TITLE:

A pilot randomised controlled trial of novel dressing and securement techniques in 101 pediatric patients.

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Author's contributions

TK, AU, CMR were involved in study inception and protocol design. TK, AU, VG, BC and JS gathered the data, GM analyzed the data, TK, CMR, AU, GM vouches for the data and the analysis, and TK, AU and CMR coordinated manuscript preparation. TK, AU, VG, BC, JS GM and CMR had intellectual contribution to the paper and approved final version for submission.

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ABSTRACT

Purpose:

To evaluate the feasibility of an efficacy trial comparing peripherally inserted central catheter (PICC) dressing and securement to prevent complication and failure.

Materials and Methods:

This pilot, three armed, randomized controlled trial was undertaken at the Royal Children's Hospital and the Lady Cilento Children's Hospital, Brisbane between April 2014 and September 2015. Pediatric participants ($n=101$; 0-18 years) were assigned to standard care (bordered polyurethane dressing, sutureless securement device); tissue adhesive (plus bordered polyurethane dressing) or integrated securement dressings. Average PICC dwell was 8.1 days (0.2 – 27.7 days). Primary outcome was trial feasibility including PICC failure. Secondary outcomes were PICC complications, dressing performance, and parent / staff satisfaction.

Results:

Protocol feasibility was established. PICC failure was: standard care, 6% (2/32); integrated securement dressing, 6% (2/31); and tissue adhesive 3% (1/32). PICC complications were 16% across all groups. Tissue adhesive provided immediate postoperative hemostasis prolonging the first dressing change to 5.5 days compared to 3.5 and 2.5 days in standard care and integrated securement dressing respectively. Bleeding was the most common reason for first dressing change: standard care ($n=18$; 75%) and integrated securement dressing ($n=11$; 69%) compared to tissue adhesive, ($n=4$; 27%). Parental satisfaction (median 9.7 out of 10; $p=0.006$) and staff feedback (9.2; $p=0.002$) was most positive for integrated securement dressing.

Conclusion:

This research suggests the safety and acceptability of different securement dressings compared to standard care; it may also reduce post insertion dressing changes. Further research is required to confirm clinical cost effective methods to prevent PICC failure.

INTRODUCTION:

The use of peripherally inserted central catheters (PICCs) for pediatrics is increasing globally [1, 2]. Unfortunately 30% of PICCs fail prior to completion of treatment due to infective, vascular or mechanical (fracture, partial or total PICC dislodgement) issues [3]. A recent meta-analysis of international observational studies [4] demonstrated high rates of failure (12.4 per 1,000 catheter days), catheter associated bloodstream infection (BSI; 3.1 per 1,000 catheter days), thrombosis (0.2 per 1,000 catheter days) and occlusion (2.2 per 1,000 catheter days). Insertion of replacement devices is resource intensive, and significantly reduces vessel health and preservation [5].

The purpose of PICC dressing and securement is three-fold: (i) stability to prevent gross movement of the catheter and maintain central position, (ii) reduce micro-motion which may cause vascular injury, (iii) protect skin puncture site from microbial entry and subsequent infection. Traditionally PICC dressing and securement included sutures and a polyurethane dressing [6]. A landmark randomized control trial in 170 adults demonstrated the superiority of a sutureless securement device (SSD; StatLock™; Bard, Georgia) over sutures, to prevent catheter-associated BSI [7]. SSDs have adhesive-backed foam anchor pads with hinged clamps for PICC wings, and are used in addition to polyurethane dressings. While this research has never been replicated in the pediatric setting, SSDs are commonly used to secure pediatric PICCs [8].

Two new PICC securement technologies might be superior to current strategies. Firstly, integrated securement dressings (ISDs) combine dressing and securement in one product, providing a single product alternative. ISDs have a reinforced border with an absorbent

barrier around the clear transparent polyurethane section to encourage movement of moisture away from the insertion site. A reinforced fabric “collar” aims to reduce movement of the external catheter extension, thereby preserving dressing integrity. Manufacturers claim no additional securement (e.g. tape) is necessary. Tissue adhesive (TA) is a medical grade ‘superglue’ (cyanoacrylate), commonly used as an alternative to sutures for wound closure [9], and recently used to improve securement of peripheral intravenous catheters [10] and non-tunneled central venous access devices (CVADs) [11]. Simonova and colleagues additionally demonstrated TA’s tensile strength, and bacteriostatic properties to avoid dislodgement and penetration by gram positive micro-organisms *in vitro* [12]. Despite the promise of these new PICC securement technologies, their clinical efficacy, cost effectiveness and acceptability with patients and staff have not been tested in the pediatric population.

The aim of this study was to pilot test feasibility aspects including intervention acceptability, compliance and recruitment of novel dressing and securement products for inpatient pediatric PICCs, prior to a full-scale efficacy randomized controlled trial. The secondary aim was to compare the product’s effectiveness to prevent PICC complications and failure due to infection, occlusion, dislodgement, thrombosis or fracture.

MATERIALS AND METHODS:

Design

An external, pilot, parallel, three-arm, randomised controlled trial (RCT) of PICC dressing and securement for paediatric patients was undertaken. The study was registered with the Australian New Zealand Clinical Trials Registry (ACTRN 12614001327673), and a protocol published [13]. The Children’s Health Service District, Queensland (HREC/13/QRCH/181) and

Griffith University (NRS/10/14/HREC) Human Research Ethics Committees provided ethics and governance approval. Informed consent was obtained from parents or legal guardians, with children providing Youth Assent when developmentally appropriate.

Study setting

The study commenced in April 2014 at the Royal Children's Hospital, Brisbane, and due to local hospital mergers, completed at the Lady Cilento Children's Hospital, Brisbane, in September 2015. These are tertiary level, specialist paediatric teaching hospitals in Brisbane, Australia providing full-spectrum health services to children and young people from birth to 18 years of age.

Sample

The target sample size was 100 participants, allowing 30 per group, plus 10% for potential attrition, determined by standard pilot trial sample size recommendations [14]. Inclusion criteria were: PICC insertion, aged < 18 years, anticipated inpatient stay for greater than 24 hours, and written informed consent by legal parent or guardian. Patients were excluded if they had a current (< 48 hours) BSI, had a diseased, burned, scarred or extremely diaphoretic skin, skin tears surrounding the PICC insertion site, known allergy to the study products, or had previously been enrolled in the study within the current hospital admission.

Participant and PICC characteristics

As described in Table 1 and Online Table E2 (online supplement), the majority of participant, PICC and insertion characteristics were balanced across the intervention groups. The majority of participants had a medical diagnosis (n=81; 80%). The mean age was 7.5 years. There was

some imbalance evident (> 10% difference between groups, not statistically significant) in skin integrity and number of insertion attempts required.

Interventions

As displayed in Figure 1, participants were randomized to receive PICC dressing and securement by:

Group 1: Standard care: Bordered polyurethane (BPU) dressing (Tegaderm® 1614 or 1616 dependent upon participant size; 3M, St Paul) and a sutureless securement device (SSD) (Statlock® VPPCSP; Bard, Georgia);

Group 2: Integrated securement dressing (ISD): ISD (SorbaView SHIELD® SV353; Centurion Medical Products, Williamston); or,

Group 3: Tissue adhesive (TA): BPU dressing (Tegaderm® 1655 or 1616 dependent upon participant size; 3M) and TA (Histoacryl®; B. Braun, Germany)

Outcomes

The primary outcome was feasibility of a full efficacy trial, established by composite analysis of elements of eligibility, recruitment, attrition, protocol adherence, missing data, parent and healthcare staff satisfaction, and effect size estimates to allow sample size calculations [14, 15]. Parent (or caregiver) and healthcare staff levels of satisfaction and acceptability of the study products were assessed using 0-10 numeric rating scale at PICC insertion and removal [16]. The parent (or caregiver) and staff were asked to rate their experience on removal to ensure consistency. The effect size estimates were based upon the proportion of PICC failure (cessation of function prior to completion of therapy) and all-cause PICC complication. The published protocol by Ullman et al provides additional definition for the elements of PICC

complication[13]. Complications were: (i) catheter-associated BSI [17]; (ii) local site infection [18]; (iii) venous thrombosis[19]; (iv) dislodgement *partial* or *complete* [18]; (v) occlusion (vi) PICC breakage [20]. Secondary outcomes are also described in full in the published protocol [13] and included: (i) individual components of PICC complication (catheter-associated BSI, local site infection, venous thrombosis, dislodgement, occlusion, breakage) as defined previously; (ii) catheter-related BSI [17]; (iii) securement-dressing failure; (iv) PICC and first securement-dressing dwell period; (v) skin safety; and (vi) direct product costs.

Study procedures

The research nurse screened operating theatre lists for patients daily, obtained written informed consent, and initiated the randomization which was web-based to ensure allocation concealment until study entry. Patients were randomly assigned in a 1:1:1 ratio with computer-generated and randomly varied block sizes of three and six. The research nurse reviewed patients daily, collected data, and ensured safety of the study participants. Participants were included in the trial until four weeks after PICC insertion, or to study withdrawal, removal of the PICC, or hospital discharge.

Data entry was undertaken by research nurses into REDCap (Research Electronic Data CAPture <http://project-redcap.org/>). Demographic and clinical data were collected to assess success of randomization, describe the participant group, and to display characteristics known to increase the risk of PICC complication and dressing integrity (e.g. comorbidities, utility, skin insertion site and technique). The Research nurses collected data on primary and secondary outcomes using the pre-defined criteria.

PICC procedures

Research nurses provided extensive pre-study education involving all clinicians involved with insertion and care of PICCs, including the study products. All PICCs (Cook[®]; Cook Medical, Bloomington; Arrow[®]; Teleflex, Morrisville; Bioflo[®]; Angiodynamics, Queensbury) were polyurethane, power injectable and inserted in an operating theatre or angiography suite.

Ultrasound was used to puncture the vessel and fluoroscopy used to confirm PICC tip placement. PICCs were inserted by a qualified consultant pediatric anesthetist, a senior anesthetic registrar or fellow in an approved anesthetic training program, or pediatric vascular access nurse practitioner, and managed by clinical staff in accordance with state and hospital policy [21]. The operator chose the PICC characteristics based on clinical judgment of patient needs, and then applied the allocated products. Local hospital policy was 2% chlorhexidine gluconate in 70% alcohol for site decontamination on insertion and subsequent dressing change unless the patient had a proven allergy. To maximize generalizability, clinical nursing staff (not research nurses) performed PICC management procedures as per hospital policy including; changing study products weekly, or as clinically indicated (e.g. interruption of dressing integrity) [21]. .

Statistical analyses

Data were exported to Stata 14.1 for management and analysis. Data cleaning of outlying figures, missing, and implausible data was undertaken prior to analysis. Missing data were not imputed. All randomized patients were analyzed on an intention-to-treat basis [22], with PICCs the unit of measurement.

Descriptive statistics (frequencies, percentages) were used to ascertain the primary outcome of feasibility for the larger trial. Comparability of groups at baseline was described across demographic, clinical and device characteristics. Incidence rates (IR) of PICC failure and complication (per 1,000 catheter days) were used to summarize the impact of the interventions; with differences evaluated by calculating 95% confidence intervals (CIs). Kaplan-Meier survival curves and log rank test were used to compare PICC failure between groups, and first dressing duration over time. Univariable Cox regressions were performed with baseline covariates at $n > 10$. Multivariable analysis was not done due to failure $n < 10$. P values of < 0.05 were considered statistically significant. Costs were calculated in 2016 Australian Dollars.

RESULTS

Feasibility outcomes

One hundred and one patients were recruited. As displayed in Figure 2, the majority of feasibility criteria were met with 74% of patients screened eligible and 91% of patients approached for consent agreed to enrol. There were no participants lost to follow up, and six patients (6%) ($n=1$, standard care; $n=3$, ISD; $n=1$, TA) did not have a PICC inserted, as the device was no longer required or insufficient theatre space prompted alternative therapy. Participant demographic data only were collected on these six patients. One patient ($< 1\%$) withdrew from the study due to skin irritation (itchiness, redness) associated with the study product (ISD); treatment continued with the PICC dressed with standard care. With parental consent, the withdrawn participant was included in the analysis due to their prolonged participation leading to the point of withdrawal. Two episodes of non-randomised SSD were incorrectly added to patients in the ISD group during the study (not at baseline). The

appropriate dressing was reapplied the next day; therefore only 2/236 (< 1%) of total studied catheter study days were affected. Multiple additional reinforcement products such as non-sterile tape (standard care $n=8$; ISD $n=2$; TA $n=7$) were applied when the edges of primary dressings were noted to lift, and tubular elastic bandage (standard care $n=29$; ISD $n=26$; TA $n=31$) were applied to the majority of patients in all study groups. No daily checks, primary or secondary outcome data were missed during the study period.

PICC failure and complications

Five percent of participants ($n=5$) experienced PICC failure (Table 2) prior to completion of treatment. PICC failure occurred in two patients (6%) in both the standard care and the ISD arms (IR 7.7 per 1,000 catheter days; 95% CI 1.9-30.9 and IR 8.5 per 1,000 catheter days; 95% CI 2.1-33.9 respectively), and one patient (3%) in TA (IR 3.4 per 1,000 catheter days; 95% CI 0.5-25.5). These results are consistent with the Kaplan-Meier curve, which displays the PICC survival of the TA group consistently higher over time (log rank $p=0.799$) (Figure 3).

Overall PICC breakage and complete dislodgement were the most common forms of PICC failure. The ISD group was the only intervention that did not have catheter failure due to complete dislodgement. There was little difference between the groups in the at-risk period of catheter failure. The median time to failure in standard care, ISD and TA was 8.0 days (inter-quartile range 4.4-11.9), 7.0 (5.0-11.8) and 7.1 (5.0 – 11.5) respectively. The Cox regression of PICC failure (Table 3) shows older age was associated with a reduced risk of failure (Hazard Ratio = 0.62; 95% CI 0.41-0.92), and when multiple attempts were required to achieve successful PICC insertion the risk of failure increased seven-fold (7.18; CI 1.19-43.3).

Complications of PICC during the study period were equally spread with five participants (16%) in each arm experiencing a complication. There were no documented episodes of catheter-associated blood stream infection. Skin complications were highest in the TA group (10/32; 31%) the majority of these were minor skin tears and resolved with no treatment other than angling the dressing away from the injury. ISD experienced the lowest number of skin complications (3/31; 10%), whilst the standard care group experienced five (16%) complications including one blister.

Staff and parental feedback

Described in Table 2, parental satisfaction with dressing and securement product was significantly higher with ISD (median 9.7 out of 10; $p=0.006$). Ease of first dressing application was equivalent across all groups; however, ease of product removal was also statistically higher in the ISD group (9.2; $p=0.002$).

Dressing and securement outcomes

As described in Table 4 mean time to first dressing change was longest for TA (5.5 days, IQR 3.5-6.5). These findings are consistent with the Kaplan Meier curve of first securement life, reflecting prolonged time to first dressing change for TA participants when compared to standard care or ISD ($p=0.087$) (Figure 4). Early first dressing change in standard care and ISD was most commonly related to bleeding at insertion site (18/32; 75% and 11/31; 69% respectively). Non-routine dressing changes per patient were also lowest in TA (0; IQR 0.0-0.5) compared to a median of 1.0 in both the standard care (IQR 0.0-2.0) and ISD (IQR 0.0-1.0) ($p=0.019$). Non-routine dressing changes in standard care arm and ISD were again related to bleeding at the insertion site. Lifting at dressing edges was another common

reason for non-routine dressing change, which occurred most frequently in the standard care arm 9/32 (36%) and least frequently in the ISD arm 2/31 (10%). Non-sterile tape to reinforce the edges of the bordered polyurethane dressing in both the standard care (8/32; 18%) and TA (7/32; 32%) arms was increased compared to ISD where additional tape was only required twice.

Direct product costs

When considering the first dressing application only, each of the experimental arms are more expensive than standard care as an SSD (Stat Lock®) is provided in most PICC insertion kits. Subsequent PICC dressing changes when considering product purchase costs alone in Australian dollars were cheapest in the ISD group (SorbaView SHIELD® SV353) (\$4.75) compared to \$6.62 for standard care and \$17.57 – \$18.47 in TA. The variability in price range is due to the use of a small or large BPU (Bordered polyurethane (BPU) dressing (Tegaderm® 1614 or 1616 dependent upon participant size). A small BPU was generally sufficient in the TA group (Histoacryl® due to the smaller surface area that required coverage, as opposed to the standard care group that generally required a large BPU to cover the SSD.

DISCUSSION

Although PICC failure (5%) and complications (16%) in this trial remain unacceptably high, alternative dressing and securement methods have not been recently examined [23]. The trial investigated innovative securement strategies not previously tested in pediatric PICCs. This pilot trial confirmed the feasibility of a large efficacy trial, using pre-determined feasibility criteria, a registered and published trial protocol [13], and rigorous methodology. As a pilot trial, the study design could not statistically test products for superiority. However,

dislodgement and fracture were the main causes of catheter failure, and partial dislodgement was the most common complication, in all groups.

Skin complications occurred in all groups, however were lowest in the ISD group (3/31; 10%) compared to (5/32; 16%) for standard care and (10/32; 31%) for TA. The majority of TA complications were minor skin tears, which resolved without treatment. Although TA was removed easily from patients' skin, repeated use at each dressing replacement led to build up on the PICC body which was difficult to remove. Use of TA at insertion only, specifically two drops at the PICC insertion site is sufficient. The average increase of two days until first dressing change in the TA group supports its use as an adjunct to other dressings, including ISD, and securement technologies to provide immediate hemostasis [24], reduce post-operative bleeding, and the need for early dressing change. A delayed first dressing change reduces the risk of accidental dislodgement and/or infection in the often distressed and un-co-operative pediatric patient[25].

Skin complications including itchiness, rash and blister were common across all groups with one participant withdrawing due to skin irritation. Altered skin integrity at pediatric PICC sites is common, potentiated by the patient's age, morbidity and additional irritation of the PICC site during dressing changes [26, 27]. Removal of adhesives can be traumatic and anxiety provoking. Identifying patients at risk for skin complication and initiating preventative strategies are vital. All products tested appear safe, and well tolerated by patients with high levels of staff and parental satisfaction with their overall performance.

PICC failure was associated with younger age and multiple insertion attempts. A recent meta-analysis of observational studies [4] also found PICC failure associated with younger age, especially in neonates. Multiple insertion attempts have not previously been cited as a predictor of PICC failure. Investment in research, education and training to improve PICC insertion technique and maintenance procedures are necessary to reduce failure, especially in these high risk populations.

Although innovative PICC securement products have higher purchase price than traditional approaches, the potential to avoid even one dressing replacement can provide overall cost-benefit. Additionally, if these strategies reduce PICC failure and complications, large savings in healthcare funds would result. The sequelae of failed PICCs include treatment delays whilst awaiting replacement PICCs, increased hospital length of stay, and threat to vessel health and preservation with additional unplanned access. Additional upfront investment in superior dressing and securement products to reduce the risk of complication and failure seems sensible, and a larger study is urgently needed to inform cost-effectiveness.

Although the pilot data provided valuable information there are limitations. Not all dressing and securement products available were evaluated in this trial. The study was carried out in inpatient wards of large tertiary pediatric hospitals in Brisbane, however pediatric intensive care unit and outpatient or home care settings were not included, limiting generalizability to these populations. Patients with pre-existing skin conditions were excluded from the study also limiting the generalizability. Participants, family members and the research staff were not blinded to the intervention; however, it is unlikely that they would cause PICC failure due to preference for study product over another. A blinded infectious diseases physician

determined outcomes of PICC associated bloodstream infection and blinded radiological personnel assessed venous thrombosis, thus ensuring validity. Study rigor was further ensured through prospective protocol registration, independent randomization, allocation concealment until study entry and dedicated research nurses.

Conclusion

These results suggest trials of innovative PICC securement are feasible; are as safe, and might be more effective than standard care; are acceptable to healthcare staff and parents, and may reduce the need for post insertion dressing change. Further research is required to definitively identify clinical, cost-effective methods to prevent PICC failure and improve reliability.

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Figure 1: PICC securement methods

^aStandard care; ^bIntegrated Securement-Dressing; ^cTissue adhesive

Figure 2: CONSORT flowchart

Table 1: Participant characteristics at baseline (n=101)

	Control	ISD	TA	Total
Group size	34 (34%)	34 (34%)	33 (33%)	101 (100%)
Age (years) ^a	6.9 (4.5; 0-16)	7.7 (4.6; 1-16)	7.8 (5.5; 0-18)	7.5 (4.8; 0-18)
Sex (male)	13 (38%)	18 (53%)	21 (64%)	52 (51%)
Skin integrity:				
- good	21 (62%)	18 (53%)	13 (39%)	52 (51%)
- fair	12 (35%)	14 (41%)	15 (45%)	41 (41%)
- poor	1 (3%)	2 (6%)	5 (15%)	8 (8%)
Skin type (white)	25 (74%)	29 (85%)	25 (76%)	79 (78%)
Comorbidities:				
- none	4 (12%)	3 (9%)	3 (9%)	10 (10%)
- one	24 (71%)	26 (76%)	23 (70%)	73 (72%)
- two or more	6 (18%)	5 (15%)	7 (21%)	18 (18%)
Diagnosis:				
- medical	28 (82%)	27 (79%)	26 (79%)	81 (80%)
- surgical	1 (3%)	3 (9%)	4 (12%)	8 (8%)
- oncology	5 (15%)	4 (12%)	3 (9%)	12 (12%)
Infection	16 (47%)	9 (26%)	14 (42%)	39 (39%)
Leucocytes low ^b (n=85)	3 (11%)	3 (10%)	4 (14%)	10 (12%)

n(%) shown unless otherwise indicated; ISD = integrated securement dressing; TA = tissue adhesive; ^a mean, standard deviation, minimum and maximum; ^b low = below 1,000 per microlitre;

Table 2: Study outcomes (n=95, analysed)

	Control	ISD	TA	p
Group size	32 (34%)	31 (33%)	32 (34%)	-
Failure:				
- number	2 (6%)	2 (6%)	1 (3%)	0.868 ^a
- modes (complications)	dislodgement (c); breakage	dislodgement (p); breakage	dislodgement (c)	-
At-risk period:				
- dwell time (days) ^b	8.0 (4.4-11.9)	7.0 (5.0-11.8)	7.1 (5.0-11.5)	-
- cath-days	259	236	279	-
IR (1,000 cath-days, 95% CI)	7.72 (1.93-30.9)	8.48 (2.12-33.9)	3.59 (0.51-25.5)	-
IRR (1,000 cath-days, 95% CI)	referent	1.10 (0.08-15.2)	0.46 (0.01-8.93)	-
Hazard Ratio (crude, 95% CI)	referent	1.06 (0.15-7.56)	0.50 (0.05-5.48)	0.799 ^c
PICC complications ^d :				
- all-cause per participant	5 (16%)	5 (16%)	5 (16%)	1.000 ^a
- dislodgement (p)	2 (6%)	3 (10%)	3 (9%)	-
- occlusion	2 (6%)	1 (3%)	1 (3%)	-
- breakage	1 (3%)	1 (3%)	0 (0%)	-
- dislodgement (c)	1 (3%)	0 (0%)	1 (3%)	-
- thrombosis	0 (0%)	1 (3%)	0 (0%)	-
Skin complications ^d :				
- all-cause per participant	5 (16%)	3 (10%)	10 (31%)	0.108 ^a
- itchiness	2 (6%)	3 (10%)	2 (6%)	-
- rash	3 (9%)	2 (6%)	2 (6%)	-
- skin tear	0 (0%)	0 (0%)	7 (22%)	-
- blister	1 (3%)	2 (6%)	1 (3%)	-
- bruising	0 (0%)	0 (0%)	1 (3%)	-
Ease of appl. (first devices) ^{b,e}	9.55 (2.15)	9.70 (1.60)	9.70 (1.25)	0.407 ^f
Difficulty of removal ^{b,e}	7.35 (6.55)	9.20 (2.10)	6.05 (7.30)	0.002 ^f
Parental satisfaction ^{b,e}	7.60 (3.80)	9.70 (2.00)	8.55 (3.05)	0.006 ^f

ISD = integrated securement dressing; TA = tissue adhesive; p = p-value; PICC = peripherally inserted central catheter; n(%) shown unless otherwise indicated; ^a Fisher's exact; ^b median and 25th/75th percentiles shown; ^c log-rank test; ^d at any time during study, could have multiple complications per patient, were not necessarily associated with Failure; ^e 0 = very difficult/unsatisfied, 10 = very easy/satisfied; ^f median test; CVAD = central vascular access device; BSI = bloodstream infection; IR = incidence rate; IRR = incidence rate ratio; cath = catheter; cath-days = catheter-days; CI = confidence interval; (c) = complete; (p) = partial; appl = application;

Table 3: Cox regression of PICC failure

	HR (95% CI)	p
Study group (referent: standard care):		
- ISD	1.08 (0.15-7.67)	
- TA	0.49 (0.04-5.41)	
Age (one year increase)	0.62 (0.41-0.92)*	0.019
Sex (male)	1.82 (0.30-11.0)	
Skin integrity (fair or poor)	1.48 (0.25-8.88)	
Skin type (brown)	cannot be calculated	
Comorbidities (two or more)	1.12 (0.12-10.0)	
Diagnosis (surgical or oncology)	3.16 (0.51-19.5)	
Infection at recruitment	1.09 (0.18-6.51)	
Leucocytes <1,000 μ L	3.56 (0.35-36.4)	
PICC placement (brachial/cephalic/other)	0.52 (0.06-4.66)	
Insertion number (subsequent)	0.20 (0.02-1.76)	
Inserted by (nurse)	0.54 (0.06-4.84)	
Multiple insertion attempts	7.18 (1.19-43.3)*	0.032
Ease of application (one better, by clinician)	1.35 (0.54-3.35)	
Received IV therapy during study	0.71 (0.08-6.33)	

*HR = hazard ratio; CI = confidence interval; ISD = integrated securement device; TA = tissue adhesive; PICC = peripherally inserted central catheter; IV = intravenous; * statistically significant at $p < 0.05$;*

Table 4: Securement device outcomes (n=95, analysed)

	Control	ISD	TA
Group size	32 (34%)	31 (33%)	32 (34%)
Securement device usage (n=88):			
- total number	61 (38%)	52 (32%)	56 (33%)
- per pt ^a	2.0 (2.0-2.0)	2.0 (1.0-2.0)	1.5 (1.0-2.0)
Days to first change ^a (n=58)	3.5 (1.5-6.5)	2.5 (1.5-6.5)	5.5 (3.5-6.5)*
Reasons for first change (n=55):			
- bleeding	18 (75%)	11 (69%)	4 (27%)
- routine	6 (25%)	5 (31%)	8 (53%)
- lifting	7 (29%)	0 (0%)	3 (20%)
- leakage	1 (4%)	1 (6%)	0 (0%)
- other	1 (4%)	0 (0%)	2 (13%)
No. of non-routine changes per pt ^a	1.0 (0.0-2.0)	1.0 (0.0-1.0)	0.0 (0.0-0.5)
Reasons for non-routine changes (n=61):			
- bleeding	19 (76%)	14 (67%)	5 (31%)
- lifting	9 (36%)	2 (10%)	3 (19%)
- leakage	1 (4%)	1 (5%)	0 (0%)
- other	1 (4%)	3 (14%)	3 (19%)
Additional securing devices ^b (n=94):			
- bandage or tubi grip	29 (67%)	26 (61%)	31 (57%)
- strips of non-sterile tape	8 (18%)	2 (20%)	7 (32%)
- foam	2 (84%)	1 (8%)	4 (40%)
- non-randomised SSD	0	2 (34%)	2 (56%)
- randomised study product	0	0	4 (27%)
- non-sterile gauze	2 (29%)	1 (8%)	0
- non-randomised BPU	0	2 (22%)	1 (8%)
- sterile gauze	0	0	2 (32%)
- sterile tape securing the hub	0	1 (22%)	1 (25%)
- other	2 (36%)	1 (21%)	2 (48%)

* $p < 0.10$ using Wilcoxon rank-sum test; pt = participant; ISD = integrated securement dressing; TA = tissue adhesive; ^a median and 25th/75th percentiles; ^b number of participants with additional securing device and approximate mean duration (as % of dwell time) shown; No. = number; SSD = sutureless securing device; BPU = bordered polyurethane dressing;

Table E1 (Online content): PICC characteristics (n=95 analysed)

	Control	ISD	TA	Total
Group size	32 (34%)	31 (33%)	32 (34%)	95 (100%)
Placement:				
- basilic	22 (69%)	24 (77%)	19 (59%)	65 (68%)
- brachial	5 (16%)	3 (10%)	6 (19%)	14 (15%)
- cephalic	5 (16%)	3 (10%)	5 (16%)	13 (14%)
- other	0 (0%)	1 (3%)	2 (6%)	3 (3%)
Subsequent insertion	17 (53%)	14 (45%)	17 (53%)	48 (51%)
Inserted by:				
- anaesthetist doctor	24 (75%)	21 (68%)	24 (75%)	69 (73%)
- nurse	8 (25%)	10 (32%)	8 (25%)	26 (27%)
Multiple insertion attempts	6 (19%)	6 (19%)	10 (31%)	22 (23%)
Ultrasound guidance used	31 (97%)	29 (94%)	28 (88%)	88 (93%)
Skin cond./hair not removed	0 (0%)	0 (0%)	1 (3%)	1 (1%)
Device size (gauge):				
- 2	0 (0%)	0 (0%)	1 (3%)	1 (1%)
- 3	23 (72%)	16 (52%)	20 (62%)	59 (62%)
- 4	9 (28%)	15 (48%)	10 (31%)	34 (36%)
- 5	0 (0%)	0 (0%)	1 (3%)	1 (1%)
Number of lumens:				
- 1	31 (97%)	30 (97%)	32 (100%)	93 (98%)
- 2	1 (3%)	1 (3%)	0 (0%)	2 (2%)
Treatment characteristics ^a :				
- continuous intravenous	7 (22%)	9 (29%)	6 (19%)	22 (23%)
- PN and/or lipids	0 (0%)	1 (3%)	4 (12%)	5 (5%)
- chemotherapy	4 (12%)	3 (10%)	1 (3%)	8 (8%)
- blood products	4 (12%)	1 (3%)	4 (12%)	9 (9%)
- antibiotics	30 (94%)	28 (90%)	29 (91%)	87 (92%)
Pt confused, agitated or drowsy ^b	3 (9%)	0 (0%)	1 (3%)	4 (4%)

frequencies and column percentages shown; PICC = peripherally inserted central catheter; ISD = integrated securement dressing; TA = tissue adhesive; cond. = condition; ^a during study period; ^b at study completion; PN = parenteral nutrition; pt = participant;