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Peripherally inserted central catheter design and material for reducing catheter failure and complications (Protocol)

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[Intervention Protocol]

Peripherally inserted central catheter design and material for reducing catheter failure and complications

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ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

To assess the effectiveness of PICC material and design in reducing catheter failure and complications.

BACKGROUND

Peripherally inserted central catheters (PICCs) are routinely inserted in adults and children who require intermediate intravascular therapy such as total parenteral nutrition (Russell 2014; Ullman 2017). PICCs are long (50 cm to 60 cm), flexible catheters usually constructed of polyurethane or silicone material. Typically inserted in the basilic, brachial or cephalic veins of the upper arm, the tip of the PICC terminates in a central vessel providing natural haemodilution of irritant infusates, such as chemotherapy. In recent decades, PICC use has increased due to perceived advantages in comparison to central venous catheters (CVCs), such as bedside placement by non-medical staff and reduced complication profile during insertion (Bertoglio 2016; Chopra 2013a; Johansson 2013). PICCs are associated with greater patient-reported satisfaction in adults requiring central venous access (Periard 2008). They have also been demonstrated to be a cost-effective intervention, with the average cost of a PICC insertion estimated at USD 690 per patient (Periard 2008), compared to approximately USD 1500 for other central vascular access devices (Di Carlo 2012). However, despite these perceived benefits, PICC complications are common, with 30% of PICCs failing prior to the completion of therapy (Shen 2009; Ullman 2015).

Description of the condition

PICC failure can occur due to infectious, mechanical or vascular complications including deep venous thrombosis (DVT), occlusion, catheter-associated blood stream infection (CABSI), dislodgement or breakage (Abedin 2008; Yamamoto 2002; Yap 2006). A recent systematic review in paediatrics found PICCs had

the second highest failure rate of all central venous access devices after haemodialysis catheters (incidence rate 12.4; 95% confidence interval (CI) 10.0 to 14.9) (Ullman 2015). Vascular complications associated with PICC failure include the development of DVT due to vein occlusion and vessel irritation. A meta-analysis of more than 29,000 adults demonstrated PICCs were associated with a higher risk of DVT than CVCs (odds ratio 2.55, 95% CI 1.54 to 4.23, P < 0.0001), with a weighted frequency of PICC-related DVT of 6.7% (95% CI 4.7 to 8.6) (Chopra 2013b). PICC-related DVTs were more prevalent in vulnerable diagnostic groups such as intensive care patients or those with an oncology diagnosis (Chopra 2013b). PICC-related thrombus is associated with increased morbidity and mortality (Chopra 2012). In paediatrics, a systematic review of 74 cohort studies found PICCs had the highest incidence of catheter occlusion or blockage per 1000 catheter days (Ullman 2015). PICC-related DVTs affect around 7% of children, with recent pilot trial data demonstrating DVTs were the primary reason for PICC failure (Kleidon 2018). However, the true incidence of PICC-related DVTs is likely to be higher due to the presence of unscreened and asymptomatic DVTs.

Infection is another serious complication associated with central venous access and PICC placement. PICC-related CABSI affects more than 5% of hospitalised adults (Chopra 2013c), and 8% of hospitalised children (Ullman 2015), with *Staphylococcus aureus* and *S epidermidis* the most commonly isolated pathogens (Ullman 2015). A cohort study of hospitalised adults (966 PICCs; 26,887 catheter days) found CABSI was associated with an increased length of stay and multi-lumen PICCs (Chopra 2014). CABSI particularly impacts vulnerable patients such as neonates (Shalabi 2015), or oncology patients (Chopra 2013c), and is associated with an almost three-fold increase in hospital mortality (Ziegler 2015). PICC failure due to CABSI is estimated to cost the USA healthcare system between USD 11,000 (Warren 2006) and USD 69,000 (Wilson 2014) per episode.

Description of the intervention

Developments in PICC material and design have been purported to reduce the incidence of PICC failure and associated complications. The interventions under consideration are innovations in PICC material and design that include power injectable polyurethane, integrated valve technology and anti-thrombogenic or antimicrobial surface modifications. Desirable properties of PICC material and design include:

- soft, flexible catheter material for patient comfort and ease of insertion, reducing procedural risks such as vessel trauma;
- mechanical stability of the outer lumen to withstand rapid injection pressures, with a corresponding internal lumen large enough to enable infusion and aspiration;
- low adherence of blood components, biofilm formation and microbial colonisation; and
- provision of cost-effective therapy.

How the intervention might work

The primary goal of central vascular access using a PICC is to facilitate the reliable delivery of infusates over a prolonged period, for both in- and outpatient settings. Choice of PICC material and design can play a vital role in preventing or reducing device failure and subsequent reinsertion procedures. Early PICCs were predominately manufactured using silicone-based materials, which were considered soft and 'stretchable' for increased patient comfort and ease of placement (Gallieni 2008). However, these PICCs had smaller internal lumens, tolerated lower injectable pressures (50 psi) and were associated with an increased risk of fracture and dislodgement (Poli 2016). Subsequent PICCs were composed of a stronger polyurethane material which tolerated higher pressures (> 100 psi) with only a small decrease in catheter flexibility. However, these first generation polyurethane PICCs were associated with an increased risk of phlebitis and vessel trauma due to the rigidity of the material (Seckold 2015). Newer polyurethane PICCs are composed of material blends, which soften with body temperature and facilitate injection pressures of up to 300 psi (power injectable), whilst maintaining catheter workability and resilience (May 2015).

Surface-modified PICCs are becoming increasingly available in clinical practice. Current approaches for introducing anti-thrombogenic properties into PICCs include the use of hydrophilic, hydrophobic or biological surfaces, and the addition of drugs (Ullman 2018). Hydrophillic surfaces - or grafted surface polymers - decrease protein reabsorption through a water-soluble surface layer, conversely hydrophobic polymers rapidly absorb proteins and have the ability to 'repel' water mass. Biological grafting entails coating the surface of the PICC with a protein that may reduce the development of thrombosis such as albumin (Freitas 2003). In vitro studies have demonstrated anti-thrombogenic PICC surface modifications that inhibit platelet activation, and adherence of blood components to the catheter wall, and can potentially lower the risk of catheter-associated venous thrombosis (Kleidon 2018). Finally, catheter coating or impregnation using drugs such as chlorhexidene may inhibit bacterial cell growth and division within the PICC. This is particularly important in CABSI, where detached microbial cells from the biofilm can re-infect the blood, leading to organism resistance to antibiotics. Antimicrobial PICCs are impregnated with an antibiotic (e.g. minocycline plus rifampicin) or antiseptic (chlorhexidine-silver sulphadiazine). Antimicrobial impregnation in CVCs has been demonstrated to reduce the risk of CABSI significantly by preventing intraluminal colonisation (Lai 2016). It is proposed that PICCs with modified materials provide protective properties, whilst not adversely impacting catheter mechanical properties (Mermel 2001; Raad 2009).

In addition to PICC material modification, innovations in PICC design, such as valved PICCs, have been created to reduce the occurrence of PICC-related complications. Valved PICCs incorporate a valve either distally in a closed-end catheter, or proximally,

where a valve is incorporated into the hub of the catheter. The valve opens with infusion or aspiration pressure (Hoffer 2001), and closes during pressure fluctuations, creating a closed system and reducing the potential for blood reflux into the catheter (Pittiruti 2014). Valve technology has been purported to reduce the risk of catheter occlusion and thrombus, thus providing a clinical benefit (Hoffer 2001; Kleidon 2018). With the increased availability of technologically modified PICCs, clinicians need to know the clinical- and cost-effectiveness of catheter modifications, and which innovations reduce PICC-associated complications and failure.

Why it is important to do this review

PICCs are associated with serious complications, a high failure rate and negative sequelae for patients and healthcare systems. PICC failures necessitating multiple PICC insertions are associated with increased complications and increased procedural complexity due to vascular anatomical changes (Yang 2012). In children, subsequent PICC placement is associated with an increased risk of DVT. A prospective cohort study found an almost six-fold increase in the risk of developing a symptomatic DVT compared to first PICC placement (95% CI 2.25 to 16.04) (Gnannt 2018). Choosing the most appropriate PICC for the patient and healthcare system is important. Determining the efficacy and safety of various PICC materials and designs may contribute to catheter selection and subsequent reduction in healthcare-related costs and PICC complications.

OBJECTIVES

To assess the effectiveness of PICC material and design in reducing catheter failure and complications.

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomised controlled trials (RCTs) that evaluate PICC design and materials. We will include clinical controlled trials in the absence of RCTs.

Types of participants

We will include people of any age, in any setting (inpatient or outpatient), who require a PICC.

Types of interventions

We will include trials comparing one type of catheter material or catheter design to standard PICCs (without design or material), or with any other modification. Modifications of PICC material and design can include, but are not limited to:

Material:

- power-injectable polyurethane;
- polyurethane;
- silicone;
- surface-modified polyurethane;
- chemical-bonded PICCs;
- medication-impregnated PICCs;
- antiseptic-coated PICCs.

Design:

- valve technology; and
- clamp,

We plan to investigate the following main comparisons:

- anti-thrombogenic surface-modified catheters versus catheters without surface modification;
- antimicrobial-impregnated catheters versus non-impregnated catheters;
- catheters with integrated-valve technology versus catheters without valve technology; and
- power-injectable polyurethane catheters versus silicone catheters.

Types of outcome measures

Primary outcomes

- Venous thromboembolism, defined as either:
  - development of symptomatic thrombosed vessel (partial or complete) at the PICC site, diagnosed via ultrasound (Frey 2006; Yamamoto 2002); or
  - symptomatic DVT as described by the trial investigator.
- PICC-associated bloodstream infection (CABSI) as defined by one of the following criteria:
  - primary bacteraemia or fungaemia with at least one positive blood culture from a peripheral vein with no other identifiable source for the bloodstream infection (BSI) other than the PICC, plus one of:
    - a positive semiquantitative (> 15 colony-forming units (cfu)); or
    - a positive semiquantitative (> 15 cfu); or
    - a quantitative (> 10^3 cfu) device culture, with the same organism (species and antibiogram) isolated from the PICC and blood;
  - two blood cultures (one from the PICC hub and one from a peripheral vein), that both meet the PICC-related BSI

criteria for quantitative blood cultures (three-fold greater colony count of growth for the same organism as from the peripheral blood), or differential time to positivity (DTP; growth of the same microbe from hub drawn blood at least two hours before growth from the peripheral blood);

- two quantitative blood cultures of samples obtained through two catheter lumens in which the colony count for the blood sample drawn through one lumen is at least three-fold greater than the colony count for the blood sample from the second lumen; or
- laboratory-confirmed BSI (LCBSI) that is not secondary to an infection at another body site (excluding mucosal barrier injury LCBSI), with PICC in place for more than two calendar days on the day of the BSI (i.e. the day of PICC placement is Day 1) and the PICC in place on the date of the event or the day before, when all elements of LCBSI, were first present together (Horan 2008).

- Occlusion: complete blockage of the PICC lumen or lumens including fibrin sheath and medication precipitate. This includes aspiration and infusion occlusion and occlusions that resolve with tissue plasminogen activator (Goossens 2016), and intraluminal thrombosis or fibrin sheath as described by the trial investigator.

- All-cause mortality.

Secondary outcomes

- Catheter failure: cessation of catheter function prior to the completion of necessary therapy.
- Incidence of PICC-related BSI: laboratory confirmed with matched organism from blood culture and catheter tip culture.
- Catheter breakage: visible split in PICC material diagnosed by leakage or radiographic evidence of infiltration or extravasation from a portion of the PICC into tissue.
- PICC dwell time: hours from insertion until removal.
- Other safety endpoints: adverse effects including any local or systemic allergic reactions to chemical or drugs used to coat, bond or impregnate PICCs.

Search methods for identification of studies

Electronic searches

The Cochrane Vascular Information Specialist aims to identify all relevant RCTs regardless of language or publication status (published, unpublished, in press, or in progress).
The Information Specialist will search the following databases for relevant trials.

- The Cochrane Vascular Specialised Register via the Cochrane Register of Studies (CRS-Web).
- The Cochrane Central Register of Controlled Trials (CENTRAL) via the Cochrane Register of Studies Online (CRSO).
- MEDLINE (Ovid MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily and Ovid MEDLINE) (1946 onwards).
- Embase Ovid (from 1974 onwards).
- CINAHL EBSCO (from 1982 onwards).

The Information Specialist has devised a draft search strategy for RCTs for MEDLINE which is displayed in Appendix 1. This will be used as the basis for search strategies for the other databases listed.
The Information Specialist will search the following trials registries:

- ClinicalTrials.gov (www.clinicaltrials.gov);
- World Health Organization International Clinical Trials Registry Platform (www.who.int/trialsearch).

Searching other resources

To identify further relevant studies we will handsearch bibliographies of all retrieved studies. We will also review references cited in previous related Cochrane Reviews.

Data collection and analysis

Selection of studies

Two review authors (JAS, TK) will independently screen titles and abstracts of retrieved studies for relevance. We will retrieve full versions of all potentially eligible studies. The same two review authors will independently screen the full papers for eligibility, using the predefined inclusion and exclusion criteria to select eligible studies. We will resolve discrepancies between review authors through discussion and consensus with a third review author (AU). To facilitate transparency in reporting, we will publish a full list of included and excluded studies with reasons for exclusion using a PRISMA flowchart (Liberati 2009).

Data extraction and management

We will extract data from eligible studies using a data extraction sheet. We will extract the following data: study characteristics, information relating to the risk of bias, primary and secondary outcome measures and outcome data. One review author (JS) will enter data into Review Manager 2014 and a second review author will independently cross-check this for accuracy and agreement. We will resolve any discrepancies through discussions and consensus with a third review author (AU). For studies with more than one report, we will extract maximum data but we will not duplicate data in analyses.

Assessment of risk of bias in included studies

Two review authors (JAS, TK) will independently assess any possible risk of bias in eligible studies using Cochrane's 'Risk of bias' assessment tool (Higgins 2011). The tool includes assessment of the following criteria:

- adequacy of sequence generation;
- adequacy of allocation concealment;
- blinding;
- incomplete outcome data;
- selective reporting; and
- other sources of bias.

We will assign a judgement of low, high or unclear risk of bias for each criterion. We will resolve discrepancies through discussion and consensus and complete a 'Risk of bias' table for each eligible study.

Measures of treatment effect

The primary analysis will involve pair-wise comparison of treatment effect between PICC material and design types, using the predefined outcomes. Effect measures for dichotomous outcomes will be calculated using risk ratios (RR) and 95% confidence intervals (CI). Effect measures for continuous outcomes will be calculated using mean difference (MD) and 95% CI. For outcomes presented as rate-per-time period we will perform inverse variance analysis using rate ratios (RaR) and standard errors (SE). If studies use different measurement scales we will analyse using standardised mean difference (SMD).

Unit of analysis issues

The unit of analysis will be based on the predefined included study design (RCT) and is likely to be per participant. We will however, include studies which define the unit of analysis as PICC and perform a sensitivity analysis to examine the potential risk of bias.

Dealing with missing data

We will attempt to obtain missing data on study methods, participants and statistics by contacting study authors. If we do not receive a response from study authors, we will analyse only the available data. We will perform quantitative analyses on an intention-to-treat basis.

Assessment of heterogeneity

We will consider methodological, statistical and clinical heterogeneity of included studies. We will investigate statistical heterogeneity using a combination of methods including visually inspecting the forest plot and the associated Chi^2 statistic (using an alpha level 0.10 to determine statistical significance). To assess the impact of trials' heterogeneity (variation in effect estimates that are not due to chance (Higgins 2011)), we will interpret the I^2 statistic using the Higgins-Thompson method (where low heterogeneity, moderate heterogeneity, and high heterogeneity can loosely be equated to 25%, 50% and 75%, respectively) (Higgins 2003). Due to anticipated clinical heterogeneity, we will use a random-effects model (Higgins 2003). We will explore clinical variation across trials using descriptive statistics to summarise participant characteristics, sample size, intervention and outcome measures.

Assessment of reporting biases

We will assess reporting bias using funnel plots if ten or more trials meet review inclusion criteria. We will report each outcome separately. We will contact study authors if further clarification of outcomes reported in methods versus outcomes reported in results is required.

Data synthesis

Initially, we will use qualitative synthesis to summarise study results. Data will be entered into Review Manager 2014. We will undertake a meta-analysis where more than one study applies the same intervention and measures the same outcome. Due to expected clinical heterogeneity, we will use a random-effects model for all analyses. Where pooled analyses are not possible, we will report the results of the individual studies separately. We will use intention-to-treat data where possible in analyses.

Subgroup analysis and investigation of heterogeneity

We will undertake the following subgroup analyses for the primary outcomes if sufficient data are available:

- paediatric participants (less than 18 years) versus adult participants (18 years or over);
- participants diagnosed with oncology or haematology pathology versus other participants;
- participants in the intensive care unit versus participants in other settings;
- inpatient versus outpatient settings; and
- participants receiving lipid and parenteral nutrition (PN) versus participants not receiving lipid and PN.

In addition to the main pair-wise analysis, we plan to investigate the following comparisons if data are available:

- PICCs with a proximal valve versus PICCs with a distal valve;
- PICCs with one type of anti-thrombotic coating versus all other anti-thrombotic coated PICCs;
- Chlorhexidine gluconate (CHG)-impregnated PICCs versus all other antimicrobial impregnated PICCs;
- minocycline-impregnated PICCs versus all other antimicrobial-impregnated PICCs; and

- rifampicin-impregnated PICCs versus all other antimicrobial-impregnated PICCs.

If sufficient data are available we will undertake comparisons of 'clustered' interventions due to the variety of PICC technology and the aim of each design or modification innovation.
PICC-associated BSI and venous thrombosis:

- PICCs with two or more modifications (e.g. anti-thrombogenic material with valve technology, antimicrobial-impregnated with valve technology, impregnation, valve technology) versus PICCs without modification .

Sensitivity analysis

We plan to conduct the following sensitivity analyses:

- excluding studies with a high risk of bias - we will only include studies that are assessed as having a low risk of bias in all key domains, namely adequate sequence generation, adequate allocation concealment, and blinding of outcome assessor for estimates of treatment effect;
- excluding studies which defined PICC as the unit of analysis.

'Summary of findings' table

We will prepare 'Summary of findings' tables using the web-based version of GRADEpro to present the findings for the main comparisons (GRADEpro GDT 2015).

- Anti-thrombogenic surface-modified catheters versus catheters without surface modification.
- Antimicrobial-impregnated catheters versus non-impregnated catheters.
- Catheters with integrated-valve technology versus catheters without valve technology.
- Power-injectable polyurethane catheters versus silicone catheters.

We will include the seven outcomes which are most clinically relevant to healthcare professionals and consumers:

- venous thromboembolism;
- PICC-associated bloodstream infection;
- all-cause mortality;
- catheter failure;
- PICC-related BSI;
- occlusion; and
- catheter breakage.

We have created a draft 'Summary of findings' table for this protocol (see Table 1). We will grade the quality of the body of evidence using the criteria developed by the GRADE Working Group (Atkins 2004). We will consider the five GRADE factors of study limitations, consistency of effect, imprecision, indirectness and publication bias to assess the quality of the body of evidence for each outcome and the body of evidence in the review as high, moderate, low or very low (GRADEpro GDT 2015; Higgins 2011).

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* *Indicates the major publication for the study*

ADDITIONAL TABLES

Table 1. Example 'Summary of findings' table

Anti-thrombogenic surface modified catheters versus catheters without surface modification for reducing the risk of peripherally inserted central catheter (PICC) failure						
Patient or population: people requiring a PICC **Settings:** in- or outpatient settings (medical or surgical intensive care units, oncology, general wards or any other inpatient or outpatient setting) **Intervention:** anti-thrombogenic surface modified PICCs **Control:** non surface modified PICCs						
Outcomes	**Illustrative comparative risks* (95% CI)**		**Relative effect (95% CI)**	**No. of Participants (studies)**	**Quality of the evidence (GRADE)**	**Comments**
	Assumed risk	**Corresponding risk**				
	Non surface modified PICCs	**Anti-thrombogenic surface modified PICCs**				
Venous thromboembolism (follow up)						
PICC-associated BSI (follow up)						
Occlusion (follow up)						
All-cause mortality (follow up)						
Catheter failure (follow up)						
PICC-related BSI (follow up)						
Catheter breakage (follow up)						

Table 1. Example 'Summary of findings' table (*Continued*)

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **BSI**: blood stream infection; **CI**: confidence intervals; **PICC**: peripherally inserted central catheter
GRADE Working Group grades of evidence **High quality:** Further research is very unlikely to change our confidence in the estimate of effect. **Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. **Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. **Very low quality:** We are very uncertain about the estimate.

APPENDICES

Appendix 1. MEDLINE search strategy

1 exp Catheterization, Central Venous/ae, is, mt [Adverse Effects, Instrumentation, Methods]
2 exp Catheterization, Peripheral/ae, is, mt [Adverse Effects, Instrumentation, Methods]
3 exp Central Venous Catheters/ae [Adverse Effects]
4 PICC*.ti,ab.
5 "Peripherally inserted central venous catheter*".ti,ab.
6 "PIC line".ti,ab.
7 "percutaneous indwelling central catheter*".ti,ab.
8 or/1-7
9 exp Equipment Design/
10 exp POLYURETHANES/
11 exp SILICONES/
12 "antimicrobial-impregnated ".ti,ab.
13 "Antiseptic coated".ti,ab.
14 bonding.ti,ab.
15 "catheter wall".ti,ab.
16 "Chemical bonded".ti,ab.
17 Clamp.ti,ab.
18 coating.ti,ab.
19 design*.ti,ab.
20 flexibil*.ti,ab.
21 impregnat*.ti,ab.
22 "injectable pressure*".ti,ab.
23 "injection pressure*".ti,ab.
24 material*.ti,ab.
25 mechanical.ti,ab.
26 micropattern.ti,ab.
27 nonstick.ti,ab.

28 non-stick.ti,ab.
29 non-valved.ti,ab.
30 polymer.ti,ab.
31 polyurethane.ti,ab.
32 "Power injectable".ti,ab.
33 rigid*.ti,ab.
34 silicone.ti,ab.
35 stretch*.ti,ab.
36 "surface modif*".ti,ab.
37 valve.ti,ab.
38 valved.ti,ab.
39 (compare adj2 complications).ti,ab.
40 or/9-39
41 8 and 40
42 randomized controlled trial.pt.
43 controlled clinical trial.pt.
44 randomized.ab.
45 placebo.ab.
46 drug therapy.fs.
47 randomly.ab.
48 trial.ab.
49 groups.ab.
50 or/42-49
51 exp animals/ not humans.sh.
52 50 not 51
53 41 and 52

CONTRIBUTIONS OF AUTHORS

JAS: conceived the review question, developed the protocol and co-ordinated the protocol development. Completed the first draft, made an intellectual contribution and approved the final version prior to submission. Guarantor of the review.

TK: conceived the review question, edited the protocol, made an intellectual contribution and approved the final version prior to submission.

HP: edited the protocol, made an intellectual contribution and approved the final version prior to submission.

RS: made an intellectual contribution and approved the final version prior to submission.

JS: edited the protocol, made an intellectual contribution and approved the final version prior to submission.

AU: conceived the review question, edited the protocol, made an intellectual contribution and approved the final version prior to submission.

DECLARATIONS OF INTEREST

JAS: none known.

TK: Griffith University has received money from Bard for employment of TK. Griffith University has received investigator-initiated research grants from Centurion Medical Products and Angiodynamics, led by TK and AU. This research was developed and completed independently from Centurion Medical Products and Angiodynamics, who had no involvement in the protocol development, data collection, data analysis or manuscript development related to the project. Griffith University has also received speaker fees (3M, Angiodynamics, Becton Dickinson, Cook Medical Specialties Australia), consultancy fees (3M, Angiodynamics, Becton Dickinson, Baxter, Cook Medical Specialties Australia), and investigator-initiated research grants from other vascular access product manufacturers (3M, Adhezion, Angiodynamics, Baxter, Becton Dickinson, Centurion Medical Products, Cook, FloMedical, Medical Specialties Australia), to support research led by TK and AU, unrelated to the PICC products included within this review. Angiodynamics provided funding for part of an RCT that will form part of the Cochrane Review. This grant was investigator-initiated and Angiodynamics did not play any part in study development, data collection, analysis or decision to publish. TK will not review this study. The review of this study will be undertaken by other authors on the review. All potential conflicts of interest have been declared in the statements above, TK declares she does not have any additional conflicts of interest. TK declares that all payments have been made to her institution and she has not received any personal gain from these bodies and none of the declared funding will bias the review.

HP: none known. HP declares she is currently employed as a senior lecturer at the School of Nursing and Midwifery, Griffith University, and holds an Early Career Fellowship for 2016-2019 supported by Asthma Australia.

RS: none known.

JS: none known.

AU: declares that Griffith University has received investigator-initiated research grants from Centurion Medical Products and Angiodynamics led by TK and AU. This research was developed and completed independently from Centurion Medical Products and Angiodynamics, who had no involvement in the protocol development, data collection, data analysis or manuscript development related to the project. Griffith University received an unrestricted investigator-initiated research grant from 3M in 2016 to support a research study on which AU is an investigator, but this study was unrelated to PICC materials and design. Griffith University received an unrestricted investigator-initiated research grant from Centurion Medical as funding for ongoing trials unrelated to PICC materials and design. Griffith University received an unrestricted investigator-initiated research grant from Angiodynamics in 2016 to support a research study, where AU is an investigator, relating to PICC materials and design. The funders were not involved in the development of the protocol, data collection, analysis or preparation of the manuscript. Griffith University has also received speaker fees in a series of lectures regarding AU's independent research related to vascular access internationally (3M), and investigator-initiated research grants from other vascular access product manufacturers (3M (research into medical adhesive-related skin injury prevalence), Adhezion, Becton Dickinson, Centurion Medical Products (for research into catheter dressings), FloMedical, Medical Specialties Australia), to support research led by TK and AU.

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NOTES

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