ORIGINAL ARTICLE

A Comparison of Peripherally Inserted Central Catheter Materials

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ABSTRACT

BACKGROUND

New catheter materials for peripherally inserted central catheters (PICCs) may reduce the risk of device failure due to infectious, thrombotic, and catheter occlusion events. However, data from randomized trials comparing these catheters are lacking.

METHODS

We conducted a randomized, controlled, superiority trial in three Australian tertiary hospitals. Adults and children who were referred for PICC placement were assigned in a 1:1:1 ratio to receive a hydrophobic or chlorhexidine PICC or a standard polyurethane PICC and were followed for 8 weeks. The primary outcome was device failure, which was a composite of infectious (bloodstream or local) or noninfectious (thrombosis, breakage, or occlusion) complications.

RESULTS

A total of 1098 participants underwent randomization; 365 were assigned to the hydrophobic group, 365 to the chlorhexidine group, and 368 to the standard-polyurethane group. Device failure occurred in 21 of 358 participants (5.9%) in the hydrophobic group, in 36 of 363 (9.9%) in the chlorhexidine group, and in 22 of 359 (6.1%) in the standard-polyurethane group (risk difference, hydrophobic vs. standard polyurethane, −0.2 percentage points [95% confidence interval {CI}, −3.7 to 3.2; P=0.89]; and chlorhexidine vs. standard polyurethane, 3.8 percentage points [95% CI, −0.1 to 7.8; P=0.06]). In the hydrophobic group as compared with the standard-polyurethane group, the odds ratio for device failure was 0.96 (95% CI, 0.51 to 1.78), and in the chlorhexidine group as compared with the standard-polyurethane group, the odds ratio was 1.71 (95% CI, 0.98 to 2.99). Complications from any cause during the period of PICC placement occurred in 77 participants (21.5%) in the hydrophobic group, in 140 (38.6%) in the chlorhexidine group, and in 78 (21.7%) in the standard-polyurethane group (odds ratio, hydrophobic vs. standard polyurethane, 0.99 [95% CI, 0.69 to 1.42]; and chlorhexidine vs. standard polyurethane, 2.35 [95% CI, 1.68 to 3.29]). No adverse events were attributable to the interventions.

CONCLUSIONS

Among adults and children who were referred for PICC placement, the risk of device failure due to noninfectious or infectious complications was not lower with hydrophobic or chlorhexidine PICCs than with standard polyurethane PICCs. (Funded by the National Health and Medical Research Council of Australia; PICNIC Australian New Zealand Clinical Trials Registry number, ACTRN12619000022167.)

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Peripherally inserted central catheters (PICCs) are used across health care settings for stable and safe administration of treatments. Over the past decade, there has been greater recognition and response to the infectious, thrombotic, and mechanical complications associated with their use.[1-4] These complications have been incorporated in health care performance measures, including those used for financial incentives and penalties.[5,6] An influx of products, practices, and technological advances has been introduced by manufacturers to reduce the risk of such complications. The development of technological innovations embedded within the PICC is a solution for reducing harm.[7]

Most conventional PICCs are made of polyurethane.[8] Advances in material technology have introduced coatings and altered surfaces with purported antithrombotic and antiinfective properties to be used with polyurethane PICCs. Hydrophobic catheter materials are commonly used in other contexts (e.g., oil spills) but are a relatively new health care technology.[8] Fluorinated hydrophobic materials, such as the BioFlo PICC (Spectrum Vascular), inhibit platelet adhesion and suppress protein procoagulant conformation.[8] Our pilot trials involving 150 children[9] and 111 adults[10] showed acceptability of the hydrophobic products and the feasibility of use in clinical trials. Antiinfective materials such as antibiotics or antiseptics have been well studied. A Cochrane review[11] that included data from 42 randomized, controlled trials and 10,405 patients concluded that there was high-quality evidence showing that antimicrobial central venous catheters reduced the risk of bloodstream infections (risk ratio, 0.62; 95% confidence interval [CI], 0.52 to 0.74). On the basis of this indication, chlorhexidine-coated PICCs have been introduced to clinical practice (Arrowg+ard Blue Advance, Teleflex). We conducted the Peripherally Inserted Central Catheter Innovation to Reduce Infections and Clots (PICNIC) trial to test the hypothesis that the risk of device failure due to complications would be lower with two technological innovations (hydrophobic and chlorhexidine PICCs) than with standard polyurethane PICCs.

METHODS

TRIAL DESIGN

The PICNIC trial was a pragmatic, multicenter, parallel-group, randomized, controlled, superiority trial designed to test each of the innovative PICCs against the standard polyurethane PICC. The trial protocol was published previously,[12] and both the protocol and the statistical analysis plan are available with the full text of this article at NEJM.org. The protocol was approved by the human ethics committees at Queensland Health, Griffith University, and the University of Queensland. The conduct of the trial was initially overseen by Griffith University (until March 2021) and was then overseen by the University of Queensland. All the participants or substitute decision makers (parents for pediatric participants) provided written informed consent. An independent data and safety monitoring board and trial steering committee provided trial oversight. Griffith University, the University of Queensland, and the funder of the trial (the National Health and Medical Research Council of Australia) had no role in the design of the trial; the collection, analysis, or interpretation of the data; or the writing of the manuscript. The first draft of the manuscript was written by the first author, and all the authors provided critical feedback and participated in the final decision to submit the manuscript for publication. No commercial entity had any role in the conception, design, or funding of this trial or in the preparation of the manuscript. The authors vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol.

PARTICIPANTS

Participants were recruited at three tertiary-referral, metropolitan hospitals (two adult and one pediatric) in Brisbane, Australia. Adults and children who were referred to the department of medical imaging or vascular access service for PICC placement and had veins sufficient to support a 4.0-French or larger device were eligible. Participation in the trial was allowed only once. Additional inclusion and exclusion criteria are provided in the Supplementary Appendix, available at NEJM.org.

RANDOMIZATION AND BLINDING

Participants were randomly assigned in a 1:1:1 ratio to receive a hydrophobic PICC (with pressure activated valve; BioFlo), a chlorhexidine-coated PICC (with external clamp; Arrowg+ard Blue Advance), or a standard polyurethane PICC (with external clamps). Randomization was performed centrally with the use of an interactive Web-based service (Griffith University) immediately before PICC insertion. Randomization was stratified according to hospital site and thrombosis risk (high or low), as defined by the Michigan Risk Score[13] for adults and history of thrombosis or cancer for pediatric participants, and was performed in randomly varying block sizes of six or nine. The Michigan Risk Score predicts the risk of deep-vein thrombosis; scores range from 0 to 10, with higher scores indicating a higher risk of deep-vein thrombosis. Outcome assessors and data analysts were unaware of the treatment-group assignments.

PROCEDURES

Hospital-based research nurses provided the assigned, prepackaged PICC to practitioners, who would insert the catheter after randomization. Practitioners inserting the PICCs were provided training by the PICC manufacturers regarding the insertion of non–standard-care PICCs. Other than PICC type, insertion, care, and management was standardized with the use of guidelines[14]; full details are provided in the Supplementary Appendix. Because this was a pragmatic trial, variations in care were noted but not considered to be protocol violations.

Data were directly entered into a secure online database (Research Electronic Data Capture [REDCap]). In addition to a review of medical records, participants were assessed in person (if admitted) or by means of telephone (if discharged) weekly for 8 weeks or until the PICC was removed, whichever occurred earlier. Demographic and clinical data on participant, provider, and device factors associated with PICC–associated complications were collected.[15,16]

OUTCOMES

The primary outcome was device failure, which was a composite of infectious or noninfectious complications severe enough to cause cessation of PICC function or necessitate its removal before completion of the intended therapy (further details are provided in the Supplementary Appendix).[1,17] Noninfectious complications included symptomatic venous thrombosis confirmed on imaging,[18] catheter breakage or splitting that is visible or confirmed on imaging),[19] or catheter occlusion (complete [i.e., ≥1 lumen cannot be flushed or aspirated][20] or partial [i.e., reduced ability to flush or aspirate, resulting in the need for thrombolytic therapy][21]). Infectious complications included PICC-associated bloodstream infection or local infection defined according to National Healthcare Safety Network criteria for central catheter–associated bloodstream infection or arterial or venous infection, with the exclusion of infections involving vascular access devices with organisms identified in the blood.[22,23]

Secondary outcomes were complications from any cause or cause-specific complications that occurred during the period of PICC placement (with or without catheter failure); duration of PICC placement; participant, parent, and staff satisfaction at the time of insertion and at trial end (assessed with the use of numerical rating scales with values ranging from 0 to 10, with higher numbers indicating increasing satisfaction)[17]; quality-adjusted life-days; and adverse events, including allergy, pain, and death. Full outcome definitions are provided in the Supplementary Appendix.

STATISTICAL ANALYSIS

We assumed that the risk of device failure would be 15% with standard polyurethane PICCs[24-26] and 7.5% with each of the hydrophobic and chlorhexidine PICCs,[9,11,27] which would give a difference in risk of 7.5 percentage points. We calculated that a sample of 366 participants in each treatment group would provide the trial with 85% power to show the superiority of each innovative PICC over the standard-care PICC, at a two-sided alpha significance level of 0.035. Consequently, we sought to enroll 1098 participants.

In the primary analysis, between-group differences in the risk of device failure were analyzed with the use of logistic regression, with the treatment-group assignment included as the main effect. Effect estimates are presented as

odds ratios with 95% confidence intervals for the comparisons between each innovative PICC and the standard polyurethane PICC. For count-based outcome variables, Poisson regression with robust standard errors was used, and effect estimates are reported as incidence rate ratios with 95% confidence intervals. For time-to-event outcomes, Cox regression was used, and effect estimates are reported as hazard ratios with 95% confidence intervals. The proportional-hazards assumption was tested graphically with the use of Kaplan–Meier curves and plots of Schoenfeld residuals against log-transformed time. The time to device failure is reported graphically with the use of Kaplan–Meier curves. For continuous outcome variables, linear regression was used, and effect estimates are reported as mean differences with 95% confidence intervals. When model assumptions were not met, median regression was used, and the effect estimates are reported as median differences with 95% confidence intervals. The stratification factors of hospital site and thrombosis risk were included as covariables in all regression models.

All outcomes were analyzed in the intention-to-treat population, which included all participants who had undergone randomization and provided outcome data. Missing data were not imputed, and a complete-case analysis was performed. A per-protocol analysis of the primary outcome assessed the effect of protocol violations, such as use of an unassigned PICC use. The per-protocol analysis included all participants who had undergone randomization and provided outcome data and was performed with the use of an instrumental variable approach.[28] Post hoc analyses were performed according to age. For secondary outcomes and subgroup analyses, formal adjustment of confidence intervals for multiplicity was not performed, and no definitive inferences should be drawn from these findings. Analyses were performed with the use of Stata statistical software, version 17.0 (StataCorp). Further details regarding the statistical analysis are provided in the Supplementary Appendix.

RESULTS

PARTICIPANTS

From September 2019 through December 2022, a total of 2325 patients who were referred to receive a PICC were assessed for eligibility; 1227 were excluded because they did not meet inclusion criteria (637 participants), declined to participate (233), or were missed because a research nurse was not available (357) (Fig. 1). A total of 1098 participants were enrolled and underwent randomization; 365 were assigned to receive a hydrophobic PICC, 365 to receive a chlorhexidine PICC, and 368 to receive a standard polyurethane PICC. The PICC was not inserted in 14 participants because of clinical reasons, and these participants were excluded from analyses, as were the 4 participants who were lost to follow-up. Data were missing for only 4 of the 1084 participants (0.4%), so a complete-case analysis was conducted. A total of 25 protocol breaches that involved insertion of the incorrect PICC occurred in the trial.

The demographic and clinical characteristics of the participants are shown in Table 1. The trial population comprised 178 pediatric participants (16.2%; mean [±SD] age, 12±3 years) and 920 adult participants (83.8%; (mean age, 57±15 years). Most participants (53.8%) had three or more coexisting medical conditions, and 41.0% had previously undergone central venous catheter placement. The inserted PICCs in this trial were most commonly dual lumen and 5.0 to 5.5 French, and most were inserted in the basilic vein. Additional participant, device, and provider characteristics are listed in Tables S1, S2, and S3 in the Supplementary Appendix.

PRIMARY OUTCOME

Device failure occurred in 21 of 358 participants (5.9%) in the hydrophobic group, in 36 of 363 (9.9%) in the chlorhexidine group, and in 22 of 359 (6.1%) in the standard-polyurethane group (risk difference, hydrophobic group vs. standard-polyurethane group, −0.2 percentage points [95% CI, −3.7 to 3.2; P=0.89]; and chlorhexidine group vs. standard-polyurethane group, 3.8 percentage points [95% CI, −0.1 to 7.8; P=0.06]). In the hydrophobic group as compared with the standard-polyurethane group, the odds ratio for device failure was 0.96 (95% CI, 0.51 to 1.78), and in the chlorhexidine group as compared with the standard-polyurethane group, the odds ratio was 1.71 (95% CI, 0.98 to 2.99) (Table 2 and Fig. 2). The results of the per-protocol analyses and analyses with stratification according to age appeared to be similar to those of the primary analysis (Fig. 2 and Tables S4, S5, and S6).

SECONDARY OUTCOMES

The mean number of device failures per 1000 catheter days was 2.2±0.5 in the hydrophobic group, 3.6±0.6 in the chlorhexidine group, and 2.1±0.5 in the standard-polyurethane group. The hazard ratio for device failure in the hydrophobic group as compared with the standard-polyurethane group was 1.07 (95% CI, 0.59 to 1.94), and the hazard ratio in the chlorhexidine group as compared with the standard-polyurethane group was 1.68 (95% CI, 0.99 to 2.86) (Table 2 and Fig. 3).

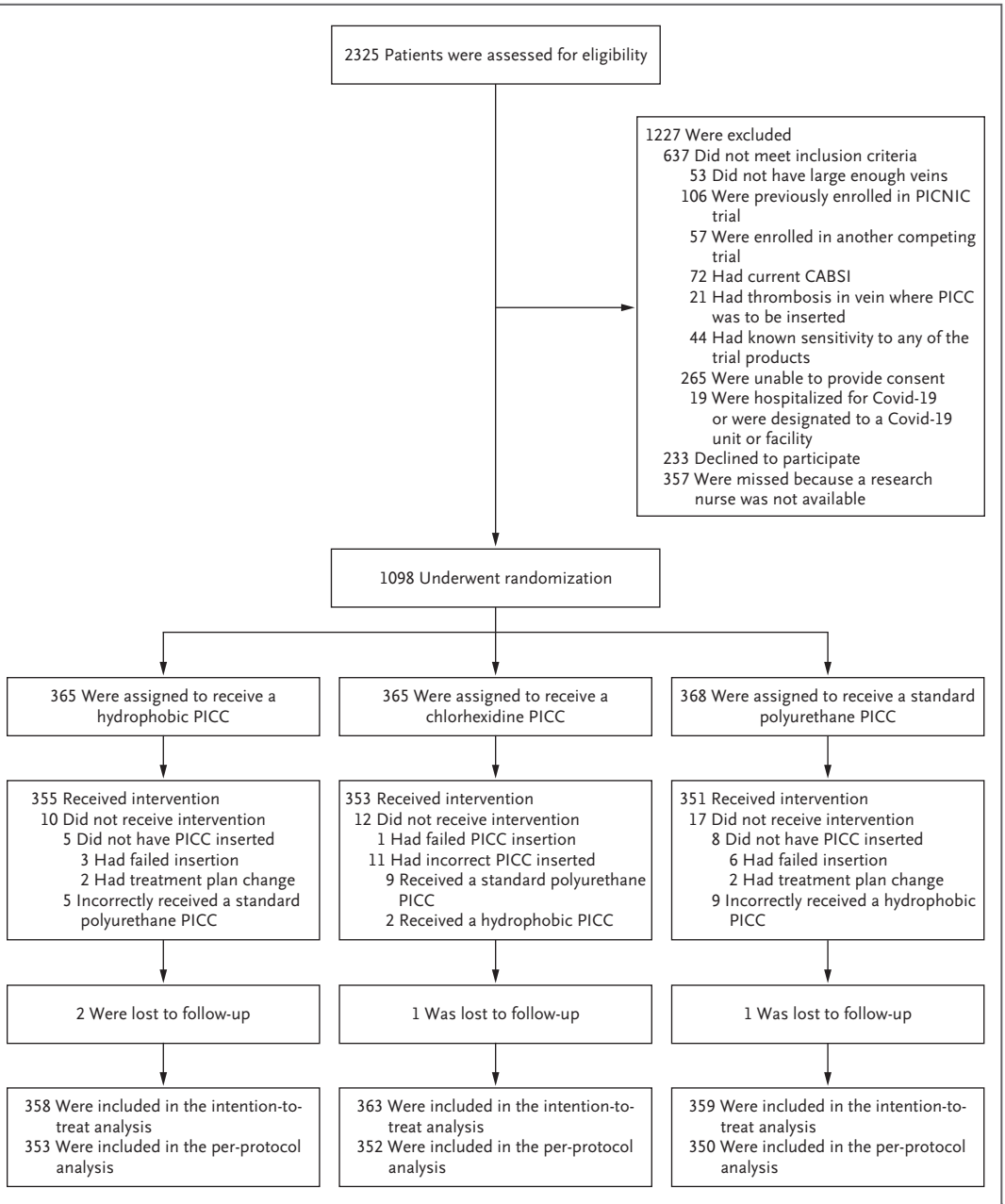


Figure 1. Screening, Randomization, and Analysis.

CABSI denotes catheter-associated bloodstream infection, Covid-19 coronavirus disease 2019, PICC peripherally inserted central catheter, and PICNIC Peripherally Inserted Central Catheter Innovation to Reduce Infections and Clots.

Table 1. Participant and Device Characteristics at Baseline.*

Characteristic	Hydrophobic PICC (N=365)	Chlorhexidine PICC (N=365)	Standard Polyurethane PICC (N=368)
Total catheter-days included in the trial — no.	9352	9986	10,324
Age — yr	50.7±22.3	50.4±21.7	49.7±21.7
Female sex — no. (%)	144 (39.5)	146 (40.0)	149 (40.5)
Hospital site — no. (%)			
Princess Alexandra Hospital	195 (53.4)	195 (53.4)	195 (53.0)
Queensland Children's Hospital	60 (16.4)	58 (15.9)	60 (16.3)
Royal Brisbane and Women's Hospital	110 (30.1)	112 (30.7)	113 (30.7)
Coexisting conditions — no. (%)			
None	45 (12.3)	49 (13.4)	40 (10.9)
1	65 (17.8)	67 (18.4)	65 (17.7)
2	63 (17.3)	61 (16.7)	52 (14.1)
3	21 (5.8)	27 (7.4)	32 (8.7)
>3	171 (46.8)	161 (44.1)	179 (48.6)
Diagnostic group — no. (%)†			
Surgical	129 (35.3)	120 (32.9)	118 (32.1)
Oncology	82 (22.5)	82 (22.5)	91 (24.7)
Hematology	54 (14.8)	54 (14.8)	52 (14.1)
Respiratory	29 (7.9)	23 (6.3)	25 (6.8)
Gastroenterology	26 (7.1)	27 (7.4)	33 (9.0)
General medical	28 (7.7)	27 (7.4)	40 (10.9)
Cardiology	20 (5.5)	27 (7.4)	8 (2.2)
Infectious diseases	11 (3.0)	15 (4.1)	12 (3.3)
First CVC in the participant's life — no. (%)	215 (58.9)	216 (59.2)	212 (57.6)
Active infection at time of recruitment — no. (%)	233 (63.8)	244 (66.8)	253 (68.8)
High thrombosis risk — no. (%)			
Adults	200 (65.6)	203 (66.1)	200 (64.9)
Children	11 (18.3)	9 (15.5)	11 (18.3)
PICC lumens — no. (%)‡			
1	46 (12.8)	50 (13.7)	48 (13.3)
2	310 (86.1)	307 (84.3)	311 (86.4)
3	4 (1.1)	7 (1.9)	1 (0.3)
PICC insertion site — no. (%)‡			
Basilic vein	322 (89.4)	306 (84.1)	305 (84.7)
Brachial vein	32 (8.8)	54 (14.8)	44 (12.2)
Other vein	6 (1.7)	4 (1.1)	11 (3.1)
EQ-5D utility index score for quality of life§			
Age >12 yr	0.73±0.29	0.76±0.28	0.74±0.29
Age ≤12 yr	0.60±0.35	0.58±0.37	0.53±0.36

* Plus–minus values are mean ±SD. Percentages may not total 100% because of rounding. CVC denotes central venous catheter, and PICC peripherally inserted central catheter.
† A participant could be in more than one diagnostic group.
‡ The number of PICC lumens and PICC insertion sites was assessed among the participants who received a PICC (360 in the hydrophobic group, 364 in the chlorhexidine group, and 360 in the standard-polyurethane group).
§ The EuroQol Group 5-Dimension (EQ-5D) questionnaire measures quality of life in five dimensions; utility scores range from –0.109 to 1, with higher scores indicating better states of health. In the hydrophobic, chlorhexidine, and standard-polyurethane groups, the EQ-5D was assessed in 47, 44, and 38 participants, respectively, among those 12 years of age or younger, and in 301, 304, and 301 participants, respectively, among those older than 12 years of age.

Complications from any cause during the period of PICC placement occurred in 77 participants (21.5%) in the hydrophobic group, in 140 (38.6%) in the chlorhexidine group, and in 78 (21.7%) in the standard-polyurethane group. The odds ratio for a complication from any cause in the hydrophobic group as compared with the standard-polyurethane group was 0.99 (95% CI, 0.69 to 1.42), and the odds ratio in the chlorhexidine group as compared with the standard-polyurethane group was 2.35 (95% CI, 1.68 to 3.29). The most frequent complication was catheter occlusion, which occurred in 17.0% of the participants in the hydrophobic group, in 33.6% in the chlorhexidine group, and in 14.2% in the standard-polyurethane group (Table 2 and Table S7).

The numbers of overall, complete, and partial occlusions are shown in Table 2. Venous thrombosis occurred in 3.1% of the participants in the hydrophobic group, in 3.3% in the chlorhexidine group, and in 6.4% in the standard-polyurethane group. PICC-associated bloodstream infections occurred in 1.4% of the participants in the hydrophobic group, in 1.7% in the chlorhexidine group, and in 1.9% in the standard-polyurethane group. Staff ease with PICC insertion and satisfaction with the insertion kit appeared to be lower with hydrophobic PICCs than with the other PICCs. Trial-group assignment had no apparent effect on quality-adjusted life-days.

ADVERSE EVENTS

Adverse events of any cause occurred in 12 participants (3.4%) in the hydrophobic group, in 4 (1.1%) in the chlorhexidine group, and in 7 (1.9%) in the standard-polyurethane group. All adverse events, including a systemic allergic reaction in 1 participant in the standard-polyurethane group, were determined by the medical monitor to be unrelated to the PICC.

DISCUSSION

The current trial did not show that the risk of device failure (a composite of infectious or noninfectious complications severe enough to cause cessation of PICC function) was lower with hydrophobic PICCs or chlorhexidine PICCs than with standard polyurethane PICCs. The number of catheter occlusion events, as well as complete and partial occlusion events, appeared to be higher with chlorhexidine PICCs than with hydrophobic or standard polyurethane PICCs. There were no apparent differences in the incidence of infectious complications among the treatment groups. We also observed numerically more complications from any cause in the chlorhexidine group than in the hydrophobic or standard-polyurethane group. The incidence of adverse events appeared to be similar in the three groups.

The current findings reflect the complexity in preventing multifactorial PICC dysfunction, with no apparent difference in the incidence of device failure or of catheter-acquired bloodstream infection according to PICC type. These results are in contrast to previous recommendations regarding PICC materials, which are mostly based on observational studies that are inadequately powered or lack robust outcome assessments.[8,10,26,27,29] Occlusion was the most common reason for device failure in the current trial, a complication rarely reported in clinical trials and international databases. Devices that occlude prevent the administration of time-sensitive therapies[30] and require costly catheter salvage interventions, such as thrombolytic agents or catheter replacement.[31] In our trial, occlusion occurred more frequently with chlorhexidine PICCs than with the other PICC types, although the reason is unclear. Occlusion may be due to the interactivity of the chlorhexidine acetate coating with sometimes-complex infusates being administered; however, previous studies have focused on chlorhexidine gluconate rather than acetate.[32,33] The results of previous studies evaluating chlorhexidine-coated PICCs[27] and centrally inserted venous catheters[11] are not similar to our findings, but occlusion is often overlooked when treatment is directed toward the prevention of catheter-acquired bloodstream infection. A pediatric cancer-care trial examining the use of ethanol-based catheter-locking solutions as a treatment and secondary prophylaxis for catheter-acquired bloodstream infections was stopped early because of catheter occlusions.[34] Further exploration of modifiable and nonmodifiable risks of PICC occlusions, including those associated with chlorhexidine coatings, are warranted.

In contrast to more expensive and less common products, PICC material and design choices are often determined by multiinstitutional product contracts that are based on perceived best

Table 2. Primary and Secondary Outcomes.*

Outcome	Hydrophobic PICC (N=358)	Chlorhexidine PICC (N=363)	Standard Polyurethane PICC (N=359)	Effect Estimate (95% CI)†	
				Hydrophobic vs. Standard Polyurethane	Chlorhexidine vs. Standard Polyurethane
Primary outcome					
Device failure — no. (%)	21 (5.9)	36 (9.9)	22 (6.1)	0.96 (0.51 to 1.78)	1.71 (0.98 to 2.99)
Secondary outcomes					
Device failure per 1000 catheter-days	2.2±0.5	3.6±0.6	2.1±0.5	1.07 (0.59 to 1.94)	1.68 (0.99 to 2.86)
Noninfectious failure — no. (%)					
Venous thrombosis	7 (2.0)	9 (2.5)	11 (3.1)	0.63 (0.24 to 1.65)	0.81 (0.33 to 2.00)
Breakage	2 (0.6)	0	1 (0.3)	2.04 (0.18 to 22.60)	NC
Occlusion‡	8 (2.2)	24 (6.6)	4 (1.1)	2.06 (0.61 to 6.93)	6.50 (2.22 to 19.01)
Infectious failure — no. (%)	5 (1.4)	4 (1.1)	6 (1.7)	0.82 (0.25 to 2.72)	0.65 (0.18 to 2.32)
PICC-associated BSI	4 (1.1)	3 (0.8)	5 (1.4)	0.79 (0.21 to 2.96)	0.58 (0.14 to 2.46)
Local infection	1 (0.3)	1 (0.3)	1 (0.3)	0.99 (0.06 to 15.90)	0.98 (0.06 to 15.72)
Complications from any cause — no. (%)	77 (21.5)	140 (38.6)	78 (21.7)	0.99 (0.69 to 1.42)	2.35 (1.68 to 3.29)
Complications per 1000 catheter-days	16.6±2.1	30.2±2.5	12.0±1.5	1.36 (0.96 to 1.92)	2.49 (1.86 to 3.32)
Noninfectious complications — no. (%)					
Venous thrombosis	11 (3.1)	12 (3.3)	23 (6.4)	0.46 (0.22 to 0.96)	0.50 (0.24 to 1.02)
Breakage	3 (0.8)	0	2 (0.6)	1.51 (0.25 to 9.12)	NC
Occlusion	61 (17.0)	122 (33.6)	51 (14.2)	1.25 (0.83 to 1.89)	3.22 (2.21 to 4.69)
Complete occlusion	32 (8.9)	87 (24.0)	18 (5.0)	1.88 (1.03 to 3.43)	6.21 (3.63 to 10.62)
Partial occlusion	41 (11.5)	82 (22.6)	37 (10.3)	1.13 (0.70 to 1.83)	2.73 (1.77 to 4.21)
Infectious complications — no. (%)§	12 (3.4)	16 (4.4)	14 (3.9)	0.83 (0.36 to 1.89)	1.22 (0.57 to 2.59)
PICC-associated BSI	5 (1.4)	6 (1.7)	7 (1.9)	0.70 (0.22 to 2.23)	0.83 (0.27 to 2.51)
Local infection	6 (1.7)	10 (2.8)	7 (1.9)	0.85 (0.28 to 2.55)	1.42 (0.53 to 3.78)

Duration of PICC placement — days	26.1±18.1	27.5±18.0	28.8±18.9	−2.7 (−5.3 to −0.2)	−1.2 (−3.8 to 1.3)
Numerical rating of satisfaction — score (interquartile range)¶					
Staff ease with PICC insertion	9.0 (7.0 to 10.0)	10.0 (9.0 to 10.0)	10.0 (9.0 to 10.0)	−0.5 (−0.7 to −0.3)	0.0 (−0.2 to 0.2)
Staff satisfaction with insertion kit	8.0 (5.0 to 10.0)	10.0 (9.0 to 10.0)	10.0 (10.0 to 10.0)	−2.0 (−2.2 to −1.8)	0.0 (−0.2 to 0.2)
Participant's or parent's overall experience with trial product	9.8 (7.7 to 10.0)	8.8 (5.9 to 10.0)	9.6 (7.4 to 10.0)	0.0 (−0.3 to 0.3)	−0.4 (−0.7 to −0.1)
Any adverse event — no. (%)	12 (3.4)	4 (1.1)	7 (1.9)	1.76 (0.68 to 4.53)	0.56 (0.16 to 1.95)
Death	12 (3.4)	4 (1.1)	6 (1.7)	2.05 (0.76 to 5.52)	0.66 (0.18 to 2.35)
Allergy	0	0	1 (0.3)	NC	NC
Quality-adjusted life-days‖					
Age 8 to ≤17 yr	14.0±12.2	15.8±13.6	12.5±10.4	2.2 (−4.3 to 8.8)	4.9 (−1.7 to 11.5)
Age ≥18 yr	27.9±31.7	28.5±18.6	27.8±18.7	0.1 (−4.6 to 4.7)	0.3 (−4.3 to 4.9)

* Plus–minus values are mean ±SD. One participant had a simultaneous bloodstream infection (BSI) and local infection. NC denotes not calculable.
† Effect estimates were adjusted for stratification factors (hospital site and thrombosis risk) and are reported as odds ratios for binary outcomes, as hazard ratios for device failure per 1000 catheter-days, as incidence rate ratios for complications per 1000 catheter-days, as mean differences for the duration of PICC placement and quality-adjusted life-days, and as median differences for numerical rating of satisfaction.
‡ All occlusive failures were complete occlusions.
§ A participant could have both types of infectious complication.
¶ Satisfaction was assessed on a numerical rating scale of 0 to 10, with higher scores indicating increasing ease, satisfaction, or experience. Staff ease and satisfaction with insertion was assessed at the time of PICC insertion; in the hydrophobic, chlorhexidine, and standard-polyurethane groups, the number of assessments was 353, 351 and 349, respectively. Each participant's or parent's experience was assessed at the time of PICC removal; in the hydrophobic, chlorhexidine, and standard-polyurethane groups, the number of assessments was 263, 272 and 269, respectively.
‖ In the hydrophobic, chlorhexidine, and standard-polyurethane groups, the number of quality-adjusted life-days was assessed in 29, 31, and 24 participants, respectively, among those 8 to 18 years of age and in 192, 198, and 191 participants, respectively, among those older than 18 years of age.

Analysis Population	Innovative PICC: Hydrophobic	Innovative PICC: Chlorhexidine	Standard Polyurethane PICC	Odds Ratio for Device Failure (95% CI)
	no. of events/total no. (%)			
Overall				
Intention-to-treat analysis				
Hydrophobic	21/358 (6)	—	22/359 (6)	0.96 (0.51–1.78)
Chlorhexidine	—	36/363 (10)	22/359 (6)	1.71 (0.98–2.99)
Per-protocol analysis				
Hydrophobic	21/353 (6)	—	22/350 (6)	0.95 (0.50–1.82)
Chlorhexidine	—	35/352 (10)	22/350 (6)	1.71 (0.96–3.03)
Hospital site				
Princess Alexandra Hospital				
Hydrophobic	10/192 (5)	—	11/190 (6)	0.89 (0.37–2.16)
Chlorhexidine	—	15/194 (8)	11/190 (6)	1.36 (0.61–3.05)
Queensland Children's Hospital				
Hydrophobic	1/57 (2)	—	1/57 (2)	1.43 (0.06–16.39)
Chlorhexidine	—	2/58 (3)	1/57 (2)	2.00 (0.18–22.69)
Royal Brisbane and Women's Hospital				
Hydrophobic	10/109 (9)	—	10/112 (9)	1.03 (0.41–2.58)
Chlorhexidine	—	19/111 (17)	10/112 (9)	2.11 (0.93–4.76)
Thrombosis risk				
High risk, adults				
Hydrophobic	17/199 (9)	—	15/198 (8)	1.14 (0.55–2.35)
Chlorhexidine	—	25/201 (12)	15/198 (8)	1.73 (0.88–3.40)
Low risk, adults				
Hydrophobic	3/102 (3)	—	6/102 (6)	0.49 (0.12–2.03)
Chlorhexidine	—	9/104 (9)	6/102 (6)	1.55 (0.53–4.51)
High risk, children				
Hydrophobic	1/11 (9)	—	0/10	NC
Chlorhexidine	—	0/9	0/10	NC
Low risk, children				
Hydrophobic	0/46	—	1/47 (2)	1.02 (0.00–39.85)
Chlorhexidine	—	2/49 (4)	1/47 (2)	1.96 (0.17–22.34)

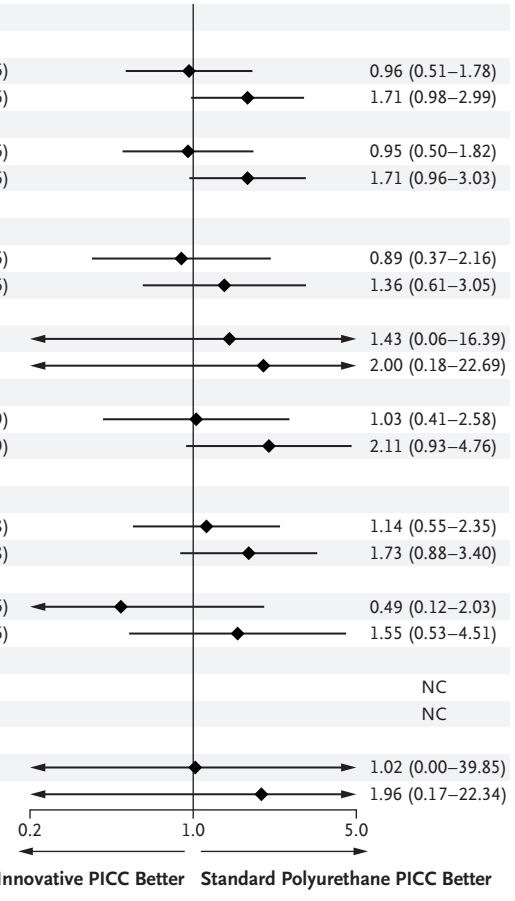


Figure 2. Overall and Subgroup Analyses of Primary Outcome.

The association between PICC type and device failure (a composite of infectious and noninfectious complications severe enough to cause cessation of PICC function or necessitating PICC removal before completion of the intended therapy) is shown for intention-to-treat and per-protocol populations and subgroups according to hospital site and thrombosis risk among adults (≥18 years of age) and children (<18 years of age). NC denotes not calculable.

price.[35] In addition, regulation is driven by risk-based classification, and for lower-risk devices, the focus is on self-certification (i.e., certification without independent verification) and conformity rather than effectiveness.[36] Despite extensive public interest, the onus is on postmarket evaluations — often sponsored by the device manufacturer — to collect clinical information on device performance. Infrastructure to rigorously evaluate devices before widespread implementation is necessary to ensure benefit for patients and health systems.

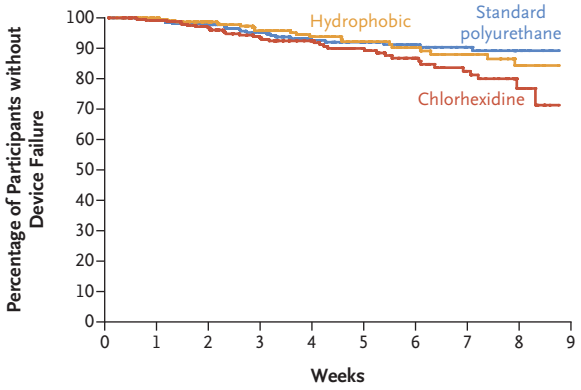
Our superiority hypothesis and sample-size calculations were based on local pilot randomized, controlled trials and observational studies; however, our primary outcome results did not show superiority of the chlorhexidine or hydrophobic PICCs over the standard polyurethane PICCs.[9,11,25-27] This result may be attributable to the fact that PICC removal because of complications is a clinically driven decision, which is often based on multifactorial patient requirements (e.g., dual lumen inserted, but only one lumen required) and health services requirements (e.g., availability of staff).[37] In addition, the PICNIC trial was conducted during the coronavirus disease

2019 (Covid-19) pandemic, when people were minimizing health care exposures, which may have also influenced decision making toward leaving partially functional PICCs in situ.

During the Covid-19 pandemic, there was also an increased focus on infection prevention and control,[38] which had the potential to influence infection outcomes; the incidence of catheter-acquired bloodstream infection in our trial was lower than historical international benchmarks.[39] However, a multisite Australian interrupted-time-series study showed a similar incidence of health care–associated infection before and during the Covid-19 pandemic (25.5 and 25.1 infections per 10,000 occupied bed-days, respectively).[38] Patients with Covid-19 were not recruited in our trial. The risk of PICC-associated venous thrombosis was similar to that in a 2013 meta-analysis[40] but higher than that in a 2021 review,[41] with venous thrombosis occurring in 6.4% of the participants who received a standard polyurethane PICC. The trend toward a reduction in the risk of PICC-associated venous thromboembolism with hydrophobic PICCs shows promise and conforms with previous laboratory and clinical evaluations.[8] However, because the current trial was not designed to test thrombosis as a primary outcome, the clinical effectiveness of hydrophobic PICCs for the prevention of thrombosis warrants further examination.

Our trial has several limitations. All outcome assessments required clinical presentation of the participant to identify device failure, and there was no routine testing or imaging; therefore, it is possible that the interventions may have an effect at a subclinical level. The trial included a pragmatic approach, based on statewide guidelines, to PICC insertion with a range of proceduralists; however, many practitioners performing the insertions were relatively unfamiliar with the PICC products and kits. It is likely that performance will improve over time as practitioners become more familiar with using the products during the insertion procedure; a lack of familiarity may have influenced the results regarding staff satisfaction.

In this trial involving adults and children who were referred for PICC placement, the risk of device failure caused by noninfectious or infectious complications was not lower with hydrophobic or chlorhexidine PICCs than with standard polyurethane PICCs.



No. at Risk

Standard polyurethane	359	314	252	203	160	132	105	88	44
Hydrophobic	358	312	231	180	129	102	84	67	37
Chlorhexidine	363	320	249	195	156	125	91	70	42

Figure 3. Device Failure According to PICC Type (Time-to-Event Analysis).
The Kaplan–Meier curves show device failure through 8 weeks after insertion.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

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