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Research paper

Central venous access device Securement and dressing effectiveness: The CASCADE pilot randomised controlled trial in the adult intensive care

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ABSTRACT

Introduction: Central venous access devices (CVADs) are a vital medical device for intensive care (ICU) patients; however, complications and failure are common, yet potentially prevented through effective dressings and securement.
Objectives/aims: The objective of this study was to test the feasibility of a randomised controlled trial (RCT) comparing standard care with three dressing and securement products to prevent CVAD failure. Secondary aims included comparing dressing and securement products on CVAD failure, microbial colonisation, and intervention costs.
Methods: A single-centre pilot RCT of ICU adult patients requiring CVADs for >24 h were randomised to four groups: (i) sutures plus chlorhexidine gluconate (CHG) dressing (standard care); (ii) standard care plus tissue adhesive (TA); (iii) two sutureless stabilisation devices (SSD) plus CHG dressing; (iv) sutures, CHG disc plus integrated securement dressing (ISD). Descriptive statistics assessed feasibility. Incidence rates (IRs) of CVAD failure were reported, with group differences compared using the Fisher exact and log-rank tests. Cox regression explored univariable risks for failure. A substudy examined bacterial colonisation of catheter tips, dressings, and skin. Cost estimates of the intervention were compared.
Results: A total of 121 participants were randomised. Study feasibility was established with no withdrawal and moderate staff acceptability; however, recruitment was low at 12%. Overall CVAD failure was seen in 14 of 114 (12%) CVADs (19 per 1000 catheter-days); highest in the SSD group (IR: 27.3 per 1000 catheter-days [95% confidence interval {CI}: 11.4–65.6]), followed by the standard care group (IR: 22.3

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per 1000 catheter-days [95% CI: 8.38–59.5]) and TA group (IR: 20.6 per 1000 catheter-days [95% CI: 6.66–64.0]), and lowest in the ISD group (IR: 8.8 per 1000 catheter-days [95% CI: 2.19–35.0]). The majority of complications (11/14, 79%) were suspected central line-associated bloodstream infection (CLABSI), of which only one was laboratory confirmed (standard care group). The cost per patient was lowest in the standard care group by an average difference of AUD $14.

Conclusion(s): A large multisite RCT examining forms of securement and dressing is feasible. ISD is the highest priority to test further as it had the lowest failure rate.

Trial registration: ACTRN12615000667516

Protocol: https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id = 368765

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1. Introduction

Central venous access devices (CVADs) are a vital medical device to facilitate the delivery of supportive and interventional medical therapies, including fluid and medication administration, haemodialysis, central venous pressure monitoring, and blood sampling in critically ill patients in intensive care units (ICUs).[1] Insertion of these devices poses significant procedural risk, and complications are common during current and subsequent CVAD use. A recent meta-analysis examining CVAD failure and complications in adult ICU patients demonstrated that 5% (95% confidence interval [CI]: 3–6%) of CVADs failed before the completion of therapy at a rate of 5.43 (4.43–6.43) per 1000 catheter-days.[2] Such complications can be mechanical (e.g., blockage, dislodgement, vein thrombosis, CVAD rupture) or infective (e.g., local or bloodstream infections).[2,3] These complications increase patient suffering, hospitalisation duration, mortality, and healthcare costs.[1,4,5]

Two key factors that can prevent CVAD complications are (i) securement – that CVADs are adequately secured to the skin to prevent dislodgment – and (ii) dressings – that the insertion site is covered to prevent infection.[6] Traditionally, CVADs were secured via sutures, under a simple polyurethane dressing. However, there is significant evidence of increased bloodstream infections and needlestick injury risks in randomised controlled trials (RCTs) comparing sutures with sutureless securement devices, although use persists because of concerns about equivalent securement efficacy.[7,8] Environmental protection is provided by sterile dressings; however, skin bacteria are the most common source of CVAD infections.[5,8] In the last decade, medication-impregnated dressings have been introduced to prevent such infections with high-quality evidence that chlorhexidine gluconate (CHG)–impregnated dressings (or discs) and reduce the risk of CVAD-related bloodstream infections (CRBSIs) compared with nonmedicated approaches (risk ratio: 0.60, 95% CI: 0.39–0.93; p = 0.02).[9,10]

Despite the traditional use of sutures to secure CVADs, critically ill patients have multiple risk factors of CVAD dislodgment and rupture, due to multiple, heavy infusion lines (causing drag) and, increasingly, light sedation and early mobilization.[11,12] Vein irritation from poor securement precipitates thrombosis and occlusion, with CVAD-associated thrombosis and occlusion observed in 10%[4–17] and 11%[4–22] of CVADs.[2] The scarcity of studies examining CVAD security warrants urgent attention and investigation.[10]

New alternative securement and dressing options that may be superior to traditional products in preventing complications are available, but these require testing for safety, efficacy, and cost-effectiveness. For example, sutureless stabilisation devices (SSDs) can be used instead of sutures, reducing suture-related infections, but the impact on other complications is less clear.[7] SSDs have large adhesive padded footplates with plastic CVAD-locking clasps which aim to reduce movement, kinking, and flow impedance and are used with polyurethane dressings. Integrated securement dressings (ISDs) are 'next-generation' polyurethane dressings with a tough fabric adhesive border and integrated catheter stabilisation device around the central polyurethane window and have been associated with improved dressing performance in small RCTs conducted on other patient/CVAD populations.[13–15] Tissue adhesive (TA) is medical-grade 'superglue' (cyanoacrylate) used as an alternative to sutures in both internal and external wounds.[16] TA also forms an occlusive healing environment and a physical barrier to microorganisms, with haemostatic properties to reduce ooze and haematomas, and preliminary evidence supports its use in some CVAD types.[13–15,17]

The ideal CVAD securement and dressing should (1) prevent accidental removal, micromotion, and pistoning; (2) block bacteria entering the wound; (3) have antimicrobial properties; (4) assist with haemostasis; (5) be comfortable for patients; (6) be easy for staff to use; and (7) be cost-effective.[11] Although many alternatives to sutures and polyurethane dressings exist, how these meet the aforementioned criteria is largely unknown, and high-quality RCTs are necessary to provide estimates of true effectiveness. To date, there is lack of high-quality evidence on the comparative efficacy of SSDs, ISDs, and TAs on CVADs for general ICU patients.[10]

2. Aim

The primary aim was to provide feasibility data for an efficacy RCT comparing standard care with three innovative dressing and securement methods (SSDs, ISDs, and TAs) for CVADs in adult ICU patients. The secondary aim was to compare the effect of dressing and securement products on (1) CVAD failure and complications (infection, occlusion, dislodgement, thrombosis, or breakage); (2) microbial colonisation of catheter tips, skin, and dressing; and, (3) healthcare costs.

3. Methods

3.1. Study design and setting

This single-site, four-armed, parallel group, superiority, pilot RCT had three experimental arms and one control arm. The trial was prospectively registered with the Australian Clinical Trial Registry (ACTRN12615000667516). The study site was a metropolitan, government-run, academic-affiliated, adult hospital in Australia with 640 beds. It has comprehensive critical care services and is an accredited level 1 trauma centre. The 28-bed ICU admits patients from all major specialties including medical, surgical, and spinal injuries, excepting burns and obstetric conditions. The ICU admits approximately 2300 patients per year, with a 1:1 registered nurse-to-patient ratio.

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3.2. Sample

Inclusion criteria were patients requiring nontunnelled CVADs (including jugular, femoral, and subclavian sites) to be inserted in the ICU, with a predicted dwell time of >24 h, and informed consent. Exclusion criteria were patients with peripherally inserted CVADs, dialysis catheters, or pulmonary artery catheters. Patients whose CVAD was to be inserted through diseased, burned, scarred, or hirsute skin; were allergic to any study product; or had previous study enrolment during the current admission were also excluded. The target sample size was 120 participants (30 per group), determined by pilot trial sample size recommendations to ensure accuracy of feasibility estimates including effect size.[18]

3.3. Intervention

Participants were randomised to four groups to receive CVAD securement and dressing by

A. Standard care: Sutures (Prolene suture [Polyamide 6 – REF 1663, Ethilon; Ethicon]) plus CHG dressing (Tegaderm CHG [REF 1658R/1659R; 3M]), the site's usual securement and dressing practice;

B. Standard care plus TA (TA group): (Prolene suture [Polyamide 6 – REF 1663, Ethilon; Ethicon), CHG dressing (Tegaderm CHG [REF 1658R/1659R; 3M]), plus TA (Histoacryl [REF 1050044; BBraun]);

C. SSD plus CHG dressing (SSD group): SSD (Statlock stabilisation device, CV Plus with Pigtail – REF CV0220]) plus CHG dressing (Tegaderm CHG [REF 1658R/1659R; 3M]);

D. Sutures, CHG disc plus ISD (ISD group): Sutures (Prolene suture [Polyamide 6 – REF 1663, Ethilon; Ethicon), CHG disc (Biopatch [REF 44150; Ethicon]) plus ISD (SorbaView SHIELD [REF SV733UDT-6; Centurion Medical Products]) (Fig. 1).

3.4. Outcome

The primary outcome was the feasibility of an efficacy RCT including eligibility (percentage of screened patients who were eligible); recruitment (percentage of eligible patients who consented); attrition and retention (percentage of randomised participants lost to follow-up or who withdrew consent); protocol adherence (percentage of randomised participants who received the allocated intervention); missing data (percentage of missing data for the primary endpoint); intervention acceptability using numeric rating scale (i.e., clinician and participant satisfaction in a 10-point scale [0 = completely dissatisfied, 10 = completely satisfied] and ease of study product application using a 10-point scale [0 = very difficult, 10 = very easy]); and effect sizes to inform future sample size estimates.[19]

The other primary outcome was CVAD failure (a composite measure of any reason for cessation of function before completion of treatment) because of

- CLABSI: a laboratory-confirmed bloodstream infection (LCBSI) that is not secondary to an infection at another body site (CDC National Healthcare Safety Network [NHSN] criteria; excludes mucosal barrier injury LCBSI), with CVAD in place for >2 calendar

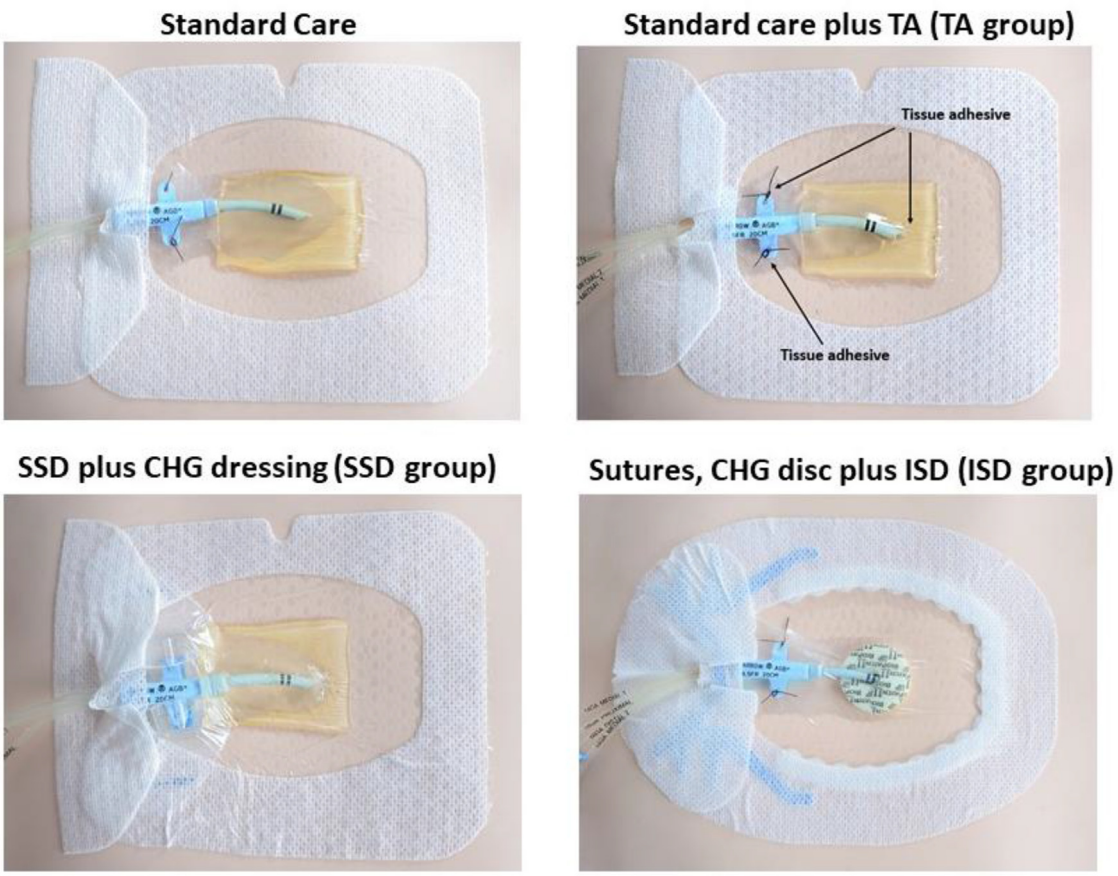

Fig. 1. Dressing and securement methods for each study group. Standard care: Sutures (Prolene suture) plus CHG dressing. Standard care plus TA (TA group): Prolene suture, CHG dressing plus TA. SSD plus CHG dressing (SSD group): SSD (Statlock stabilisation device) plus CHG dressing. Sutures, CHG disc plus ISD (ISD group): Sutures (Prolene suture, CHG disc (Biopatch plus ISD). TA = tissue adhesive; SSD = sutureless stabilisation device; CHG = chlorhexidine gluconate; ISD = integrated securement dressing.

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days when all elements of LCBSI were first present together,[20] determined by a blinded infectious disease specialist.
- Suspected central line-associated bloodstream infection (CLABSI): suspected CVAD-related infection diagnosed by a treating clinician that resulted in CVAD removal.[2,21]
- Local infection: purulent phlebitis confirmed with a positive CVAD semiquantitative tip culture, but with negative or no blood culture.[20]
- Dislodgement: partial dislodgement – change in external CVAD length from hub to skin, as measured by marking closest to the hub, or CVAD removal because the tip is no longer in the superior vena cava (diagnosed by X-ray/leakage from the site on injection); complete dislodgement – CVAD body completely leaves the vein.[8]
- Occlusion: partial occlusion – ≥1 lumens cannot be flushed and/or aspirated; complete occlusion – all lumens cannot be flushed and/or aspirated.[22]
- Thrombosis: development of thrombosed vessel (partial or complete) at the CVAD site diagnosed on ultrasound as requested by the treating clinician for suspected thrombosis.[23]
- CVAD breakage: visible split in CVAD material diagnosed by leakage or radiographic evidence of extravasation from a portion of the CVAD into surrounding tissue.[24]

Secondary outcomes were CVAD complications during treatment (whether resolvable or causing CVAD removal) including infection (local and CLABSI), dislodgement (partial, complete), occlusion, thrombosis, and breakage.

- CLABSI was further categorised as CVAD-related bloodstream infection (laboratory-confirmed with matched organism from blood and catheter tip culture) or not.[20]
- All bloodstream infections: positive blood cultures meeting the CDC NHSN criteria for LCBSI.[20]
- Primary bloodstream infections: LCBSIs (as aforementioned) that are not related to an infection at another site.[20]
- Securement dressing failure: clinically indicated securement dressing replacement less than seven days from application because of loose, missing, bloodstained, diaphoresis, or secretion-soaked dressings.[8]
- CVAD and first securement dressing dwell time: hours from insertion/application until removal.
- Safety endpoints: skin rash, skin tears, blisters, pruritis, significant haematoma and bruising, and local or systemic allergic reaction.
- Cost estimates of time to apply, secure, and change dressings and related costs.
- Microbiological laboratory examination of bacterial colonisation of catheter tips, dressing products, and skin swabs from under trial dressings.
- We had planned to test tensile strength of removed CVADs to consider any interaction with TA, but this was not possible within the resources available.

3.5. Recruitment and randomisation

A research nurse (ReN) screened the electronic medical records of all ICU admissions for potential participants daily, obtained written informed consent from participants or their substituted decision-maker, and accessed the randomised allocation. Randomisation was conducted via a centralised Web-based service (https://www151.griffith.edu.au/) using a 1:1:1:1 ratio with randomly varied block sizes of four and eight, stratified by site of insertion: jugular or other, which ensured allocation concealment until study entry. CVAD dressings prevented the ability to blind clinicians and patients. Blinded scientists in the hospital and research laboratories performed all cultures, a blinded radiologist defined thrombotic outcomes, and a blinded infectious diseases specialist confirmed all cases of CLABSIs.

3.6. CVAD procedures

This was a pragmatic RCT to maximise generalisability; therefore, ReN involvement in CVAD insertion, application of study products, or CVAD care was limited. ReNs provided initial education and demonstration of the application of study products and CVAD care for the medical and nursing staff and were available for questions during the study. The inserting clinician (specialist medical consultant, or registrar enrolled in a specialist training program) typically applied the first study product, and ICU nurses undertook subsequent replacements if needed. Study products were in preprepared packs and ReNs liaised with the inserting clinicians to ensure familiarity with the study products. CVAD inserters used a large sterile drape and gown and prepared the skin with 2% CHG in 70% isopropyl alcohol. The CVAD inserter selected a site (e.g., jugular, subclavian, and femoral) by ultrasound for insertion and CVAD type (e.g. lumens) based on clinical judgement of participant needs (Arrow^{+}ard Blue PLUS™ Antimicrobial/polyurethane catheter: 20-cm triple and quadruple lumens were routinely used) and then applied the allocated products. The CVAD tip location was confirmed by X-ray for jugular and subclavian insertions. CVAD insertion was conducted as per the Australian and New Zealand Intensive Care Society guidelines.[25]

3.7. Data collection

The ReNs used REDCap (Research Electronic Data CAPture, Vanderbilt) to collect demographic (age, sex, Acute Physiology and Chronic Health Evaluation [APACHE] 2 and 3 scores, weight, length of ICU stay), clinical (diagnosis, comorbidities, skin integrity, skin colour, white blood cell count, existing infection, existing wound/drain/tracheostomy/stoma, patients level of consciousness, ability to mobilise, and sweatiness), and CVAD characteristics (CVAD type, insertion side, subsequent device, inserter, previous experience with the product, the number of lumens, and multiple insertion attempts) and outcome data. The ReNs asked inserters to rate ease of study product application using a 10-point scale (0 = very difficult, 10 = very easy) and recorded the number of times they had previously used the study product. The ReN checked participants daily during the weekdays to inspect the CVAD and dressing securement products for protocol adherence. Participants were assessed for study outcomes. Product replacements/reinforcements, including tape, and the reasons for these were recorded.

Data were collected at CVAD removal on the reason for removal including any complications, dwell time, and infusates. Final data included microbiological data, ICU length of stay, and mortality at 48 h ss after CVL removal. Clinical staff ordered blood, CVAD tip, and other cultures if participants were suspected of a CVAD infection (usual practice). Where possible, on the day of removal, the ReN asked the participant about satisfaction with the study products on a 10-point scale (0 = completely dissatisfied, 10 = completely satisfied).

3.8. Microbiological method

Microbiological testing was conducted in one laboratory external to the study site. The skin swab, catheter tip, CHG dressing/disc, and SSD swab samples were purposively sampled and

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aseptically collected at the time of removal and evaluated using next-generation sequencing (MiSeq; Illumina) for 16 participants (four per group). Two centimetres of skin surface area around the insertion site was swabbed using a 'dry swab' moistened with sterile saline water. A twisting back/forth motion 10 times was used to swab the area. Skin swab samples were placed in a glycerol stock. Swabs and collected catheter tips were cultured on blood agar plates and incubated at 37 °C for 24 h, and then bacterial colony counting was conducted. The CHG dressings and disc were aseptically removed from the transport container and placed onto horse blood agar (HBA) with light pressure for 10 s. The SSDs were swabbed with 0.9% saline-moistened sterile swabs and streaked across the entire HBA plate. These were reincubated for 72 h for slow-growing species. Species were identified morphologically, biochemically, and genetically through DNA sequencing of representative colonies if necessary. Samples were characterised through identification of microbial species and the colony-forming units (CFUs).

3.9. Data analysis

Feasibility outcomes were assessed using descriptive statistics. All randomised participants were analysed on an intention-to-treat basis. Baseline group comparisons were described across demographic, clinical, and device characteristics. Incidence rates of CVAD and dressing failure per 1000 device-days or 100 devices were reported to summarise treatment impact, with group differences tested using the Fisher exact and log-rank tests. Kaplan–Meier survival curves were drawn to compare CVAD failure, complication, and first dressing duration over time.

Secondary endpoints were compared between groups using parametric/nonparametric techniques as appropriate. Cox regressions tested the effect of baseline variables (e.g., insertion site, antimicrobial catheters, delirium) on failure. A P-value < 0.05 was considered statistically significant. Missing values were not imputed.

Total per-participant and per-group costs were calculated as the cumulative costs of initial product application and any replacements needed. The cost of the initial application included all materials and consumables in addition to labour cost for a senior registrar doctor (including 25% on-cost) using an average time of three insertions measured during the study (convenience sample). The cost of dressing changes included materials and consumables in addition to labour cost for a registered nurse (including 25% on-cost) using an average time of three dressing changes measured during the study (convenience sample). To allow for the different rate of dressing changes during the study between the groups (calculated as the total number of dressing changes divided by the number of participants, per group), the calculated cost of one dressing change was multiplied with this group-specific ratio. Cost estimates of the intervention product and staffing costs were compared between study groups. There were 12 participants selected, ensuring equal distribution across study arms. The procedural time associated with CVAD product application at insertion and dressing changes was collected by the ReN using a stopwatch. Detailed costings of equipment/materials were calculated through a review of current site hospital costings (2018), and staff costings were calculated using current Australian state award wages.[26] Costs were reported in Australian Dollars (2018).

For the microbiology testing, microbial species were identified culturally, and the predominant species described for each collection component (catheter tip, swab, CHG dressing, SSD, CHG disk). Microbial load was measured as CFUs per specimen, categorised in the standard ranges of 0, 1–14, 15–29, 30–300, and > 301 (including too numerous to count [TNTC])[27]. Counts below 15 CFUs were considered possible contamination except for counts on catheter tips which were considered colonisation.[27]

4. Results

4.1. Participant and catheter characteristics

The baseline characteristics are described in Table 1. There were 31 (26%) participants in the standard care group, 29 (24%) in the TA group, 30 (25%) in the SSD group, and 31 (26%) in the ISD group. A total of 736 catheter-days were studied, with an average of 6.4 days dwell time per device. Participants were of high acuity; around 30% had four or more comorbidities, most were unable to mobilise (64%) at CVL removal, and half were confused, agitated, or drowsy (54%). Most CVADs were inserted in an internal jugular vein (70%) and had quadruple lumens (83%). There were some imbalances (>10%) of baseline variables between groups. Standard care participants were more likely to be male and to have a trauma diagnosis and a quadruple lumen CVAD than participants in other groups. The SSD group had considerably more surgical emergency patients than other groups. The ISD group had the greatest incidence of mechanical ventilation (97%). The ISD and SSD groups had more participants with comorbidities than the standard care or TA group. TA and ISD groups had the greatest proportion of junior registrar–inserted CVADs. TA participants were least likely to have 'good skin' and most likely to have a medical diagnosis.

The trial recruited from February 2016 until July 2018 during which time 1141 patients were assessed for eligibility, of which 976 (86%) met inclusion criteria (see Fig. 2). Thirty-three refused participation, and 121 ICU participants were recruited (12% of those assessed for eligibility) and randomised (Fig. 2); 115 participants received the intervention and included in the analysis (95% of those randomised) with the primary outcome data from 114 participants (99% of those who received the intervention) analysed. Retention was 100% (no attrition/loss to follow-up). Six participants (5%) were excluded after randomisation because of not meeting the inclusion criteria (five did not receive a nontunnelled CVAD and one had previously participated).

Difficulties in recruitment included that CVADs were frequently inserted outside office hours preventing study inclusion, emergent CVAD insertion precluding prior consent, and failure to capture due to the ReN not being contacted before CVAD insertion. There were three participants (3%) with protocol deviations in the standard care group, three participants in the TA group, five participants in the SSD group, and three ISD participants in 912 study days (2% of study days). Please see the details of protocol deviations in the Supplementary Material 1 table.

Overall, acceptability of the interventions was similar across study groups (Table 2). The previous experience of doctors with the intervention products were highest in the standard care group (27; 96%) followed by the SSD group (19; 83%), TA group (6; 25%), and ISD group (4; 14%). The ISD group had the lowest (worst) scores in the 'ease of dressing applications', 'participant satisfaction', and 'nurse confidence' categories, and the standard care group had the highest (best) scores for 'participant satisfaction', 'nurse satisfaction', and nurse confidence'. The TA group had the lowest nurse satisfaction with dressing removal scores.

4.2. CVAD failure and complications

The overall incidence rate of catheter failure was 12% (14/114) of CVADs [19.0 (11.3–32.1) per 1000 catheter-days]. The incidence was highest in the SSD group at 27.3 (11.4–65.6) per 1000 catheter-days and lowest in the ISD group at 8.76 (2.19–35.0) (Table 2).

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Table 1
Participant characteristics by study group at baseline.

Characteristic	*n*	Standard care	TA	SSD	ISD	**Total**
Group size[a]	121	31 (26)	29 (24)	30 (25)	31 (26)	121 (100)
Age (years)[b]	115	50.7 (20.3)	53.1 (14.9)	53.4 (18.3)	57.1 (15.3)	53.6 (17.3)
APACHE II score[b]	120	20 (7)	22 (8)	20 (7)	19 (6)	20 (7)
APACHE III score[b]	120	65 (26)	76 (33)	71 (30)	64 (25)	69 (29)
Length of stay in the ICU (days)[c]	120	11 (10)	11 (7)	10 (15)	10 (10)	11 (10)
Weight (kg)[b] (n = 84)	115	84 (22)	79 (23)	87 (22)	86 (25)	84 (23)
Males	115	24 (80)	17 (65)	16 (55)	21 (70)	78 (68)
Diagnosis	115					
Medical: other		4 (13)	10 (38)	9 (31)	9 (30)	32 (28)
Trauma		10 (33)	5 (19)	4 (14)	8 (27)	27 (23)
Medical: sepsis		8 (27)	3 (12)	3 (10)	2 (7)	16 (14)
Medical: respiratory		4 (13)	3 (12)	2 (7)	5 (17)	14 (12)
Surgical emergency		2 (7)	1 (4)	7 (24)	3 (10)	13 (11)
Other		2 (7)	4 (15)	4 (14)	3 (10)	13 (11)
Comorbidities	115					
None		8 (27)	7 (27)	6 (21)	5 (17)	26 (23)
One, two, or three		12 (40)	11 (42)	14 (48)	15 (50)	52 (45)
Four or more		10 (33)	8 (31)	9 (31)	10 (33)	37 (32)
Skin integrity	114					
Good		14 (48)	7 (27)	11 (38)	12 (40)	44 (39)
Fair		11 (38)	15 (58)	10 (34)	13 (43)	49 (43)
Poor		4 (14)	4 (15)	8 (28)	5 (17)	21 (18)
Skin colour	114					
Pale white		4 (14)	4 (15)	8 (28)	2 (7)	18 (16)
White		23 (79)	16 (62)	12 (41)	22 (73)	73 (64)
Light brown		2^{7}	3^{12}	2^{7}	2^{7}	9^{8}
Moderate brown		0 (0)	1^{4}	2^{7}	2^{7}	5^{4}
Dark/deeply pigmented brown		0 (0)	2^{8}	5^{17}	2^{7}	9^{8}
Mechanically ventilated		23 (77)	22 (85)	25 (86)	29 (97)	99 (86)
WBC < 1.0×10^{9}	115	4^{13}	2^{8}	3^{10}	5^{17}	14^{12}
Blood cultures taken <48 h ss prior	115	23 (77)	9^{35}	20 (69)	19 (63)	71 (62)
Infection (any)	115	5^{33}	5 (36)	4^{24}	4^{27}	18^{30}
Wound present	115	13 (43)	12 (46)	15 (52)	18 (60)	58 (50)
Drain present	115	7^{23}	5^{19}	4^{14}	10^{33}	26^{23}
Tracheostomy present	115	2^{7}	1^{4}	3^{10}	1^{3}	7^{6}
Stoma present	115	3^{10}	2^{8}	3^{10}	2^{7}	10^{9}
Treatment characteristics at baseline						
CVAD type	115					
Internal jugular		22 (73)	18 (69)	18 (62)	22 (73)	80 (70)
Femoral		2^{7}	3^{12}	6^{21}	3^{10}	14^{12}
Subclavian		6^{20}	5^{19}	5^{17}	5^{17}	21^{18}
Insertion side: right	115	17 (57)	16 (62)	13 (45)	23 (77)	69 (60)
Inserted by	114					
Senior registrar		15 (50)	13 (50)	24 (83)	14 (48)	66 (58)
Junior registrar		10^{33}	12 (46)	4^{14}	14 (48)	40^{35}
Other		5^{17}	1^{4}	1^{3}	1^{3}	8^{7}
Number of lumens	115					
Triple		3^{10}	3^{12}	5^{17}	7^{23}	18^{16}
Quad		27 (90)	23 (88)	23 (79)	23 (77)	96 (83)
Quin		0 (0)	0 (0)	1^{3}	0 (0)	1^{1}
Multiple insertion attempts	112	6^{21}	3^{12}	5^{17}	5^{17}	19^{17}

mod = moderate; pigm = pigmented; dx = dressing.
[a] Frequencies and row percentages shown.
[b] mean (standard deviation) shown; frequencies and column percentages shown, unless otherwise noted.
[c] median (interquartile range); CVAD = central venous access device; standard care group = control with Prolene suture plus CHG dressing; TA: tissue adhesive; SSD = sutureless securement device; ISD = integrated securement device.

These rates were not statistically different between any experimental group and the control group on log-rank testing (p = 0.26–0.92) or on the Kaplan–Meier curves (Supplementary Material 2). The majority of failures (11/14; 61%) were suspected CLABSI, but only one of these was laboratory-confirmed CLABSI. Skin reactions were not statistically significant between groups, although the SSD group had the most reactions (two skin rashes, one skin tear, one bruising, one pruritis, and one local allergic reaction) followed by the ISD group (two skin rashes, one pruritis, and one local allergic reactions). There was one skin tear in the standard care group and two skin rashes in the TA group. On univariable regression, the hazard ratio of CVAD failure was 0.89 (0.20–3.99) for the TA group, 1.23 (0.33–4.59) for the SSD group, and 0.35 (0.06–1.91) for the ISD group, with a darker skin colour being the only variable significantly associated with failure (hazard ratio: 1.52 [1.03–2.22]) (Supplementary Material 3).

4.3. Microbiology

The dwell time of the catheters sampled for microbiology testing ranged from 6 to 18 days with those specimens colonised >301 CFU having a dwell time between six and eight days

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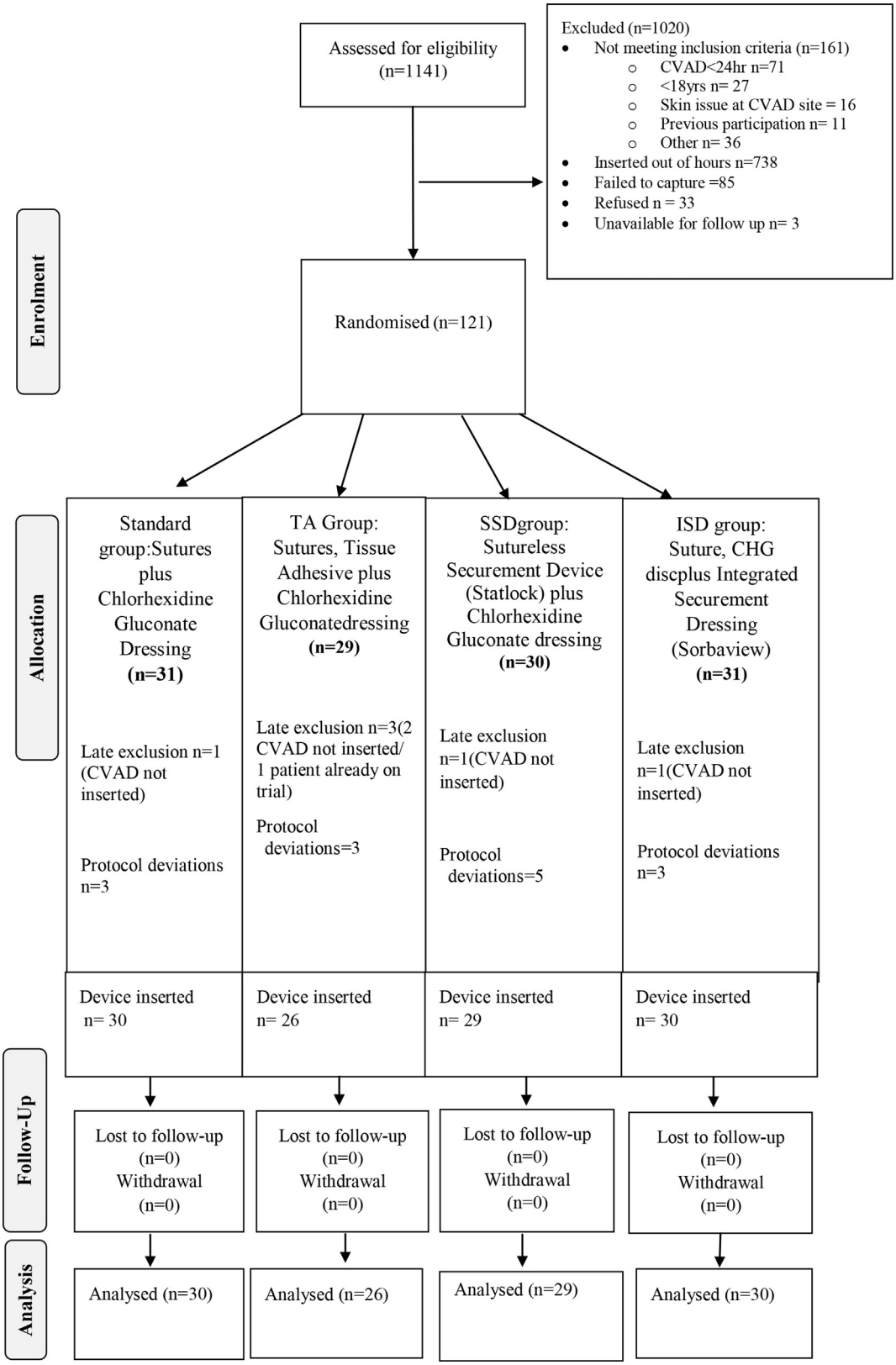

Fig. 2. CONSORT flow chart. CHG = chlorhexidine gluconate; standard care = control with Prolene suture plus CHG dressing; TA = tissue adhesive; SSD = sutureless securement device; ISD = integrated securement device; CVAD = central venous access device. Please note: The detailed description of the protocol deviations are listed in Supplementary Material 1.

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Table 2
CVAD failure and complications.

Characteristic	N	Standard care	TA	SSD	ISD	p-values
CVAD failure (%)[a]	114	4 (13)	3 (12)	5 (18)	2 (7)	0.641[a]
Dwell time[b] (days)	115	6.0 (2.2)	5.6 (3.4)	6.3 (4.3)	7.6 (3.7)	
Device-days	115	179	145	183	228	
Incidence rate (95% CI)[c]		22.3 (8.38–59.5)	20.6 (6.66–64.0)	27.3 (11.4–65.6)	8.8 (2.19–35.0)	
Incidence rate ratio (95% CI)[c]		ref.	0.92 (0.14–5.47)	1.22 (0.26–6.17)	0.39 (0.04–2.74)	
p-value of log-rank test		ref.	0.924	0.866	0.255	0.460
Primary outcome						
Reasons of CVAD failure[d]	18					
Suspected CLABSI		3	1	5	2	
Partial occlusion		1	1	0	0	
Dislodgement		0	1	0	0	
Thrombosis		0	1	0	0	
Local skin breakdown		0	0	0	0	
Other[g]		1	0	1	0	
Laboratory-confirmed CLABSI		1	0	0	0	
Secondary outcomes						
Skin reactions at removal[e]	114					
Rash		0	1	2	0	
Residue		0	1	0	0	
Pruritis		0	0	1	0	
Dressing/securement failure[f]	111	13 (43)	10 (42)	11 (41)	17 (57)	
Complications during treatment						
CVAD complications						
Local infection (including suspected)	114	0	0	0	0	
CLABSI (including suspected)	115	5	1	6	2	
Dislodgment (including partial)	114	0	1	0	0	
Occlusion (including partial)	115	2	1	0	2	
Thrombosis	115	0	1	0	0	
Breakage	114	0	0	0	0	
Serious adverse events	115					
Death		3	7	4	1	
Positive blood culture		1	0	0	0	
Other[g]		1	0	1	0	
Feasibility: comparison of acceptance of dressing interventions by clinicians						
Ease of dressing application (0–10)[f,h]	115	7.1 (3.6)	6.5 (3.7)	7.8 (2.3)	6.0 (4.0)	
Participant satisfaction with product (0–10)[f,h]	115	10.0 (0.0)	10.0 (0.0)	10.0 (6.0)	5.0 (4.0)	
Nurse satisfaction with removal (0–10) [f,i]	115	9.0 (2.0)	6.5 (4.0)	7.0 (4.0)	9.0 (7.0)	
Nurse confidence in product (0–10) [f,i]	115	8.0 (4.0)	5.0 (2.0)	7.5 (4.0)	4.5 (3.5)	

Frequencies and column percentages shown, unless otherwise noted.
Standard care = control with Prolene suture plus CHG dressing.
TA = tissue adhesive.
SSD = sutureless securement device.
ISD = integrated securement device.
CVAD = central venous access device.
BSI = bloodstream infection.
CLABSI = central line-associated bloodstream infection.
CI = confidence interval.
Frequencies and row percentages shown.
[a] Fisher exact test.
[b] Mean (standard deviation) shown.
[c] Per 1000 device-days.
[d] May have one or more outcomes per catheter.
[e] Defined as replacement before seven days for loose, soiled, or missing dressings.
[f] Median (interquartile) shown.
[g] Other complications at removal included: allergic reaction to chlorhexidine in the SSD group; suspected air embolus on removal of CVL in the standard care group.
[h] 0 = worst 10 = best.
[i] 0 = very difficult,10 = very easy;.

(Supplementary Material 4). Microbiological analysis indicated that one of 16 (6%) catheter tips from the TA group was colonised (CFUs >15).

For CVAD site swabs, there were three (30%) samples colonised with >15 CFUs. Two samples were colonised with 15–29 CFUs, and one sample with >300 CFUs. Sixty percent of the 10 CHG dressing samples were colonised, with bacteria isolated on all samples in the SSD group (3/3). Twenty-five percent (1/4) of the CHG disc (ISD group) were colonised with >15 CFUs. No SorbaView dressings (ISD group) were tested for microbiology analysis as the CHG component was the consistent part tested between all four study arms. One (25%) Statlock sample (SSD group) had 30–300 CFUs. Overall, microbial colonisation of the products was evident across study arms.

4.4. Cost estimate

The cost estimate per patient of standard care was lowest (A$70) followed by the SSD group (A$81), the ISD group (A$90), and TA group (A$95) (Table 3). On average, the TA group required the most time on initial application (9.1 min), and the SSD group required the most time on dressing changes (16.3 min). The ISD group had the

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Table 3
Cost estimate of dressing interventions per patient.

Interventions	Study group			
	Standard care (n = 3)	TA (n = 3)	SSD (n = 3)	ISD (n = 3)
Initial application				
Materials and consumables	$ 39.18	$ 50.98	$ 40.20	$ 43.18
Per minute labour rate[a]	$ 1.25	$ 1.25	$ 1.25	$ 1.25
Insertion time (minutes) average	5.8	9.1	6.7	6.9
Total per patient	$ 46.43	$ 62.31	$ 48.60	$ 51.76
Dressing changes during trial				
Average number of changes per patient[c]	1.27	1.00	1.00	1.53
Materials and consumables	$ 12.92	$ 24.88	$ 19.87	$ 16.92
Per minute labour rate[b]	$ 0.79	$ 0.79	$ 0.79	$ 0.79
Change time (minutes) average	7.6	10.2	16.3	10.5
Total per patient	$ 23.99	$ 32.95	$ 32.78	$ 38.69
Grand total	**$70.00**	**$95.00**	**$81.00**	**$90.00**

[a] Senior registrar = average hourly rate $60/hr.
[b] Registered nurse = average hourly rate $38/hour.
[c] Derived from the number of changes divided by study sample size. Standard care = control with Prolene suture plus CHG dressing; TA = tissue adhesive; SSD= sutureless securement device; ISD = integrated securement device.

highest number of changes per participant (1.53) followed by the standard care group (1.27).

5. Discussion

This is the first pilot RCT examining the feasibility and effectiveness of usual CVAD securement and dressing, in comparison with three innovative methods in general ICU adult patients, and the first in any setting to compare the effectiveness of CHG dressing versus CHG disc with an ISD dressing. Feasibility outcomes were positive overall, with excellent retention, attrition, protocol adherence, and staff acceptability. Of all randomised patients, only one patient had some missing outcome data not included in the final analysis. Recruitment was challenging within the current protocol (i.e., CVAD insertion in ICU, ReN availability), with 122 participants recruited over 29 months. It is predicted that these challenges would be improved within a future efficacy trial, by including multiple sites, with increased research staffing availability and recruitment of CVADs inserted perioperatively, thereby increasing recruitment rates. In addition, deferred or waived consent as used in other ICU trials could increase the recruitment rates.[28] Protocol adherence could be enhanced with closer supervision by research team members and project champions. A future two-group superiority RCT would need at least 389 participants per group to test a hypothesis of 13% (standard care) versus 7% (ISD) CVAD failure with an alpha of 0.8.

Although the ISD group had the lowest incidence rate of catheter failure, in comparison with previous trials, the ISD group also had the lowest scores in the 'ease of dressing applications', 'participant satisfaction', and 'nurse confidence' categories.[13–15] Clinicians who applied the study products were least familiar with two components of this treatment arm and, given the slow recruitment, had little chance to become familiar with it, both of which may have contributed to these lower scores. There was some negative feedback about this group because clinicians were unable to visualise the CVAD insertion site with the CHG disc in situ. In addition, if the dressing required replacement, some nurses reported difficulty changing the dressing because of the CHG disc adhering to the ISD dressing and surrounding the CVAD. A future trial requires additional training and exposure to dressing techniques for clinicians to increase acceptability.

The overall incidence of CVAD failure was 12% (14/114), with most cases (11/14; 79%) due to suspected CLABSI. Although these rates are higher than previously reported, they should not be compared with current literature as evidence because this is a pilot study. Similarly, the trial sample size does not allow statistical testing of hypotheses, and CVAD failure was highest in the SSD group and lowest in the ISD group, suggesting that ISD followed by TA and then SSD would be the priorities for testing in future trials. Removal due to suspected infection was more common than reported in a meta-analysis of CVAD outcomes in similar populations (4% [3–6]),[2] is consistent with a recent observational study and a systematic review, and warrants further investigation because many lines may be unnecessarily removed.[2,21] In this study, only one of the suspected CLABSIs was in fact confirmed, thus giving support to consideration of a 'watch and monitor' strategy in the effort to reduce unwarranted CVAD removal with the potential need for insertion of a new devise. Previous studies[29–31] investigated the effects of immediate, deferred, or no removal of CVADs suspected of infection and found no difference in morbidity or mortality between groups (antibiotic treatment and frequent monitoring were used).

There were few noninfectious complications (two partial occlusions, one dislodgement, and one thrombosis) which due to the pilot design cannot be tested for differences between groups. Only one dislodgment occurred, demonstrating the effectiveness of securement with both sutures and SSD methods which appeared equally effective in this trial. A similar trial by Rickard et al.[11] demonstrated substantially fewer dislodgements when sutures were added to TA plus a simple polyurethane dressing.

The SSD group and ISD group had the most CVAD-associated skin impairment, most likely due to strong adhesives used in these products.[32,33] Application of skin barrier solutions was not a routine practice at this site, but such products are strongly recommended before dressing application in the Infusion Therapy Standards of Practice as they have demonstrated ability to prevent erythema and skin stripping after adhesive removal.[32,34,35]

The microbiology analyses showed significant colonisation in some patients under the CHG dressing as well as the CHG disc. This is concerning as the CHG products are designed to suppress the growth of such colonisation. The presence of CHG-resistant bacteria was also shown in a previous microbiology study in which CHG-resistant genes were highly prevalent on hospital patients' skin.[36] Bacterial growth was predominant with common skin bacteria although there was one *Staphylococcus aureus*–positive specimen in the ISD group.

Standard care was the cheapest intervention studied. We focussed on a cost estimate and did not account for the cost of

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complications which was beyond the scope of this study. With this costing and until further evidence from future RCTs, the standard care approach is the most cost-effective.

Although the study provided valuable information, there are several limitations. The study was carried out at a single facility, limiting generalisability to other populations and clinical settings. As a pilot study, despite randomisation, there were some imbalanced risk factors between groups, and the sample size was inadequate to test statistical hypotheses. Participants, clinicians, and research staff were not blinded to the study interventions; however, it is unlikely that this influenced the study outcomes. Importantly, the statistician, infectious disease physicians, and radiologists were blinded to intervention, improving study validity. Despite these limitations, this study demonstrated the safety and feasibility of all study interventions and processes.

6. Conclusions

The overall catheter failure rate continues to be of concern from both a patient impact and institutional expense perspective, and new trials are urgently needed. A large multisite RCT examining the four forms of securement and dressings is feasible. Investigation of ISD would be the highest priority to test further as it had the lowest failure rate of the four arms.

Ethical approval

Ethical approval was granted from the hospital and university human research and ethics committees (HREC/13/QRBW/454, GU Ref No: NRS/10/14/HREC). Informed consent was gained from all study participants (patient or substitute decision-maker), before study commencement. All deidentified data were entered via REDCap with password protection. Data will be securely retained for five years.

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Authorship

All authors have made substantial contributions to all of the following: (1) the conception and design of the study, acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; (3) final approval of the version to be submitted.

Contributions

M.L.M., A.J.U., and C.M.R. conceptualised the study, designed the data collection instruments, drafted the initial manuscript, and reviewed and revised the final manuscript. M.C.D. and M.M.P. performed the data collection. M.M.T. drafted the initial manuscript and reviewed and revised the final manuscript. M.G.M. carried out the analyses and reviewed and revised the manuscript. L.Z. and M.M.B. carried out the microbiology analyses and reviewed and revised the manuscript. E.G.P. provided clinical expertise in the design of the data collection instrument and reviewed and revised the final manuscript. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.aucc.2019.10.002.

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