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Research paper

Polyhexamethylene biguanide discs versus unmedicated dressings for prevention of central venous catheter–associated infection in the intensive care unit: A pilot randomised controlled trial to assess protocol safety and feasibility

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ABSTRACT

Background: Central venous catheters are prone to infectious complications, affecting morbidity, mortality and healthcare costs. Polyhexamethylene biguanide-impregnated discs at the catheter insertion site may prevent local and bloodstream infection; however, efficacy has not been established in a critical care setting.

Objective: The objective of this study was to pilot test polyhexamethylene biguanide–impregnated discs compared to standard unmedicated dressings for central venous catheter infection prevention in critically ill patients.

Methods: This was a single-centre pilot randomised controlled trial. Adults admitted to intensive care requiring a central venous catheter for >72 h were eligible. Patients with a current bloodstream infection, concurrent central venous catheter, chlorhexidine or polyhexamethylene biguanide allergy, or sensitive skin were excluded. Patients were randomised to receive standard central venous catheter dressings with/without polyhexamethylene biguanide discs.

Outcome measures: The primary outcome was feasibility, defined by patient eligibility, recruitment, retention, protocol adherence, missing data, and staff satisfaction. Secondary outcomes included: central

Abbreviations: CHG, chlorhexidine gluconate; CVC, central venous catheter; ICU, intensive care unit; PHMB, polyhexamethylene biguanide.

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line–associated infection; primary bloodstream infection; local infection; skin complications; device/dressing dwell time; serious adverse events, and cost-effectiveness.

Results: Of 309 patients screened, 80 participants were recruited with 98% (n = 78) receiving an internal jugular catheter which dwelled for a median of 5 days (interquartile range = 4.0, 6.0). Feasibility criteria were predominantly met (recruitment 88%; retention 100%; protocol fidelity 91%); however, eligibility criteria were not met (32%; most commonly owing to short predicted catheter dwell). Staff acceptability criteria were met, with 83% of staff scoring dressing application and removal ≥7 on a numerical rating scale. There were no central line–associated bloodstream infections and no local infections. Insertion site itch occurred in 4% (control [n = 0], intervention [n = 3]) of participants, while 32% (24/76) reported pain, and 46% (35/76) tenderness.

Conclusions: Polyhexamethylene biguanide discs appear safe for central venous catheter infection prevention. Feasibility of a large efficacy trial was established with some modifications to screening processes. Large, adequately powered randomised controlled trials are needed to test the infection prevention hypotheses.

1. Introduction

Central venous catheters (CVCs) are inserted in large veins to deliver intravenous therapy and monitor central venous pressures in critically ill patients admitted to the intensive care unit (ICU).[1] Whilst integral to patient treatment, CVCs are associated with significant risk, the most serious being infection.[2] Central line–associated bloodstream infection (CLABSI) increases patient morbidity, mortality and healthcare costs,[3] with an estimated 250,000 CLABSIs occurring every year in the USA alone,[2] each costing on average an additional USD$56,000.[4] In Australian ICUs, CLABSI surveillance data indicate 0.46 episodes per 1000 catheter days,[5] although a systematic review and meta-analysis of observational studies and randomised controlled trials (RCTs) reported CVC CLABSI rates as high as 5.28 episodes per 1000 catheter days.[6] Each CLABSI episode has been estimated to cost an additional AUD$14,000,[7] and increase the length of ICU admission by more than 4 days.[8]

Clinical interventions, such as the use of antimicrobial-impregnated dressings and discs at the CVC insertion site, have been introduced to lower CLABSI rates and the resultant healthcare burden. Such dressings aim to reduce microorganism growth and migration through the CVC insertion site, along the intravascular catheter and into the bloodstream.[9] A Cochrane review demonstrated that any type of antimicrobial-impregnated dressings reduced the incidence of CLABSI compared with other dressing types, primarily in the intensive care setting.[10] At an individual trial level, a multicentre study by Timsit et al reported that CLABSI rates could be significantly reduced with the use of chlorhexidine gluconate (CHG)–impregnated dressings compared with standard care even in the setting of already low bloodstream infection (BSI) rates.[11]

Consequently, CHG-impregnated dressings and discs are recommended for inclusion in CLABSI care bundles.[12] However, while effective at reducing CLABSI, CHG dressings can be associated with significantly increased adverse skin events compared with non-impregnated dressings in some patients.[13] Recently, polyhexamethylene biguanide (PHMB), an antiseptic with antiviral and antibacterial qualities, currently used in chronic wound dressings, has been investigated as an alternative to CHG for device dressings. Although PHMB share similar properties to CHG, it has a relatively low incidence of adverse skin events.[14–17] PHMB has been reported as more effective at inhibiting growth of many organisms responsible for CLABSI, including *Staphylococcus aureus, Enterococcus* sp. and *Enterobacter* sp., compared with CHG.[18] In contrast to CHG, there is currently no evidence of PHMB microbial resistance.[19]

When impregnated into a foam disc (Kendall™ AMD Foam Disc, Cardinal Health, Waukegan, IL, USA) suitable for the insertion site of vascular access devices, the manufacturer states PHMB will inhibit microorganism growth for up to 7 days.[20] In Australia, PHMB-impregnated discs are currently half the cost of widely used CHG-impregnated discs, but there is limited research regarding their comparative ability to prevent CVC-related infections. A single-centre feasibility trial in peripherally inserted central catheters showed that PHMB discs are safe,[15] but they have not yet been tested in a critical care environment.

2. Methods

2.1. Aims and objectives

The aim of this trial was to test the feasibility of conducting a large-scale, parallel-group RCT by assessing the methodology and rigour of methods planned for the larger study, in addition to obtaining initial effect estimates for infection prevention and adverse events.

2.2. Setting

This pilot RCT was conducted in an Australian tertiary referral hospital between the 31st July, 2019, and 3rd February, 2020. Participants included general and post-cardiac surgery ICU cohorts from a 28-bed unit and were recruited either in the ICU or preoperatively.

2.3. Ethical approval

Ethical approval was provided by the human research ethics committees of The Prince Charles Hospital (HREC/19/QPCH/51795) and Griffith University (Ref No: 2019/376).

2.4. Participants

Patients were eligible for study inclusion if they were (i) 18 years or older; (ii) anticipated to require a CVC for more than 72 h; and (iii) able to provide informed written consent. Patients were ineligible if they (i) had a current laboratory-confirmed BSI (reported within the previous 48 h); (ii) had a concurrent CVC anticipated to be in situ for greater than 24 h; (iii) were non–English-speaking without an interpreter; (iv) had a known allergy to CHG or PHMB; (v) had preexisting dermatitis/rash/burns at the CVC insertion site;

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and/or (vi) had previously been enrolled in the study. Sample size was set at 80 patients (40 per arm) as per recommendations for pilot trial sample size.[21]

2.5. Consent

Eligible patients, or their legally authorised representative, were approached by a research nurse who explained study interventions and processes before providing them with a study-specific information sheet and consent form. Informed consent was provided by the patient or their legally authorised representative before study enrolment. If the patient's legally authorised representative was not present at the time of CVC insertion, temporary consent was obtained via telephone and followed with written consent at the earliest opportunity.

2.6. Outcome measures

2.6.1. Primary outcomes

Feasibility criteria and limits were determined based on criteria used in previous pilot trials of similar nature.[15,22]

1. Feasibility of the study interventions and protocol
   a. Eligibility (>80% of screened patients meeting all inclusion and no exclusion criteria)
   b. Recruitment (>80% of eligible patients providing informed consent)
   c. Retention (<5% of recruited patients lost to follow-up or withdrawing consent)
   d. Protocol fidelity (>90% of randomised patients receiving their allocated intervention)
   e. Missing data (<5% of total primary clinical outcome [secondary outcome 1] data unable to be collected)
   f. Staff satisfaction with study interventions (>80% scoring $\geq$7 on a 0–10 numerical rating scale [on application and removal of intervention and control dressings])

2.6.2. Secondary outcomes

1. CLABSI: a laboratory-confirmed BSI where an eligible BSI organism is identified that is unrelated to an infection at another site, the patient exhibits at least one of fever (>38.0 °C), chills, or hypotension (National Healthcare Safety Network common commensal organisms only), and an eligible central line is present on the day of or day before the event[23]
2. Primary BSI: a laboratory-confirmed BSI where an eligible BSI organism is identified that is unrelated to an infection at another site, the patient exhibits at least one of fever (>38.0 °C), chills, or hypotension (National Healthcare Safety Network common commensal organisms only)[23]
3. Local infection: defined as an arterial or venous infection excluding infections involving vascular access devices with organisms identified in the blood. Patients must have purulent drainage from the vascular site, or exhibit at least one of fever (>38.0 °C), pain, erythema or heat involved at the vascular site AND more than 15 CFU cultured from the intravascular tip[24]
4. Skin complications: a composite of any skin complication surrounding the CVC site including contact/allergenic dermatitis, pressure injury, skin rash/tears/blisters, and/or self-reported pruritus[25]
5. Device and dressing functional dwell time (time to removal and time to first dressing change)
6. Serious adverse events (death and CLABSI)
7. Healthcare costs: dressing purchase cost, number of dressings used, and cost of staff time for dressing application and replacement (subset of six participants)

Protocol violations were defined as cases where the patient never received their allocated dressing combination. Protocol deviations were defined as cases where the patient initially received the allocated treatment but then subsequently received a non-allocated treatment or initially did not receive the allocated treatment but subsequently did receive the correct treatment.

2.7. Randomisation and blinding

Randomisation was via a centralised web-based program (Griffith University Randomisation Service, https://randomisation.griffith.edu.au/) generated in a 1:1 ratio using randomly allocated block sizes of four and six. Randomisation allocation was concealed until each patient's study entry. The patient, research staff, and clinical staff were not blinded to the randomisation allocation owing to the nature of the intervention being tested. However, microbiology staff and infectious diseases specialists were blinded for outcome assessment.

2.8. Study interventions

Participants were randomised into two groups:

Arm 1 (Control): Foam stabilising dressing (EasI-V™ foam securement device [664M, 5.8 cm × 7.6 cm], ConvaTec, Skillman, USA) and polyurethane dressing (IV3000 Orange Handle [4925, 10 cm × 14 cm], Smith and Nephew, Watford, UK) (Fig. 1).

Arm 2 (Intervention): PHMB disc (Kendall™ Antimicrobial Foam Disc [55511AMD, 1-inch diameter 4-mm hole, 4-mm thick, Covidien, Basingstoke, UK] *plus* control) (Fig. 1).

Randomised dressings were applied for the entire duration of the CVC dwell. Control dressings were chosen based on standard care of the participating ICU.

2.9. Catheter insertion and care

Catheter type (including the use of antimicrobial-impregnated CVCs) and length was selected at the discretion of the treating clinician, and catheters were inserted in accordance with Centers for Disease Prevention and Control recommendations[12] and standard hospital policy.[26] Hand hygiene, maximal sterile barrier precautions, and aseptic technique were observed during catheter insertion. Skin was prepared with alcoholic chlorhexidine gluconate or tincture of iodine. After device insertion, the research nurse provided the allocated dressing combination to the inserting clinician, who applied each dressing with supervision or assistance as required. Clinical staff members were responsible for CVC care and maintenance after insertion as per hospital policy, including dressing changes every 7 days or more frequently if indicated (e.g.,

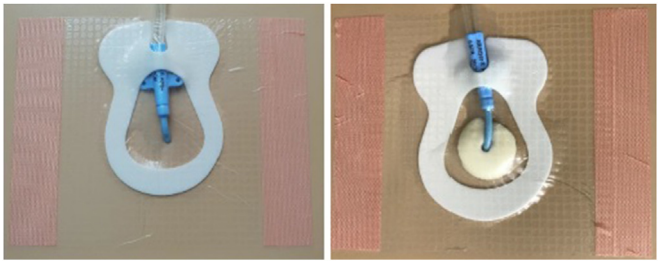

Fig. 1. Control dressing combination (left); Intervention dressing combination (right).

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soiled, loose, or moist). Bedside staff members were provided the randomised dressings by the research team. Extensive education regarding study procedures was provided to all clinical staff members before, and during, the study. CVC removal was at the discretion of the treating team, and microbiological specimens, such as CVC tips, insertion site swabs, and blood cultures, were collected only if clinically indicated.

2.10. Data collection

Data were collected on a paper-based form and transferred to Research Electronic Data Capture platform (REDCap; project-redcap.org).[27,28] Variables were collected by research nurses at the time of study enrolment, daily until CVC removal (except weekends), at the time of CVC removal, and 48 h after CVC removal as per Table 1. Study participants self-reported any itch at the insertion site (mild/moderate/severe). Staff satisfaction of the study products was rated by medical officers (on application) or registered nurses (on removal).

Cost data were collected by retrospectively selecting six random participants and calculating the total cost of dressing application and removal for each device's total dwell time, with item costs based on 2019 Queensland Health store prices and wages based on Queensland Health nursing wage rates (Clinical Nurse Level 6.2 AUD$48.80/hr). Time estimates for application and removal of dressings were determined using a simulated dressing scenario.

2.11. Data analysis

Before analysis, data were cleaned for implausible and/or outlying figures, and missing data located where possible. Data were exported from REDCap to STATA, version 15 (College Station, TX: StatCorp LLC) and analysed using intention-to-treat principles. Missing data were not imputed. Feasibility outcomes were reported descriptively as percentages and analysed against predetermined acceptability criteria. Clinical outcomes were reported descriptively between groups. Categorical data were summarised as frequency and percentages. Means and standard deviations were reported for normally distributed data, and medians and interquartile ranges were used to report nonnormally distributed data.

Infection data (i.e., those fields pertaining to potential BSI, CLABSI, and local infection) were collated by the study team and then provided to an infectious disease specialist outside the main study team who determined the presence or absence of CLABSI, primary BSI, and local infection using published definitions.[23,24]

2.12. Trial Registration

Australia and New Zealand Clinical Trials Registry: ACTRN12619000918123.

3. Results

There were 309 patients screened between 30th July, 2019, and 29th January, 2020, with 86 randomised and 80 included in the final analysis as six patients never received the allocated intervention (Fig. 2). Demographic and CVC characteristics were largely balanced between the two groups (Table 2). Participants were predominantly male (73%), older than 65 years, undergoing elective surgery (88%), with most suffering from chronic disease (61% > 3 comorbidities). Five percent of patients (4/80) had wounds at enrolment, while one patient had a suspected BSI ([control: n = 1, intervention: n = 0] negative growth after 5 days) and another had a confirmed varicella-zoster infection at the time of enrolment

Table 1
Data collected.

Enrolment	Daily check	Upon CVC removal	48 h after CVC removal
• Age • Sex • Height • Weight • Dominant side • Skin type (Fitzpatrick scale) • Skin integrity at CVC insertion site • Hospital admission date • ICU admission date • ICU admission diagnosis • Comorbidities • Wounds present • Current suspected/laboratory-confirmed infections • CVC insertion date/time • CVC insertion site • No. of CVC lumens • Difficult insertion • No. of insertion attempts • Skin preparations used • Hair at insertion site • Hair clipped before insertion • Diaphoresis • Dressing application date/time • Randomised dressing combination applied • Staff satisfaction with dressing application [0–10 scale (10 = extremely easy)]	• Device still in situ • Indications for CVC use • No. of lumens in use • Other intravascular devices in situ • Randomised dressing in situ • Insertion site visible • No. of dressing changes • Reasons for dressing changes o Dressing lifting o Sweating o Leakage o Skin reaction o Bleeding o Purulent discharge o Oozing • Dressing appearance • Diaphoresis (Y/N) • Level of consciousness • Skin complications o Rash o Blister o Skin tear o Bruising o Papules o Self-reported itch • Pain & tenderness at insertion site • Erythema & swelling at insertion site	• CVC removal date/time • Reason for CVC removal • CVC-related complications o Occlusion o Unable to aspirate o Infiltration o Too painful to tolerate o Leaking o Accidental removal o Suspected CLABSI/local infection o Impaired limb circulation o Extravasation • Staff satisfaction with dressing removal (upon CVC insertion) • Skin complications (as per daily check) • Pain & tenderness at insertion site • Erythema & swelling at insertion site • Patient mobility • Neurological status • Intravenous antibiotics	• Mortality • Date/time of death • SAEs • Nosocomial infections • CVC tip culture results • CVC insertion site swab results • Blood culture results • Treatments commenced for CVC-related infections

BMI = body mass index; CVC = central venous catheter; ICU = intensive care unit; SAE = serious adverse event.

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(control: n = 0, intervention: n = 1). Most CVCs placed were quadruple lumen (94%), were inserted in the operating theatre (95%), were inserted into the right internal jugular vein (95%), and were not antibiotic coated (86%). Sutures were used to secure the CVC at the insertion site in 95% of patients. CVC failure, defined as premature removal of the CVC before the end of therapy, occurred in 7% of control group patients and 6% of intervention group patients (15 and 12.5 episodes of failure per 1000 catheter days, respectively). Two patients died whilst enrolling in the study, but these serious adverse events were not related to the study intervention.

Of the 309 patients screened, 98 met eligibility criteria (32% eligible); therefore, the feasibility criteria were not met (Table 3). Patients were most likely to be ineligible as they were not anticipated to require a CVC for more than 72 h (97/223, 43%). Informed consent was obtained from 86 of the 98 eligible patients (88%) thereby fulfilling the recruitment feasibility criteria, with 12% (12/98) of eligible patients (or their next of kin) declining to participate. No patients withdrew or were lost to follow-up, meeting the retention criteria. Protocol fidelity was maintained with 91% (78/86) of randomised patients receiving the correct dressing allocation upon CVC insertion; however, 18% (14/78) initially received the correct dressing but then deviated from the dressing allocation in the subsequent days (control: n = 7, intervention: n = 7). Two participants (2%) (control: n = 1, intervention: n = 1) constituted protocol violations as they never received the allocated dressing combination but were still included in the final analysis. All data for the main clinical outcome of CLABSI could be collected; therefore, the missing data feasibility criteria were met. Staff satisfaction with dressing application and removal met feasibility criteria with 83% of scores ≥7 (control application 9.0 [median, interquartile range {IQR} = 7.0, 10.0]; intervention application 8.0 [median, IQR = 6.0, 9.0]; removal in both study arms 10.0 [median, IQR = 9.0, 10.0]).

There were no confirmed CLABSIs or local insertion site infections in either study group. However, four CVCs (5%, 2 in each group) were removed owing to a clinical suspicion of CLABSI, and one of these four was also suspected of local infection (control [n = 1]) (Table 4). Of the four devices removed for suspected CLABSIs, three had CVC tips sent for culture; all were negative. A further five CVC tips (control [n = 2], intervention [n = 3]) were sent for culture upon removal even when infection was not suspected and, similarly did not culture organisms >15 CFU.

Skin complications (itch underneath the CVC dressing) were reported by 4% of patients (control [n = 0], intervention [n = 3]), all of which were mild and self-resolved with no targeted treatment. One-third of participants (32%, control [n = 11], intervention [n = 13]) reported some degree of pain, and nearly half (46%, control [n = 19], intervention [n = 16]) reported some degree of CVC insertion site tenderness during the CVC dwell. No evidence of

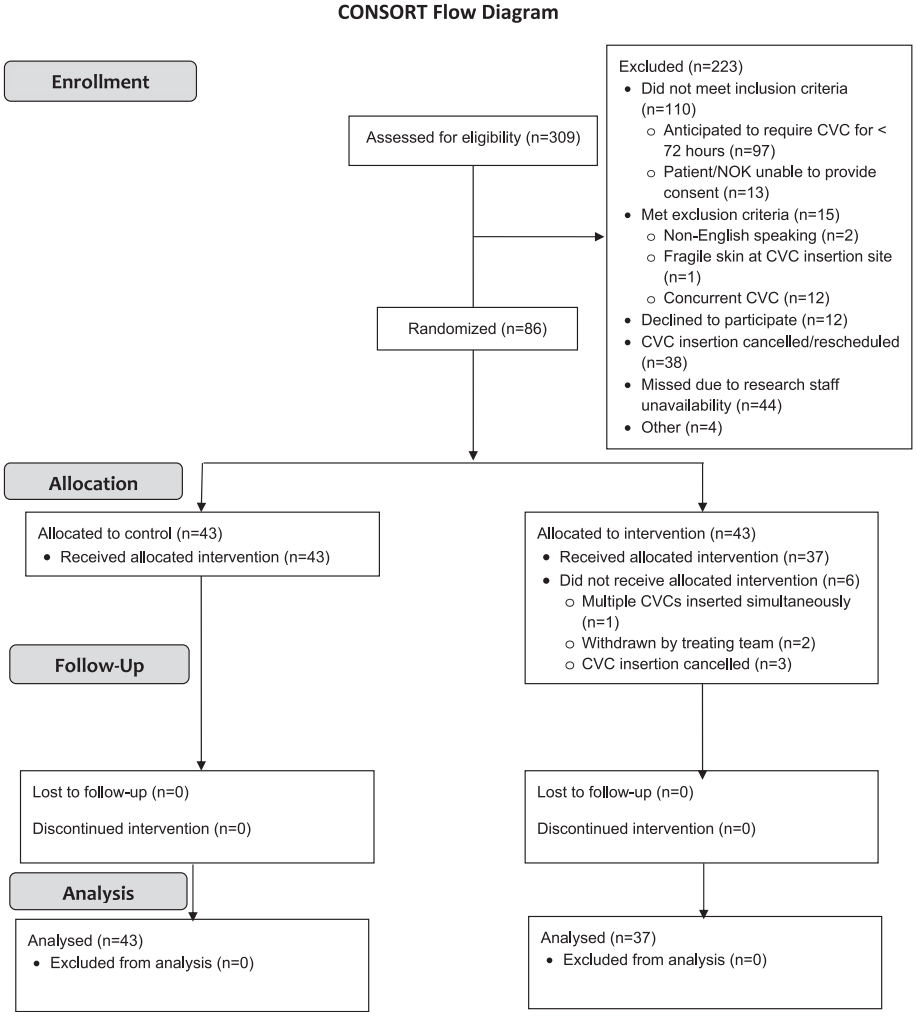

Fig. 2. CONSORT flow diagram.

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Table 2
Randomised patient and device characteristics.

Characteristic	Control	Intervention	Total
Group size	43	37	80
Age in years, median (IQR)	71 (63–75)	68 (58–73)	69 (62–73)
Male	31 (72)	27 (73)	58 (73)
Skin integrity			
Good	15 (35)	18 (49)	33 (41)
Fair	25 (58)	17 (46)	42 (53)
Poor	3 (7)	2 (5)	5 (6)
Intensive care admission			
Planned	39 (91)	31 (84)	70 (88)
Emergent	2 (5)	4 (11)	6 (8)
Interhospital transfer	2 (5)	2 (5)	4 (5)
No. comorbidities			
0	0 (0)	1 (3)	1 (1)
1	2 (5)	2 (5)	4 (5)
2	6 (14)	2 (5)	8 (10)
3	10 (23)	8 (22)	18 (23)
>3	25 (58)	24 (65)	49 (61)
IV antibiotics administered during enrolment	32 (74)	25 (68)	57 (71)
CVC insertion location			
R) internal jugular	42 (98)	34 (92)	76 (95)
L) internal jugular	1 (2)	1 (3)	2 (3)
R) femoral	0 (0)	1 (3)	1 (1)
L) femoral	0 (0)	1 (3)	1 (1)
Number of CVC lumens			
4	41 (95)	34 (92)	75 (94)
5	2 (5)	3 (8)	5 (6)
Antibiotic-coated CVC	6 (14)	5 (14)	11 (14)
Current wound	1 (2)	3 (8)	4 (5)
Confirmed infection			
Varicella-zoster virus	0 (0)	1 (3)	1 (1)
Suspected infection			
Bloodstream	1 (2)	0 (0)	1 (1)

Results are presented as frequencies and proportions unless otherwise stated.
CVC = central venous catheter; IV = intravenous; IQR = interquartile range.

specific hypersensitivity or anaphylaxis was observed in either treatment group.

There were 200 catheter days in the control group and 160 catheter days in the intervention group. Median device functional dwell time was the same across the two treatment groups (both medians = 5 days; IQR = 4, 6). Forty-two (55%) patients required a dressing change during their CVC dwell (60% control; 50% intervention), with a collective total of 84 dressing changes (n = 50 control; n = 34 intervention). Time to first dressing change was shorter in the intervention group (25.5 h, IQR = 16.9, 43.8) than the control group (29.8 h, IQR = 18.0, 72.8). The most common reason for dressing change was adhesive failure (dressing lifting) (39% [33/84], control 42%; intervention 35%) with limited use of additional bordered (3%) and nonbordered dressings (6%) to maintain dressing adhesion.

A cost analysis was performed in a convenience-sampled (based on research staff availability) subset of six participants (control [n = 3], intervention [n = 3]). At the time of recruitment, each control dressing cost AUD$3.06 and each intervention dressing cost AUD$7.56. Application of the intervention dressing combination (1 min, 24 s) took 9 s longer than application of the control dressing combination (1 min, 15 s). Removal of the dressing took the same amount of time between groups (16 s). No dressing changes were required in the intervention group and four were required in the control arm (Table 5). Mean cost per patient (including replacement dressings and staff time) allocated to the control group was AUD$11.37, while the mean cost per patient in the intervention group was AUD$8.92.

Table 3
Protocol feasibility outcomes.

Feasibility criteria	Predetermined threshold	Result
Eligibility	>80% screened patients eligible	32%
Recruitment	>80% eligible patients consented	88%
Retention	<5% patients lost to follow-up/withdrew consent	100%
Protocol fidelity	>90% randomised patients receiving allocated intervention	91%
Missing data	<5% of primary clinical outcome data missing	0%
Staff satisfaction[a]	>80% staff scoring ≥7 on a 0–10 rating scale	83%

[a] n = 68 (application of dressing) and n = 47 (removal of dressing).

4. Discussion

This pilot RCT is the first to assess feasibility and safety of a protocol to evaluate the effect of PHMB-impregnated discs on CVC infection prevention in the ICU. The primary aim of this study was to examine feasibility outcomes while also collecting safety and clinical data. Recruitment, retention, protocol fidelity and missing data feasibility criteria were met, indicating study processes in these areas were sound and could be translated to a larger trial. The eligibility feasibility criterion was not met, primarily owing to many screened patients (elective cardiac surgical) not anticipated to require their CVC for more than 72 h. Efficiencies could be found in screening processes by targeting patient groups with longer expected lengths of stay, specifically the general ICU population or those surgical patients undergoing more complex procedures. An efficacy trial comparing PHMB discs with standard CVC dressings in the adult ICU population is feasible with slight modifications to the target population.

CHG is a critical antimicrobial component of infection prevention initiatives, and there is a lack of robust head-to-head trials comparing CHG and PHMB in the evidence base, particularly in the vascular access literature. The evidence surrounding PHMB safety and efficacy is small in scale and not well controlled;[16] however, PHMB appears to have a broader spectrum of action than CHG[18,29] and has been used in the wound care setting to inhibit wound biofilm formation and decrease wound pain and size without leading to bacterial resistance.[30–34] Importantly, PHMB has been shown to inhibit the growth of Coagulase-negative staphylococci, *S. aureus*, enterococci and Candida species, pathogens commonly responsible for CLABSIs.[18,35] Furthermore, a pilot RCT conducted comparing CHG- and PHMB-impregnated discs for reduction in CLABSI in peripherally-inserted central catheters found PHMB safe to use; however, this trial was not powered to detect significant differences in clinical infection outcomes.[15] These advantages, combined with the lower cost of PHMB-impregnated discs than similar CHG products and ongoing concern surrounding chlorhexidine-resistant microorganisms[36–38] make PHMB-impregnated foam discs a potentially efficacious method for CLABSI and local infection prevention in both long- and short-term CVCs.

Although not a study endpoint, we demonstrated in this RCT that the application of a PHMB disc to standard securement dressings does not negatively impact overall dressing integrity with lower rates of device and dressing failure and dressing changes seen in the intervention group. This is an important consideration as dressing disruption is a major risk factor for catheter-related infections, which increase in likelihood by three-fold after the second dressing disruption.[39] We also found no instances of CVC failure owing to confirmed CLABSI or local infection in this study. This was expected owing to the small sample size in addition to the relatively short dwell times in this study, which was not designed to detect differences in clinical outcomes. It does, however, have implications for future studies with primary infection outcomes, suggesting that future trials might benefit from a CLABSI

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Table 4
Device and patient outcomes.

Outcome	Control	Intervention	Total
Group size	43	37	80
Infection outcomes			
Central-line associated infection (CLABSI)	0 (0)	0 (0)	0 (0)
Primary bloodstream infection	0 (0)	2 (5)	2 (3)
Local infection	0 (0)	0 (0)	0 (0)
Skin complications			
Itch[a]	0 (0)	3 (8)	3 (4)
Pain[b]	11 (27)	13 (37)	24 (32)
Tenderness[b]	19 (46)	16 (46)	35 (46)
Erythema[c]	0 (0)	0 (0)	0 (0)
Swelling[c]	0 (0)	1 (3)	1 (1)
Device dwell time (days), median (IQR)	5 (4–6)	5 (4–6)	5 (4–6)
Time to first dressing change (hours), median (IQR)[d]	29.8 (18.0 −72.8)	25.5 (16.9 −43.8)	26.4 (17.4 −66.3)

Results are presented as frequencies and percentages unless otherwise stated.
IQR, interquartile range.
[a] n = 42 control and n = 36 intervention.
[b] n = 41 control and n = 35 intervention.
[c] n = 42 control and n = 34 intervention.
[d] n = 23 control and n = 16 intervention.

comparative design with primary outcomes centred on skin complication or dressing change frequency.

Compared with standard care, application of the PHMB disc slightly increased the time to apply the dressings and total cost of each dressing. However, use of the PHMB disc did not increase removal time as the disc, which adhered to the foam and polyurethane dressings, was removed in one motion with the other two dressings. In the subset of participants used for the cost analysis, there were four dressing changes required in the control group, but no dressing changes required in the intervention group. This resulted in the overall cost for the control group dressings being higher than that for the intervention group, despite initial increased cost in the intervention group. This may demonstrate the potential cost-effectiveness of PHMB disc use in this setting owing to reduced incidence of CLABSI and associated healthcare costs, but a larger RCT is needed to explore this further.

While the rate of protocol deviations experienced in this trial was equal across groups and was similar to that of other CVC dressing RCTs,[1,15,40] this pilot trial has highlighted several areas in which the protocol may be enhanced before undertaking a larger trial. For example, three patients in the intervention group reported itch underneath their dressing, but this was difficult to assess owing to the disc obscuring visualisation of the insertion site. It may be useful in a larger scale RCT to protocolise actions to take when patients in either treatment group experience itch (i.e., when to remove the dressing to assess the skin versus when to leave the dressing in situ). Likewise, shorter length CVCs (i.e., 11 cm) were found to not accommodate disc application as they needed to be inserted to the hub to achieve correct tip position and therefore left insufficient space for disc placement. Exclusion criteria could be modified in a larger scale RCT to exclude those patients planned to receive a shorter length CVC, but doing so would limit the use ofPHMB discs as an infection prevention strategy to those with longer length CVCs.

Before this trial is translated into a fully powered RCT, a number of design elements would have to be amended in the protocol. For example, the implications of antimicrobial-impregnated CVC use in conjunction with PHMB discs on the data would have to be considered. While some hospitals use antimicrobial-impregnated catheters as standard care, it may be prudent to exclude antimicrobial-impregnated CVCs to recruit a pragmatic sample size, given CLABSI as the primary outcome has such a low event rate. Previously published RCTs in the adult ICU setting with CLABSI as the primary outcome have required sample sizes of approximately 300 participants per group,[41] and a similar sample is anticipated when this trial progresses to a larger RCT.

The study limitations included the pilot trial design, which resulted in an imbalance in group numbers, largely owing to case cancellations occurring in the intervention arm which would be unlikely to occur in a larger trial. This trial was also conducted at a single centre, and so results may not be generalisable to other institutions. Additionally, owing to the nature of the intervention, study participants, and clinical and research staff could not be blinded to the study allocation; however, microbiology staff members and infectious diseases specialists could be blinded for data analyses. The cost comparisons were calculated on a subset of six participants and did not account for the cost of additional dressings and securements (outside the allocated intervention dressings). The cost estimate will therefore be an underestimation of actual costs. Finally, funding limitations meant that research staff hours were restricted, and after-hours data could not be collected. This resulted in missing some daily data but did not affect outcomes as these data were able to be collected retrospectively. In a larger trial, the number of daily data variables may need to be reduced so as to limit the amount of missing data.

Current guidelines recommend the use of CHG-impregnated dressings to reduce the incidence of CVC-related infection, however infection remains one of the major causes of CVC-related morbidity. This, combined with the increasing prevalence of CHG resistance and CHG-associated adverse skin events, suggests more evidence is needed to inform alternative infection prevention protocols and products which may have a higher efficacy, lower costs and less microbial resistance than CHG-based interventions. PHMB could provide an alternative to CHG, but further high-quality RCTs are required to definitively determine its clinical applicability and efficacy, particularly in vascular access.

Table 5
Mean cost (AUD) per patient (subset of six participants).

Component	Control	Intervention
Dressings applied at insertion	3.06 (0)[a]	7.56 (0)[b]
Initial dressing application labour	1.02 (0)	1.14 (0)
Replacement dressings cost[†]	4.08 (1.77)	0 (0)
Replacement dressing removal labour	0.29 (0.13)	0 (0)
Replacement dressing application labour	1.36 (0.59)	0 (0)
Final dressing removal labour	0.22 (0)	0.22 (0)
Total cost	**$11.37 (3.06)**	**$8.92 (0)**

All values are presented as mean (standard deviation) in AUD.
[a] IV3000 dressing = AUD$1.30 each; EasI-V dressing = AUD$1.76 each.
[b] IV3000 dressing = AUD$1.30 each; EasI-V dressing = AUD$1.76 each; PHMB disc = AUD$4.50 each.

5. Conclusion

PHMB discs appear to be safe for infection prevention at CVC insertion sites. It would be feasible to assess the clinical efficacy of PHMB-impregnated discs for CVC infection prevention in a larger definitive trial. Innovative solutions are required to continue efforts to minimise infectious CVC-associated complications in the ICU.

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CRediT authorship contribution statement

India Pearse: Methodology, Investigation, Funding acquisition, Project administration, Investigation, Data curation, visualisation, Writing – original draft, Writing – review & editing. **Nicole Marsh:** Conceptualisation, Funding acquisition, Methodology, Writing – original draft, Writing – review & editing. **Claire M. Rickard:** Conceptualisation, Funding acquisition, Methodology, Writing – original draft, Writing – review & editing. **Amanda J. Ullman:** Conceptualisation, Funding acquisition, Methodology, Writing – original draft, Writing – review & editing. **Emily Larsen:** Methodology, Resources, Data curation, Writing – original draft, Writing – review & editing. **Anita Pelecanos:** Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Nicola McGuinness:** Investigation, Data curation, visualisation, Writing – original draft, Writing – review & editing. **Lacey Irvine:** Investigation, Data curation, Writing – original draft, Writing – review & editing. **Ivan L. Rapchuk:** Supervision, Writing – original draft, Writing – review & editing. **Marc Ziegenfuss:** Supervision, Writing – original draft, Writing – review & editing. **Amanda Corley:** Conceptualisation, Methodology, Funding acquisition, Supervision, Investigation, visualisation, Writing – original draft, Writing – review & editing.

Conflict of interest

None.

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