Routine Catheter Lock Solutions in Pediatric Cancer Care
A Pilot Randomized Controlled Trial of Heparin vs Saline

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Background: Central venous access devices (CVADs) are integral to cancer care provision. Despite the high prevalence of CVAD complications in children with cancer, preventative strategies are understudied. Objective: The aim of this study was to assess study feasibility, occlusive events, thrombolytic use, adverse events, and direct costs of catheter lock solutions. Methods: A single-center, parallel-group, pilot randomized controlled trial was undertaken at a tertiary-referral pediatric hospital in Australia. Children 18 years or younger with an oncological or malignant hematological condition and a CVAD were eligible. Participants were 1:1 randomized to (1) normal or (2) heparinized (10–100 U/mL; CVAD-type dependent) saline lock solutions. Results: Of 217 children assessed for eligibility, 61 were recruited and randomized to normal (n = 30; 3850 CVAD days) or heparinized (n = 31; 4036 CVAD days) saline. Eligibility (52%) and recruitment (54%) feasibility targets were not met. Protocol adherence was high (95% assessments), with no attrition. Parent/clinician satisfaction of interventions was high (median, 10/10 clinicians/parents). Complete CVAD occlusion occurred in heparin only (n = 2, 6.7% CVADs; incidence rate [IR], 0.49/1000 CVAD days [0.06–1.78]). Central venous access device partial occlusion was detected in 23.3% of CVADs in heparin (n = 7; IR, 2.73/1000 CVAD days [1.36–4.87]) and 13.8% of CVADs in normal saline (n = 4; IR, 2.59/1000 CVAD days [1.24–4.77]). Thrombolytic agents were used in 16.7% heparin (5 CVADs) and 3.5% normal saline (1 CVAD). Adverse events did not differ between groups. Conclusion: Multisite randomized controlled trials examining CVAD locks are safe, but strategies and resources to increase recruitment and eligibility are required. Implications for Practice: Both routine CVAD lock solutions seem safe but may not prevent all forms of CVAD-associated harm.

In pediatric cancer care, the insertion of a central venous access device (CVAD) is necessary to facilitate the safe and reliable administration of anticancer drugs and supportive therapies, and for blood sampling, while minimizing the risk for multiple, painful venipunctures. Consequently, the adoption of CVADs, including peripherally inserted central catheters (PICCs), and tunneled and totally implanted CVADs, has led to increased quality of care and quality of life for children with cancer. However, 1 in 3 CVADs in pediatric cancer care becomes infected, thrombosed, or blocked during treatment. These events disrupt and complicate treatment delivery and recovery trajectory, significantly impacting morbidity and mortality.

Central venous access device–associated bloodstream infections (CABSIs) have been a considerable focus for improvement across cancer care. However, in pediatric cancer care, CVAD occlusion (ie, blockage) remains common, occurring in 6% of all CVADs and affecting 14% to 36% of children with long-term CVADs (estimated incidence rate [IR] of 1.35 per 1000 catheter days). Aspirate occlusion (inability to aspirate) and infuse occlusion (inability to infuse medication) occur secondary to fibrin buildup, medication precipitate, catheter tip thrombus, or tip malposition against vessel or chamber walls, leading to catheter rupture if excessive flushing force is applied. As a result, CVAD failure often occurs and is associated with treatment delays and device replacement. In addition, children with cancer who have a blocked CVAD have a significantly increased risk of vessel thrombosis and local or systemic infection. Catheter lock solutions are routine interventions aimed to promote CVAD performance by preventing CVAD-associated adverse events, especially occlusion. Solutions dwell in the CVAD tubing between therapy administration (between 24 hours and 8 weeks) and are used as routine CVAD lock solutions in pediatric cancer care and beyond.

Historically low-dose heparin (10–100 U/mL) was instilled, then was aspirated before the next therapy administration, and was primarily selected because of its anticoagulant properties. However, the effectiveness of heparin to prevent thrombotic occlusion for extended periods is questionable, given its short half-life (60–90 minutes). In addition, there is a risk of bleeding due to accidental administration of heparin during the aspiration procedure or overdose due to incorrect dilution. Comparatively, normal saline (0.9% sodium chloride) relies on the movement of the solution to physically clear the catheter of blood or fibrin.
buildup. To date, research in adult cancer populations has shown promise for using normal saline as a lock solution to prevent potential complications associated with heparin use, including the risk of heparin-induced thrombocytopenia and accidental heparin administration. However, a recent Cochrane review comparing the clinical effects of normal saline with those of heparin to prevent occlusion concluded that there was insufficient evidence to establish the efficacy of normal saline to prevent complications of CVADs in pediatric cancer care. The same review also found that there was insufficient evidence to suggest heparin was necessary to prevent occlusion, CABSI, or the effects of prolonged catheter placement.

Despite the high prevalence of CVAD-associated adverse events in children with cancer and the commonality of routine CVAD lock procedures, it is unclear which routine practice (normal or heparinized saline) is more effective at preventing CVAD complications. Catheter lock solution practices vary widely, because of the limited quality evidence to guide clinical decision making. It is necessary to establish the efficacy and safety of strategies aimed at preventing occlusive events using randomized controlled trials (RCTs); however, the feasibility and safety of conducting an RCT in pediatric cancer care has not yet been established. Therefore, this study aimed to test the safety and feasibility of an equivalence RCT comparing heparinized saline with normal saline (0.9% sodium chloride) for locking CVADs in pediatric cancer care.

### Methods

#### Study Design

A single-center, parallel-group, pilot RCT was undertaken at a tertiary-referral pediatric hospital in Australia between July 2019 and September 2020, to establish the feasibility of an effectiveness trial, as recommended in the Canadian Clinical Trial Programmatic research approach. Data related to the feasibility of the intervention, occlusion events, and CVAD performance (including complications and removals) were prospectively collected during the participant’s admission. This study was prospectively registered with the Australian and New Zealand Clinical Trial Registry (ACTRN12619000393156) and is reported in accordance with the Consolidated Standards of Reporting Trials statement. Approval to undertake the project was provided by Children’s Health Queensland Human Research Ethics Committee (HREC/18/QCHQ/46862) and Griffith University Human Research Ethics Committee (GU 2019/199).

#### Participants

The study was undertaken in the Oncology Services Group (inpatient and outpatient facilities) of Queensland Children’s Hospital, Brisbane, Australia. Queensland Children’s Hospital is the tertiary-referral teaching hospital for pediatric cancers in Queensland, Australia.

All children younger than 18 years, with a CVAD in situ (including PICCs, and tunneled [eg, Hickmans; Becton Dickinson, US (Becton, Dickinson and Company, Franklin Lakes, United States)] and totally implanted [eg, PORT-A-CATH; BBraun, US (B. Braun; Melsungen, Germany)] CVADs), and who had been given a diagnosis of an oncological or malignant hematological condition were eligible for inclusion. Children who were under an end-of-life care pathway, had a preexisting coagulopathic condition not related to the current diagnosis or treatment (eg, hemophilia A and B or other factor deficiencies, immune thrombocytopenic purpura, Von Willebrand’s disease), had a coagulation disorder related to the current diagnosis or treatment (eg, disseminated intravascular coagulopathy), were undergoing current treatment with PEG-asparaginase (due to influences on coagulation), had an allergy to heparin, had a bone marrow transplant planned, were admitted to the pediatric intensive care unit or to a regional hospital or alternative healthcare facility, or had previously participated in the study were not included in the study.

#### Interventions

Participants were randomized to receive CVAD locks (administered when the CVAD was not planned to be in use for >24 hours) with either of the following:

1. Normal saline: 0.9% sodium chloride 10 mL
2. Heparinized saline: per CVAD type (as per local clinical practice guideline; Cochrane review). Peripherally inserted central catheter and tunneled CVADs: sodium heparin 50 U/5 mL; 1–2 mL per catheter lumen. Totally implanted CVADs: sodium heparin 100 U/mL; 2 mL

All other aspects of CVAD management were per local clinical guidelines, which are based on international standards.

In particular, this included manual pulsatile flushing with normal saline between access, routine relocking every 7 days (for PICCs and tunneled CVADs) or 6 to 8 weeks (totally implanted CVADs), no routine prophylactic systemic heparin therapy, goal catheter tip positioning in the cavoatrial junction, and aseptic nontouch technique for all access episodes.

#### Study Outcomes

The primary outcomes were as follows: (1) “study feasibility,” determined based on eligibility (percentage of screened patients meeting all inclusion and no exclusion criteria), recruitment (percentage of eligible patients providing informed consent), retention/attrition (percentage of recruited patients lost to follow-up or withdrawing consent), protocol fidelity (percentage of randomized patients receiving their allocated intervention), missing data (percentage of total data unable to be collected by study staff), and parent/caregiver and staff satisfaction with the interventions (percentage of parents/caregivers and staff scoring ≥7 on an 11-point numeric rating scale at study completion), and (1) “occlusive events,” described proportionally and per 1000 catheter days, and assessed using the Catheter Injection and Aspiration classification system. Secondary outcomes include use of thrombolytic agents (eg, alteplase), CVAD fracture (visible split during or after flushing or infusion), venous thrombosis (thrombosed CVAD vessel or fibrin sheath occluding lumen diagnosed via ultrasound or venography, confirmed by blinded radiologist), CABSI (as per Centers of Disease Control National Healthcare Safety Network criteria), medication error (incorrect dose instilled, with or without clinical sequelae), and differences in direct healthcare costs (products, investigation, and clinical time).
Sample Size

Sample size calculations were based on acquisition of feasibility outcomes, with 30 participants per treatment group determined to be adequate to identify feasibility of study procedures, and provide estimates of treatment effect for future investigations.29,30

Study Procedures

Inpatient and outpatient oncology admission lists were screened for eligible patients daily (Monday-Friday only) by the research nurse. After extensive consultation with clinicians, eligible patients and their parents/caregivers were approached by the research nurse for written informed consent. Participants were randomized to treatment allocation by the research nurse using a secure Web-based computer-generated central randomization service in a ratio of 1:1 and stratified per CVAD device (PICC, tunneled cuffed CVAD, totally implanted CVAD), using a randomly variable permuted block size (2, 4), to avoid allocation prediction. The research nurse checked patients daily when admitted to hospital, or weekly when attending outpatient appointments, to inspect the CVAD, ensure intervention fidelity, collect data, and ensure safety of the study participants. Allocated lock solutions were prescribed by medical staff in the electronic medical record. To maximize protocol adherence, point-of-care education resources were provided and pre-prepared packs and labels were used to remind clinicians of the locking regimen to be followed for each participant, including laminated education resources at the infusion pump.

Participants were included in the trial for 6 weeks, or until study withdrawal, upon CVAD removal, or on admission to a regional facility or pediatric intensive care unit. The intervention was not amenable to blinding of patients, clinical staff, or research nurses; however, physicians were blinded to treatment allocation when assessing infectious (infectious disease physician) and thrombosis (radiologist) outcomes. Data analysis was conducted with blinding to group.

Deidentified data collection was undertaken via Research Electronic Data CAPture (http://project-redcap.org/). The research nurse collected data on primary and secondary outcomes using the predefined criteria. Demographic and clinical data were prospectively collected to assess success of randomization and describe the participant group.

Statistical Methods

Before analysis, data cleaning of outlying observations was undertaken, and a random 5% sample of source data was reentered and checked. Missing data were not imputed. Analysis was conducted as “intention to treat,” with the participant as the unit of measurement. Baseline characteristics for each of the groups are presented using frequencies and percentages (categorical variables) and means and standard deviations (normally distributed continuous variables) or median and interquartile range (nonnormally distributed variables). For this pilot trial, the primary analysis tested the feasibility of the statistical analysis for a definitive trial. Comparability of groups at baseline was assessed using clinically significant differences. Frequency and IR (with 95% confidence intervals) of device occlusion were used to summarize the impact of the intervention. Primary end points were compared between groups using log-rank test for equality of survivor function and clinically significant differences. Statistical tests were considered significant at the 95% level (P < .05, 2-tailed). Stata (version 15; StataCorp, College Station, Texas) was used for statistical analysis.

Cost Analysis

A cost analysis from the health sector perspective was undertaken to estimate the incremental difference in total per-patient costs. Differences in the cost of the solution (heparinized and normal saline), use of ultrasound or other diagnostic imaging, and cost of treating complications (ie, occlusive events, thrombolytic agents, venous thrombosis, CABSI, heparin-induced thrombocytopenia) were included. All other healthcare costs associated with the patient episode were not included because they were not expected to differ between groups as a result of the intervention. Costs were estimated based on the number of episodes or events multiplied by the cost per episode and limited to where resource use differed between groups and complications, which were numerically different between groups. The number of heparin episodes was estimated based on management protocol. Most complication treatment costs were sourced from a previous cost analysis conducted at the same hospital.31 Partial occlusions were modeled on standard treatment practice at the site and informed by expert opinion and cost using local hospital pricing arrangements. As cost data are skewed, a general linear model was performed using a gamma family, log-link specification. Postregression estimation was used to test the difference in mean costs per person. All costs were presented in 2020 Australian dollars ($1 AUD = US$0.77).

Results

Participant and Device Characteristics

Of the 217 children assessed for eligibility, 61 were recruited and randomized to either the heparin (n = 31, 4036 CVAD days) or normal saline (n = 30, 3850 CVAD days) condition. Two children had late exclusions (postrandomization), due to clinical plans for future procedures meeting exclusion criteria; thus, 59 children were included in the final data analysis (Figure 1).

Feasibility

Despite not meeting prespecified cutoffs for eligibility (52%) and recruitment (54%) feasibility criteria, 95% of participants in the intervention groups achieved protocol fidelity. In addition, there were no attrition (high retention) or missing data. Parent/caregiver satisfaction was high (median, 10/10; interquartile range [IQR], 8–10), with 52 (88.1%) rating their satisfaction with their allocated treatment as 7 out of 10 (median, 10/10; IQR, 8–10). Similarly, 46 (78.0%) of healthcare practitioners rated their satisfaction with their patient’s treatment allocation.
as 7 out of 10 (median, 10/10; IQR, 8–10). Feasibility outcomes are summarized in Table 1.

Participant and Device Characteristics

Participant and device characteristics are summarized in Table 2. Most participant data were evenly distributed across intervention heparin and normal saline groups, including age, primary diagnosis, location at recruitment, and device type.

Occlusive Events

As reported in Table 3, complete CVAD occlusion occurred in heparin only (n = 2, 6.7%; IR, 0.49 [0.06–1.78]), whereas partial occlusion was detected in 7 CVADs in heparin (23.3%; IR, 2.73 [1.36–4.87]) and 4 CVADs in normal saline (13.8%; IR, 2.59 [1.24–4.77]; 10 events; Table 3). These results are consistent with the Kaplan-Meier curve, which displays the days to first complete occlusion and first partial occlusion (Figures 2A, B) for normal saline were predominantly higher over time (complete: log-rank test, P = .17; partial: log-rank test, P = .38).

Secondary Clinical Outcomes

Also reported in Table 3, overall, the number of thrombolytic agents administered was higher in heparin (n = 5, 16.7%) compared with normal saline (n = 1, 3.5%), with venous thrombosis confirmed in heparin only (n = 1, 3.3%). Central venous access device–associated bloodstream infection was detected in 1 CVAD across both heparin (3.3%; IR, 0.25 [0.01–1.38]) and normal saline (3.5%; IR, 0.26 [0.01–1.44]). Similarly, use of ultrasound or other diagnostic imaging was equal between both heparin (n = 2, 6.7%; IR, 0.74 [0.15–0.22]) and normal saline (n = 2, 6.7%; IR, 0.78 [0.16–0.23]). No CVAD fracture, heparin-induced thrombocytopenia, or medication errors were
Cost of heparin per person was $0.74 ($22.40/30) compared with $0.19 ($5.45/29) for normal saline. The total incremental cost difference between patients, including the cost of complications, who received heparin and those who received normal saline was substantial but not statistically significantly different ($258.17, P = .255; Table 4). Most of the incremental cost difference was driven by the cost of complications; however, owing to small numbers (eg, 1 thrombosis event reported in either group. Cost of heparin per person was $0.74 ($22.40/30) compared with $0.19 ($5.45/29) for normal saline. The total incremental cost difference between patients, including the cost of complications, who received heparin and those who received normal saline was substantial but not statistically significantly different ($258.17, P = .255; Table 4). Most of the incremental cost difference was driven by the cost of complications; however, owing to small numbers (eg, 1 thrombosis event

Table 2 • Participant and Device Characteristics (N = 59; 7886 CVAD Days)

| Characteristic          | Variable                                | Heparin (N = 30; 4036 CVAD Days) | Normal Saline (N = 29; 3850 CVAD Days) |
|-------------------------|-----------------------------------------|----------------------------------|----------------------------------------|
| Age, y                  | Median (IQR)                            | 7 (5-10)                         | 6 (4-9)                                |
| Gender (male)           |                                         | 21 (70.0)                        | 18 (62.1)                              |
| Primary diagnosis       | ALL                                      | 8 (26.7)                         | 9 (31.0)                               |
|                         | Lymphoma                                | 6 (20.0)                         | 3 (10.3)                               |
|                         | Bone tumors                             | 4 (13.3)                         | 5 (17.2)                               |
|                         | AML                                      | 5 (16.7)                         | 2 (6.9)                                |
|                         | Neuroblastoma                           | 2 (6.7)                          | 4 (13.8)                               |
|                         | Brain and CNS                           | 2 (6.7)                          | 2 (6.9)                                |
|                         | Rhabdomyosarcoma                        | 0 (0.0)                          | 2 (6.9)                                |
|                         | Other (eg, Wilms tumor, other sarcomas) | 3 (10.0)                         | 2 (6.9)                                |
| Location at recruitment | Outpatient                              | 17 (56.7)                        | 18 (62.1)                              |
|                         | Inpatient                               | 13 (43.3)                        | 11 (37.9)                              |
| Infection at recruitment|                                         | 0 (0.0)                          | 2 (6.9)                                |
| CVAD type               | Tunneled cuffed                         | 16 (53.3)                        | 16 (55.2)                              |
|                         | Totally implanted                       | 11 (36.7)                        | 11 (37.9)                              |
|                         | PICC                                     | 3 (10.0)                         | 2 (6.9)                                |
| CVAD lumens             | Single                                   | 11 (36.7)                        | 14 (48.3)                              |
|                         | Double                                   | 19 (63.3)                        | 15 (51.7)                              |
| CVAD tip position       | SVC/RA Junction                         | 10 (33.3)                        | 17 (58.6)                              |
|                         | SVC                                      | 8 (26.7)                         | 2 (6.9)                                |
|                         | RA                                       | 8 (26.7)                         | 4 (13.8)                               |
|                         | Unknown                                  | 4 (13.3)                         | 6 (20.7)                               |
| CVAD dwell before study participation, d | Median (IQR) | 45 (13–141)                    | 57 (17–07)                             |
| Viscous medication during study |                        | 22 (73.3)                        | 19 (65.5)                              |
| Reason for study end    | Death                                    | 0 (0.0)                          | 0 (0.0)                                |
|                         | CVAD removal                             | 5 (16.7)                         | 2 (6.9)                                |
|                         | End of study period                      | 23 (76.7)                        | 23 (79.3)                              |
|                         | Other (including hospital transfer)      | 2 (6.7)                          | 4 (13.8)                               |

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CNS, central nervous system; CVAD, central venous access device; IQR, interquartile range; PICC, peripherally inserted central catheter; RA, right atrium; SVC, superior vena cava.

Table 3 • Clinical Outcomes (per Device and per 1000 Catheter Days)

| Characteristic          | Variable                                | Heparin (N = 30; 4036 CVAD Days) | Normal Saline (N = 29; 3850 CVAD Days) |
|-------------------------|-----------------------------------------|----------------------------------|----------------------------------------|
| Occlusive events        | Complete occlusion                       | 2 (6.7% CVADs)                   | 0 (0.0)                                |
|                         | Partial occlusion                        | IR, 0.49 (0.06–1.78)             | IR, 0                                  |
|                         |                                          | 7 (23.3% CVADs)                  | 4 (13.8% CVADs)                        |
|                         |                                          | IR, 2.73 (1.36–4.87)             | IR, 2.59 (1.24–4.77)                   |
|                         | Thrombolytic agents                      | 5 (16.7% CVADs)                  | 1 (3.4% CVADs)                         |
|                         |                                          | IR, 1.49 (0.55–3.32)             | IR, 1.04 (0.28–2.66)                   |
| CVAD fracture           | 0                                       | 0                                | 0                                      |
| Venous thrombosis       | Suspected                                | 0                                | 0                                      |
|                         | Confirmed                                | 1 (3.3%)                         | 0                                      |
| Catheter associated bloodstream infection | 1 (3.3% CVADs) | IR, 0.25 (0.01–1.38)             | IR, 0.26 (0.01–1.44)                   |
| Heparin-induced thrombocytopenia | 0 (0.0%)                              | 0 (0.0%)                         | 0 (0.0%)                              |
| Medication error        | 0 (0.0%)                                | 0 (0.0%)                         | 0 (0.0%)                              |
| Ultrasound/diagnostic imaging | 2 (6.7% CVADs) | IR, 0.74 (0.15–0.22)             | IR, 0.78 (0.16–0.23)                   |

Abbreviations: CVAD(s), central venous access device(s); IR, incidence rate.
costing $7045), these were not statistically significantly different between the 2 groups.

**Discussion**

Central venous access devices are integral for quality cancer care provision but are associated with adverse events that have been linked with significant and potentially life-threatening complications in up to 46% of children with cancer. However, fundamental practices such as catheter lock solutions, which may reduce these events, remain understudied. Within this pilot trial, we have demonstrated the safety and potential feasibility of answering this common and important research question.

In Australia, treatment protocols require attendance at the specialist, tertiary center for acute components; however, a substantial proportion of follow-up care is provided in local regional centers. For pragmatic reasons, within this feasibility study, we were not able to include children managed by home care services, or returning to regional shared-care units, with 37 children ineligible for participation. Regional settings, and children based in regional settings, deserve to participate in research, and infrastructure needs to be developed to enable multisite studies in pediatric cancer care, including follow-up in regional settings. In particular, the benefit of a reliable lock solution for these families is evident. It would enhance their ability to receive as much treatment as possible close to home without compromising the CVAD, reducing travel and accommodation costs as well as interruptions to the family routines associated with traveling to the specialist center for maintenance CVAD care in between treatments. Regional centers and home care services are integral to patient outcomes in a shared-care model, and their contribution to CVAD maintenance and care should be represented in future research.

To date, emphasis has been placed on the clinical importance of the catheter lock solution to maintain catheter function; however, other nursing-led interventions such as catheter flushing (ie, manual injection of sodium chloride to rinse or clean the catheter) and the interval of changing lock solutions may be equally valuable and worthy of future study. In this study, despite anticoagulant properties, heparin was descriptively associated with a higher rate of complete and partial occlusion as well as venous thrombosis, resulting in substantively greater but not statistically significant costs. Although these results are not powered for clinical or statistical significance, the effectiveness of heparin over extended periods remains questionable. The process of in vivo catheter occlusion is complex and multifactorial, not simply based on blood clotting or deposit of blood proteins or cells.

**Table 4** Cost Comparisons Between Intervention Group

| Characteristic            | Variable         | Heparin (N = 30) | Normal Saline (N = 29) |
|---------------------------|------------------|-----------------|------------------------|
|                           | Episodes     | Cost per Episode (A$) | Total Cost (A$) | Episodes    | Cost per Episode (A$) | Total Cost (A$) |
| Solution used (heparin/saline) | 112 0.20 | 22.40 109 0.05 | 2.22 5.45  |
| Occlusive events          | Complete occlusion | 2 239.00 | 478.00 0 | 239.00 0.00 |
|                           | Partial occlusion | 11 32.10 | 353.10 10 | 32.10 321.00 |
| Thrombolytic agents       | 6 99.00 | 594.00 4 | 99.00 396.00 |
| Venous thrombosis         | Confirmed | 1 7045.00 | 7045.00 0 | 7045.00 0.00 |
| Total cost                | — | — 8492.50 | — 722.45 |
| Cost A$ per person, mean (SD) | 283.08 (1342.73) | 24.91 (98.51) |
| Difference between group means (95% confidence interval), P* | -258.17 (-703.09 to 186.74) | .255 |

Abbreviation: A$, Australian dollars.

Cost per episode was derived from previous work.

*Estimated using general linear model, gamma family log link.
be a result of the flush technique used to administer the intervention by nurses, rather than the catheter lock solution itself. For example, Guiffant et al. demonstrated in an in vitro study the superiority of a pulsatile flush (aka “push-pause”) to a laminar flush technique to remove thrombotic and other materials from catheter materials. Further clinical trials are needed to confirm the clinical impact of the variations in flush technique and subsequent catheter patency.

The goal of a catheter lock solution is to maintain a functional catheter by preventing infective, thrombotic, and occlusive complications. To date, the existing literature has been unable to determine the effects of intermittent flushing of heparin versus normal saline to prevent occlusion in long-term central venous catheters in infants and children. However, other therapeutic solutions are available. Antimicrobial catheter locks, including antibiotic locks, have been used as a catheter salvage technique to treat individual episodes of CABSI. However, in the interest of antibiotic stewardship, these are not practical as a prophylactic intervention. A multisite RCT demonstrated alternative anti-infective solutions such as ethanol locks to be ineffective as a treatment strategy (relative risk [RR], 1.0; 95% confidence interval [CI], 0.6–1.6; P = .98) and secondary prophylaxis of CABSI in high-risk populations (hazard ratio, 1.2; 95% CI, 0.5–2.6; P = .7) and to be associated with more catheter occlusion than normal saline (RR, 1.8 [95% CI, 1.1–2.9]). A systematic review of taurodilone (antimicrobial lock solution) use in pediatric patients demonstrated a significant reduction in CABSI (RR, 0.23; 95% CI, 0.13–0.40; P < .00001); however, the quality of evidence was low. In early observational studies, new catheter lock solutions with both antimicrobial and anticoagulating properties such as taurodilone citrate and 4% tetrasodium ethylenediaminetetraacetic acid show promise in reducing the risk of catheter occlusion and infection; however, adequately powered clinical trials evaluating the safety and efficacy of these strategies are necessary.

Although we used robust methods, our trial had some limitations. This was a feasibility study and therefore not powered to detect clinical outcomes. In addition, it was undertaken in a single, pediatric hospital in a specific subset of patients (excluding children receiving PEG-asparaginase) over a relatively short follow-up period (up to 6 weeks) because of funding limitations, thereby limiting external generalizability. There was some imbalance in diagnostic group, number with single lumens, and tip position that could potentially have influenced occlusion development, although this is to be expected in a pilot trial design. Clinicians, participants, family members, and research staff were not blinded to the intervention; however, it is unlikely this would have influenced clinical decision making. The data analyst was blinded for analysis, as was the infectious disease consultant (determining infectious outcomes) and radiology consultant (determining thrombotic outcomes). Despite these limitations, our study had important strengths. It was designed and reported in accordance with best practice standards, with a priori protocols including outcome criteria definition and statistical analysis approach.

### Conclusion

Current nursing practices to prevent CVAD occlusion and other complications vary widely, because of the limited quality evidence to guide clinicians in the best practices for preventing occlusions and other CVAD adverse events. We have demonstrated that we can (it is safe) and should (it is valuable) study catheter locks and other CVAD management practices in pediatric cancer care. In particular, future studies should extend the follow-up period and revise exclusion criteria to include children receiving PEG-asparaginase, and regional centers and home care services, where patients could most benefit from an efficient lock solution between cancer treatments across populations.

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