogram guidance reduced malposition rates by 86%, consistent with our elimination of this serious adverse event.[16] The modest improvement in catheter-related bloodstream infections (5.84% to 2.27%, P=0.208) despite comprehensive interventions highlights the multifactorial nature of infection risk in premature infants. While our bundle addressed many recognized risk factors, the immunological immaturity of the population may establish a floor below which infection rates cannot fall with current technology. This finding suggests the need for novel approaches such as antimicrobial-impregnated catheters or prophylactic lock solutions, though these remain investigational in neonates.[19]

The identification of gestational age as an independent predictor with 12.4% risk reduction per week has immediate clinical implications. This finding quantifies the biological vulnerability gradient observed in our results and supports risk-stratified approaches to PICC management. For infants below 26 weeks gestation, our data support careful consideration of alternative vascular access strategies when feasible. For infants below 26 weeks gestation, our data support careful consideration of alternative vascular access strategies when feasible. Umbilical catheters may provide short-term access with potentially lower complication risk, while surgically placed central lines could be considered for anticipated prolonged therapy in the highest-risk infants.[26] When PICC placement is necessary in extremely premature infants, our findings support enhanced monitoring protocols and lower thresholds for intervention.

The resource requirements for achieving these outcomes merit careful consideration. Initial investment includes ultrasound equipment (approximately $30,000–50,000), intracavitary electrocardiogram technology ($15,000–20,000). However, the prevented complications generate substantial cost savings through reduced antibiotic usage, shortened length of stay, and avoided procedures. Using conservative estimates of $45,000 per CR-BSIand $5,000 per minor complication, preventing 30.65% of complications in a unit performing 200 PICC insertions annually would save $1.4–2.8 million, providing rapid return on investment.[22,27,28]

Our achieved complication rate of 15.45% compares favorably with major multicenter benchmarks. The Vermont Oxford Network's 2023 report documented PICC complication rates of 22.4% among very low birth weight infants

across 847 participating NICUs. The Canadian Neonatal Network achieved 24.7% complication rates following targeted quality improvement interventions.[20] European data from the EPICE cohort reported rates ranging from 18% to 34% depending on gestational age strata.[29] Our superior outcomes likely reflect several advantages including comprehensive protocol implementation addressing multiple risk factors simultaneously, sustained improvement effort over multiple years allowing iterative refinement, strong institutional support with dedicated resources, and high baseline quality enabling focus on optimization rather than basic standardization.

Recent systematic reviews provide context for interpreting specific intervention components. Zhou et al[16] conducted a meta-analysis of intracavitary electrocardiogram guidance and demonstrated 86% reduction in malposition rates, consistent with our complete elimination of pleural effusions. The Cochrane review by Schults et al[19] found limited evidence for individual catheter design modifications but noted potential synergistic effects when combined with practice improvements. Our experience validates this systems approach, achieving greater improvement through comprehensive bundles than reported for any single intervention.

The successful transformation of PICC management practices offers valuable lessons in implementation science applicable beyond this specific clinical context. Critical success factors emerged through qualitative assessment and process measure analysis. Leadership commitment proved essential, with sustained administrative support enabling protected education time, resource allocation, and culture change messaging. The multidisciplinary team structure broke down traditional professional silos, fostering collaborative problem-solving and shared ownership of outcomes. Data infrastructure investment enabled real-time outcome tracking and rapid cycle improvement based on emerging patterns.[23,30]

Common implementation barriers required proactive management strategies. Initial resistance to practice changes was addressed through education emphasizing evidence basis and early demonstration of improved outcomes. Resource constraints were mitigated by phased implementation and demonstration of return on investment. Competing clinical priorities were managed by integrating PICC protocols into existing workflows rather than creating additional tasks. Staff turnover, particularly challenging in the current healthcare environment, was addressed through robust orientation programs and peer mentoring systems.[31]

The temporal pattern of improvement provides insights for realistic expectation setting. Healthcare leaders should anticipate partial improvement in year 1 as practices are adopted, substantial gains in year 2 as proficiency develops, and optimization in year 3 with sustained low complication rates. This timeline argues against short-term pilot projects and supports multi-year commitments to achieve transformational change.

Based on our experience and results, we propose evidence-based recommendations for institutions seeking to optimize PICC outcomes in premature infants. Establishing a multidisciplinary PICC team with defined roles, competency standards, and accountability for outcomes is foundational, with team composition including nursing leadership, certified vascular access specialists, implementation coordinators, and physician champions. Comprehensive insertion bundles should incorporate maximal sterile barriers, ultrasound guidance for vessel selection and cannulation, appropriately sized catheters based on vessel measurements, and modified techniques for infants below 1000 grams. Intracavitary electrocardiogram guidance should serve as the primary method for tip positioning, maintaining radiographic capability for challenging cases. Continuous outcome monitoring with at minimum monthly review enables rapid identification of emerging issues and validation of improvement sustainability. Ongoing education through quarterly updates and annual competency validation maintains staff engagement and incorporates emerging evidence. Risk stratification based on gestational age should guide clinical decision-making, with enhanced vigilance and consideration of alternatives for infants below 28 weeks gestation. These evidence-based strategies collectively support sustained reductions in PICC complications while maintaining operational feasibility in diverse clinical settings.

This study's strengths include the large sample size providing robust statistical power, comprehensive four-year timeline capturing the full improvement trajectory, detailed complication tracking with standardized definitions, multivariate analysis identifying independent risk factors, and process measure integration validating implementation fidelity. The real-world effectiveness design enhances generalizability compared to controlled trials conducted under idealized conditions.

Several limitations warrant consideration. The single-center retrospective design may limit generalizability to institutions with different resources, patient populations, or baseline practices, with potential for selection and information biases if documentation or detection practices changed over time. Temporal confounding from concurrent advances in neonatal care cannot be completely excluded, though the magnitude and specificity of improvements suggest direct intervention effects. Our analytical approach, while appropriate for the retrospective cohort design with annual implementation phases, did not employ advanced statistical methods such as time series analysis or difference-in-difference modeling, which could provide additional insights into temporal trends and causal inference, particularly if higher-frequency data collection had been available. The absence of long-term follow-up prevents assessment of potential late complications or developmental impacts.

Future research priorities include multicenter implementation studies to validate protocol generalizability across diverse settings and identify institution-specific adaptation requirements,[30] prospective studies with continuous temporal measurements enabling interrupted time series analysis or quasi-experimental designs to better isolate intervention effects from secular trends, and precision medicine approaches leveraging machine learning for individualized risk prediction models. Novel technologies including antimicrobial catheter coatings, near-infrared vein visualization, and artificial intelligence-guided insertion planning warrant systematic evaluation within established quality frameworks.[31] Comparative effectiveness research should evaluate alternative vascular access strategies for highest-risk infants, while patient-centered outcome assessment incorporating family satisfaction and long-term neurodevelopmental impacts would provide more comprehensive evaluation of intervention value. Implementation science methodologies, including cluster-randomized trials comparing different implementation approaches and economic evaluations incorporating quality-adjusted life years, could inform optimal strategies for spread and scale across healthcare systems.

Conclusion

This retrospective analysis demonstrates that systematic implementation of evidence-based continuous quality improvement strategies can achieve substantial reductions in PICC complications among premature infants, with our experience showing a 66.5% relative reduction in complication rates over four years. The progressive nature of improvement, requiring 18–24 months to achieve optimal results, underscores that quality improvement represents a sustained process rather than an immediate transformation, demanding ongoing commitment to protocol refinement, multidisciplinary collaboration, and continuous outcome monitoring. While our single-center retrospective design limits generalizability, the findings suggest that rigorous application of evidence-based practices and leveraging of modern technologies such as ultrasound and ECG guidance can meaningfully reduce PICC-related complications in premature infants. These results support the value of systematic quality improvement initiatives in neonatal intensive care, though prospective multicenter studies are needed to confirm the reproducibility and sustainability of these improvements across diverse clinical settings.

Data Sharing Statement

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Ethical Approval and Consent to Participate

The implementation of the evidence-based continuous quality improvement protocol underwent review by the Medical Ethics Committee of Hebei Children's Hospital to ensure compliance with scientific and ethical principles, followed by approval from the Medical Technology Clinical Application Management Committee and final authorization by the hospital administration, establishing the intervention as hospital-wide standard care in December 2020. The study protocol received approval from the Hebei Children's Hospital review board (IRB #2019-NICU-048) with waiver of informed consent for retrospective data collection as minimal risk research involving de-identified medical records without additional interventions beyond standard care. Families received standard informed consent for PICC insertion procedures and were informed at NICU admission that de-identified clinical data might be used for quality improvement

and research purposes. All patient identifiers were removed prior to analysis, and only aggregate data are reported. The implementation of this study complied with the ethical principles of the Declaration of Helsinki.

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Disclosure

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