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PILOT STUDY

# Controlling peripheral intravenous catheter failure by needleless connector design: A pilot randomised controlled trial

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## Abstract

**Aim:** To test the feasibility of a study protocol that compared the efficacy of neutral- and negative-pressure needleless connectors (NCs).

**Design:** A single-centre, parallel-group, pilot randomised control trial.

**Methods:** Our study compared neutral-(intervention) and negative-pressure (control) NCs among adult patients in an Australian hospital. The primary feasibility outcome was measured against predetermined criteria (e.g. eligibility, attrition). The primary efficacy outcome was all-cause peripheral intravenous catheter failure, analysed as time-to-event data.

**Results:** In total, 201 (100 control; 101 intervention) participants were enrolled between March 2020 and September 2020. All feasibility criteria were met except eligibility, which was lower (78%) than the 90% criterion. All-cause peripheral intravenous catheter failure was significantly higher in the intervention group (39%) compared to control (19%).

**Conclusion:** With minor modifications to participant screening for eligibility, this randomised control trial is feasible for a large multicentre randomised control trial. The neutral NC was associated with an increased risk of peripheral intravenous catheter failure.

**Implications for the Profession and/or Patient Care:** There are several NC designs available, often identified by their mechanism of pressure (positive, negative and neutral). However, NCs can contribute to peripheral intravenous catheter failure. This is the first randomised controlled trial to compare neutral and negative NC designs.

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Negative pressure NCs had lower PIVC failure compared to neutral NCs, however the results might not be generalisable to other brands or treatment settings. Further high-quality research is needed to explore NC design.

**Reporting Method:** Study methods and results reported in adherence to the CONSORT Statement.

**Patient or Public Contribution:** No patient or public contribution.

**KEYWORDS**
adult nursing, clinical trial, clinical, evidence-based nursing, health services research, nursing practice, nursing research, randomised controlled trials

## 1 | INTRODUCTION

Peripheral intravenous catheters (PIVCs) are the most frequently used vascular access device for intravenous treatment in hospitalised patients (Webster et al., 2019). A needleless connector (NC) allows a PIVC to directly connect to an administration set or syringe without the use of needles. First introduced in the 1990s, NCs have successfully reduced the incidence of needlestick injuries among healthcare workers (Flynn et al., 2018), and are associated with reduced incidence of catheter-related bloodstream infections (CRBSIs) and phlebitis (irritation to the vein wall) compared with alternative stopcock products (Ronen et al., 2017). NCs are recommended by the Centers for Disease Control and Prevention (CDC) and the Infusion Nurses Society (Gorski et al., 2021; O'Grady et al., 2011). With the majority of vascular access devices requiring a NC, there are billions purchased each year (Rickard et al., 2017; Slater et al., 2017; Tuffaha et al., 2018).

Despite the use of NCs, PIVC failure before treatment completion remains unacceptably high, with reported replacement PIVC insertions required for up to 69% of patients (Marsh et al., 2018b; Marsh et al., 2018c; Ozger et al., 2021; Rickard et al., 2018). This causes discomfort to the patient and increased cost (both in products and in staff time) to organisations (Cooke et al., 2018; Helm et al., 2015). There are several reasons for catheter failure; in part, it could be due to the type of NC in use. Currently there are a plethora of NCs, manufactured from various materials and with different structural designs (Gorzek & LaDisa Jr., 2021). Recent novel NCs have features thought to improve patient safety and decrease the risk of CRBSI. These features include a flat surface for easy decontamination; a clear design to allow visualisation of a PIVC flush; and an open fluid pathway to increase intravenous fluid/flush flow rate (Rosenthal, 2020). NCs' internal structural design can also offer different fluid displacement properties. This determines the direction of fluid movement on connection and disconnection of syringes/infusions to an NC (Rosenthal, 2020). Negative pressure NCs, on the completion of access or flushing, create a negative displacement. This allows a small amount of blood to move back into the catheter (reflux) (Curran, 2016), *theoretically* increasing the risk of complications such as occlusion or infection. More recently, manufacturers have created NCs comprising mechanical valves with neutral pressure thought to limit blood reflux into the PIVC upon accessing the NC (Rosenthal, 2020). Recent randomised controlled trials (RCTs) have compared NC design and displacement properties for central venous and arterial catheters with a focus on infection outcomes (Delgado et al., 2020; Koeppen et al., 2019). However, different types of NCs are yet to be compared for patients with PIVCs. This RCT tested the feasibility of the study protocol and efficacy of a neutral pressure NC.

**What does this paper contribute to the wider global clinical community?**

- This pilot trial established the feasibility of a large multicentre randomised controlled trial.
- The findings provide evidence that different NC designs can influence PIVC failure, and information to support clinical decision making about NC choice.

## 2 | METHODS

### 2.1 | Trial design, participants and setting

A single centre, parallel group, pilot randomised controlled trial comparing neutral and negative displacement NCs reported using the CONSORT Statement (Data S1). Patients from general medical and surgical wards at a large teaching hospital (>900 beds) were screened by Research Nurses (ReNs) between March and September 2020. Patients were eligible to participate if they required a PIVC for more than 24 h, were 18 years or older, and able to provide informed written consent. Patients were excluded if they were a non-English speaker without an interpreter, had a current bloodstream infection, were on a palliative care pathway, receiving critical care treatment or were previously enrolled on the study.

### 2.2 | Interventions

Patients were randomised to receive either the intervention (neutral displacement NC–*MicroClave*® Clear, ICU Medical) or the control (negative displacement NC–*SmartSite*™ BD) treatment (Figure 1).

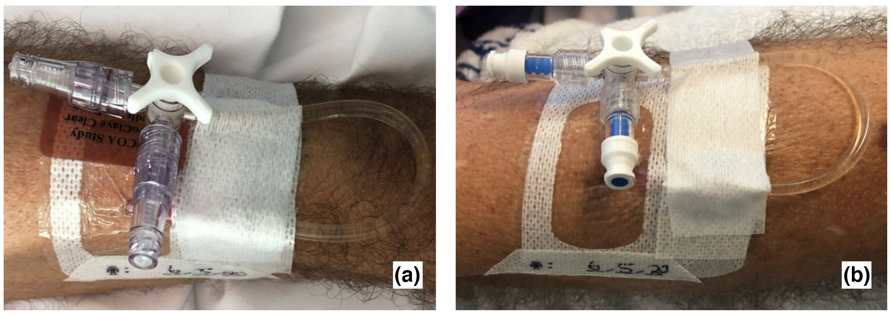


FIGURE 1 Needless connectors, (A) neutral displacement needleless connector; (B) negative displacement needleless connector. [Colour figure can be viewed at wileyonlinelibrary.com]

## 2.3 | Ethics statement

Human Research Ethics Committee approval was obtained from the Royal Brisbane and Women's Hospital (HREC/2018/QRBW/48811) and Griffith University (Ref. 2019/573). Trial methods were prospectively registered on 8 August 2019 with the Australian New Zealand Clinical Trials Registry (ACTRN12619001091190).

## 2.4 | Primary outcomes

The primary outcomes were feasibility and efficacy. The feasibility of conducting an adequately powered RCT was measured against predetermined criteria, based on locally conducted vascular access pilot RCTs (Marsh et al., 2018b; Marsh, Larsen, Genzel, et al., 2018). Feasibility was defined as eligibility (≥90% of screened patients eligible), recruitment (≥90% of eligible patients consent to trial participation), retention and attrition (≤5% of participants lost to follow up, including those who withdrew consent), protocol adherence (≥90% of randomised participants receive their randomised intervention), missing data (≤5% data missing) and patient satisfaction (scored 0 = dissatisfied to 10 = completely satisfied).

All-cause PIVC failure (a measure of efficacy) was defined as premature device removal before the end of therapy due to phlebitis, infiltration/extravasation, occlusion (with or without leakage), local or CRBSI (Centers for Disease Control and Prevention National Healthcare Safety Network, 2020).

## 2.5 | Secondary outcomes

Secondary outcomes included *individual PIVC failure types*: phlebitis (pain or tenderness ≥2 on a 11-point scale, or two or more signs/symptoms of pain, tenderness, erythema, swelling, palpable cord or purulent discharge) (Marsh et al., 2021; Rickard et al., 2023), infiltration (the movement of IV fluids into the surrounding tissue) with or without extravasation (i.e. infiltration resulting in damage to surrounding tissue) (Marsh et al., 2020), occlusion (the PIVC will not flush or leaks when flushed), dislodgement/accidental removal, local infection (defined as any positive skin swab growth, with insertion site swabs taken only as per treating team's decision) (Centers for Disease Control and Prevention National Healthcare Safety Network, 2020), and CRBSI (blood/tip cultures taken only as per treating team's decision) (Centers for Disease Control and Prevention National Healthcare Safety Network, 2020). Additional secondary outcomes included PIVC dwell time (from the time of PIVC insertion until removal due to either device failure, routine replacement or the completion of IV therapy) and cost analysis (staff resources, equipment and PIVC failure resource usage with previously developed cost estimations (Tuffaha et al., 2014).

## 2.6 | Sample size

For this pilot study, the recruitment target was 100 participants per group (total 200). The study was not powered to find statistical significance, but rather to assess the feasibility of the protocol for a larger definitive study. The sample size is adequate in the literature for the purpose of feasibility assessment (Whitehead et al., 2016).

## 2.7 | Randomisation, sequence allocation, concealment and blinding

A ReN screened the wards daily to identify patients who met the inclusion and did not meet the exclusion criteria. Eligible, consenting patients were randomised (1:1 ratio) using a web-based randomisation service (randomisation.griffith.edu.au) with varying block sizes of two and four. Due to the nature of the intervention, it was not possible to blind clinical staff or ReNs to study allocation. However, the Infectious Diseases expert assessing the secondary outcome of CRBSI and the data analyst were blinded to group allocation.

## 2.8 | Device insertion and maintenance

PIVCs were inserted by clinical staff (nurses and doctors) or ReNs who had achieved PIVC insertion accreditation as per local hospital policy. All PIVCs were Insyte™ Autoguard™ Blood Control (non-winged) catheters (BD) with a 10 cm extension tubing and bonded three-way connector (Connecta™, Becton Dickinson). Skin preparation was with 3 M SoluPrep™ and NC decontamination was performed with Alcohol Prep Pads (Reynard). NCs were not routinely replaced during therapy.

## 2.9 | Data collection

Data were collected directly into an electronic data platform supported by REDCap™ (Research Electronic Data Capture, Software

Version 6.10.6 © 2016 Vanderbilt University) hosted on a Griffith University server (Harris et al., 2009). All data were entered using a unique participant identifier number only re-identifiable through a separate screening log, which was kept in a secure location on-site.

At the time of recruitment, the ReN collected the patient's baseline demographic data (e.g. age, gender, diagnosis) and PIVC characteristics (e.g. gauge, insertion site, vein quality (Hallam et al., 2016)). All study participants were visited daily to assess the insertion site for patient-reported pain/tenderness, redness, swelling, palpable cord, leakage and purulence. When the PIVC was removed, the ReN recorded the time and reason for removal.

## 2.10 | Statistical analysis

Feasibility outcomes are reported descriptively and were analysed against predetermined acceptability criteria. An intention-to-treat analysis framework was used, with the unit of analysis taken as one PIVC per patient. Data cleaning was performed but missing data were not imputed. PIVC failure was compared between study groups with chi-square and log-rank tests, and by calculating the incidence rate and hazard ratios. Kaplan–Meier survival curves were generated. Co-variables to be tested in Cox regression analyses were pre-selected based on prior knowledge of risk factors and were eligible for inclusion in the multivariable model at a univariable $p < 0.20$. Correlations between co-variables was considered before model building. The final multivariable model was derived by stepwise manual removal of variables at $p \geq 0.05$. The removed variables were retested one-by-one in the final model to confirm their exclusion. The proportional hazards assumption was tested for each variable and for the final model. Statistical significance was declared at two-sided $p < 0.05$. Stata 16 (StataCorp. 2019. College Station, TX: StataCorp LLC.) was used for data management and analysis.

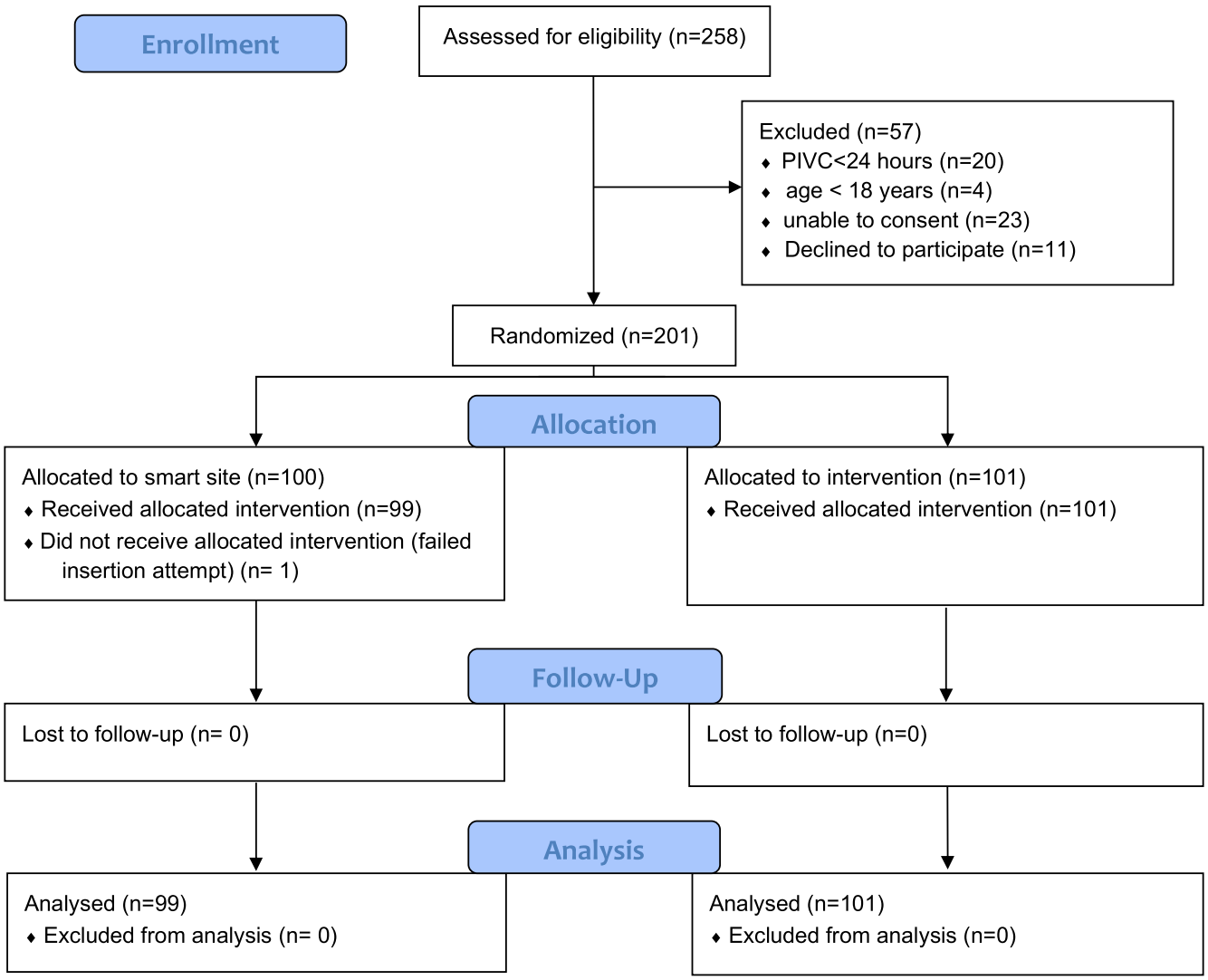


FIGURE 2 CONSORT Flow Diagram. [Colour figure can be viewed at wileyonlinelibrary.com]

## 3 | RESULTS

### 3.1 | Feasibility outcomes

A total of 258 medical and surgical patients were screened (Figure 2), and of these, 201 (78%) were eligible for study inclusion; this was lower than the a priori established eligibility target (≥90%). One patient in the control group was excluded as they did not have a PIVC inserted. All other feasibility criteria were met, with no patients lost to follow up, and no missing outcome data.

### 3.2 | Patient and PIVC characteristics

Demographic characteristics (Table 1) were similar between groups. Patients were on average male (56%), overweight (body mass index of 28.4), and had two or more (77%) comorbidities. Most PIVCs were a 22 gauge (79%), inserted in the forearm (85%), and inserted by a nurse (85%) (Table 2). Approximately one third (36%) of PIVCs were placed with ultrasound guidance and 27% of patients experienced two or more insertion attempts. The most common reason for PIVC placement was IV antibiotic administration (60%). Over one quarter of patients (27%) had their NC accessed on at least 16 occasions during PIVC dwell.

### 3.3 | Efficacy outcomes

The primary outcome of all-cause failure was statistically significantly higher ($p=0.002$) in the intervention neutral displacement NC group (39%) compared to the standard care (control) negative displacement NC group (19%) (Table 3). The incidence rates between the study groups had a ratio of 1.85 (95% confidence interval [CI] 1.05–3.40; log-rank test $p=0.028$) (Table 3, Figure 3) and an adjusted hazard ratio of 1.92 (95% CI 1.10–3.37) (Table 4). Catheter dwell times were similar between groups, with a median of 2.5 days (interquartile range [IQR] 1.8–3.9) in the control negative displacement NC group and 2.6 days (IQR 1.3–4.9) for the neutral displacement NCs. The most common individual PIVC complication was phlebitis, which was higher in the neutral displacement NC group (25%) compared with the control negative displacement NC (12%). Infiltration (4% vs. 1%), occlusion (5% vs. 2%), and dislodgement (6% vs. 3%) were higher in the neutral displacement NC group. There was no incidence of local infection or CRBSI in either group (Table 3).

## 4 | DISCUSSION

This pilot RCT of NCs was undertaken in response to reported high PIVC failure rates at local and international levels, noting particular

**TABLE 1** Baseline characteristics.

| | *n* | Negative (control) | Neutral (intervention) | Total |
|---|---|---|---|---|
| Group size | 201 | 100 (50%) | 101 (50%) | 201 (100%) |
| Age (years)[a] | 201 | 58.2 (16.3) | 55.7 (18.1) | 56.9 (17.3) |
| Gender: males | 201 | 57 (57%) | 55 (54%) | 112 (56%) |
| BMI[a] | 200 | 27.8 (6.9) | 29.0 (8.8) | 28.4 (7.9) |
| Reason for admission | 201 | | | |
| surgical | | 76 (76%) | 78 (77%) | 154 (77%) |
| medical | | 21 (21%) | 21 (21%) | 42 (21%) |
| cancer | | 3 (3%) | 2 (2%) | 5 (2%) |
| Comorbidities | 201 | | | |
| none | | 9 (9%) | 14 (14%) | 23 (11%) |
| one | | 15 (15%) | 14 (14%) | 29 (14%) |
| two | | 17 (17%) | 17 (17%) | 34 (17%) |
| three | | 28 (28%) | 18 (18%) | 46 (23%) |
| four or more | | 31 (31%) | 38 (38%) | 69 (34%) |
| Infection at baseline | 201 | 64 (64%) | 65 (64%) | 129 (64%) |
| Vein quality | 200 | | | |
| excellent | | 22 (22%) | 17 (17%) | 39 (20%) |
| good | | 21 (21%) | 22 (22%) | 43 (22%) |
| fair | | 21 (21%) | 24 (24%) | 45 (22%) |
| poor | | 35 (35%) | 38 (38%) | 73 (36%) |

Abbreviation: BMI, body mass index.

[a]Mean (standard deviation) shown.

**TABLE 2** Device characteristics.

| | *n* | Negative (control) | Neutral (intervention) | Total |
|---|---|---|---|---|
| Group size | 200 | 99 (50%) | 101 (50%) | 200 (100%) |
| Inserted by | 200 | | | |
| Research nurse | | 88 (89%) | 82 (81%) | 170 (84%) |
| Registered nurse | | 0 (0%) | 2 (2%) | 2 (2%) |
| Vascular access service | | 9 (9%) | 10 (10%) | 19 (10%) |
| Doctor | | 2 (2%) | 6 (6%) | 8 (4%) |
| Other | | 0 (0%) | 1 (1%) | 1 (<1%) |
| Device size | 200 | | | |
| 22 g | | 21 (21%) | 20 (20%) | 41 (20%) |
| 20 g | | 78 (79%) | 80 (79%) | 158 (79%) |
| 18 g | | 0 (0%) | 1 (1%) | 1 (<1%) |
| Inserting department | 200 | | | |
| Ward | | 98 (99%) | 101 (100%) | 199 (100%) |
| Theatre | | 1 (1%) | 0 (0%) | 1 (<1%) |
| Inserted on dominant side | 200 | 50 (50%) | 53 (52%) | 103 (51%) |
| Inserted at | 200 | | | |
| Forearm | | 84 (85%) | 84 (83%) | 168 (84%) |
| Upper arm | | 10 (10%) | 10 (10%) | 20 (10%) |
| Wrist/hand | | 5 (5%) | 5 (5%) | 10 (5%) |
| Cubital fossa | | 0 (0%) | 2 (2%) | 2 (1%) |
| Insertion attempts | 200 | | | |
| One | | 74 (75%) | 72 (71%) | 146 (73%) |
| Two | | 18 (18%) | 21 (21%) | 39 (20%) |
| Three or more | | 7 (7%) | 8 (8%) | 15 (8%) |
| Ultrasound-guided insertion | 200 | 38 (38%) | 34 (34%) | 72 (36%) |
| Needleless connector at insertion | 200 | | | |
| Single | | 4 (4%) | 5 (5%) | 9 (4%) |
| Double | | 95 (96%) | 96 (95%) | 191 (96%) |
| Connections at insertion | 200 | | | |
| 3-way tap with needleless connector/s | | 96 (97%) | 97 (96%) | 193 (96%) |
| Needless connector only | | 3 (3%) | 4 (4%) | 7 (4%) |
| Administration set connected (ever) | 200 | 55 (56%) | 57 (56%) | 112 (56%) |
| Highest rate of infusion during trial | 112 | | | |
| ≤ 20 mL/h | | 14 (25%) | 20 (35%) | 34 (30%) |
| > 20 mL/h but ≤100 mL/h | | 24 (44%) | 24 (42%) | 48 (43%) |
| > 100 mL/h | | 17 (31%) | 13 (23%) | 30 (27%) |
| Antimicrobial received | 200 | 55 (56%) | 65 (64%) | 120 (60%) |
| Fluids received | 200 | 46 (46%) | 49 (49%) | 95 (48%) |
| Electrolyte/vitamin/mineral received | 200 | 33 (33%) | 31 (31%) | 64 (32%) |
| Antiemetic/gastric protection received | 200 | 30 (30%) | 27 (27%) | 57 (28%) |
| Analgesics received | 200 | 27 (27%) | 27 (27%) | 54 (27%) |
| Sedation received | 200 | 19 (19%) | 17 (17%) | 36 (18%) |
| Blood product received | 200 | 11 (11%) | 13 (13%) | 24 (12%) |
| Contrast received | 200 | 4 (4%) | 4 (4%) | 8 (4%) |
| Corticosteroid received | 200 | 4 (4%) | 4 (4%) | 8 (4%) |

TABLE 2 (Continued)

| | *n* | Negative (control) | Neutral (intervention) | Total |
|---|---|---|---|---|
| Diuretic received | 200 | 6 (6%) | 2 (2%) | 8 (4%) |
| Heparin infusion received | 200 | 2 (2%) | 3 (3%) | 5 (2%) |
| Insulin received | 200 | 1 (1%) | 3 (3%) | 4 (2%) |
| Chemotherapy received | 200 | 1 (1%) | 0 (0%) | 1 (<1%) |
| Sedation and diuretic | 200 | 1 (1%) | 0 (0%) | 1 (<1%) |
| Other medications received | 200 | 5 (5%) | 6 (6%) | 11 (6%) |
| No medications received | 200 | 4 (4%) | 2 (2%) | 6 (3%) |
| Number of accesses during trial | 136 | | | |
| Zero | | 4 (6%) | 3 (4%) | 7 (5%) |
| One–five | | 24 (35%) | 26 (39%) | 50 (37%) |
| 6–10 | | 16 (23%) | 14 (21%) | 30 (22%) |
| 11–15 | | 7 (10%) | 5 (7%) | 12 (9%) |
| 16–20 | | 9 (13%) | 6 (9%) | 15 (11%) |
| 21–higher | | 9 (13%) | 13 (19%) | 22 (16%) |
| Subsequent IV device inserted | 200 | 64 (65%) | 62 (61%) | 126 (63%) |

Abbreviations: IV, intra-vascular; VA, vascular access device.

TABLE 3 Study outcomes.

| | Negative (control) | Neutral (intervention) | *p*-value |
|---|---|---|---|
| Group size | 99 (50%) | 101 (50%) | |
| All-cause PIVC failure | 19 (19%) | 39 (39%) | 0.002[a] |
| Dwell time (days)[b] | 2.5 (1.8–3.9) | 2.6 (1.3–4.9) | |
| Dwell time (patient-days) | 298 | 330 | |
| Incidence rate of failure (95% CI)[c] | 63.7 (40.7–99.9) | 118.1 (86.3–161.7) | |
| Incidence rate ratio (95% CI) | reference | 1.85 (1.05–3.40) | 0.028[d] |
| Complications | | | |
| Phlebitis | 12 (12%) | 25 (25%) | 0.021[a] |
| Dislodgement/accidental removal | 3 (3%) | 6 (6%) | 0.321[a] |
| Infiltration | 1 (1%) | 4 (4%) | 0.181[a] |
| Occlusion | 2 (2%) | 5 (5%) | 0.260[a] |
| Local infection | 0 (0%) | 0 (0%) | |
| Catheter-related bloodstream infection | 0 (0%) | 0 (0%) | |
| Serious adverse events[e] | | | |
| Death | 1 | 3 | |
| Unplanned ICU admission | 2 | 1 | |

Abbreviations: CI, confidence interval; ICU, intensive care unit; PIVC, peripherally inserted venous catheter; VAD, vascular access device.

[a]Chi-squared test

[b]Median (25th–75th percentiles) shown

[c]Per 1000 device-days

[d]Log-rank test

[e]Unrelated to trial participation.

concern about the harmful impact failure has on patients' future vascular access opportunities (Hallam et al., 2016). The aim of this study was to compare negative and neutral displacement NCs on feasibility and efficacy outcomes. All a priori feasibility criteria were met, except for eligibility, therefore with minor adjustments to screening processes this study protocol would be feasible for a

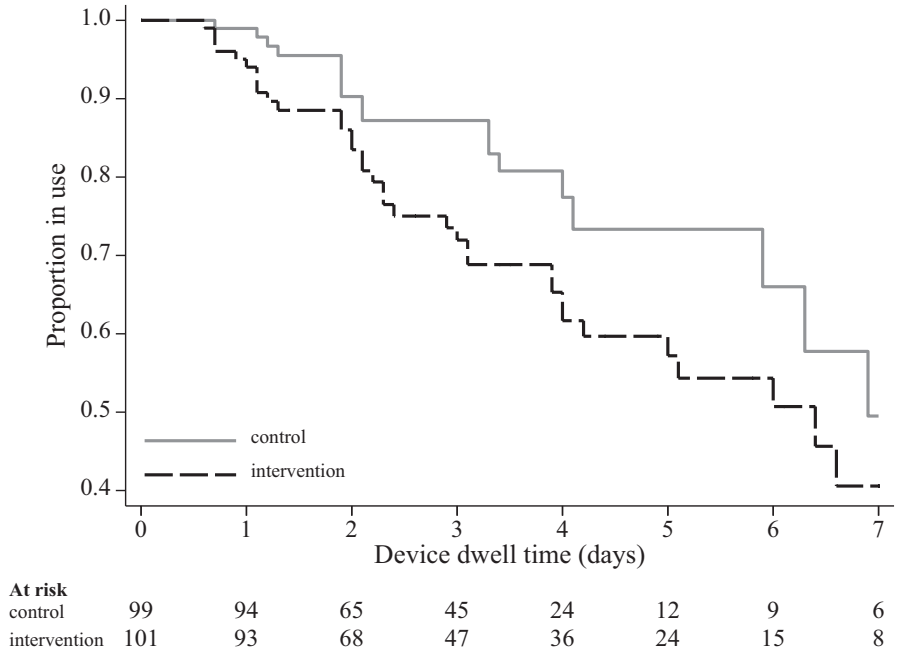


**FIGURE 3** Kaplan–Meier survival estimates by study group.

| | Univariable (crude) HR | Multivariable (adjusted) HR |
|---|---|---|
| Intervention (ref: control) | 1.85 (1.06–3.25)** | 1.92 (1.10–3.37)** |
| Age (10-year incremental increase) | 0.98 (0.84–1.15) | [a] |
| Females (ref: males) | 2.13 (1.25–3.60)*** | 2.19 (1.29–3.73)*** |
| Inserted by ReN (ref: others) | 0.58 (0.28–1.20)* | [a] |
| Insertion in lower forearm (ref: other) | 0.59 (0.331–1.12)* | [a] |
| 22 g catheter size (ref: 20 g) | 1.62 (0.90–2.91)* | [a] |

**TABLE 4** Cox regression of all-cause PIVC failure.

*Note*: 95% confidence intervals shown in parentheses.

Abbreviations: HR, hazard ratio; ref, reference category; ReN, Research Nurse.

[a]Removed from multivariable model at $p \geq 0.05$.

*$p < .020$; **$p < 0.05$; ***$p < 0.01$.

larger, definitive RCT. Our primary efficacy outcome was all-cause PIVC failure, with an absolute difference of 20% favouring the standard care (control) negative displacement NC. Although this was a pilot trial, we detected both clinically and statistically significant results.

Our study found a twofold higher phlebitis rate in the (intervention) neutral displacement NC (25%) compared to the (control) negative displacement NC group (12%). Phlebitis has been previously associated with vessel irritation caused by catheter movement in areas of flexion, and the administration of irritant or vesicant medications (e.g. contrast) (Gorski et al., 2021; Marsh et al., 2018c). These variables were unlikely to have influenced our study results as there were low numbers of PIVCs placed in the wrist and cubital fossa (<7% in both groups) and irritant medications/fluids were equally distributed in both the control and intervention group. However, the flow rate through a PIVC is influenced by add on devices, such as extension tubing or the type of NC attached (Berman et al., 2020; Hadaway, 2018). Although both NCs included in this study are described as having a straight fluid path to decrease the risk of haemolysis or blood residual, the neutral NC (*MicroClave*) flow rate is 165 mL per minute compared to the standard care negative displacement NC (*SmartSite)* flowrate of 133 mL per minute (Hadaway, 2012). This, coupled with a lack of nursing staff familiarity with a new product, might have inadvertently increased the rate at which PIVC flushes were delivered via the neutral NC compared to the standard care negative NC group. Higher infusion rates are reported to increase vessel injury and vein wall stress in computational fluid dynamic models (Piper et al., 2018). This might have contributed to phlebitis, the most frequently reported complication in this study. Future research needs to explore the impact of NCs, and other connections, and their influence upon flow rates and phlebitis. We also recommend future studies are underpinned with an implementation science framework to ensure the use of strategies (e.g. staff training) that promote clinical change uptake (Xu et al., 2023).

Our study also found only small differences in occlusion rates between negative (2%) and neutral (5%) displacement NCs. It is possible that the movement of fluid and blood through the NC facilitates accumulation of debris within the catheter, leading to lumen occlusion or

biofilm development and thereby increasing the risk of CRBSI (Gorski et al., 2021; Hull et al., 2017). The potential risk for complication is likely heightened with clinician confusion or non-compliance with the complex clamping and disconnecting sequences, as seen with negative displacement NCs (Curran, 2016). This is in contrast to the modern neutral displacement NC that avoids confusion by not requiring a clamping action before disconnection (Hull et al., 2017). Concerns of fluid displacement for NCs were recently explored in a laboratory study that used a computerised optical measuring system to measure fluid volume. They found higher volume displacement with negative NCs (9.73–50.34 μL) compared to neutral NCs (3.60–10.80 μL) (Hull et al., 2017). Although this suggests a higher risk of occlusion with negative NCs, our results did not reflect this, with a higher occlusion in the neutral NC group. We were unable to explore the potential risk for CRBSI with no reported infections in either group.

A limitation of this study was the inability to blind nursing and research staff to the study intervention due to the obvious differences between NCs. This limitation, which is common in device trials, was partially overcome by blinding the statistician for data analysis. A further limitation is that although our results indicate a statistically significant outcome, this study was designed as a pilot RCT. Therefore, rigorous multi-site RCTs are required to test NCs within different patient populations and to include a broader range of IV medication, flush and fluid administration practices. We were also unable to measure patient satisfaction, as participants reported not understanding how to score satisfaction for an add on device to their PIVC. However, a strength of this study was that all decisions around clinical need and care of the PIVC were made by the bedside nurse and medical team, which supports the generalisability of our results.

## 5 | CONCLUSION

High rates of PIVC failure place patients at risk of avoidable harm. These results suggest less failure and PIVC complications with negative NCs. NC efficacy and safety need further testing in a large multi-centre RCT, including a broader patient population.

### AUTHOR CONTRIBUTIONS

All authors meet authorship criteria and are in agreement with the content of the manuscript. NM, EL, SK, KD, CB, BH, ALM, JF and CMR designed the study. CO collected data. GM, NM, EL analysed the data. NM, EL, CO drafted the first version of the manuscript. All authors approved the final version for submission.

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### CONFLICT OF INTEREST STATEMENT

NM: Griffith University and The University of Queensland have received on her behalf investigator-initiated grants from 3 M, Cardinal Health and Eloquest, and consultancy payments from 3 M and Becton Dickinson for expert advice/ educational sessions. EL: affiliate (University of Queensland) has received, on her behalf: an investigator-initiated research grant from Eloquest Healthcare, unrelated to this work; EL was also awarded scholarship for conference attendance, by Angiodynamics, unrelated to this work. SK: employer has received, on her behalf, monies for scholarship attendance from Becton Dickinson, unrelated to this work. CMR: Employers (Griffith University or The University of Queensland) have received on her behalf: investigator-initiated research or educational grants from 3 M, Becton Dickinson-Bard; Cardinal Health, Eloquest Healthcare; and consultancy payments for educational lectures/expert advice from 3 M, Becton Dickinson-Bard. CO, KD, GM, BH, CB, ALM, JF: The authors declare no conflict of interest.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

### STATISTICIAN ON THE AUTHORSHIP TEAM

Dr Gabor Mihala. The author(s) affirm that the methods used in the data analyses are suitably applied to their data within their study design and context, and the statistical findings have been implemented and interpreted correctly.

### TRIAL REGISTRATION

Trial methods were prospectively registered on 8 August 2019 with the Australian New Zealand Clinical Trials Registry (ACTRN12619001091190), https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=377895&isReview=true.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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