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Securing All intraVenous devices Effectively in hospitalised patients - The SAVE Trial: study protocol for a multi-centre, randomised controlled trial.

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Title

Securing All intraVenous devices Effectively in hospitalised patients - The SAVE Trial: study protocol for a multi-centre, randomised controlled trial.

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ABSTRACT

Introduction: Over 70% of all hospital admissions have a peripheral intravenous device (PIV) inserted, however the failure rate of PIVs is unacceptably high, with up to 69% of these devices failing before treatment is complete. Failure can be due to dislodgement, phlebitis, occlusion/infiltration, and/or infection. This results in interrupted medical therapy; painful phlebitis and reinsertions; increased hospital length of stay, morbidity and mortality from infections; and wasted medical/nursing time. Appropriate PIV dressing and securement may prevent many cases of PIV failure but little comparative data exists regarding the efficacy of various PIV dressing and securement methods. This trial will investigate the clinical- and cost-effectiveness of four methods of PIV dressing and securement in preventing PIV failure.

Methods and Analysis: A multi-centre, parallel-group, superiority randomised controlled trial with four arms: three experimental groups (tissue adhesive; bordered polyurethane dressing; sutureless securement device) and one control (standard polyurethane dressing) is planned. There will be a three-year recruitment of 1708 adult patients, with allocation concealment until randomisation by a centralised web-based service. The primary outcome is PIV failure which includes any of: dislodgement, occlusion/infiltration, phlebitis and infection. Secondary outcomes include: types of PIV failure; PIV dwell time; costs; device colonisation; skin colonisation; patient and staff satisfaction. Relative incidence rates of device failure per 100 devices and per 1,000 device days with 95% confidence intervals will summarise the impact of each dressing, and test differences between groups. Kaplan-Meier survival curves (with log rank Mantel-Cox test) will compare device failure over time. P-values of <0.05 will be considered significant. Secondary endpoints will be compared between groups using parametric or nonparametric techniques appropriate to level of measurement.

Ethics and dissemination: Ethical approval has been received from Queensland Health (HREC/11/QRCH/152) and Griffith University (NRS/46/11/HREC). Results will be published according to the CONSORT statement and presented at relevant conferences.

Trial Registration: Australian New Zealand Clinical Trial Registry ACTRN 12611000769987.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first large scale, independent multi-centre randomised controlled trial to investigate the efficacy and cost-effectiveness of PIV dressing and securement methods to prevent PIV failure.
- The trial examines a novel Tissue Adhesive securement method for the first time in PIVs.
- This is a pragmatic trial, with PIVs inserted and cared for by general staff in two adult hospitals, not specialist teams or researchers.
- Microbiology endpoints will be analysed by blinded scientists, and infection outcomes assigned by a blinded infectious disease specialist outcome assessor.
- It will not be possible to blind the dressing and securement intervention/control from clinical staff, patients or research nurses.
- Patients with existing skin problems, severe diaphoresis or frail skin are excluded from the study so results will not be generalisable to these groups

INTRODUCTION

Peripheral intravenous devices (PIVs) are the most commonly used medical device world-wide: almost all hospital patients need one or more to receive intravenous treatment.[1-2] Failure rates of these devices are unacceptably high, affecting up to 69% of patients receiving therapy.[3-7] Of these, 10% simply fall out, despite having a dressing in place, with patients then unable to receive treatment.[5] Other PIVs become painful or occluded and must also be replaced. Such failure rates for an essential device are unacceptable and indicate that current dressings and securement methods are inadequate, with much failure potentially preventable with improved effective dressing and securement.

Intravenous devices

About 90% of all vascular catheters are peripheral PIVs.[8] Approximately 330 million PIVs are sold in the United States of America (USA) alone each year.[9] The external component of PIVs require securement to the skin, with dressings and other securements used to ensure PIVs do not dislodge and fall out, or move out of the vein and into surrounding tissue. Effective securement also minimises PIV micro-motion within the vessel, which irritates the vein wall, causing inflammation presenting as pain, swelling and PIV occlusion/infiltration.[6, 10] Micro-motion may also encourage skin bacteria to enter the PIV wound, causing infection risk.

PIV failure

PIV failure occurs when the PIV can no longer be used for treatment. Failure can be mechanical (dislodgement, occlusion, infiltration), vascular (phlebitis), or infectious (localised or bloodstream infections). PIV failure is an important detrimental patient outcome that causes: (a) interruptions to medical treatment and compromised patient safety from lost vascular access; (b) painful phlebitis lasting for days or weeks at the PIV site, even after removal; (c) potentially increased hospital length of stay and mortality from PIV-associated bloodstream infection; (d) additional needlesticks for replacement PIV insertions; and (e) replacement PIVs in poorer quality veins with exponentially higher risk of device failure and need for central venous catheter insertion with even greater infectious

and other complication risks.[11-12] Studies have reported high PIV failure rates, up to 69%.[3-7] Inadequate dressing and securement is likely a factor in most PIV failures, with one study reporting 71% of PIVs are inadequately secured.[13]

PIV dressing and securement

Despite its obvious importance, the study of effective approaches to PIV dressing and securement has received little attention.[10, 14] The earliest PIV dressing and securement was with simple tape or gauze-tape, with plastic film dressings becoming prominent in the 1980s.[15-16] An early systematic review found plastic films to have higher infection risk than gauze-tape[17] and this spurred the development of the modern standard polyurethane dressings (SPU) which are transparent and semi-permeable to oxygen, carbon dioxide and water vapour.[18] SPUs (e.g. Tegaderm™, 3M, St Paul or IV3000, Smith & Nephew, Hull) have been standard care for many years.[19] In contrast with gauze-tape dressings that are generally limited to short-term use, SPUs allow visualisation of the insertion site and can be left in place for up to 7 days if not soiled, loose or wet.[18, 20] Suturing is not recommended as this increases infection.[20]

Two new approaches to PIV dressing and securement are bordered polyurethane (BPU) and sutureless securement devices (SSDs). BPUs retain the central polyurethane component of SPUs with an added adhesive border of foam or cloth (e.g. Veni-Gard® I.V. Stabilization Dressing, CONMED, Utica). One BPU manufacturer (Tegaderm™ IV Advanced Securement Dressing, 3M™ St Paul, Minnesota) reports it has nearly twice the pull-out force of SPU, however there is scant independent data on the effectiveness of BPUs.[21-22] For example, Needham et al studied four different BPU and SPUs, but the small sample size of 78 precluded statistical comparisons.[22] BPU use is not yet widespread, likely due to increased costs over SPU and lack of convincing data to support its implementation.

SSDs are used in conjunction with SPUs. They have a large adhesive padded footplate with a PIV-locking or gripping clasp (e.g. StatLock®, Bard Access Systems, Murray Hill; Grip-Lok, Vygon, Ecouen; Hubguard®, Centurion, Williamston). They are designed to reduce movement, dislodgement,

kinking and flow impedance.[10] A manufacturer-initiated, non-randomised study reporting data from 10,164 patients in 63 hospitals, observed PIV failure reduced from 71% to 17% ($p<0.001$) when securement was with SSD (and SPU) compared to tape (and SPU), with significant estimated cost savings.[23] A manufacturer-sponsored and analysed randomised controlled trial (RCT) (N=302) reported BPU to have a 25% lower purchase price than SSD, and PIV failure rates at 96 hours of 52% for SSD, and 62% for BPU.[1] It remains unclear whether BPU or SSD has more benefit over traditional less expensive SPU dressings.

Tissue Adhesive

Another potential product to assist with PIV securement is Tissue Adhesive (TA) which is medical grade 'superglue' (cyanoacrylate). TA is used mainly to close skin lacerations and wounds as an alternative to sutures or staples, but also to repair gastric varices, inguinal hernias, bones, tendons and retinal detachments.[24-25] TA has haemostatic properties that may reduce post insertion bleeding, haematomas and associated infection risk. The use of TA to secure vascular access devices has only been reported in two case reports.[26-27] In these, TA was completely successful in securing approximately 100 epidural and central venous devices with no skin reactions or mechanical problems reported.[26-27] Epidural fall out was reduced from 12% to 4% but little data was provided on study methods or sample characteristics.[26]

The pull-out force required to dislodge PIVs secured with either SPU, BPU, SSD, TA or no dressing (control) was tested in an experimental model.[28] Compared with no dressing, neither SPU nor BPU significantly increased the pull-out force required to dislodge the PIV, although this may have been an underpowered comparison. In contrast, TA and SSD significantly increased the pull-out force, and TA resulted in a bond which was four times as strong as an SPU dressing.[28] The bactericidal properties of TA include inhibition of all Gram-positive organisms, including methicillin-resistant *Staphylococcus aureus* (MRSA), the predominant organisms in PIV infections. [29] We demonstrated that TA inhibits *Staphlycoccus aureus* and *Staphylococcus epidermidis* both under the TA, and down the PIV tunnel at 18 and 72 hours dwell time.[28] Given the strong results from non-controlled

clinical reports and *in vitro* work, TA may assist in avoiding PIV failure by reducing pistoning and accidental removal, with additional benefits being infection prevention and comfort for patients.

PIV dressing and securement remains a poorly-researched area of patient safety and has been identified as a priority area for improvement.[23] Previous research is limited by small samples, non-randomised designs and manufacturer involvement. Moreover, there has been no specific study comparing the cost-effectiveness of different PIV dressing and securement approaches, which vary widely in purchase price but may be more cost-effective if they reduce PIV failure. This study will test the efficacy, cost-effectiveness and acceptability to patients and professionals of TA (used with SPU), BPU, and SSD (used with SPU), against current care (SPU alone) to assist policy makers with decision making about the best dressing and securement choice for patients with PIVs.

METHODS AND ANALYSIS

The study will be a multi-centre, parallel group superiority RCT with four arms: three experimental groups (TA, BPU and SSD) and one control (SPU). There will be a three year recruitment of 1708 adult patients from two large teaching hospitals in south-east Queensland, Australia. Comprehensive assessment of effectiveness, cost-effectiveness, and acceptibility will be performed in line with the Medical Research Council model for evaluating complex interventions.[30] This will include smaller qualitative components including staff survey and focus groups. The protocol is version 1 dated 6 October 2011.

Outcome Measures

Primary Outcome

1. PIV failure: composite of any unplanned PIV removal, prior to completion of therapy. This includes: dislodgement (complete), occlusion (PIV will not infuse, or leakage occurs when fluid infused), phlebitis (2 or more of pain/tenderness, redness, swelling, purulence, and/or a palpable cord), or infection (laboratory confirmed local or bloodstream infection).[20, 31]

Secondary Outcomes

1. PIV and dressing/securement dwell time: Time in hours from insertion/application until removal.
2. Costs: Direct costs to the hospital for device management, including costs of PIV replacement in addition to the effects of dressing choice (randomised product and any additional tape or reinforcements).
3. Types of PIV failure will be analysed as secondary outcomes (dislodgement, occlusion, phlebitis, and infection).
4. PIV colonisation (>15 colony forming units [cfu]) from a purposive 10% subset of devices. [32]
5. Skin colonisation (>15cfu) from a purposive 10% subset of patients.[32]
6. Patient (overall with product) and staff satisfaction (with removal) ranked on a 10 point scale.

Setting and Sample

Patients will be recruited from the medical and surgical areas, and critical care departments at the Royal Brisbane and Women's Hospital and the Princess Alexandra Hospital, Queensland, Australia. Only one PIV will be studied per patient. The study hospitals together have approximately 500,000 separations per annum. Inclusion criteria are: ≥ 18 years of age; and requires a PIV with expected use greater than 24 hours. Exclusion criteria will be: non-English speaking patients without interpreter; PIV to be inserted through burned or diseased skin (e.g. blisters, sunburn, bruising, rash or skin infections); severe diaphoresis; known allergy to any study product; terminal/palliative care patients; current skin tear, or clinician believes patient is at high risk of a skin tear; or previously enrolled in the study.

Sample size and study power

We hypothesise a difference (reduced failure rate) for each of the three alternative treatments against control. For each, we will measure difference in outcomes for pairs of treatments (i.e. Group (G)1

(SPU – controls) vs G2 (TA); G1 vs G3 (BPU); G1 vs G4 (SSD) - that is, in turn the three alternatives versus the control). Sample sizes were calculated for three inequality tests of two proportions. Our recent trial of 3283 patients in the same study hospitals showed failure rates of 40% using SPU.[33] We hypothesise that TA, BPU and SSD will each reduce failure by an absolute proportion of 10%, therefore to 30%. A 10% absolute difference in PIV failure incidence was also observed in a previous study of SSD and BPU, and would be clinically important to detect.[1, 23] PASS (Power Analysis & Sample Size system, NCSS, Utah) was used to calculate the sample required to reduce the 40% device failure rate (controls) to 30% in each of the three experimental groups with 90% power at p=0.05. This results in each group requiring 388 patients i.e. a total of 1552 PIVs. We will add 10% to allow for potential attrition, therefore 1708 patients in total.

Recruitment, randomisation, allocation concealment and blinding

Research nurses (ReNs), not clinicians, will screen patients on a daily basis, gain informed consent, and perform randomisation for each patient at the time of study entry. Randomisation will be via a centralised web-based service provided by Griffith University. This will ensure full compliance with best practice standards for computerised randomisation generation and allocation concealment until study entry. Randomisation will be stratified by hospital site, and in a 1:1:1:1 ratio between the four study groups. Block randomisation will be used with random variation in block sizes to further ensure allocation concealment. PIV dressings are not amenable to blinding of patients, clinical staff or ReNs. However, there is no suggestion in the literature or our practice that clinical staff or patients would sabotage medical devices to favour one group. This is an independent academic study, with no product manufacturer having any involvement in the research.

Insertion and care of the PIV dressings and securements

PIVs will be inserted, and dressing and securements applied by clinical nurses, medical staff, or the ReNs using standard policies in place throughout Queensland Health. The study sites do not have dedicated intravenous (IV) teams to perform insertions, although there are a small number of IV nurse

consultants who provide education and undertake surveillance. Extensive education will be delivered to staff on how to apply, care for and remove the study products. All study products will be changed weekly or earlier if they are not clean, dry and intact, as recommended by the Centres of Disease Control (CDC).[20] Strips of non-sterile tape on the IV tubing will be permitted in all groups as per usual practice, and this will be documented.

Data collection

The ReNs, all of whom have had study-specific database training, will directly enter data in the clinical areas using portable password protected electronic devices with a purpose-built RedCAP database and form-based interface. All data is de-identified at this point and only identifiable within the database by specific study number. The master list of participants will be kept separately to the study database in a different password protected computer program at the hospital sites. Patient characteristics collected by ReNs at baseline will be: age, sex, estimated weight category, diagnostic group, dominant limb, co-morbidities, length of stay, immunodeficiency, current infection, IV therapy (including antimicrobial), skin integrity, skin type, and the presence of a wound, drain, tracheostomy or intestinal stoma. PIV characteristics collected will be: device type, insertion site, PIV gauge, side of insertion, clinical area/ward, inserter discipline, insertion difficulty, initial/subsequent PIV, skin preparation (including disinfectants and clipping), use of gloves for insertion, and the addition of extension tubing and injection ports. After PIV removal, the following data will be collected: reason for PIV removal, dwell time, infusates given, oral antibiotic therapy, number of additional vascular access devices in place, phlebitis signs and symptoms, level of consciousness, mobility level, delirium status, hospital length of stay and hospital mortality. Clinical staff will order blood and PIV cultures from patients suspected of PIV related infection as per usual practice and the ReNs will access the results. Clinically instigated cultures will be performed by blinded scientists in the hospital laboratories. Routine culturing is unnecessary and leads to comparable infection rates as those performed on clinical suspicion.[10] The ReNs will visually inspect PIVs daily and assess for phlebitis (redness, pain/tenderness, swelling, purulence, palpable cord or vein streak); dressing integrity (including any dressing change and/or addition of secondary securement products) and any

residue, rash, blister, itchiness or tearing of skin on dressing removal (adverse event). At device removal, the ReN will ask the patient (if able) about their satisfaction with the dressing and securement on a 10 point scale (0 = completely dissatisfied, 10 = completely satisfied). The person removing the dressing will be asked to rate the difficulty of removing the product (0 = very difficult, 10 = very easy). A Study Manager (reporting to the Chief Investogator) will audit data quality, completeness and protocol adherence with site visits for initial training and then for monitoring at least bimonthly. Because trial participation is relatively short (approximately 1 week) and participants will remain hospitalised, high rates of retention and follow-up are expected. A purposive sample of 150 clinical staff (about 10% of staff involved in the trial) will be invited to participate in a brief researcher-developed survey about study products and trial involvement. Further, 10-15 key clinical and policy staff will be invited to participate in a brief semi-structured interview about perceived barriers/enablers of implementation of the results, using a nominal group technique.

Data Analysis

The Principal Investigator, Study Manager and Trial Statistician will have access to the final datset. All randomised patients will be analysed by intention to treat, regardless of treatment received. The patient will be the unit of measurement, with only one PIV studied per patient. Comparability of groups at baseline for risk of device failure will be assessed. Relative incidence rates of device failure per 100 devices and per 1000 device days with 95% confidence intervals will summarise the effectiveness of each dressing and securement, and test for differences between groups. Kaplan-Meier survival curves (with log rank Mantel-Cox test) will compare device failure over time. Secondary endpoints will be compared between groups using parametric or nonparametric techniques as appropriate. In addition to group, multivariate regression (Cox) models will test the association between patient and device characteristics and device failure (e.g. age, PIV insertion site). Missing data will be modelled for best- and worst-case outcomes to assess for potential effect on overall results. A per-protocol analysis will assess the effect of protocol violations. P values of <0.05 will be considered significant. We do not expect effect sizes to vary between sites, however, variability will

be assessed, and if necessary, adjustment made in the model, with consideration of potential institutional differences in practice variables. Survey data will be described and interview data thematically analysed for issues that provide contextualisation of the RCT results, and inform implementation of findings into practice.

Estimating cost parameters and cost-effectiveness analysis

Direct costs to the hospital for device management will be captured including purchase costs of dressings and securements, any additional tape or reinforcements, the costs incurred by PIV failure (e.g. PIV replacement or antibiotics to treat PIV infections). Adverse event costs will be obtained from hospital cost centres for precise estimates, given the likely variability in costs between participants, reasons for admission, and hospitals. Detailed resource use for dressing and securement replacement will be recorded for 100 replacements selected at random (25 per device per group). Resources to be recorded include nurse/doctor time for replacement; waiting times for treatment; and equipment (e.g. dressings). The study will determine the hours of nursing and medical time required for replacement, wage costs per minute and the cost of treatments. These data will be used to estimate total resource use and costs for each of the groups over the study period. A cost analysis using ANCOVA or non-parametric bootstrapping techniques (dependent on the distribution of the cost data) will be undertaken from the public hospital perspective to compare mean total costs for the four treatment groups. Explanatory clinical and demographic variables (in addition to group) will be explored. A cost-effectiveness analysis will also be undertaken to estimate the incremental cost of each study product alternative per additional PIV failure avoided, compared to SPU. This will indicate the device securement that would provide the best value for money if implemented more widely in clinical practice.

Microbiological testing and endpoints

To further inform the infection outcomes, a sub-study (purposive 10%) will have ReNs take PIV tip and skin cultures (from under the dressing) immediately after PIV removal.[13] These specimens will

be transferred to the laboratory, with skin swabs streaked onto non-selective agar, and PIV tip segments roll-plated.[32] After 24 hours of incubation, plates will be examined for bacterial colony counts. The plates will then be re-incubated for 72 hours to enable growth of slow-growing species. Species identification will be determined morphologically, biochemically and if required genetically (e.g. Polymerase Chain Reaction and Sequencing). Samples will be scored for presence of bacteria, the total cfu, and species present. The added workload and cost mean this is not feasible for the entire sample. For patients who consent, we will store recovered microorganisms for use in potential future infection control studies.

In vitro antimicrobial properties

We will also investigate the antimicrobial properties of each dressing.[34] These tests are similar to the Minimum Inhibitory Concentration evaluations for antibiotics. A confluent bacterial monolayer on the surface of solid agar will be produced by plating liquid bacterial suspensions. An aliquot of TA will be dropped onto one point of the agar plate. We will do this for unpolymerised, semi-polymerised and fully polymerised TA. For SPU, BPU and SSD, a 0.5 cm disc will be cut and laid on the plate, incubated and the zone of inhibition determined. We will also examine growth under each specimen. Bacteria associated with PIV infection will be used (*Staphylococcus epidermidis*, *Staphylococcus aureus*, *Pseudomonas aeroginosa*, *Stenotrophomonas maltophilia)*.[35-36] A modification of this method will also be used to investigate bacterial migration between the dressing and securement products and the agar surface, modelling bacterial migration at the skin/PIV interface. Proportions colonised between study groups will be compared with non-parametric techniques.

ETHICS AND DISSEMINATION OF RESULTS

Ethical and safety considerations

Human Research Ethics Committee approvals have been granted by Queensland Health (HREC/11/QRCH/152) and Griffith University (NRS/46/11/HREC), and the trial is registered with the Australian New Zealand Clinical Trials Registry (ACTRN 12611000769987). Written informed

consent will be obtained from participants or representatives to participate in this trial, with an additional option to consent for the data and specimens collected to be stored and used in future infection control studies. Consent can be withdrawn from the trial participation for use of the study products and/or data collection if participants change their mind. In these cases, the trial products would be removed (if the participant requests) and replaced with SPU dressings. Serious adverse events (deaths, ICU admissions, PIV-related bloodstream infections) will be monitored and reported to the Human Research and Ethics Committees (HREC). Because of the rapid recruitment expected in the trial, there are no plans for interim analyses or safety data monitoring beyond that reported to the HREC. The Study Manager will communicate important protocol modifications or clarifications to relevant parties (investigators, ReNs, HREC, trial registry).

Dissemination of results

The prevention of medical device failure, improved well-being, hospital patient satisfaction, and responsible use of the health dollar are all of high interest to stakeholders, including the general community. To disseminate results widely, the investigators will present results locally and at relevant international meetings. The study can be expected to be published in an influential medical journal and be rapidly translated into clinical policies. Additional processes to promote research translation into practice will be sought e.g brief practical articles in professional newspapers.

DISCUSSION

PIV device failure is a common problem and affects millions of people each year. Improved dressing and securement is likely to prevent many cases of PIV failure. However, despite a high clinical need and the high costs to hospitals for products given the significant volume of use, there is a paucity of studies reporting the efficacy of alternative dressing and securement methods. Rigorous assessment of the efficacy and cost-effectiveness of PIV dressing and securement methods is therefore needed to guide clinical decision making. If failure rates can be reduced by 10%, this would prevent more than 30 million PIV failures and re-insertions in the USA each year alone, with phenomenal associated

reductions in health costs and nursing/medical time.[9] The results from this large RCT will have significant impact on international health policies, decrease hospital budgets, reduce nursing/medical workloads and improve patient experiences.

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AUTHORS CONTRIBUTIONS

Study conception: CMR, NMM, JW, JFF

Protocol design and funding application: CMR, NMM, JW, EGP, MRM, DM, JAW, KRD, HR, AM, JC, JY, OT, JG, JFF

Manuscript preparation and approval of final manuscript: CMR, NMM, JW, EGP, MRM, EL, SK, DM, JAW, MAC, KRD, HR, AM, JC, JY, OT, JG, AC, JFF

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COMPETING INTERESTS STATEMENT

Professor Claire M Rickard

CMR's employer has received on her behalf: unrestricted research and educational grants from 3M, BBraun, BD, Carefusion, Centurion; consultancy payments for educational lectures based on her research from 3M, Bard, BBraun, BD, Carefusion and Teleflex; and consultancy payments for a research project from BD.

Nicole Marsh

NMM's employer has received on her behalf consultancy payments for educational lectures based on her research, and an unrestricted research grant from BD.

Professor Joan Webster

Nil

Professor E Geoffrey Playford

Nil

Dr Matthew R McGrail

Nil

Emily Larsen

Nil

Dr David McMillan

Nil

Dr Md Abu Choudhury

Nil

A/Prof Jennifer A Whitty

JAW's employer has received on her behalf: consultancy payments from Coloplast Denmark.

Kimble R Dunster

Nil

Dr Heather Reynolds

Nil

Professor Andrea Marshall

Nil

Dr Julia Crilly

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REFERENCES

1. Bausone-Gazda D, Lefaiver CA, Walters C-A. A randomized controlled trial to compare the complications of 2 peripheral intravenous catheter-stabilization systems. *J Infus Nurs* 2010;33(6):371-84.

2. Zingg W, Pittet D. Peripheral venous catheters: an under-evaluated problem. *Int J Antimicrob Agents* 2009;34(Suppl 4):S38-42.

3. Bolton D. Improving peripheral cannulation practice at an NHS Trust. *Br J Nurs* 2010;19(21):1346, 8-50.

4. Harwood IR, Greene LM, Kozakowski-Koch JA, et al. New peripherally inserted midline catheter: a better alternative for intravenous antibiotic therapy in patients with cystic fibrosis. *Pediatr Pulmonol* 1992;12:233-9.

5. Rickard CM, McCann D, Munnings J, et al. Routine resite of peripheral intravenous devices every 3 days did not reduce complications compared with clinically indicated resite: a randomised controlled trial. *BMC Med* 2010;8:53.

6. Royer T. Improving short peripheral IV outcomes: a clinical trial of two securement methods. *JAVA* 2003;8(4):45-9.

7. Smith B. Peripheral intravenous catheter dwell times. A comparison of 3 securement methods for implementation of a 96-hour scheduled change protocol. *J Infus Nurs* 2006;29(1):14-7.

8. Ezingeard E, Coudrot M, Guyomarc'h S, et al. Evaluation of colonisation of peripheral venous catheters inserted by prehospital emergency service teams (SMUR) in France. *J Hosp Infect* 2009;72(2):169-75.

9. Hadaway L. Short peripheral intravenous catheters and infections. *J Infus Nurs* 2012;35(4):230-40.

10. Frey AM, Schears GJ. Why are we stuck on tape and suture? A review of catheter securement devices. *J Infus Nurs* 2006;29(1):34-8.

11. Bregenzer T, Conen D, Sakmann P, et al. Is routine replacement of peripheral intravenous catheters necessary? *Arch Intern Med* 1998;158(2):151-6.

12. Naimer SA, Temira F. Evaluation of techniques for intravenous catheter and tubing fixation. *Military Med* 2004;169(1):79-81.

13. Van Gessel H, McCavana C. Increased incidence of infections associated with peripheral IV cannulae: recognition, investigation, interventions. *Aust Infect Cont* 2006;11:39-45.

14. Sheppard K, Ledesma M, Morris N, et al. A prospective study of two intravenous catheter securement techniques in a skilled nursing facility. *J Intraven Nurs* 1999;22(3):151-6.

15. Campbell H, Carrington M. Peripheral IV cannula dressings: advantages and disadvantages. *Br J Nurs* 1999;8(21):1420-7.

16. Smith B, Royer, TI. New standards for improving peripheral I.V. catheter securement. *Nursing* 2007;37(3):72-4.

17. Hoffmann KK, Weber DJ, Samsa GP, et al. Transparent polyurethane film as an intravenous catheter dressing: a meta-analysis of the infection risks. *JAMA* 1992;267(15):2072-6.

18. Maki DG, Ringer M. Evaluation of dressing regimens for prevention of infection with peripheral intravenous catheters: gauze, a transparent polyurethane dressing, and an iodophor-transparent dressing. *JAMA* 1987;258(17):2396–403.

19. NSW Health. Nursing management of arterial catheters in critically ill patients. Sydney: Arterial Guidelines Development Network, Intensive Care Coordination and Monitoring Unit. 2007.

20. O'Grady NP, Alexander M, Burns LA, et al. Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis* 2011;52(9):e162-93.

21. Callaghan S, Copnell B, Johnston L. Comparison of two methods of peripheral intravenous catheter securement in the pediatric setting. *J Infus Nurs* 2002;25(4):256-64.

22. Needham R, Strehle EM. Evaluation of dressings used with local anaesthetic cream and for peripheral venous cannulation. Evaluation. *Paed Nurs* 2008;20(8).

23. Schears GJ. Summary of product trials for 10,164 patients: comparing an intravenous stabilizing device to tape. *J Infus Nurs* 2006;29(4):225-31.

24. Aukerman DF, Sebastianelli WJ, Nashelsky J. Clinical inquiries. How does tissue adhesive compare with suturing for superficial lacerations? *J Fam Pract* 2005;54(4):378.

25. Singer AJ, Thode HCJ. A review of the literature on octylcyanoacrylate tissue adhesive. *Am J Surg* 2004;187(2):238-48.

26. Wilkinson JN, Fitz-Henry J. Securing epidural catheters with Histoacryl glue. *Anaesthesia* 2008;63(3):324.

27. Wilkinson JN, Sheikh N, Jayamaha J. Tissue adhesive as an alternative to sutures for securing central venous catheters. *Anaesthesia* 2007;62(9):969-70.

28. Simonova G, Rickard C, Dunster K, et al. Cyanoacrylate tissue adhesives - effective securement technique for intravascular catheters: in vitro testing of safety and feasibility. *Anaes Intens Care* 2012;40(3):460-6.

29. Wilkinson JN, Chikhani M, Mortimer K, et al. The antimicrobial effect of Histoacryl skin adhesive. *Anaesthesia* 2008;63(12):1382-4.

30. Craig P, Dieppe P, Macintyre S, et al. Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ* 2008;337:a1655.

31. Webster J, Clarke S, Paterson D, et al. Routine care of peripheral intravenous catheters versus clinically indicated replacement: randomised controlled trial. *BMJ* 2008;337(a339).

32. Maki DG, Weise CE, Sarafin HW. A semiquantitative culture method for identifying intravenous-catheter-related infection. *NEJM* 1977;296(23):1305–9.

33. Rickard CM, Webster J, Wallis MC, et al. Routine versus clinically indicated replacement of peripheral intravenous catheters: a randomised controlled equivalence trial. *Lancet* 2012;380(9847):1066-74.

34. Bhende S, Rothenburger S, Spangler DJ, et al. In vitro assessment of microbial barrier properties of Dermabond topical skin adhesive. *Surg Infect* 2002;3:251-7.

35. Donlan RM. Biofilms and device-associated infections. *Emerg Infect Dis* 2001;7(2):277-81.

36. Sherertz RJ, Raad II, Belani A, et al. Three-year experience with sonicated vascular catheter cultures in a clinical microbiology laboratory. *J Clin Micro* 1990;28(1):76-82.

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	_____1_____
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	_____3_____
	2b	All items from the World Health Organization Trial Registration Data Set	_____n/a_____
Protocol version	3	Date and version identifier	_____8_____
Funding	4	Sources and types of financial, material, and other support	_____16_____
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	_____1 & 16___
	5b	Name and contact information for the trial sponsor	17
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	_____16_____
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	DSMC p14

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	_____5-8___
	6b	Explanation for choice of comparators	_____5-8___
Objectives	7	Specific objectives or hypotheses	_____8_____
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	___8_____
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	__9_____
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	__9_____
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	___10_____
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	____N/A_____
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	_10-11_____
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	_____N/A_____
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	_____8-9
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	___11-12_____

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	_____9-10_____
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	_____n/a_____
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	____10_____
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	_____10_____
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	____10_____
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	___10, 11_____
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	__N/A_____
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	___11-12_____
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	____15_____

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	___11_____
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	___12___
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	_____12____
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	__12_____
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	__14-15_____
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	_____14-15____
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	_____14_____
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	_____ 12_____
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	_____14_____
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	__15_____

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	____n/a_____
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	____n/a_____
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	___11_____
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	____16-18__
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	_____12_____
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	___n/a_____
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	__15_____
	31b	Authorship eligibility guidelines and any intended use of professional writers	__n/a_____
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	___n/a_____
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	__n/a
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	____14-15_____

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

BMJ Open

Securing All intraVenous devices Effectively in hospitalised patients - The SAVE Trial: study protocol for a multi-centre, randomised controlled trial.

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Primary Subject Heading:	Evidence based practice
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Title

Securing All intraVenous devices Effectively in hospitalised patients - The SAVE Trial: study protocol for a multi-centre, randomised controlled trial.

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ABSTRACT

Introduction: Over 70% of all hospital admissions have a peripheral intravenous device (PIV) inserted, however the failure rate of PIVs is unacceptably high, with up to 69% of these devices failing before treatment is complete. Failure can be due to dislodgement, phlebitis, occlusion/infiltration, and/or infection. This results in interrupted medical therapy; painful phlebitis and reinsertions; increased hospital length of stay, morbidity and mortality from infections; and wasted medical/nursing time. Appropriate PIV dressing and securement may prevent many cases of PIV failure but little comparative data exists regarding the efficacy of various PIV dressing and securement methods. This trial will investigate the clinical- and cost-effectiveness of four methods of PIV dressing and securement in preventing PIV failure.

Methods and Analysis: A multi-centre, parallel-group, superiority randomised controlled trial with four arms: three experimental groups (tissue adhesive; bordered polyurethane dressing; sutureless securement device) and one control (standard polyurethane dressing) is planned. There will be a three-year recruitment of 1708 adult patients, with allocation concealment until randomisation by a centralised web-based service. The primary outcome is PIV failure which includes any of: dislodgement, occlusion/infiltration, phlebitis and infection. Secondary outcomes include: types of PIV failure; PIV dwell time; costs; device colonisation; skin colonisation; patient and staff satisfaction. Relative incidence rates of device failure per 100 devices and per 1,000 device days with 95% confidence intervals will summarise the impact of each dressing, and test differences between groups. Kaplan-Meier survival curves (with log rank Mantel-Cox test) will compare device failure over time. P-values of <0.05 will be considered significant. Secondary endpoints will be compared between groups using parametric or nonparametric techniques appropriate to level of measurement.

Ethics and dissemination: Ethical approval has been received from Queensland Health (HREC/11/QRCH/152) and Griffith University (NRS/46/11/HREC). Results will be published according to the CONSORT statement and presented at relevant conferences.

Trial Registration: Australian New Zealand Clinical Trial Registry ACTRN 12611000769987.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first large scale, independent multi-centre randomised controlled trial to investigate the efficacy and cost-effectiveness of PIV dressing and securement methods to prevent PIV failure.
- The trial examines a novel Tissue Adhesive securement method for the first time in PIVs.
- This is a pragmatic trial, with PIVs inserted and cared for by general staff in two adult hospitals, not specialist teams or researchers.
- Microbiology endpoints will be analysed by blinded scientists, and infection outcomes assigned by a blinded infectious disease specialist outcome assessor.
- It will not be possible to blind the dressing and securement intervention/control from clinical staff, patients or research nurses.
- Patients with existing skin problems, severe diaphoresis or frail skin are excluded from the study so results will not be generalisable to these groups

INTRODUCTION

Peripheral intravenous devices (PIVs) are the most commonly used medical device world-wide: almost all hospital patients need one or more to receive intravenous treatment.[1-2] Failure rates of these devices are unacceptably high, affecting up to 69% of patients receiving therapy.[3-7] Of these, 10% simply fall out, despite having a dressing in place, with patients then unable to receive treatment.[5] Other PIVs become painful or occluded and must also be replaced. Such failure rates for an essential device are unacceptable and indicate that current dressings and securement methods are inadequate, with much failure potentially preventable with improved effective dressing and securement.

Intravenous devices

About 90% of all vascular catheters are peripheral PIVs.[8] Approximately 330 million PIVs are sold in the United States of America (USA) alone each year.[9] The external component of PIVs require securement to the skin, with dressings and other securements used to ensure PIVs do not dislodge and fall out, or move out of the vein and into surrounding tissue. Effective securement also minimises PIV micro-motion within the vessel, which irritates the vein wall, causing inflammation presenting as pain, swelling and PIV occlusion/infiltration.[6, 10] Micro-motion may also encourage skin bacteria to enter the PIV wound, causing infection risk.

PIV failure

PIV failure occurs when the PIV can no longer be used for treatment. Failure can be mechanical (dislodgement, occlusion, infiltration), vascular (phlebitis), or infectious (localised or bloodstream infections). PIV failure is an important detrimental patient outcome that causes: (a) interruptions to medical treatment and compromised patient safety from lost vascular access; (b) painful phlebitis lasting for days or weeks at the PIV site, even after removal; (c) potentially increased hospital length of stay and mortality from PIV-associated bloodstream infection; (d) additional needlesticks for replacement PIV insertions; and (e) replacement PIVs in poorer quality veins with exponentially higher risk of device failure and need for central venous catheter insertion with even greater infectious

and other complication risks.[11-12] Studies have reported high PIV failure rates, up to 69%.[3-7] Inadequate dressing and securement is likely a factor in most PIV failures, with one study reporting 71% of PIVs are inadequately secured.[13]

PIV dressing and securement

Despite its obvious importance, the study of effective approaches to PIV dressing and securement has received little attention.[10, 14] The earliest PIV dressing and securement was with simple tape or gauze-tape, with plastic film dressings becoming prominent in the 1980s.[15-16] An early systematic review found plastic films to have higher infection risk than gauze-tape[17] and this spurred the development of the modern standard polyurethane dressings (SPU) which are transparent and semi-permeable to oxygen, carbon dioxide and water vapour.[18] SPUs (e.g. Tegaderm™, 3M, St Paul or IV3000, Smith & Nephew, Hull) have been standard care for many years.[19] In contrast with gauze-tape dressings that are generally limited to short-term use, SPUs allow visualisation of the insertion site and can be left in place for up to 7 days if not soiled, loose or wet.[18, 20] Suturing is not recommended as this increases infection.[20]

Two new approaches to PIV dressing and securement are bordered polyurethane (BPU) and sutureless securement devices (SSDs). BPUs retain the central polyurethane component of SPUs with an added adhesive border of foam or cloth (e.g. Veni-Gard® I.V. Stabilization Dressing, CONMED, Utica). One BPU manufacturer (Tegaderm™ IV Advanced Securement Dressing, 3M™ St Paul, Minnesota) reports it has nearly twice the pull-out force of SPU, however there is scant independent data on the effectiveness of BPUs.[21-22] For example, Needham et al studied four different BPU and SPUs, but the small sample size of 78 precluded statistical comparisons.[22] BPU use is not yet widespread, likely due to increased costs over SPU and lack of convincing data to support its implementation.

SSDs are used in conjunction with SPUs. They have a large adhesive padded footplate with a PIV-locking or gripping clasp (e.g. StatLock®, Bard Access Systems, Murray Hill; Grip-Lok, Vygon, Ecouen; Hubguard®, Centurion, Williamston). They are designed to reduce movement, dislodgement,

kinking and flow impedance.[10] A manufacturer-initiated, non-randomised study reporting data from 10,164 patients in 63 hospitals, observed PIV failure reduced from 71% to 17% ($p<0.001$) when securement was with SSD (and SPU) compared to tape (and SPU), with significant estimated cost savings.[23] A manufacturer-sponsored and analysed randomised controlled trial (RCT) (N=302) reported BPU to have a 25% lower purchase price than SSD, and PIV failure rates at 96 hours of 52% for SSD, and 62% for BPU.[1] It remains unclear whether BPU or SSD has more benefit over traditional less expensive SPU dressings.

Tissue Adhesive

Another potential product to assist with PIV securement is Tissue Adhesive (TA) which is medical grade 'superglue' (cyanoacrylate). TA is used mainly to close skin lacerations and wounds as an alternative to sutures or staples, but also to repair gastric varices, inguinal hernias, bones, tendons and retinal detachments.[24-25] TA has haemostatic properties that may reduce post insertion bleeding, haematomas and associated infection risk. The use of TA to secure vascular access devices has only been reported in two case reports.[26-27] In these, TA was completely successful in securing approximately 100 epidural and central venous devices with no skin reactions or mechanical problems reported.[26-27] Epidural fall out was reduced from 12% to 4% but little data was provided on study methods or sample characteristics.[26]

The pull-out force required to dislodge PIVs secured with either SPU, BPU, SSD, TA or no dressing (control) was tested in an experimental model.[28] Compared with no dressing, neither SPU nor BPU significantly increased the pull-out force required to dislodge the PIV, although this may have been an underpowered comparison. In contrast, TA and SSD significantly increased the pull-out force, and TA resulted in a bond which was four times as strong as an SPU dressing.[28] The bactericidal properties of TA include inhibition of all Gram-positive organisms, including methicillin-resistant *Staphylococcus aureus* (MRSA), the predominant organisms in PIV infections. [29] We demonstrated that TA inhibits *Staphlycoccus aureus* and *Staphylococcus epidermidis* both under the TA, and down the PIV tunnel at 18 and 72 hours dwell time.[28] Given the strong results from non-controlled

clinical reports and *in vitro* work, TA may assist in avoiding PIV failure by reducing pistoning and accidental removal, with additional benefits being infection prevention and comfort for patients.

PIV dressing and securement remains a poorly-researched area of patient safety and has been identified as a priority area for improvement.[23] Previous research is limited by small samples, non-randomised designs and manufacturer involvement. Moreover, there has been no specific study comparing the cost-effectiveness of different PIV dressing and securement approaches, which vary widely in purchase price but may be more cost-effective if they reduce PIV failure. This study will test the efficacy, cost-effectiveness and acceptability to patients and professionals of TA (used with SPU), BPU, and SSD (used with SPU), against current care (SPU alone) to assist policy makers with decision making about the best dressing and securement choice for patients with PIVs.

METHODS AND ANALYSIS

The study will be a multi-centre, parallel group superiority RCT with four arms: three experimental groups (TA, BPU and SSD) and one control (SPU). There will be a three year recruitment of 1708 adult patients from two large teaching hospitals in south-east Queensland, Australia. Comprehensive assessment of effectiveness, cost-effectiveness, and acceptibility will be performed in line with the Medical Research Council model for evaluating complex interventions.[30] This will include smaller qualitative components including staff survey and focus groups. The protocol is version 1 dated 6 October 2011.

Outcome Measures

Primary Outcome

1. PIV failure: composite of any unplanned PIV removal, prior to completion of therapy. This includes: dislodgement (complete), occlusion (PIV will not infuse, or leakage occurs when fluid infused), phlebitis (2 or more of pain/tenderness, redness, swelling, purulence, and/or a palpable cord), or infection (laboratory confirmed local or bloodstream infection).[20, 31]

Secondary Outcomes

1. PIV and dressing/securement dwell time: Time in hours from insertion/application until removal.
2. Costs: Direct costs to the hospital for device management, including costs of PIV replacement in addition to the effects of dressing choice (randomised product and any additional tape or reinforcements).
3. Types of PIV failure will be analysed as secondary outcomes (dislodgement, occlusion, phlebitis, and infection).
4. PIV colonisation (>15 colony forming units [cfu]) from a purposive 10% subset of devices. [32]
5. Skin colonisation (>15cfu) from a purposive 10% subset of patients.[32]
6. Patient (overall with product) and staff satisfaction (with removal) ranked on a 10 point scale.

Setting and Sample

Patients will be recruited from the medical and surgical areas, and critical care departments at the Royal Brisbane and Women's Hospital and the Princess Alexandra Hospital, Queensland, Australia. Only one PIV will be studied per patient. The study hospitals together have approximately 500,000 separations per annum. Inclusion criteria are: ≥ 18 years of age; and requires a PIV with expected use greater than 24 hours. Exclusion criteria will be: non-English speaking patients without interpreter; PIV to be inserted through burned or diseased skin (e.g. blisters, sunburn, bruising, rash or skin infections); severe diaphoresis; known allergy to any study product; terminal/palliative care patients; current skin tear, or clinician believes patient is at high risk of a skin tear; or previously enrolled in the study.

Sample size and study power

We hypothesise a difference (reduced failure rate) for each of the three alternative treatments against control. For each, we will measure difference in outcomes for pairs of treatments (i.e. Group (G)1

(SPU – controls) vs G2 (TA); G1 vs G3 (BPU); G1 vs G4 (SSD) - that is, in turn the three alternatives versus the control). Sample sizes were calculated for three inequality tests of two proportions. Our recent trial of 3283 patients in the same study hospitals showed failure rates of 40% using SPU.[33] We hypothesise that TA, BPU and SSD will each reduce failure by an absolute proportion of 10%, therefore to 30%. A 10% absolute difference in PIV failure incidence was also observed in a previous study of SSD and BPU, and would be clinically important to detect.[1, 23] PASS (Power Analysis & Sample Size system, NCSS, Utah) was used to calculate the sample required to reduce the 40% device failure rate (controls) to 30% in each of the three experimental groups with 90% power at p=0.05. This results in each group requiring 388 patients i.e. a total of 1552 PIVs. We will add 10% to allow for potential attrition, therefore 1708 patients in total.

Recruitment, randomisation, allocation concealment and blinding

Research nurses (ReNs), not clinicians, will screen patients on a daily basis, gain informed consent, and perform randomisation for each patient at the time of study entry. Randomisation will be via a centralised web-based service provided by Griffith University. This will ensure full compliance with best practice standards for computerised randomisation generation and allocation concealment until study entry. Randomisation will be stratified by hospital site, and in a 1:1:1:1 ratio between the four study groups. Block randomisation will be used with random variation in block sizes to further ensure allocation concealment. PIV dressings are not amenable to blinding of patients, clinical staff or ReNs. However, there is no suggestion in the literature or our practice that clinical staff or patients would sabotage medical devices to favour one group. This is an independent academic study, with no product manufacturer having any involvement in the research.

Insertion and care of the PIV dressings and securements

PIVs will be inserted, and dressing and securements applied by clinical nurses, medical staff, or the ReNs using standard policies in place throughout Queensland Health. The study sites do not have dedicated intravenous (IV) teams to perform insertions, although there are a small number of IV nurse

consultants who provide education and undertake surveillance. Extensive education will be delivered to staff on how to apply, care for and remove the study products. All study products will be changed weekly or earlier if they are not clean, dry and intact, as recommended by the Centres of Disease Control (CDC).[20] Strips of non-sterile tape on the IV tubing will be permitted in all groups as per usual practice, and this will be documented.

Data collection

The ReNs, all of whom have had study-specific database training, will directly enter data in the clinical areas using portable password protected electronic devices with a purpose-built RedCAP database and form-based interface. All data is de-identified at this point and only identifiable within the database by specific study number. The master list of participants will be kept separately to the study database in a different password protected computer program at the hospital sites. Patient characteristics collected by ReNs at baseline will be: age, sex, estimated weight category, diagnostic group, dominant limb, co-morbidities, length of stay, immunodeficiency, current infection, IV therapy (including antimicrobial), skin integrity, skin type, and the presence of a wound, drain, tracheostomy or intestinal stoma. PIV characteristics collected will be: device type, insertion site, PIV gauge, side of insertion, clinical area/ward, inserter discipline, insertion difficulty, initial/subsequent PIV, skin preparation (including disinfectants and clipping), use of gloves for insertion, and the addition of extension tubing and injection ports. After PIV removal, the following data will be collected: reason for PIV removal, dwell time, infusates given, oral antibiotic therapy, number of additional vascular access devices in place, phlebitis signs and symptoms, level of consciousness, mobility level, delirium status, hospital length of stay and hospital mortality. Clinical staff will order blood and PIV cultures from patients suspected of PIV related infection as per usual practice and the ReNs will access the results. Clinically instigated cultures will be performed by blinded scientists in the hospital laboratories. Routine culturing is unnecessary and leads to comparable infection rates as those performed on clinical suspicion.[10] The ReNs will visually inspect PIVs daily and assess for phlebitis (redness, pain/tenderness, swelling, purulence, palpable cord or vein streak); dressing integrity (including any dressing change and/or addition of secondary securement products) and any

residue, rash, blister, itchiness or tearing of skin on dressing removal (adverse event). At device removal, the ReN will ask the patient (if able) about their satisfaction with the dressing and securement on a 10 point scale (0 = completely dissatisfied, 10 = completely satisfied). The person removing the dressing will be asked to rate the difficulty of removing the product (0 = very difficult, 10 = very easy). A Study Manager (reporting to the Chief Investogator) will audit data quality, completeness and protocol adherence with site visits for initial training and then for monitoring at least bimonthly. Because trial participation is relatively short (approximately 1 week) and participants will remain hospitalised, high rates of retention and follow-up are expected. A purposive sample of 150 clinical staff (about 10% of staff involved in the trial) will be invited to participate in a brief researcher-developed survey about study products and trial involvement. Further, 10-15 key clinical and policy staff will be invited to participate in a brief semi-structured interview about perceived barriers/enablers of implementation of the results, using a nominal group technique.

Data Analysis

The Principal Investigator, Study Manager and Trial Statistician will have access to the final datset. All randomised patients will be analysed by intention to treat, regardless of treatment received. The patient will be the unit of measurement, with only one PIV studied per patient. Comparability of groups at baseline for risk of device failure will be assessed. Relative incidence rates of device failure per 100 devices and per 1000 device days with 95% confidence intervals will summarise the effectiveness of each dressing and securement, and test for differences between groups. Kaplan-Meier survival curves (with log rank Mantel-Cox test) will compare device failure over time. Secondary endpoints will be compared between groups using parametric or nonparametric techniques as appropriate. In addition to group, multivariate regression (Cox) models will test the association between patient and device characteristics and device failure (e.g. age, PIV insertion site). Missing data will be modelled for best- and worst-case outcomes to assess for potential effect on overall results. A per-protocol analysis will assess the effect of protocol violations. P values of <0.05 will be considered significant. We do not expect effect sizes to vary between sites, however, variability will

be assessed, and if necessary, adjustment made in the model, with consideration of potential institutional differences in practice variables. Survey data will be described and interview data thematically analysed for issues that provide contextualisation of the RCT results, and inform implementation of findings into practice.

Estimating cost parameters and cost-effectiveness analysis

Direct costs to the hospital for device management will be captured including purchase costs of dressings and securements, any additional tape or reinforcements, the costs incurred by PIV failure (e.g. PIV replacement or antibiotics to treat PIV infections). Adverse event costs will be obtained from hospital cost centres for precise estimates, given the likely variability in costs between participants, reasons for admission, and hospitals. Detailed resource use for dressing and securement replacement will be recorded for 100 replacements selected at random (25 per device per group). Resources to be recorded include nurse/doctor time for replacement; waiting times for treatment; and equipment (e.g. dressings). The study will determine the hours of nursing and medical time required for replacement, wage costs per minute and the cost of treatments. These data will be used to estimate total resource use and costs for each of the groups over the study period. A cost analysis using ANCOVA or non-parametric bootstrapping techniques (dependent on the distribution of the cost data) will be undertaken from the public hospital perspective to compare mean total costs for the four treatment groups. Explanatory clinical and demographic variables (in addition to group) will be explored. A cost-effectiveness analysis will also be undertaken to estimate the incremental cost of each study product alternative per additional PIV failure avoided, compared to SPU. This will indicate the device securement that would provide the best value for money if implemented more widely in clinical practice.

Microbiological testing and endpoints

To further inform the infection outcomes, a sub-study (purposive 10%) will have ReNs take PIV tip and skin cultures (from under the dressing) immediately after PIV removal.[13] These specimens will

be transferred to the laboratory, with skin swabs streaked onto non-selective agar, and PIV tip segments roll-plated.[32] After 24 hours of incubation, plates will be examined for bacterial colony counts. The plates will then be re-incubated for 72 hours to enable growth of slow-growing species. Species identification will be determined morphologically, biochemically and if required genetically (e.g. Polymerase Chain Reaction and Sequencing). Samples will be scored for presence of bacteria, the total cfu, and species present. The added workload and cost mean this is not feasible for the entire sample. For patients who consent, we will store recovered microorganisms for use in potential future infection control studies.

In vitro antimicrobial properties

We will also investigate the antimicrobial properties of each dressing.[34] These tests are similar to the Minimum Inhibitory Concentration evaluations for antibiotics. A confluent bacterial monolayer on the surface of solid agar will be produced by plating liquid bacterial suspensions. An aliquot of TA will be dropped onto one point of the agar plate. We will do this for unpolymerised, semi-polymerised and fully polymerised TA. For SPU, BPU and SSD, a 0.5 cm disc will be cut and laid on the plate, incubated and the zone of inhibition determined. We will also examine growth under each specimen. Bacteria associated with PIV infection will be used (*Staphylococcus epidermidis*, *Staphylococcus aureus*, *Pseudomonas aeroginosa*, *Stenotrophomonas maltophilia)*.[35-36] A modification of this method will also be used to investigate bacterial migration between the dressing and securement products and the agar surface, modelling bacterial migration at the skin/PIV interface. Proportions colonised between study groups will be compared with non-parametric techniques.

ETHICS AND DISSEMINATION OF RESULTS

Ethical and safety considerations

Human Research Ethics Committee approvals have been granted by Queensland Health (HREC/11/QRCH/152) and Griffith University (NRS/46/11/HREC), and the trial is registered with the Australian New Zealand Clinical Trials Registry (ACTRN 12611000769987). Written informed

consent will be obtained from participants or representatives to participate in this trial, with an additional option to consent for the data and specimens collected to be stored and used in future infection control studies. Consent can be withdrawn from the trial participation for use of the study products and/or data collection if participants change their mind. In these cases, the trial products would be removed (if the participant requests) and replaced with SPU dressings. Serious adverse events (deaths, ICU admissions, PIV-related bloodstream infections) will be monitored and reported to the Human Research and Ethics Committees (HREC). Because of the rapid recruitment expected in the trial, there are no plans for interim analyses or safety data monitoring beyond that reported to the HREC. The Study Manager will communicate important protocol modifications or clarifications to relevant parties (investigators, ReNs, HREC, trial registry).

Dissemination of results

The prevention of medical device failure, improved well-being, hospital patient satisfaction, and responsible use of the health dollar are all of high interest to stakeholders, including the general community. To disseminate results widely, the investigators will present results locally and at relevant international meetings. The study can be expected to be published in an influential medical journal and be rapidly translated into clinical policies. Additional processes to promote research translation into practice will be sought e.g brief practical articles in professional newspapers.

DISCUSSION

PIV device failure is a common problem and affects millions of people each year. Improved dressing and securement is likely to prevent many cases of PIV failure. However, despite a high clinical need and the high costs to hospitals for products given the significant volume of use, there is a paucity of studies reporting the efficacy of alternative dressing and securement methods. Rigorous assessment of the efficacy and cost-effectiveness of PIV dressing and securement methods is therefore needed to guide clinical decision making. If failure rates can be reduced by 10%, this would prevent more than 30 million PIV failures and re-insertions in the USA each year alone, with phenomenal associated

reductions in health costs and nursing/medical time.[9] The results from this large RCT will have significant impact on international health policies, decrease hospital budgets, reduce nursing/medical workloads and improve patient experiences.

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AUTHORS CONTRIBUTIONS

Study conception: CMR, NMM, JW, JFF

Protocol design and funding application: CMR, NMM, JW, EGP, MRM, DM, JAW, KRD, HR, AM, JC, JY, OT, JG, JFF

Manuscript preparation and approval of final manuscript: CMR, NMM, JW, EGP, MRM, EL, SK, DM, JAW, MAC, KRD, HR, AM, JC, JY, OT, JG, AC, JFF

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COMPETING INTERESTS STATEMENT

Professor Claire M Rickard

CMR's employer has received on her behalf: unrestricted research and educational grants from 3M, BBraun, BD, Carefusion, Centurion; consultancy payments for educational lectures based on her research from 3M, Bard, BBraun, BD, Carefusion and Teleflex; and consultancy payments for a research project from BD.

Nicole Marsh

NMM's employer has received on her behalf consultancy payments for educational lectures based on her research, and an unrestricted research grant from BD.

Professor Joan Webster

Nil

Professor E Geoffrey Playford

Nil

Dr Matthew R McGrail

Nil

Emily Larsen

Nil

Dr David McMillan

Nil

Dr Md Abu Choudhury

Nil

A/Prof Jennifer A Whitty

JAW's employer has received on her behalf: consultancy payments from Coloplast Denmark.

Kimble R Dunster

Nil

Dr Heather Reynolds

Nil

Professor Andrea Marshall

Nil

Dr Julia Crilly

Nil

Professor Jeanine Young

Nil

Dr Ogilvie Thom

Nil

Dr John Gowardman

Nil

Amanda Corley

Nil

Professor John F Fraser

Nil

REFERENCES

1. Bausone-Gazda D, Lefaiver CA, Walters C-A. A randomized controlled trial to compare the complications of 2 peripheral intravenous catheter-stabilization systems. *J Infus Nurs* 2010;33(6):371-84.

2. Zingg W, Pittet D. Peripheral venous catheters: an under-evaluated problem. *Int J Antimicrob Agents* 2009;34(Suppl 4):S38-42.

3. Bolton D. Improving peripheral cannulation practice at an NHS Trust. *Br J Nurs* 2010;19(21):1346, 8-50.

4. Harwood IR, Greene LM, Kozakowski-Koch JA, et al. New peripherally inserted midline catheter: a better alternative for intravenous antibiotic therapy in patients with cystic fibrosis. *Pediatr Pulmonol* 1992;12:233-9.

5. Rickard CM, McCann D, Munnings J, et al. Routine resite of peripheral intravenous devices every 3 days did not reduce complications compared with clinically indicated resite: a randomised controlled trial. *BMC Med* 2010;8:53.

6. Royer T. Improving short peripheral IV outcomes: a clinical trial of two securement methods. *JAVA* 2003;8(4):45-9.

7. Smith B. Peripheral intravenous catheter dwell times. A comparison of 3 securement methods for implementation of a 96-hour scheduled change protocol. *J Infus Nurs* 2006;29(1):14-7.

8. Ezingeard E, Coudrot M, Guyomarc'h S, et al. Evaluation of colonisation of peripheral venous catheters inserted by prehospital emergency service teams (SMUR) in France. *J Hosp Infect* 2009;72(2):169-75.

9. Hadaway L. Short peripheral intravenous catheters and infections. *J Infus Nurs* 2012;35(4):230-40.

10. Frey AM, Schears GJ. Why are we stuck on tape and suture? A review of catheter securement devices. *J Infus Nurs* 2006;29(1):34-8.

11. Bregenzer T, Conen D, Sakmann P, et al. Is routine replacement of peripheral intravenous catheters necessary? *Arch Intern Med* 1998;158(2):151-6.

12. Naimer SA, Temira F. Evaluation of techniques for intravenous catheter and tubing fixation. *Military Med* 2004;169(1):79-81.

13. Van Gessel H, McCavana C. Increased incidence of infections associated with peripheral IV cannulae: recognition, investigation, interventions. *Aust Infect Cont* 2006;11:39-45.

14. Sheppard K, Ledesma M, Morris N, et al. A prospective study of two intravenous catheter securement techniques in a skilled nursing facility. *J Intraven Nurs* 1999;22(3):151-6.

15. Campbell H, Carrington M. Peripheral IV cannula dressings: advantages and disadvantages. *Br J Nurs* 1999;8(21):1420-7.

16. Smith B, Royer, TI. New standards for improving peripheral I.V. catheter securement. *Nursing* 2007;37(3):72-4.

17. Hoffmann KK, Weber DJ, Samsa GP, et al. Transparent polyurethane film as an intravenous catheter dressing: a meta-analysis of the infection risks. *JAMA* 1992;267(15):2072-6.

18. Maki DG, Ringer M. Evaluation of dressing regimens for prevention of infection with peripheral intravenous catheters: gauze, a transparent polyurethane dressing, and an iodophor-transparent dressing. *JAMA* 1987;258(17):2396–403.

19. NSW Health. Nursing management of arterial catheters in critically ill patients. Sydney: Arterial Guidelines Development Network, Intensive Care Coordination and Monitoring Unit. 2007.

20. O'Grady NP, Alexander M, Burns LA, et al. Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis* 2011;52(9):e162-93.

21. Callaghan S, Copnell B, Johnston L. Comparison of two methods of peripheral intravenous catheter securement in the pediatric setting. *J Infus Nurs* 2002;25(4):256-64.

22. Needham R, Strehle EM. Evaluation of dressings used with local anaesthetic cream and for peripheral venous cannulation. Evaluation. *Paed Nurs* 2008;20(8).

23. Schears GJ. Summary of product trials for 10,164 patients: comparing an intravenous stabilizing device to tape. *J Infus Nurs* 2006;29(4):225-31.

24. Aukerman DF, Sebastianelli WJ, Nashelsky J. Clinical inquiries. How does tissue adhesive compare with suturing for superficial lacerations? *J Fam Pract* 2005;54(4):378.

25. Singer AJ, Thode HCJ. A review of the literature on octylcyanoacrylate tissue adhesive. *Am J Surg* 2004;187(2):238-48.

26. Wilkinson JN, Fitz-Henry J. Securing epidural catheters with Histoacryl glue. *Anaesthesia* 2008;63(3):324.

27. Wilkinson JN, Sheikh N, Jayamaha J. Tissue adhesive as an alternative to sutures for securing central venous catheters. *Anaesthesia* 2007;62(9):969-70.

28. Simonova G, Rickard C, Dunster K, et al. Cyanoacrylate tissue adhesives - effective securement technique for intravascular catheters: in vitro testing of safety and feasibility. *Anaes Intens Care* 2012;40(3):460-6.

29. Wilkinson JN, Chikhani M, Mortimer K, et al. The antimicrobial effect of Histoacryl skin adhesive. *Anaesthesia* 2008;63(12):1382-4.

30. Craig P, Dieppe P, Macintyre S, et al. Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ* 2008;337:a1655.

31. Webster J, Clarke S, Paterson D, et al. Routine care of peripheral intravenous catheters versus clinically indicated replacement: randomised controlled trial. *BMJ* 2008;337(a339).

32. Maki DG, Weise CE, Sarafin HW. A semiquantitative culture method for identifying intravenous-catheter-related infection. *NEJM* 1977;296(23):1305–9.

33. Rickard CM, Webster J, Wallis MC, et al. Routine versus clinically indicated replacement of peripheral intravenous catheters: a randomised controlled equivalence trial. *Lancet* 2012;380(9847):1066-74.

34. Bhende S, Rothenburger S, Spangler DJ, et al. In vitro assessment of microbial barrier properties of Dermabond topical skin adhesive. *Surg Infect* 2002;3:251-7.

35. Donlan RM. Biofilms and device-associated infections. *Emerg Infect Dis* 2001;7(2):277-81.

36. Sherertz RJ, Raad II, Belani A, et al. Three-year experience with sonicated vascular catheter cultures in a clinical microbiology laboratory. *J Clin Micro* 1990;28(1):76-82.

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	_____1_____
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	_____3_____
	2b	All items from the World Health Organization Trial Registration Data Set	_____n/a_____
Protocol version	3	Date and version identifier	_____8_____
Funding	4	Sources and types of financial, material, and other support	_____16_____
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	_____1 & 16___
	5b	Name and contact information for the trial sponsor	17
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	_____16_____
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	DSMC p14

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	_____5-8___
	6b	Explanation for choice of comparators	_____5-8___
Objectives	7	Specific objectives or hypotheses	_____8_____
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	___8_____
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	__9_____
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	__9_____
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	___10_____
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	____N/A_____
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	_10-11_____
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	_____N/A_____
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	_____8-9
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	___11-12_____

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	_____9-10_____
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	_____n/a_____
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	____10_____
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	_____10_____
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	____10_____
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	___10, 11_____
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	__N/A_____
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	___11-12_____
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	____15_____

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	___11_____
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	___12___
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	_____12____
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	__12_____
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	__14-15_____
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	_____14-15____
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	_____14_____
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	_____ 12_____
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	_____14_____
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	__15_____

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	____n/a_____
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	____n/a_____
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	___11_____
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	____16-18__
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	_____12_____
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	___n/a_____
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	__15_____
	31b	Authorship eligibility guidelines and any intended use of professional writers	__n/a_____
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	___n/a_____
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	__n/a
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	____14-15_____

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.