Prevention of Peripheral Intravenous Catheter Failure

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Prevention of Peripheral Intravenous Catheter Failure

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Abstract

Background

Peripheral intravenous catheters (PVCs) are essential to modern healthcare and are the most frequently used vascular access device. They provide a quick, simple, and cost-effective method to gain vascular access, and up to 70% of hospitalised patients will receive at least one PVC during their admission; a large proportion of these are inserted by registered nurses. PVCs however frequently develop complications associated with their insertion and use which result in catheter failure. PVC failure interrupts important intravenous (IV) treatment, such as antibiotics or chemotherapy, and may result in longer hospital stays and increased healthcare costs. Evidence-based nursing practice is vital for the prevention of PVC complications and failure.

Aims and objectives

The overarching aim of this research was to identify effective methods to prevent PVC failure. There were two objectives to guide the two research phases: 1) to determine modifiable risk factors associated with PVC failure and complications; and 2) to evaluate the feasibility of large randomised controlled trial (RCT) of a vascular access specialist versus a generalist PVC inserter model to prevent PVC failure.

Design

This research was underpinned by the Medical Research Council Framework for the Evaluation of Complex Interventions and consisted of two study phases: a multivariate regression analysis of an existing large dataset; and a pilot randomised control trial comparing the generalist inserter with a vascular access specialist for PVC placement. A

systematic review with meta-analysis on PVC failure and a critical review of literature evaluating the effectiveness of a specialist versus a generalist PVC inserter model to prevent failure were also undertaken to clearly identify the compelling need for the arch.

Phase 1

Setting: Medical and surgical wards of a Queensland tertiary hospital

Sample: Adult patients requiring a PVC

Measurements: Demographic, clinical, and potential PVC risk factors had been collected for a prospective cohort study. Failure outcomes were noted if the catheter had complications at removal.

Main Result

Data from 1,000 patients were analysed. Catheter failure occurred in 512 (32%) of 1578 PVCs. Occlusion/infiltration risk factors were: IV flucloxacillin [Hazard Ratio (HR) 1.98, 95% confidence interval (CI) [1.19–3.31], 22-gauge PVCs [HR 1.43, 95% CI 1.02–2.00], and female patients [HR 1.48, 95% CI 1.10–2.00]. Phlebitis was associated with: female patients [HR 1.81, 95% CI 1.40–2.35], bruised insertion sites [HR 2.16, 95% CI 1.26–3.71], IV flucloxacillin [HR 2.01, 95% CI 1.26–3.21], and dominant side insertion [HR 1.39, 95% CI 1.09–1.77]. Dislodgement risks were a paramedic insertion [HR 1.78, 95% CI 1.03–3.06]. Each increase by 1 in the average number of daily PVC accesses was associated [HR 1.1, 95% CI 1.03–1.20]–[HR 1.14, 95% CI 1.08–1.21] with occlusion/infiltration, phlebitis and dislodgement. Additional securement products were associated with less [HR 0.32, 95% CI 0.22–0.46]–[HR 0.63, 95% CI 0.48–0.82] occlusion/infiltration, phlebitis and dislodgement.

Phase 2

Setting: Medical and surgical wards of a Queensland tertiary hospital

Sample: 138 patients who were over the age of 18 and required a PVC for greater than 24 hours.

Study Design: Single-centre, parallel-group, pilot RCT

Interventions: Participants were randomised to have their PVC inserted by either:

- a Vascular Access Specialist (VAS), who for this trial was a member of an intravenous therapy team for over 20 years as well as a hospital and university educator of clinicians to place PVCs; or
- generalist inserters, who were accredited PVC inserters who placed the catheter as per usual hospital policy.

Primary and secondary outcomes

Feasibility outcomes were achieved: 92% of screened patients were eligible; two patients refused participation; there was no attrition or missing outcome data. PVC failure was higher with generalists 27/50 (54%) than for VAS 33/69 (48%) [228 vs 217 per 1000 PVC days; Incidence Rate Ratio 1.05, 95% CI 0.61–1.80]. There were no local or PVC-related infections in either group. All PVCs (n = 69) were successfully inserted in the VAS group. In the generalist group, 19 (28%) patients did not have a PVC inserted. There was inadequate data available for the cost-effectiveness analysis, but the mean insertion procedure time was two minutes in the VAS group and 11 minutes in the generalist group. Overall satisfaction with the PVC was measured on an 11-point scale (0 = not satisfied and 10 = satisfied) and higher in the VAS group (n = 43; median = 7) compared to the

generalist group (n = 20; median = 4.5). The multivariable model identified medical diagnosis and bed-bound status as significantly associated with higher PVC failure, and securement with additional non-sterile tape was significantly associated with lower PVC failure.

Conclusion

This PhD research has revealed the high rate of PVC failure in acute care hospitals, and extends existing evidence related to PVC failure and identified modifiable risk factors. These results, which include several newly identified risk factors for PVC failure, will inform education programs to improve inserter skill development and clinician management of PVCs to reduce catheter failure. The PhD work has confirmed the feasibility and need for a large, multi-centre RCT to test PVC insertion models and provides the first randomised data to support the VAS model as preferable to the generalist inserter model. PVC failure is a significant worldwide problem which, until now, appears unacknowledged and unaddressed. Effective nursing interventions and a strong evidence base for practice are vital for preventing poor outcomes for patients with PVCs. This PhD research identifies areas for improvement, and an urgent health system and professional response is needed.

Statement of originality

This work has not previously been submitted for a degree or diploma in any university. To the best of my knowledge and belief, the thesis contains no material previously published or written by another person except where due reference is made in the thesis itself.

Nicole Marsh

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List of Abbreviations

ANZCTR	Australian and New Zealand Clinical Trial Registry
AVA	Association for Vascular Access
BD	Becton Dickinson
BMI	Body Mass Index
BSI	Blood stream infection
CCU	Coronary Care Unit
CDC	Centers for Disease Control and Prevention
CDIM	Communicable Diseases Infection Management branch
CI	Confidence Interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CONSORT	Consolidated Standards of Reporting Trials
CRBSI	Catheter-Related Blood Stream Infection
eCRT	electronic Case Report Form
ED	Emergency Department
EMBASE	Excerpta Medica DataBASE
GYN	Gynaecology
HR	Hazard Ratio
HREC	Human Research Ethics Committee
IDD	Infectious Disease Department
ICU	Intensive Care Unit
IR	Incidence Rate
IV	Intravenous
IVTT	Intravenous Therapy Team
MED	Medical ward/unit
MeSH	Medical Subject Headings

MOOSE	Meta-analysis of Observational Studies in Epidemiology
MRC	Medical Research Council
NR	Not Reported
OB	Obstetrics
OPD	Outpatient Department
OT	Operating Theatre
p	*p*-value
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis
n	Number of participants
OR	Odds Ratio
PubMed	Public/Publisher MEDLINE database
PVC/PIV	Peripheral Intravenous Catheter
RBWH	Royal Brisbane and Women's Hospital
RCT	Randomised Controlled Trial
REDCap	Research Electronic Data Capture
ReN	Research Nurse
SD	Standard Deviation
STROBE	Strengthening the Reporting of Observational studies in Epidemiology
SURG	Surgical ward/unit
UK	United Kingdom
USA	United States of America
VAS	Vascular Access Specialist
VAD	Vascular Access Device
WHO	World Health Organization

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Dissemination of study results

Peer-reviewed publications

1. Marsh, N., Webster, J., Ullman, A. J., Mihala, G., Cooke, M., & Rickard, C. M. Peripheral intravenous catheter failure and complications in adults: a systematic review and meta-analysis. *BMJ Open.* [Prepared for submission]
2. Marsh. N., Webster, J., Cooke, M., & Rickard, C. M. (2017). The RELIABLE trial (RELiable Intravenous Access By Line Experts): A pilot randomised controlled trial protocol of expert versus generalist peripheral intravenous catheter insertion. *Vascular Access*, *3*(2), 3–7.
3. Marsh, N., Webster, J., Larsen, E., Mihala, G., Cooke, M., & Rickard, C. M. (2018). Observational study of peripheral intravenous catheter outcomes in adult hospitalised patients – a multivariable analysis of peripheral catheter failure. *Journal of Hospital Medicine*, *13*(2), 83–89.
4. Marsh, N., Webster, J., Larsen, E., Genzel, J., Cooke, M., Mihala, G., Cadigan, S., & Rickard C. M. (2018). Expert versus generalist peripheral intravenous catheter insertion: A pilot randomised controlled. *Trials*, *19*(564), 1–10.

Invited conference presentations

1. Marsh, N., & Rickard, C. M. (2018, September). *Reliable intravenous access by line experts (the RELIABLE Pilot Trial)* comparing *PIV insertion by generalists with insertion by a vascular access specialist.* Association for Vascular Access (AVA) Conference, Columbus, Ohio, USA.

2. Marsh, N. (2018, June). *Different transparent dressings – different problems.* World Congress Vascular Access (WoCoVA), Copenhagen, Denmark. [Note: results from Phase 1 presented]

3. Marsh, N. (2018, June). *Securement of PIVs*. World Congress Vascular Access (WoCoVA), Copenhagen, Denmark. [Note: results from systematic review and Phase 1 presented]

4. Marsh, N., & Rickard, C. M. (2017, September). *The peripheral intravenous catheter journey – a prospective cohort study of 1000 patients.* Association for Vascular Access (AVA) Conference, Phoenix, Arizona, USA.

5. Marsh, N., & Rickard, C. M. (2017, September). *Secure my intravenous line effectively – (the SMILE trial). Innovative peripheral intravenous (PIV) dressing techniques to reduce PIV failure.* Association for Vascular Access (AVA) Conference, Phoenix, Arizona, USA. [Note: results from Phase 1 presented]

6. Moureau, N., Marsh, N., & Zhang, L. (2016, September). *Evaluation of skin colonization and placement of catheter exit sites.* Association for Vascular Access (AVA) Conference, Orlando, Florida, USA. [Note: results from Phase 1 presented]

Oral abstract presentations

1. Marsh, N. (2018, November). *How often are patients experiencing local and catheter-related bloodstream infections within an adult population? A systematic review of peripheral venous catheter complications and failure.* Australasian College for Infection Prevention and Control (ACIPC), Brisbane.
2. Marsh, N. (2017, May). *Life cycle of peripheral intravenous catheters: a prospective cohort study of 1000 patients.* Australian Vascular Access Society (AVAS) 2nd Scientific Meeting, Perth.

Poster presentations

1. Marsh, N., Webster, J., Ullman, A., Mihala, G., Cooke, M., & Rickard, C. M. (2018). *Peripheral intravenous catheter failure and complications in adults: a systematic review*. 27th Annual Royal Brisbane and Women's Hospital Healthcare Symposium, Brisbane. *Winner of the Cecilia Brazil Nursing Research Award.*
2. Marsh, N., Webster, J., Larsen, E., Genzel, J., Cooke, M., Mihala, G., Cadigan, S., & Rickard, C. M. (2018). *Expert versus generalist inserters for peripheral intravenous catheter insertion: pilot randomised controlled trial*. 27th Annual Royal Brisbane and Women's Hospital Healthcare Symposium, Brisbane.
3. Marsh, N., Webster, J., Larsen, E., Cook, M., Mihala, G., & Rickard, C. M. (2016, June). *Identifying risk factors for peripheral intravenous catheter failure from a prospective cohort study of 1000 patients*. World Congress Vascular Access (WoCoVA), Lisbon, Portugal.
4. Marsh, N., Webster, J., Larsen, E., Cook, M., & Rickard, C. M. (2016). *Identifying risk factors for peripheral intravenous catheter failure from a prospective cohort study of 1000 patients.* Royal Brisbane and Women's Hospital Healthcare Symposium, Brisbane. *Winner of the Cecilia Brazil Nursing Research Award*.

List of published work included in thesis

Section 11.1 of the Griffith University Code for the Responsible Conduct of Research (Criterial for authorship), in accordance with moral rights of authors under Australian copyright law contained in the *Intellectual Property Policy*, states:

To be named as an author, a researcher must have made a substantial scholarly contribution to the creative or scholarly work that constitutes the research output and be able to take public responsibility for at least that part of the work they contributed. Attribution of authorship depends to some extent on the discipline and publisher policies, but in all cases, authorship must be based on substantial contributions in one or more of:

- conception and design of the research project
- analysis and interpretation of research data
- drafting or making significant parts of the creative or scholarly work or critically revising it so-as-to contribute significantly to the final output.

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- Offer authorship to all people, including research trainees, who meet the criteria for authorship listed above, but only those people.
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- Include in the list of authors only those who have accepted authorship.

- Appoint one author to be the executive author to record authorship and manage correspondence about the work with the publisher and other interested parties. Any part of an article that is critical to its main conclusion must be the responsibility of at least one author.

Included in this thesis are four papers, in Chapter 2, 3, 4 and 5, co-authored by my supervisors and other researchers. My contribution to each paper is outlined at the front of appropriate chapters. The bibliographic details/status for these papers including all co-authors are:

Chapter 2:

Prepared for submission

Marsh, N., Webster, J., Ullman, A. J., Mihala, G., Cooke, M., & Rickard, C. M. Peripheral intravenous catheter failure and complications in adults: a systematic review and meta-analysis. *BMJ Open.*

Chapter 3:

Marsh. N., Webster, J., Cooke, M., & Rickard, C. M. (2017). The RELIABLE trial (RELiable Intravenous Access By Line Experts): A pilot randomised controlled trial protocol of expert versus generalist peripheral intravenous catheter insertion. *Vascular Access*, *3*(2), 3–7.

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Chapter 4:

Marsh, N., Webster, J., Larsen, E., Mihala, G., Cooke, M., & Rickard, C. M. (2018). Observational study of peripheral intravenous catheter outcomes in adult hospitalised

patients – a multivariable analysis of peripheral catheter failure. *Journal of Hospital Medicine*, *13*(2), 83–89.

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Chapter 5:

Marsh, N., Webster, J., Larsen, E., Genzel, J., Cooke, M., Mihala, G., Cadigan, S., & Rickard C. M. (2018). Expert versus generalist peripheral intravenous catheter insertion: A pilot randomised controlled. *Trials*, *19*(564), 1–10.

(Copyright approval as per Appendix C)

Chapter 1 — Introduction

Introduction

Peripheral intravenous catheters (PVCs) are used for the short-term delivery of intravascular fluids and medications. They are the most commonly used of all vascular access devices with worldwide annual sales of approximately 2 billion each year (Rickard & Ray-Barruel, 2017). A recent study to quantify the utilisation of vascular access devices in Queensland public hospitals found that in 2016, 2,690,000 PVCs were purchased, accounting for 97.8% of all vascular access devices (Tuffaha et al., 2018). Peripheral intravenous catheters are an essential element of modern healthcare with a reported 70% of hospitalised patients requiring at least one PVC per hospital admission (Zingg & Pittet, 2009). For such an important device, PVCs remain susceptible to catheter failure and complications such as phlebitis and infiltration. Practices for reducing complications remain unclear, and there is a need to provide better guidance for clinicians.

This research has sought to synthesise evidence on and quantify PVC failure and complications with a focus on identifying modifiable and non-modifiable risk factors in order to inform the testing of a PVC insertion model that prevents catheter failure. This chapter will provide the background to the extent of the problem of PVC failure and complications, outline current PVC insertion practices and guidelines, and argue the significance of the research, as well as detail the conceptual framework, research aims and questions for the study.

Background

A PVC is a flexible hollow tube that is progressed over a needle and into a peripheral vein, typically the cephalic or basilic vein of the forearm or the metacarpal vein of the hand, creating direct access to a patient's vascular system (Campbell & Bowden, 2011; Gabriel, 2010; McCallum & Higgins, 2012; O'Grady et al., 2011). PVCs come in an array of sizes, ranging from 14–24 gauge (largest to smallest) and lengths from 25–45 mm (Dougherty, 2008a; Gabriel, 2010). Catheter size selection is important, as it influences the speed at which infusions can be administered. A large gauge, short length PVC will deliver an infusion more quickly than a small gauge, long length PVC (Gabriel 2005).

Peripheral intravenous catheters have progressed considerably from their first incarnation with a goose quill, silver, glass and steel tubes, to modern materials that claim low irritation to the vein, such as Vialon™, Teflon™, polyvinylchloride and polyurethane (Dougherty, 2008b; Zhang, Keogh, & Rickard, 2013). Catheters made from Teflon™ and polyurethane are associated with lower infection rates than those made from polyvinylchloride or polyethylene (O'Grady et al., 2011). However, some healthcare environments have not progressed to modern PVCs and still use steel needle catheters. Such catheters are reported to increase the risk of infiltration and extravasation, and subsequent device failure (O'Grady et al., 2011).

Commercially, there is a plethora of differently designed PVCs available to clinicians. These include catheters with additional wings that help attach the device to the skin, or access points that allow the administration of medications without interrupting an intravenous (IV) infusion (Dougherty, 2008b). Other PVCs have been designed to include extension tubing as part of the device, cutting down on the number of additional products being added to the catheter (López et al., 2014). Many healthcare settings use safety

catheters to reduce the risk of needlestick injury. These products have a passive or user-activated safety feature that shields the stylet or needle introducer before it is removed from the catheter, protecting the inserter from needlestick injury (Adams, 2012; Dougherty, 2008b).

Clinical use of a PVC

The insertion of a PVC is considered the fastest, simplest, and most cost-effective method to gain vascular access and is particularly useful for the short-term delivery of IV fluids, medications, blood products, and contrast media (Sabri, Szalas, Holmes, Labib, & Mussivand, 2012). The use of a PVC allows medicine concentrations to be met quickly and overcomes the limitations of patients who are fasting, or who are unable or refusing to take oral medications (Lavery & Ingram, 2006).

There are three ways in which IV therapy may be administered via PVC: bolus injection, intermittent infusion, and continuous infusion. The administration method selected depends on the type of IV therapy being delivered and the patient's clinical condition (Dychter, Gold, Carson, & Haller, 2012; Lavery & Ingram, 2006). Bolus infusions are used when a quick response or high blood concentration is needed (Lavery & Ingram, 2006). They are ideal for patients requiring fluid restriction or whose medicine is not chemically stable in solution (Dychter et al., 2012; Lavery & Ingram, 2006). Intermittent infusions offer similar benefits as a bolus injection, but reduce the risk of an adverse event related to speed-shock (the sudden adverse physiologic reaction to IV medications delivered too quickly) or medication reaction (Lavery & Ingram, 2006). A continuous infusion offers the benefits of a constant blood level of the administered product and therefore a constant effect (Dychter et al., 2012). Intermittent and continuous

infusions both increase the patient's risk of fluid overload and the possibility of an infusion error if the IV therapy is run too quickly or slowly (Dychter et al., 2012).

Historically, international guidelines related to the management of PVCs recommended routine replacement or re-site of PVCs every 72–96 hours to avoid catheter-related problems, specifically phlebitis (O'Grady et al., 2011). More recently, based on high-quality level 1 evidence (Webster, Osborne, Rickard, & New, 2015), this recommendation has been changed. Current guidelines now propose that a PVC may remain in place if it is functional and there are no clinical indications for its removal (Bodenham et al., 2016; Infusion Nurses Society, 2016; Loveday et al., 2014). The change reinforces the importance of assessing the patient's PVC site, including skin and vein integrity at every change of shift (Infusion Nurses Society, 2016). Additionally, if the new recommendation is to provide benefit to patients and reduce replacement costs, it is important to ensure that PVCs remain in place and functional for the duration of IV therapy. However, traditionally this has not been easy.

PVC failure and complications

Failure rates of PVCs prior to completion of therapy are alarmingly high, with the incidence of unscheduled re-insertions or device failure reported to range from 33%–69% (Bausone-Gazda, Lefaiver, & Walters, 2010; Dillon et al., 2008; Rickard, McCann, Munnings, & McGrail, 2010). This high failure rate remains true even in large academic facilities (Bausone-Gazda et al., 2010; Dillon et al., 2008; Rickard et al., 2012; Webster et al., 2008).

The most frequently reported sources of failure are phlebitis (irritation or inflammation of the vein wall), occlusion (blockage), infiltration/extravasation (IV

fluids/vesicant therapy moving into surrounding tissue), partial dislodgement or accidental removal, leakage, and infection (Bolton, 2010; Rickard et al., 2012; Webster et al., 2008).

Phlebitis is the irritation or inflammation of a vein wall, and when associated with thrombus formation is referred to as thrombophlebitis (McCallum & Higgins, 2012; Ray-Barruel, Polit, Murfield, & Rickard, 2014; Zingg & Pittet, 2009). Phlebitis has been the focus of research and commentary on PVC complications (Higginson & Parry, 2011; Ray-Barruel et al., 2014; Tagalakis, Kahn, Libman, & Blostein, 2002). It can have either a mechanical, chemical, or bacterial origin (Gabriel, 2010; Ray-Barruel et al., 2014).

Mechanical phlebitis is the result of a pistoning or rubbing motion of the PVC within the vein, damaging the tunica intima of the vessel wall (Campbell & Bowden, 2011; Gabriel, 2010). Causative factors associated with mechanical phlebitis are often linked to the physical features of the catheter itself (Helm, Klausner, Klemperer, Flint, & Huang, 2015; Macklin, 2003). A larger gauge catheter has been shown to increase the risk of mechanical phlebitis, presumably because it leaves less buffer room between the PVC and the vein wall (Campbell & Bowden, 2011; Helm et al., 2015; Macklin, 2003; Wallis et al., 2014). Longer length PVCs have been shown to decrease phlebitis risk when compared with shorter length catheters, possibly by providing greater stabilisation of the catheter and letting the PVC tip rest in the larger width, proximal veins (Helm et al., 2015; Macklin, 2003). Catheters composed of newer polyurethane materials that are less stiff than previous PVC materials have been associated with lower rates of phlebitis (Helm et al., 2015). This is probably due to the flexibility of the newer products creating less friction within the vein wall (Helm et al., 2015; Macklin, 2003). The location of the PVC insertion site can also increase the risk of mechanical phlebitis, particularly if the catheter is placed near a joint (Higginson & Parry, 2011) or if the PVC is poorly secured to the skin, allowing gross

movement of the catheter in the vein (Higginson & Parry, 2011; Macklin, 2003). Catheters inserted near a vein valve or at visible venous bifurcations will also have an increased risk of phlebitis due to the movement of the PVC tip (Macklin, 2003).

Chemical phlebitis occurs when IV medications or fluids irritate the vein wall (Higginson & Parry, 2011; McCallum & Higgins, 2012). Normal blood pH is approximately 7.4. When alkaline or acidic infusates are injected into a small vessel with insufficient blood flow, inadequately diluted, or infused too rapidly, the alteration in pH or osmolality can cause irritation of the vein (Macklin, 2003; McCallum & Higgins, 2012). Symptoms typically occur along the PVC tract or above the PVC tip, and can result in a palpable cord or dilated superficial vein (Macklin, 2003).

Infective phlebitis occurs when micro-organisms track along the insertion site and into the catheterised vein, irritating the vessel wall (Gabriel, 2010; Tagalakis et al., 2002). Causes include a breach in aseptic technique at insertion or during standard PVC maintenance that leads to colonisation of the internal or external PVC surface (Helm et al., 2015; Higginson & Parry, 2011). This type of colonisation can lead to biofilm formation, providing the ideal environment for the proliferation of bacteria, which can cause a local phlebitis reaction and have the potential to result in a catheter-related blood stream infection (CRBSI) (Higginson & Parry, 2011).

A recent systematic review focusing on phlebitis identified over 71 different phlebitis assessment scales (Ray-Barruel et al., 2014). Ray-Barruel explains that “it is unclear how best to assess phlebitis as no existing scale has undergone rigorous psychometric testing” (Ray-Barruel et al., 2014). Consequently, it is easy to see why phlebitis rates vary so widely between studies (2.6% to 67.2%) (Catney et al., 2001; Karadeniz, Kutlu, Tatlisumak, & Ozbakkaloglu, 2003; Rickard et al., 2010; Rickard et al.,

2012; Webster et al., 2008). Generally, phlebitis is characterised by a combination of tenderness/pain, erythema, oedema, purulent discharge, or a palpable cord, and results in the inability to use the PVC to gain vascular access i.e., PVC failure (Gabriel, 2010; Gallant & Schultz, 2006; Maki & Ringer, 1991; Tagalakis et al., 2002). However, in recent studies, phlebitis has been diagnosed using only one sign, usually erythema (Marsh, Webster, et al., 2018)

Occlusion, which can be partial or complete, is the inability to infuse fluids or medications through a previously functioning PVC (Helm et al., 2015). Occlusion can be mechanical in origin, such as the kinking of the catheter itself, or the position of the catheter tip against the vein wall may block the flow of infusates (Helm et al., 2015). Occlusion can also occur from irritation or trauma to the catheterised vein wall, leading to a release of thromboplastic substances and platelets. This process promotes the clotting of blood and can result in narrowing or complete occlusion of the catheterised vein (Gabriel, 2010; Royer, 2003). Occlusion of a PVC often results in infiltration of IV fluid or medications into the surrounding tissue or leaking from the insertion site (Gabriel, 2010).

Infiltration is the inadvertent leakage of a non-vesicant solution into surrounding tissues (Dychter et al., 2012). It may occur if the PVC pierces the vessel wall during insertion, if the PVC moves partially or completely outside the vein during the delivery of IV fluids, or if the vessel wall does not seal around the catheter, resulting in a slow leak of fluids into the surrounding tissues (Dougherty, 2008a). Infiltration can present with signs at the insertion site of stretched or blanched skin, oedema, cool skin temperature, and leakage of IV fluids (Rosenthal, 2007) (See Figure 6). The patient may also complain of discomfort or a tight feeling at the insertion site (Rosenthal, 2007). Although injury due to infiltration is often considered minor and usually resolves without any intervention, there have been

reports of long-term disability due to the inflammatory reactions related to the infiltrate solution in the surrounding tissue or the compression of surrounding tissue due to a large volume of fluid (Doellman et al., 2009).

Extravasation is the leakage of a vesicant solution, such as contrast media or chemotherapy medications, into surrounding tissues (Dychter et al., 2012). A vesicant is defined as any IV medication or fluid that could cause severe tissue damage, blistering, or necrosis once it leaves the vascular system and enters the surrounding tissues (Hadaway, 2007). The early signs and symptoms for extravasation are similar to infiltration, but the patient often complains of a burning, stinging pain (Dougherty, 2008a). Consequences from extravasation are often serious and can result in scarring, functional limitations, and the need for surgical intervention or even amputation (Hadaway, 2007).

Infiltration and extravasation may result from poor vascular access or fragile veins being unable to cope with the pressure, volume, or irritant nature of IV medications (Dougherty, 2008a). Patients identified as being at highest risk of fragile veins include: older adults; those receiving anticoagulants or corticosteroids; patients with communication impairment; and patients with chronic diseases such as cancer, diabetes, or cardiovascular disease (Dougherty, 2008a, 2010). Infiltration and extravasation may also be the result of clinical factors such as: poor PVC insertion technique; too large a catheter for the diameter of the vein; PVC site in a dominant hand or a region of joint flexion; multiple venepuncture attempts; poor PVC securement to the skin; poor monitoring of an infusion; and the inability of patients or clinicians to recognise the signs and symptoms of infiltration and extravasation (Doellman et al., 2009; Dougherty, 2008a).

Dislodgement, the partial or complete movement of a PVC out of the vein, occurs when there is poor securement of the catheter to the skin, or with patient interference

(Campbell & Bowden, 2011). Dislodgement or accidental removal reportedly accounts for up to 20% of catheter failures (Bolton, 2010; Dillon et al., 2008). A poorly secured catheter is often painful for a patient, and dislodgement results in catheter failure, delaying IV therapy and necessitating the insertion of a new IV device.

Infections associated with PVCs are thought to occur infrequently; however, many may go undetected due to short dwell time and quick discharge of patients who have this type of device (Hadaway, 2012). The skin normally acts as a protective barrier against bacteria accessing the body; PVC insertion creates an opportunity for contamination (Gabriel, 2010). Micro-organisms can cause local infection and may track along the surface of the PVC to contaminate the catheter tip and then the bloodstream (Morris & Heong Tay, 2008; O'Grady et al., 2011) (See Figure 7). The most common signs and symptoms of a local PVC-related infection are pain, erythema, pus, and palpable venous cord, whereas the more serious CRBSI presents with fever, chills, headache, tachycardia, and nausea/vomiting (Dychter et al., 2012). Of all the types of vascular access devices used clinically, PVCs are reported to have the lowest rate of CRBSI (0.1% per PVC, 0.5 per 1000 PVC days) (Maki, Kluger, & Crnich, 2006).

Potential extrinsic sources of PVC infection include: 1) clinicians' hands contaminating add-on devices, such as 3-way taps, extension sets, hubs, and syringe tips; 2) the lack of a clean, dry, intact dressing over the insertion site; or 3) injections including flushes or aspiration of blood from a closed IV system (Campbell & Bowden, 2011). Further intrinsic sources of infection include damaged fluid containers, contaminated IV fluids, PVCs, or equipment such as syringe drivers (Campbell & Bowden, 2011).

Failure of a PVC from any cause has significant implications for patient outcomes and experience, as well as healthcare budget. Repeated PVC replacements can lead to

venous access difficulties, increasing the need for more frequent replacements and the possibility of requiring a central venous access device (Marsh, Webster, Mihala, & Rickard, 2015; Monreal et al., 1999). Replacement of a PVC requires a new skin puncture, causing patient discomfort and providing an additional entry point for bacteria. The interruption to IV treatment also increases the likelihood of a longer hospital admission, placing a greater financial burden on the healthcare system by requiring additional clinical staff time, the replacement of dressings, catheters and IV administration sets (Dillon et al., 2008; Tagalakis et al., 2002).

Risk factors for PVC complications

High rates of PVC failure and subsequent catheter replacement necessitate a clearer understanding of the insertion and maintenance-related causes of catheter failure. A number of studies conducted in adults have identified associated risk factors for PVC failure, and these are presented in Table 1.1.

The PVC gauge has been identified as a risk factor for catheter failure: in particular, small gauge catheters (22 gauge or smaller diameter) (Abolfotouh, Salam, Bani-Mustafa, White, & Balkhy, 2014; Wallis et al., 2014) and large gauge catheters 18 gauge of larger diameter) (Catney et al., 2001; Cicolini, Bonghi, Di Labio, & Di Mascio, 2009; do Rego Furtado, 2011b; Lanbeck, Odenholt, & Paulsen, 2002; Wallis et al., 2014). This is best explained by Wallis et al. (2014) through a secondary analysis of a large data set of 5907 PVCs, which found that larger diameter PVCs have an increased risk of failure caused by phlebitis and smaller diameter catheters are at greater risk of accidental dislodgement.

Peripheral intravenous catheters inserted in the hand (Cicolini et al., 2009; Dillon et al., 2008; Karadeniz et al., 2003), anterior cubital fossa (do Rego Furtado, 2011b; Uslusoy

& Mete, 2008), or over a joint (Kaur, Thakur, Kaur, & Bhalla, 2011; Saini, Agnihotri, Gupta, & Walia, 2011) have also been associated with an increased risk of catheter failure. The movement of a PVC site over a joint increases the micro movement of the PVC within the vein and has been connected with an increased rate of phlebitis (Kaur et al., 2011; Saini et al., 2011).

Advances in healthcare have had a positive effect on prolonging life, and it is expected that the number of people over the age of 65 years will increase 6% by the year 2030 (Dychter et al., 2012). The ageing vein experiences atrophy of the connective tissue, compromising the endothelium layer of the vein wall (Schelper, 2003). This atrophy can lead to a paper thin vein wall that may fail or rupture when catheterised with a vascular access device (Schelper, 2003). An increased risk of PVC failure among the elderly has been reported in cohort studies (Karadeniz et al., 2003).

Device failure has also associated with PVCs that have inserted whilst patients are in the emergency department. A prospective study conducted in two tertiary hospitals found a 20% higher rate of PVC-associated *Staphylococcus aureus* infections with PVCs inserted in the emergency department compared to those inserted in the wards (Stuart et al., 2013). This high rate of infection associated with emergency PVC insertion has resulted in the Centers for Disease Control and Prevention (CDC) recommending PVCs inserted in emergency situations are replaced within 48 hours of placement (O'Grady et al., 2011).

Although previous research has identified a number of risk factors for PVC failure, there are limitations to this research, such as small study sizes (Bai, Zang, & Yu, 2013; Goransson & Johansson, 2012; Karadeniz et al., 2003), data collected retrospectively (Fields et al., 2012), or secondary analysis from an existing data set potentially introducing a sampling bias (McNeill, Hines, & Phariss, 2009; Wallis et al., 2014). Additionally, there

has been a lack of consideration of other important risk factors that may be associated with catheter failure, such as multiple PVC insertion attempts.

Table 1.1: Risk Factors for PVC Failure

PVC related risk factors	Patient related risk factors	Other risk factors
Small gauge (Abolfotouh, Salam, Bani-Mustafa, White, & Balkhy, 2014)[a], (Wallis et al., 2014)[b]	Female (Abolfotouh et al., 2014); (Dillon et al., 2008)[c]; (Hirschmann et al., 2001)[c]; (Wallis et al., 2014)	Emergency inserted (Saini et al., 2011)[d]; (do Rego Furtado, 2011b)[e]; (Uslusoy & Mete, 2008)[c]
Large gauge (Catney et al., 2001)[c]; (Cicolini et al., 2009)[f]; (Lanbeck et al., 2002)[c]; (do Rego Furtado, 2011b; Wallis et al., 2014)	Age (Karadeniz et al., 2003)[g]; (Singh, Bhandary, & Pun, 2008)[e]; (Saini et al., 2011);	Intravenous medications (e.g. antibiotics) (Salgueiro-Oliveira, Veiga, & Parreira, 2012)[c]; (Abolfotouh et al., 2014; Catney et al., 2001; do Rego Furtado, 2011b; Lanbeck et al., 2002; Singh et al., 2008; Uslusoy & Mete, 2008; Wallis et al., 2014)
PVC dwell time (Kaur et al., 2011)[c]; (Cicolini et al., 2009; do Rego Furtado, 2011b; Hirschmann et al., 2001)	Co-morbidities (Nassaji-Zavareh & Ghorbani, 2007)[c]; (do Rego Furtado, 2011b)	Not using an intravenous therapy team or vascular access specialist (Palefski & Stoddard, 2001)[c]; (Wallis et al., 2014)
Site (hand, joint, anterior cubital fossa) (Cicolini et al., 2009; Dillon et al., 2008; do Rego Furtado, 2011b; Karadeniz et al., 2003; Kaur et al., 2011; Saini et al., 2011; Uslusoy & Mete, 2008)	Current infection (any type) (Wallis et al., 2014)	
Subsequent PVC (Grüne et al., 2004)[C]; (Gallant & Schultz, 2006; Wallis et al., 2014)		

[a] Insertion risk factors not collected; **[b]** secondary analysis from an existing data set; [c] PVC inserters and/or clinical staff caring for catheter collected study data; [d] Unclear who collected outcome data; [e] one day audit; [f] limited variables collected; [g] small study (less than 100 participants)

PVC insertion models

Many risk factors associated with PVC failure can be directly related to PVC insertion (e.g. choice of catheter gauge and insertion site), which is the focus of this PhD thesis in terms of developing an intervention to prevent failure. Placement of a PVC is the most frequently performed invasive procedure in hospitals. Different models for insertion are used by different healthcare facilities. Some hospitals have PVC insertions conducted at the bedside by generalist clinicians (nurses and doctors with varying skill levels and job descriptions). This approach focuses on the short-term goal of achieving PVC placement, with an underlying belief that a lack of specific expertise rarely has negative outcomes (Robertson, 1995), such as subsequent PVC failure. Other hospitals employ vascular access specialists (VAS), almost always nurses, either as part of a dedicated team or within the existing nursing framework for PVC insertion and clinician education. It is thought that their higher level and more specific expertise enhances patient care, decreases the incidence of infusion complications, and ultimately saves costs associated with clinician time, materials, and length of hospital stay (Palefski & Stoddard, 2001).

Current local (Department of Health, 2015) and international guidelines (Infusion Nurses Society, 2016; Intravenous Nursing New Zealand, 2011; O'Grady et al., 2011) provide limited direction on PVC insertion models or on maintenance, often deferring to local health institution requirements (Table 1.2). In Australia, there is no national credentialing for a minimum level of expertise and decision-making skill for clinicians inserting a PVC. In Queensland, practice is guided by the Communicable Diseases Infection Management Branch (CDIM). These guidelines recommend that a competent clinician should insert a PVC, but no definition is provided for what constitutes a competent clinician, other than the need for the completion of competency assessments as

per the local healthcare facility. This results in a variation of knowledge, skill, experience, and expertise for PVC inserters across healthcare settings (Vizcarra et al., 2014).

The challenge for local and international guiding bodies is the lack of robust randomised controlled trials (RCTs) that have tested the effectiveness of different skill levels on successful PVC insertion, and prevention of subsequent device failure and complications. This was highlighted in a recent Cochrane Systematic Review comparing VAS teams for device insertion and the prevention of failure, which reported that no RCTs have been published exploring the use of VAS teams for any type of vascular access device (Carr, Higgins, Cooke, Mihala, & Rickard, 2018). However, observational studies have reported benefits of IV therapy team (IVTT) or VAS in reducing the risk of PVC failure (Carr, Glynn, Dineen, & Kropmans, 2010; Palefski & Stoddard, 2001; Wallis et al., 2014). This reduction is found to be due in part to IVTTs' higher first-time PVC insertion success rates and lower risk of catheter-related complications, compared with nurses and doctors who have not had specialist training in PVC access (Carr, Higgins, Cooke, Mihala, & Rickard, 2014).

Consequently, in the absence of evidence from high-quality RCTs, it is impossible to produce comprehensive clinical practice guidelines for the best PVC insertion model.

Table 1.2: PVC insertion and maintenance guidelines

Guideline (Year)	Country of Origin	Recommendation
Peripheral Intravenous Catheter (PIVC) (Queensland Health) (2015)	Australia	➢ "Only competent staff (or training staff supervised by competent staff) should insert IVDs[a]." (*p*. 3) ➢ "All staff involved in the insertion and maintenance of IVDs should complete all competency assessments as required by the healthcare facility." (*p*. 3)
Provisional Infusion Therapy Standards of Practice (Intravenous Nursing New Zealand) (2011)	New Zealand	➢ "Competency validation is the responsibility of the clinician and employing organisation." (*p*. 11) ➢ "Validation is performed initially and/or reviewed as required." (*p*. 11) ➢ "Competency validation is set by the individual clinician's regulatory body." (*p*. 11)
Infusion Therapy Standards of Practice (Infusion Nurses Society) (2016)	USA	➢ "The clinician is responsible and accountable for attaining and maintaining competence with infusion therapy administration and VAD[b] insertion and/or management within her or his scope of practice." (*p*. S18) ➢ "Competency validation shall be performed initially and on an ongoing basis." (*p*. S18) ➢ "Competency validation shall be documented in accordance with organizational policies." (*p*. S18)
Guidelines for the Prevention of Intravascular Catheter-Related infections (Centers for Disease Control and Prevention) (2011)	USA	➢ "Educate healthcare personnel regarding the indications for intravascular catheter use, proper procedures for the insertion and maintenance of intravascular catheters, and appropriate infection control measures to prevent intravascular catheter-related infections." (*p*. 9) ➢ "Periodically assess knowledge of and adherence to guidelines for all personnel involved in the insertion and maintenance of intravascular catheters." (*p*. 9) ➢ "Designate only trained personnel who demonstrate competence for the insertion and maintenance of peripheral and central intravascular catheters." (*p*. 10)

[a] IVD = intravascular device; [b] VAD = vascular access device

The recently reported high rates of PVC failure and associated catheter related complications suggest that current PVC insertion and management practices require improvement. Rigorous synthesis of the incidence of PVC failure and PVC complications is therefore important, to highlight the extent of the problem for clinicians, policy makers, and manufacturers. Identifying risk factors for failure, both modifiable and non-modifiable, and identifying the effect of VAS versus generalist insertion models on PVC complications would inform health services, allowing them to provide effective PVC insertion and resulting in a much-needed reduction in PVC failure. Preventing PVC failure is an important outcome not only for patients but also for clinicians and healthcare facilities.

Research Title

Prevention of peripheral intravenous catheter failure.

Significance

The results from this research provide new evidence to help decrease catheter-related complications resulting in PVC failure. In published literature, PVC failure has been identified as a significant problem in individual studies. However, this data has never been synthesised to accurately identify both the incidence of and risk factors associated with PVC failure. The evidence from the systematic review and meta-analysis (Chapter 2) and the multivariable analysis (Phase 1) in this PhD study highlight the global significance of this problem and areas requiring immediate prioritisation, such as improving PVC insertion practices (Phase 2).

The insertion of a PVC has been identified as the most labour-intensive activity associated with PVC care, and takes an average of 10–20 minutes to perform (Dychter et al., 2012). If multiple attempts are required to insert the catheter, this has a significant

impact on labour and equipment costs. A recent economic analysis of data from a multi-site Queensland RCT of catheter replacement reported that the mean cost for PVC replacement was AU$69.30 per hospital admission, with outlays of AU$47.80 in equipment and AU$21.50 in staff wages (Tuffaha et al., 2014).

The cost of treating PVC complications, such as infiltration, thrombophlebitis, and infection, must be added to the cost of removing and replacing a PVC (Helm et al., 2015). Each episode of catheter-associated blood stream infection increases healthcare costs by prolonging hospital admission on average 7–14 days (Dychter et al., 2012). The associated treatment costs per episode have been reported in the USA to range from US$3,000 to $56,000 and in Australia from AU$3,000 to $29,000 (Raad, Hanna, & Maki, 2007; Spencer, 2011).

This PhD research provides new evidence on the best workforce model for PVC insertion from the results of a pilot RCT. Prior to this work, the level of skill of the PVC inserter has been described as a risk factor for catheter failure (Carr et al., 2010; Wallis et al., 2014). However, there has never been an RCT investigating the benefit of a VAS. The results of the pilot trial also provide new evidence that a systematic approach to not only PVC insertion, but also PVC maintenance, is necessary for this essential medical device.

In summary, gaps remain in our knowledge about why PVCs fail. Decreasing catheter-related complications is important for patients and for healthcare facilities and is the focus of this PhD. The findings from the two phases of this research provide new evidence to improve practices around PVC insertion and maintenance.

Conceptual Framework

The conceptual framework underpinning this PhD is the Medical Research Council (MRC) Framework for the Evaluation of Complex Interventions as outlined in Figure 1 (Craig et al., 2008). Craig et al. argue for a phased approach when there is uncertainty around a complex intervention; pilot trials informed by evidence are an important step to clarify any shortcomings of trial design and processes before conducting a definitive study (Craig et al., 2008). This framework highlights that the best evidence-base comes from carefully planned feasibility and pilot testing, involving the evaluation of study outcomes, the implementation of study results into practice, and the surveillance and monitoring of these implementations (Craig et al., 2008). This is an ongoing process involving development, testing, evaluation, and implementation.

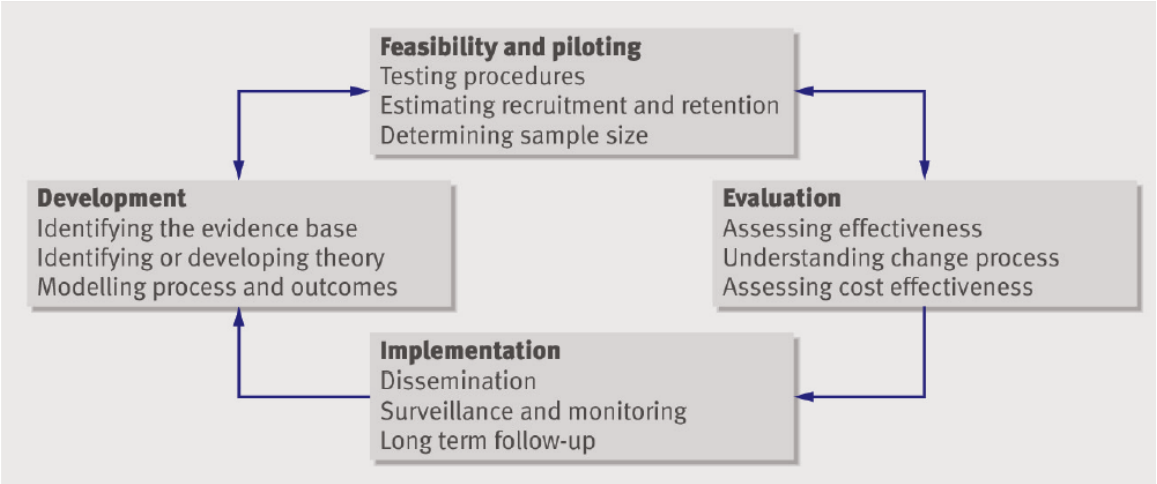

Figure 1.1: Medical Research Council framework

(Permission to reproduce image Appendix D)

The structure of this PhD reflects the 'Development' and 'Feasibility and piloting' elements of this Framework by firstly conducting a systematic review and meta-analysis to establish the global PVC failure and catheter complication rates. Following on from this, Phase 1 of this PhD research comprised a multivariable analysis of data from a large

observational study that was performed to identify both the modifiable and non-modifiable risk factors associated with PVC failure. In Phase 2, a pilot RCT was conducted to establish the feasibility of undertaking a large, multi-centre RCT comparing the clinical outcomes and cost effectiveness of two different PVC insertion models (generalist model versus VAS model).

Research Aim and Questions

The overarching aim of this PhD research was to identify effective methods to prevent PVC failure. The objectives were to:

1. Determine the modifiable risk factors associated with PVC failure and complications; and
2. Evaluate the feasibility of a large RCT of VAS versus a generalist PVC inserter model to prevent failure.

The research was conducted in two phases, which were designed to achieve the objectives and the overall aim.

Phase 1 comprised the multivariable analysis and publication of data from a prospective cohort study, data which had been collected before enrolling in this research program. This Phase addressed Objectives 1 and 2. The research questions for Phase 1 were:

1. What are the risk factors associated with PVC failure in the adult in-patient population?
2. What are the potentially modifiable risk factors associated with PVC failure in the adult in-patient population to inform insertion knowledge and practices?

Phase 2 targeted Objective 2 and comprised a pilot RCT comparing the impact of PVC insertion by a VAS with insertion by any clinician (generalist model, standard practice) on PVC failure. This phase addressed the following research question:

3. Is it feasible to conduct a full-scale RCT trial to compare the effectiveness of PVC insertion by a vascular access expert versus insertion by usual practice on the incidence of PVC failure in the adult population?

Structure of this Document

This thesis includes six chapters and appendices as follows:

Chapter 1: provides the introduction to the research context, significance, conceptual framework, research aim, objectives, and questions for the study.

Chapter 2: contains two parts: Part 1 is a comprehensive systematic review and meta-analysis of observational studies and the control group of RCTs; and Part 2 is a critique of literature about the benefit of a VAS. The systematic review and meta-analysis (Part 1) is formatted for submission to the peer-reviewed journal *BMJ Open.*

Chapter 3: describes the methods used in Phase 1 and Phase 2 of the research completed for this thesis. The methods for the cohort study (Phase 1) are described including: setting, recruitment, data collection, multivariable analyses and ethical considerations. The methods used in the pilot RCT (Phase 2) are described in a protocol which was published in the peer-reviewed journal *Vascular Access*.

Chapter 4: presents the study results for Phase 1. This section contains a manuscript reporting Phase 1 results published in the peer-reviewed *Journal of Hospital Medicine,* which has a journal impact factor of 2.331.

Chapter 5: presents the study results for Phase 2. This section contains a manuscript reporting Phase Two results published in the peer-reviewed journal *Trials*, which has a journal impact factor of 2.343.

Chapter 6: provides an overview of study methods and findings. It discusses the results from Phase 1 and Phase 2 in relation to the research aim and questions, as well as relevant literature. Finally, it contains recommendations based on the PhD findings for clinical practice, education, healthcare policy, and future research, as well as the study conclusions.

Summary

The research results presented in this thesis provide new evidence to help prevent catheter-related complications resulting in PVC failure. This is an important clinical objective which will have substantial benefit for patient outcomes.

This chapter has introduced the research problem and significance of the research conducted in this PhD. It contains an overview of the research aim, questions, design, and thesis structure. Chapter 2 critiques the literature to provide an understanding of how often and why PVCs fail, to highlight the extent of this worldwide problem and to identify gaps in knowledge that informed this PhD research. It also includes a critique of the evidence from studies investigating the potential benefit of a VAS model to prevent PVC failure.

Chapter 2 — Literature Review

Introduction

Failure of PVCs is a common and expensive problem in healthcare. Replacing a PVC may be upsetting and painful for the patient (Cooke et al., 2018; Larsen, Keogh, Marsh, & Rickard, 2017); it may also delay important treatment and increase hospital length of stay (Royer, 2003; Tagalakis et al., 2002). Although several studies have reported the frequency and types of PVC failure, there has been no systematic synthesis of this information. This chapter contains two parts. The first part provides a systematic review and meta-analysis of the extent of the problem worldwide, in the form of a co-authored paper prepared for submission to the peer-reviewed journal *BMJ Open*. This systematic review identified the most commonly occurring and most commonly studied causes of PVC failure. This assisted in prioritising these complications to identify both modifiable and non-modifiable risk factors associated with PVC failure (Phase 1).

In the second part of this chapter, a critique of the literature about the potential benefit of a VAS model of PVC insertion for preventing PVC failure follows the systematic review. The critique highlights the research gaps and provides the rationale for Phase 2 of the PhD research. Findings from the systematic review combined with the critique of the research related to a VAS model of insertion informed the conception and development of the pilot study, which tested the VAS insertion model intervention to reduce risk factors associated with failure. This meets the development stage of the framework underpinning this PhD research by identifying the current evidence base to guide this PhD research (Craig et al., 2008).

Part 1 — Peripheral Intravenous Catheter Failure and Complications in Adults: A Systematic Review and Meta-Analysis [Publication 1]

Statement of contribution to co-authored paper

The bibliographic details of the co-authored paper, prepared for submission, including all authors, are:

Marsh, N., Webster, J., Ullman, A. J., Mihala, G., Cooke, M., & Rickard, C. M. Peripheral intravenous catheter failure and complications in adults: a systematic review and meta-analysis. *BMJ Open.*

My contribution to the paper included: Study conception, protocol design, literature search, data extraction, quality assessment, data analysis, data interpretation, development of tables and figures, preparation of manuscript, and final responsibility for the decision to submit publication.

(Signed)
Nicole Marsh (Date) 16/12/2018

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(Countersigned) (Date) 22/01/2019

Supervisor: Professor Claire M Rickard

Peripheral intravenous catheter failure and complications in adults: a systematic review and meta-analysis

Abstract

Objectives

Peripheral intravenous catheters (PVCs) are essential to modern healthcare and the most frequently used vascular access device, but system-wide understanding of complications is lacking. We undertook this systematic review to summarize and quantify peripheral intravenous catheter failure and individual catheter-related complications.

Design

Systematic review and meta-analysis

Data sources and data analysis

We searched Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, CINAHL and EMBASE (2000 to the 24th of October 2018) for observational studies and randomised controlled trials in English that reported peripheral intravenous catheters (PVC) failure or PVC-related complications. In addition, a search was conducted through clinical trial registries (ClinicalTrials.gov, WHO International Clinical Trials Registry Platform and EU Clinical Trials Registry) and the reference list of included studies to identify any additional studies to be included in the review.

Data collection and data analysis

Two review authors independently screened, extracted data and performed quality assessment for included studies.

Results

31 randomised controlled trials and 70 observational studies were included (74,798 participants). Failure occurred in 36.5% catheters (95% confidence interval [CI] 32.5–40.6%) or 116.8 failures per 1000 catheter days. Individual complications were: phlebitis 16.8% [95% CI 13.9–20.0%]; infiltration 13.6% [11.0–16.4%]; occlusion 7.8% [5.6–10.4%]; leakage 7.3% [4.7–10.3%]; pain 6.4% [4.8–8.2%]; dislodgement 5.9% [4.8–7.2%]; local infection 0.6% [< 0.1–1.6%]; catheter related blood stream infection < 0.1% [< 0.1–< 0.1%] or < 0.1 per 1000 catheter days [< 0.0–0.3].

Conclusion

This large review shows that catheter failure is a significant worldwide problem, affecting one in three PVCs, and is rarely due to infection. New, substantial, and multi-specialty efforts are needed to address catheter failure and its sequelae of treatment disruption, increased health costs and poor patient experiences and outcomes.

Review Registration

PROSPERO registration number: CRD42016043722. (Appendix E)

Strengths and limitations of this study

- Our systematic review of 101 studies provides the first, large scale understanding of how often and in what way PVCs fail.
- We have identified that PVC failure related bloodstream infection was very low, and our review has set a new benchmark for PVC-related bloodstream infection, < 0·1% per 1000 days.

- Limited numbers of studies reported the number of catheter days for included participants, limiting our ability to present incidence rate of all events per 1000 catheter days.
- Phlebitis was defined variously by different authors, limiting our ability to represent a homogeneous phlebitis rate.

Introduction

Vascular accesses devices (VADs) are essential to modern health care allowing the direct administration of supportive and interventional therapy into the bloodstream (Campbell & Bowden, 2011). Many different types of VADs are in use, the most common is the peripheral intravenous catheter (PVC) (Zingg & Pittet, 2009). This flexible hollow tube is typically inserted into a peripheral vein of the forearm or hand (Gabriel, 2010), and used for short-term delivery of intravenous (IV) fluids, medications, blood products and contrast media (Dougherty, 2008b; Sabri et al., 2012). peripheral intravenous catheters are a quick, simple and cost-effective method to gain vascular access (Sabri et al., 2012); up to 70% of hospitalised patients will receive at least one PVC during their admission (Zingg & Pittet, 2009).

peripheral intravenous catheters frequently develop complications leading to catheter failure, with individual studies reporting incidence up to 69% (Marsh, Webster, Mihala, et al., 2015). This has consequences for patients and for healthcare budgets, since around two billion PVCs are sold globally each year (Rickard & Ray-Barruel, 2017). The need for repeated catheter re-insertions is not only painful, but can result in venous access depletion (Hawes, 2007), which increases the likelihood of requiring a central venous

access device (Monreal et al., 1999) - a more costly device with higher risk for significant complications. peripheral intravenous catheter failure interrupts important IV treatment such as antibiotics or chemotherapy, and may result in longer hospital stays, and increased healthcare costs (Dillon et al., 2008; Tagalakis et al., 2002).

Peripheral intravenous catheter fail for a number of reasons, but over the last two decades phlebitis has been the focus of PVC complications and failure (Higginson & Parry, 2011; Ray-Barruel et al., 2014; Tagalakis et al., 2002). Phlebitis is the irritation or inflammation of a vein wall related to the presence of a catheter, and when associated with thrombus formation, is referred to as thrombophlebitis (McCallum & Higgins, 2012; Ray-Barruel et al., 2014; Zingg & Pittet, 2009). Another frequently reported PVC-related complication is partial or complete catheter occlusion. Occlusion is the inability to infuse fluids or medications through a previously functioning catheter (Helm et al., 2015).

Infiltration or the inadvertent leakage of a non-vesicant solution into surrounding tissues is also a potential PVC complication (Dychter et al., 2012). Leakage may occur if the catheter pierces the vessel wall during insertion; if it moves partially or completely outside the vein during the delivery of IV fluids; or if the vessel wall does not seal around the catheter, resulting in a slow leak of fluids into the surrounding tissues (Dougherty, 2008a).

Peripheral intravenous catheter remain partially external to the body requiring fixation to the skin. If the PVC is inadequately secured, movement of the catheter in and out of the vein is possible. This pistoning action may lead to partial or complete dislodgement (Zingg & Pittet, 2009), and irritate or damage the internal blood vessel wall.

The skin, which normally acts as a protective barrier against bacteria accessing the body, is breached when a PVC is inserted, and bacteria may enter the blood via the external or internal surfaces of the catheter, or may cause local infection (Morris & Heong Tay, 2008; O'Grady et al., 2011; Smith, 2006). Local PVC-related infection is indicated by pain, erythema, pus, and palpable venous cord, whereas catheter-related blood stream infection (CRBSI) presents with fever, chills, headache, tachycardia, and nausea/vomiting (Dychter et al., 2012). PVCs had the lowest rate of CRBSI of all vascular catheters (0·1% per PVC, 0·5 per 1000 PVC days) in a review including older PVC materials such as Teflon (Maki et al., 2006). A more recent review also estimated bloodstream infections in PVCs at 0·5 per 1000 days, however quality assessments were not undertaken, and the primary endpoint was undefined (Mermel, 2017).

Pain is the most common patient-reported symptom of phlebitis, but may also signify failure from infiltration, occlusion, or infection (Dychter et al., 2012; Ray-Barruel et al., 2014; Zingg & Pittet, 2009). Patients also report a strong association with pain when recalling their PVC failure (Larsen et al., 2017).

Although studies commonly report PVC failure, the rates of this important phenomenon have never been synthesised. The objective of this review was to estimate the worldwide incidence of PVC failure and complications in adults.

Methods

Search strategy and selection criteria

This systematic literature review and meta-analysis of the incidence of PVC failure and complications was reported using the Moose guidelines (Meta-analysis of observation studies in epidemiology) (Stroup et al., 2000).

We searched the Cochrane Central Register of Controlled Trials (CENTRAL; the Cochrane Library), MEDLINE, CINAHL and EMBASE on the 24th of October 2018 to identify relevant cohort and randomized controlled trials (RCTs)that reported PVC failure or PVC-related complications. In consultation with a health librarian, a search strategy was developed that included appropriate Medical subject heading (MeSH) terms such as: *Catheterization, Peripheral*; *Catheter Obstruction; Vascular Access Devices; Phlebitis; and Thrombophlebitis.* We restricted the search to full-text, published articles written in English. We pre-registered the study with the International Prospective Register of Systematic Reviews (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=43722).

All cohort studies (prospective or retrospective) that investigated PVC failure and complications in adults, requiring a PVC in a healthcare setting since the year 2000 were eligible. This timeframe was selected as it reflects the use of modern PVC polyurethane materials. We also included control groups from RCTs as they represented usual practice in the study setting. Case studies, non-peer reviewed publications, and qualitative research were excluded.

The review's primary outcome was a composite, defined as catheter failure from any cause before the completion of treatment. Secondary outcomes were catheter-related complications: 1) Phlebitis: as defined by the study author; 2) Occlusion: as defined by the study author and including the inability to infuse intravenous therapy; 3) Infiltration/extravasation: as defined by the study author; 4) Dislodgement/accidental removal: as defined by the study author and including the partial or complete migration of the PVC from the vein; 5) Leakage: as defined by the study author and including the leakage of fluid from the insertion site; 6) CRBSI: with laboratory confirmation of the

catheter as the source of infection (O'Grady et al., 2011); 7) Suspected CRBSI: as defined by the study author; 8) Local infection: as defined by the study author and including purulent discharge from the insertion site; and 9) Pain as defined by the study author and related to the PVC.

Two review authors (NM and JW) independently assessed titles and abstracts for study inclusion. A third author's (AU) judgment was sought when differences of opinion were not resolved by unanimity or when review authors (NM and JW) were named on included studies. We also reviewed reference lists of retrieved studies to identify additional eligible reports. After screening, the full texts of eligible articles were retrieved.

Data extraction and quality assessment

NM and JW independently extracted data using a customised data extraction form. Any disagreement was resolved by a third author (AU) who also independently extracted data when NM or JW were named on included studies. Where required we attempted to contact study authors to collect missing data. Extracted data included: author name, year published, country, clinical setting, age, gender, study design, number of participants, and incidence (or rate/1,000 days) of outcomes.

Independently, review authors (NM and JW) assessed observational studies for quality and risk of bias using the following STROBE elements (The STrengthening the Reporting of OBservational studies in Epidemiology statement: Guidelines for reporting observational studies): clear study objective; consistency and rigor of outcome measures; research methods; and completeness of outcome reporting (Vandenbroucke et al., 2014; von Elm et al., 2014). Randomised controlled trials were assessed using the 'Risk of Bias' tool from the Cochrane Handbook of Systematic Reviews of Interventions (Higgins, 2011).

Data analysis

Cohort studies and RCT outcomes deemed eligible for data synthesis were presented using descriptive statistics. Dichotomous outcomes were pooled after Freeman-Tukey Double Arcsine Transformation using random-effects meta-analysis (DerSimonian and Laird method); estimates of heterogeneity were taken from inverse-variance fixed-effect models (Nyaga, Arbyn, & Aerts, 2014). Continuous outcomes and their Poisson confidence intervals were meta-analysed using random-effects models (DerSimonian and Laird method); estimates of heterogeneity were taken from the Mantel-Haenszel model (R. Harris et al., 2008); lower CI boundaries below zero were reported as zero. Heterogeneity between studies was assessed using the I^2 statistic, categorized as low (< 25%), moderate (25%–75%), or high (> 75%) (Higgins, 2011). Analysis was with Stata 12 (Stata Corp, College Station, Texas, USA). Statistical significance was $p < 0.05$.

Planned subgroup analyses compared PVC failure due to complications between: emergency department and other departments/all hospital; and, developed and developing economies (United Nations World classification (Nations, 2016)). Analysis was described as proportion of failure or PVC-related complication and presented with 95% CI. Sensitivity analyses were conducted comparing pooled proportion of PVC failure and PVC-related complications between: retrospective and prospective studies; and studies with ≥ 100 participants compared to < 100 participants.

Patient and public involvement

No patients or public were involved in this study.

Results

The search generated 17,381 records. Figure 2.1 flowchart identifies the reasons for inclusion and exclusion and is formatted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher, Liberati, Tetzlaff, & Altman, 2009). After removing duplicates and screening titles and abstracts, 130 full text articles were assessed for inclusion. Following full text screening, 29 articles were excluded as they: studied other VAD types (Renard, Guerci, Leguerrier, & Boizel, 2010; Thamby, 2013; Yilmaz et al., 2007); were audits (Brady, Bruno, Marchionni, & Paquet, 2016; Chiu et al., 2015; do Rego Furtado, 2011b; Malach et al., 2006; Powell, Tarnow, & Perucca, 2008); did not provide per PVC data (A. Jackson, 2012; Karadeniz et al., 2003; Norton et al., 2013; Roszell & Jones, 2010); had different outcome definitions (Aulagnier et al., 2014; Coomarasamy, Wint, & Saleh, 2014; Dunda et al., 2015; Groll, Davies, Mac Donald, Nelson, & Virani, 2010; Holder, Stutzman, & Olson, 2017; Kagel & Rayan, 2004; Mahmoud et al., 2017; Oto, Imanaka, Konno, Nakataki, & Nishimura, 2011; Prunet et al., 2008; Smith, 2006; van der Mee-Marquet, 2007); reported vascular access procedures (Benham, Culp, Wright, & McCowan, 2007; Chukhraev, Grekov, & Aivazyan, 2000; Ortiz et al., 2014); were secondary analyses or commentaries on data already included (Danski, Oliveira, Johann, Pedrolo, & Vayego, 2015; Lanbeck et al., 2002; Myrianthefs, Karatzas, & Baltopoulos, 2005). Additional information was provided from authors for nine studies (Bugden et al., 2016; Forni et al., 2012; Keogh et al., 2016; Marsh, Webster, et al., 2018; Rickard et al., 2010; Rickard et al., 2012; Van Donk, Rickard, McGrail, & Doolan, 2009; Webster et al., 2008; Webster, Lloyd, Hopkins, Osborne, & Yaxley, 2007).

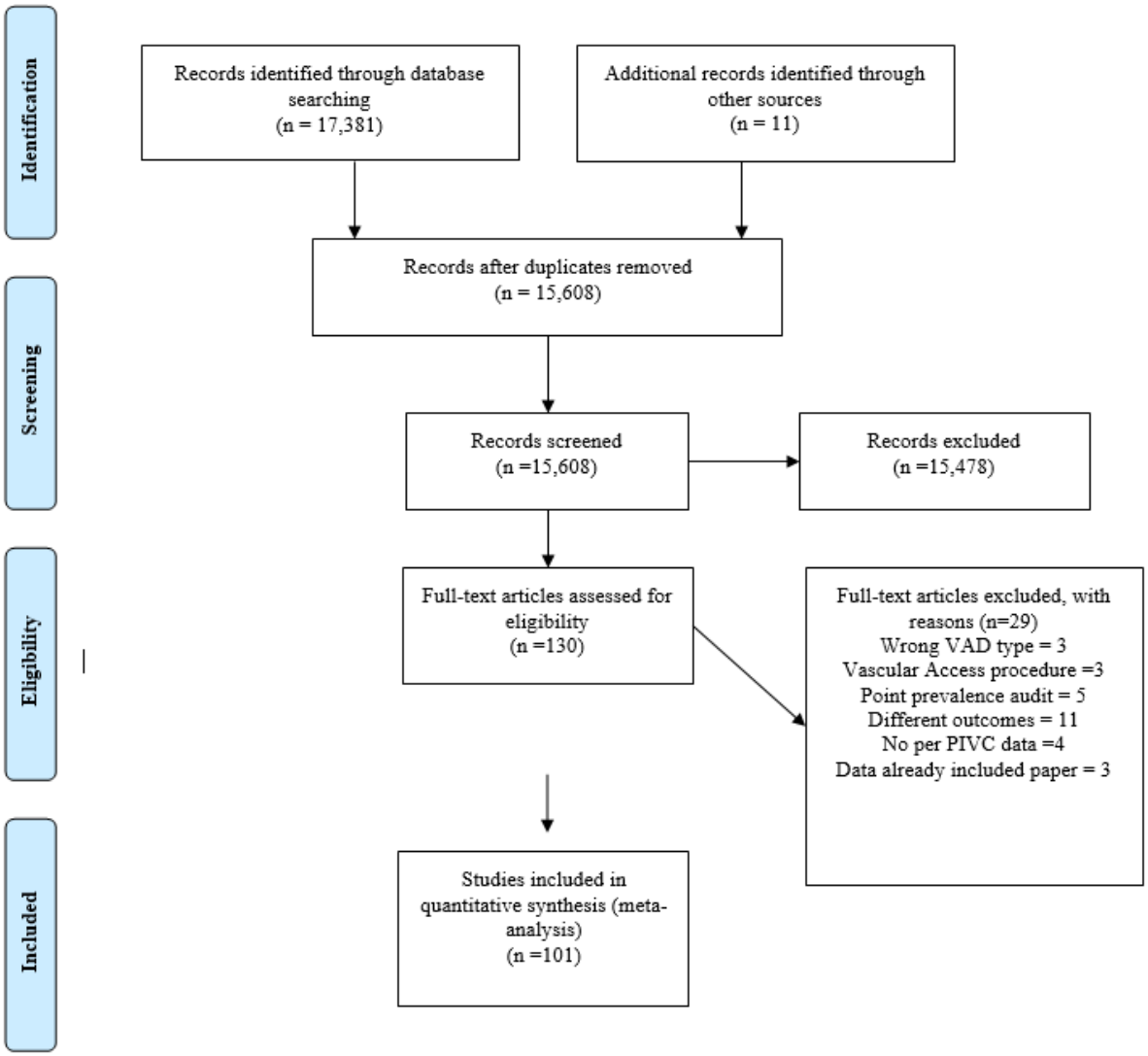

Figure 2.1: PRISMA flow chart of study selection

Characteristics of included studies

A total of 70 cohort studies (64 prospective; six retrospective) and 31 RCTs were included (74,798 participants). Studies were from Europe (Abbas, de Vries, Shaw, & Abbas, 2007; Barker, Anderson, & MacFie, 2004; Bertolino et al., 2012; Bolton, 2010; Bonnici, 2012; Bridey et al., 2018; Chico-Padrón et al., 2011; Cicolini et al., 2009; Cicolini et al., 2014; Cornely, Bethe, Pauls, & Waldschmidt, 2002; Creamer, McCarthy, Tighe, & Smyth, 2002; Curran, Coia, Gilmour, McNamee, & Hood, 2000; Dillon et al., 2008; do Rego Furtado, 2011a; Elia et al., 2012; Forni et al., 2012; Goransson & Johansson, 2012; Grüne et al., 2004; Günther et al., 2016; Hasselberg, Ivarsson, Andersson, & Tingstedt, 2010; Hirschmann et al., 2001; Johansson, Pilhammar, Khalaf, & Willman, 2008; Lanbeck et al., 2002; López et al., 2014; Martinez et al., 2009; Mestre et al., 2013; Mestre et al., 2012; Miliani et al., 2017; Palese et al., 2016; Panadero, Iohom, Taj, Mackay, & Shorten, 2002; Periard et al., 2008; Salgueiro-Oliveira et al., 2012; Vandenbos et al., 2003), North America (Adhikari, Blaivas, Morrison, & Lander, 2010; Anderson, 2016; Ascoli, Deguzman, & Rowlands, 2012; Bahl et al., 2018; Bausone-Gazda et al., 2010; Boyce & Yee, 2012; Catney et al., 2001; Dargin, Rebholz, Lowenstein, Mitchell, & Feldman, 2010; Datar, Gutierrez, Schertz, & Vachharajani, 2018; Fakih et al., 2012; Fields et al., 2012; Gallant & Schultz, 2006; Gregg, Murthi, Sisley, Stein, & Scalea, 2010; McNeill et al., 2009; Meng, Nguyen, Patel, Mlynash, & Caulfield, 2018; Niesen, Harris, Parkin, & Henn, 2003; Palefski & Stoddard, 2001; Pandurangadu, Tucker, Brackney, & Bahl, 2018; Royer, 2003; Schears, 2006; White, 2001; Zarate, Mandleco, Wilshaw, & Ravert, 2008), Asia (Abolfotouh et al., 2014; Atay, Şen, & Cukurlu, 2018; Benaya, Schwartz, Kory, Yinnon, & Ben-Chetrit, 2015; Erdogan & Denat, 2016; Fujita & Namiki, 2008; Fujita, Namiki, Suzuki, & Yamamoto, 2006; Gupta, Mehta, Juneja, & Trehan, 2007; Haddad, Waked, & Zein, 2006; Karadag & Görgülü, 2000; Kaur et al., 2011; Lee et al., 2009; Murayama et al.,

2017; Nassaji-Zavareh & Ghorbani, 2007; Nishanth, Sivaram, Kalayarasan, Kate, & Ananthakrishnan, 2009; Pasalioglu & Kaya, 2014; Ronen, Shlomo, Ben-Adiva, Edri, & Shema-Didi, 2017; Saini et al., 2011; Sarafzadeh, Sepehri, & Yazdizadeh, 2012; Singh et al., 2008; Takahashi et al., 2017; P. C. Tan, Mackeen, Khong, Omar, & Azmi, 2016; Y. H. G. Tan, Tai, Sim, & Ng, 2017; Tanabe et al., 2016; Uslusoy & Mete, 2008; R. Wang, Luo, He, Li, & Zhang, 2012; R Wang et al., 2015; Xu, Hu, Huang, Fu, & Zhang, 2017; Zhu, Wang, & Wen, 2016), South America (Danski et al., 2015; Enes, Opitz, Faro, & Pedreira, 2016; Rojas-Sánchez, Dora Inés, & Fabio Alberto, 2015; Salles et al., 2007; Urbanetto et al., 2017; Urbanetto, Peixoto, & May, 2016), and Australia (Bugden et al., 2016; Carr, Rippey, et al., 2018; Keogh et al., 2016; Marsh, Webster, Flynn, et al., 2015; Marsh, Webster, et al., 2018; Rickard et al., 2018; Rickard et al., 2010; Rickard et al., 2012; Taylor, 2003; Van Donk et al., 2009; Webster et al., 2008; Webster et al., 2007). Participants were most frequently from medical/surgical departments, but all specialties were represented. Table 2.1 contains further study characteristics. For the analysis, we combined comparison groups from 14 cohort studies: PVC dwell time (< 96 compared with > 96 hours) (Ascoli et al., 2012; Gallant & Schultz, 2006); dressings and securements (Royer, 2003; Salles et al., 2007; Schears, 2006; Zarate et al., 2008); types of PVC(Karadag & Görgülü, 2000; Tanabe et al., 2016); upper and lower extremity insertions (Benaya et al., 2015); PVC inserter (infusion nurse compared with a generalist nurse) (Palefski & Stoddard, 2001); needleless connectors or cap (Ronen et al., 2017); ultrasound compared to traditional approach (Adhikari et al., 2010); and pre-post bundle intervention (Cicolini et al., 2014). We also combined the intervention and control groups of six RCTs because all groups used similar practices recommended in international guidelines (Günther et al., 2016; Haddad et al., 2006; Keogh et al., 2016; P. C. Tan et al., 2016). These comparisons were: new generation transparent compared with a traditional

transparent dressing (Günther et al., 2016; Rickard et al., 2018); 72 compared to 96-hour PVC resite (Haddad et al., 2006); forearm compared to hand insertions (P. C. Tan et al., 2016); ultrasound compared to landmark insertions (Bridey et al., 2018); and four routinely used PVC flushing practices (Keogh et al., 2016).

Table 2.1: Characteristics of included studies

Author (year)	Country	Study Design (Sample size) Retrospective (cohort) Prospective (cohort) RCT	Setting
Curran (2000)	UK	Prospective (2934)	Ward; theatre; other
Karadag (2000)	Turkey	Prospective (255)	CCU
Catney (2001)	USA	Prospective (411)	MED; SURG; surgical OPD
Hirschmann (2001)	Austria	Prospective (1132)	Wards, OT; OPD
Palefski (2001)	USA	Prospective (776)	Hospital wide; home infusion agency
White (2001)	USA	Prospective (305)	Hospital wide
Cornely (2002)	Germany	Prospective (364)	Hematology; oncology; IDD
Creamer (2002)	Ireland	Prospective (554)	MED; SURG
Lanbeck (2002)	Sweden	Prospective (1386)	IDD
Panadero (2002)	Ireland	RCT (30)	Elective surgery
Niesen (2003)	USA	Prospective (146)	OB
Royer (2003)	USA	Prospective (275)	MED; SURG
Taylor (2003)	Australia	Prospective (390)	MED; SURG
Vandenbos (2003)	France	RCT (26)	ED
Barker (2004)	UK	Prospective (2495)	MED; SURG
Grune (2004)	Germany	Prospective (146)	MED; SURG; geriatrics, radiotherapy; neurology; orthopedics; GYN; OB
Fujita (2006)	Japan	Prospective (361)	SURG
Gallant (2006)	USA	Prospective (789)	Cardiac Surgical unit; Cardiac set down unit
Haddad (2006)	Lebanon	RCT (221)	Internal medicine/IDD; pneumology/gastroenterology department
Schears (2006)	USA	Prospective (15,004)	MED
Abbas (2007)	UK	Prospective (86)	ED

Gupta (2007)	India	RCT (35)	Cardiac surgery
Nassaji-Zavareh (2007)	Iran	Prospective (300)	MED; SURG
Salles (2007)	Brazil	Prospective (120)	SURG
Webster (2007)	Australia	RCT (103)	MED; SURG
Dillon (2008)	Ireland	Prospective (368)	MED; SURG
Fujita (2008)	Japan	Prospective (361)	SURG
Johansson (2008)	Sweden	Prospective (343)	MED; SURG; IDD
Periard (2008)	Switzerland	RCT (29)	MED
Singh (2008)	Nepal	Prospective (230)	MED; SURG; ICU; GYN; OB
Uslusoy (2008)	Turkey	Prospective (568)	SURG
Webster (2008)	Australia	RCT 376	MED; SURG
Zarate (2008)	USA	Prospective (432)	ED
Cicolini (2009)	Italy	Prospective (427)	MED; SURG
Lee (2009)	Taiwan	Prospective (6538)	MED; SURG
Martinez (2009)	Spain	RCT (332)	IDD
McNeill (2009)	USA	Prospective (80)	MED; SURG; ED; Radiology; ONC; renal therapy
Nishanth (2009)	India	RCT (21)	Major abdominal surgery
Van Donk (2009)	Australia	RCT (95)	Hospital in the home
Adhikari (2010)	USA	Retrospective (764)	ED
Bausone-Gazda (2010)	USA	RCT (152)	Level 1 trauma centre
Bolton (2010)	UK	Retrospective (1000)	ED; elective and specialized divisions
Dargin (2010)	USA	Prospective (75)	ED
Gregg (2010)	USA	Retrospective (147)	ICU
Hasselberg (2010)	Sweden	Prospective (413)	SURG
Rickard (2010)	Australia	RCT (177)	MED; SURG
Chico-Padron (2011)	Spain	RCT (29)	SURG; CCU
Do Rego Furtado (2011a)	Portugal	Prospective (286)	SURG
Fields (2012)	USA	Retrospective (151)	ED
Kaur (2011)	India	Prospective (200)	ED; surgical OPD

Saini (2011)	India	Prospective (168)	ED; medical and surgical OPD
Ascoli (2012)	USA	Retrospective (490)	Hospital wide
Bertolino (2012)	Italy	RCT (107)	MED
Bonnici (2012)	Malta	Prospective (285)	MED
Boyce (2012)	USA	Prospective (24)	Progressive care; Medical and Surgical ICU
Elia (2012)	Italy	RCT (50)	High dependency unit
Fakih (2012)	USA	Prospective (4434)	MED; SURG
Forni (2012)	Italy	RCT (521)	Orthopedic patients
Goransson (2012)	Sweden	Prospective (83)	Pre-hospital emergency services
Mestre (2012)	Spain	Prospective (2145)	MED; SURG; ICU
Rickard (2012)	Australia	RCT (1690)	MED; SURG
Salgueiro-Oliveira (2012)	Portugal	Prospective (315)	MED
Sarafzadeh (2012)	Iran	Prospective (320)	OT; pediatric*; internal disease; GYN; ED; IDD; ICU; CCU
Wang (2012)	China	RCT (181)	Gastroenterology or hepatic disease
Mestre (2013)	Spain	Prospective (2145)	Hospital wide
Abolfotouh (2014)	Saudi Arabia	Prospective (359)	MED; SURG; IDD
Cicolini (2014)	Italy	Prospective (1498)	MED; SURG
López (2014)	Spain	RCT (599)	MED; SURG
Pasalioglu (2014)	Turkey	Prospective (439)	IDD
Benaya (2015)	Israel	Prospective (103)	MED
Marsh (2015)	Australia	RCT (21)	MED; SURG
Rojas-Sánchez (2015)	Colombia	Prospective (198)	ED
Wang (2015)	China	RCT (125)	Liver cirrhosis
Anderson (2016)	USA	Prospective (95)	MED; SURG; ICU; ED
Bugden (2016)	Australia	RCT (190)	ED
Danski (2015)	Brazil	RCT (79)	Clinical and surgical services
Enes (2016)	Brazil	Prospective (122)	MED
Erdogan (2016)	Turkey	Prospective (347)	Neurosurgical clinic
Gunther (2016)	France	RCT (434)	Medical ICU

Keogh (2016)	Australia	RCT (160)	MED; SURG
Palese (2016)	Italy	Prospective (1262)	ED
Tan (2016)	Singapore	RCT (307)	OB
Tanabe (2016)	Japan	Prospective (407)	Hospital wide
Urbanetto (2016)	Brazil	Prospective (361)	Hospital wide
Zhu (2016)	China	Prospective (189)	ED
Miliani (2017)	France	Prospective (815)	MED; SURG
Murayama (2017)	Japan	Prospective (5316)	MED; SURG
Ronen (2017)	Israel	Prospective (789)	Head and neck surgery
Takahashi (2017)	Japan	Prospective (200)	MED
Tan (2017)	Singapore	Prospective (282)	MED; SURG
Urbanetto (2017)	Brazil	Prospective (447)	Hospital wide
Xu (2017)	China	RCT (317)	Hepatobiliary surgical
Atay (2018)	Turkey	Prospective (532)	Hospital wide
Bahl (2018)	USA	RCT (37)	ED
Bridey (2018)	France	RCT (104)	ICU
Carr (2018)	Australia	Prospective (391)	ED
Datar (2018)	USA	Retrospective (277)	ICU
Marsh (2018)	Australia	Prospective (1578)	MED; SURG
Meng (2018)	USA	Prospective (291)	Hospital wide
Pandurangadu (2018)	USA	Prospective (86)	ED
Rickard (2018)	Australia	RCT (845)	MED; SURG

USA: United States of America; UK: United Kingdom; RCT: randomized controlled trial; MED: medical ward/unit; SURG: surgical ward/unit; OPD: outpatient department; CCU: cardiac coronary unit; ICU: intensive care unit; OT: operating theatre; IDD: infectious diseases department; ED: emergency department; OB: obstetrics; GYN: gynaecology *Patients < 16 years excluded

Quality assessment

Reporting quality in 70 included cohort studies was mixed. Outcome measures were defined in all but 13 studies (Anderson, 2016; Ascoli et al., 2012; Bolton, 2010; Datar et al., 2018; Dillon et al., 2008; Fujita et al., 2006; Gregg et al., 2010; Hasselberg et al., 2010; Hirschmann et al., 2001; Pandurangadu et al., 2018; Royer, 2003; Schears, 2006; Vandenbos et al., 2003); a clear objective or question was lacking in two studies (Fujita & Namiki, 2008; Mestre et al., 2013); and only 11 studies provided sample size justification (Abbas et al., 2007; Abolfotouh et al., 2014; Boyce & Yee, 2012; Cicolini et al., 2014; Dargin et al., 2010; Dillon et al., 2008; Fakih et al., 2012; Fields et al., 2012; Marsh, Webster, et al., 2018; Zhu et al., 2016).

The majority of RCTs had low risk of bias for random sequence generation (21/31, 68%), but only 14/31 (45%) clearly described the method of allocation concealment (Supplementary Table 2.1). Although blinding of participants and personnel was not possible in all but one of the RCTs, we did not consider this a potential bias. Blinding of outcome assessors was poorly reported, with minimal or no information reported by 30/31 (97%) trials, and outcome assessors aware of group allocation in 4/31 (13%) RCTs (Barker et al., 2004; Bertolino et al., 2012; Gupta et al., 2007; Panadero et al., 2002).

Supplementary Table 2.1: Risk of Bias

Author (year)	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Bahl (2018)	Low	Low	Unclear	High	High	Low	Low
Barker (2004)	Unclear	Unclear	Unclear	High	Low	Low	Low
Bausone-Gazda (2010)	Low	Unclear	Unclear	Unclear	Low	Low	High
Bertolino (2012)	Low	High	Unclear	High	Low	Low	Unclear
Bridey (2018)	Unclear	Low	Unclear	High	Low	Low	Low
Bugden (2016)	Unclear	Unclear	Unclear	Unclear	Low	Low	Low
Chico-Padron (2011)	Low	High	Unclear	Unclear	Low	Low	Unclear
Danski (2015)	Unclear	Unclear	Unclear	Unclear	Low	Low	Low
Elia (2012)	Unclear	Unclear	Unclear	Unclear	Low	Low	Low
Forni (2012)	Low	Low	Unclear	Unclear	Low	Low	Low
Lopez (2014)	Low	Unclear	Unclear	Unclear	Low	Low	Unclear
Gunther (2016)	Low	Unclear	Unclear	Unclear	Unclear	Low	Unclear
Gupta (2007)	Unclear	Unclear	Unclear	High	Unclear	Low	Unclear
Haddad (2006)	Unclear	Unclear	Unclear	Unclear	Low	Low	Low
Keogh (2016)	Low	Low	Unclear	Unclear	Low	Low	Low
Marsh (2015)	Low	Low	Unclear	Unclear	Low	Low	Low
Martinez (2009)	Low	Low	Unclear	Unclear	Low	Low	Low
Niesen (2003)	Low	Unclear	Low	Low	Low	Low	Low
Nishanth (2009)	Low	Low	Unclear	Unclear	Low	Low	Unclear
Panadero (2002)	Unclear	Unclear	Unclear	High	High	Low	Low
Periard (2008)	Low	Unclear	Unclear	Unclear	Low	Low	Unclear
Rickard (2010)	Low	Low	Unclear	Unclear	Low	Low	Low
Rickard (2012)	Low	Low	Unclear	Unclear	Low	Low	Low
Rickard (2018)	Low	Low	Unclear	Unclear	Low	Low	Low

Tan (2016)	Low	Low	Unclear	Unclear	Low	Low	Low
Van Donk (2009)	Unclear	Low	Unclear	Unclear	Low	Low	Low
Wang (2012)	High	High	Unclear	Unclear	Low	Low	Low
Wang (2015)	Low	Unclear	Unclear	Unclear	Low	Unclear	Low
Webster (2007)	Low	Low	Unclear	Unclear	Low	Low	Low
Webster (2008)	Low	Low	Unclear	Unclear	Low	Low	Low
Xu (2017)	Low	Unclear	Unclear	Unclear	Low	Low	Low

Low: Low risk of bias; Unclear: Unclear risk of bias; High: high risk of bias

Synthesis of results

Table 2.2 displays the pooled proportion and incident rate (IR) per 1000 catheter days of PVC failure (any complication). Peripheral intravenous catheter failure incidence was 36.5% [32.5%–40·6%]. The pooled incident rate (IR) for overall PVC failure was 116.8 per 1000 catheter days [74.2–159.5] in 13 included studies (total 75,569 catheter days). Study heterogeneity was high (I^2 = 97·9%).

Individual PVC complications are reported in Table 2.2. Pooled phlebitis was 16·8% [13.9–20.0%] in 82 studies, with an IR of 37.7 [27.4–48.0] per 1000 catheter days (14 studies). Study heterogeneity was high (I^2 = 99.4%). Phlebitis was the most frequently reported outcome, as well as the most highly prevalent complication (Figure 2). Pooled infiltration was 13·6% [11.0–16·4%] reported in 44 studies, constituting the second most common PVC complication, followed by occlusion (7·8%), leakage (7·3%), pain (6.4%), and dislodgement (5·9%).

Infection outcomes were the least frequently reported and least common complication. The pooled proportion for diagnosed CRBSI was < 0·1% [< 0·1–< 0·1%] (14 studies) and < 0·1 per 1000 days, [< 0.1–0.3], (7 studies). Pooled suspected CRBSI (8 studies) was < 0.1% of PVCs [< 0·1–< 0·1%], with local infection in 12 studies being a pooled 0·6% [< 0·1–1·6%].

Table 2.2: Proportion and incidence rates of PVC complications in included studies

Event	Proportion of events					Incidence Rate of events per 1000 catheter-days				
	Studies	PVCs	Outcomes	Pooled%	95% CI	Studies	Catheter-days	Outcomes	Pooled IR	95% CI
Failure	36	34,031	10,670	36.5 [c,d]	32.5–40.6	13	75,569	3,309	116.8 [c,d]	74.2–159.5
Phlebitis	82	64,427	7,012	16.8[c,d]	13.9–20.0	14	75,569	1,496	37.7 [c,d]	27.4–48.0
Occlusion	34	18,962	1,525	7.8 [c,d]	5.6–10.4	11	71,286	828	26.1 [c,d]	17.1–35.0
Infiltration	44	25,728	3,097	13.6 [c,d]	11.0–16.4	9	74,076	960	32.2 [c,d]	22.4–42.0
Dislodgement	40	19,802	1,338	5.9 [c,d]	4.8–7.2	15	83,192	832	19.5[c,d]	12.2–26.7
Leakage	18	9,376	525	7.3 [c,d]	4.7–10.3	6	16,775	212	18.0 [c,d]	9.4–26.5
CRBSI	14	16,190	12	< 0.1 [a,e]	< 0.1–< 0.1	7	23,462	2	< 0.1 [a,e]	< 0.1–0.3
Suspected CRBSI	8	3,138	15	< 0.1 [b,e]	< 0.1–< 0.1	7	57,279	15	0.2 [a,d]	0.1–0.4
Local infection	12	14,729	215	0.6 [c,d]	< 0.1–1.7	7	16,348	41	1.8 [c,d]	< 0.1–3.7
Pain	26	18,602	1,075	6.4 [c,d]	4.8–8.2	9	68,082	435	21.2 [c,d]	11.3–31.2

CI = confidence interval; CRBSI = catheter-related bloodstream infection; heterogeneity of studies: [a] low, [b] moderate and [c] high; effect-size test: [d] significant and [e] non-significant; IR = incidence rate; PVC = peripheral intravenous device.

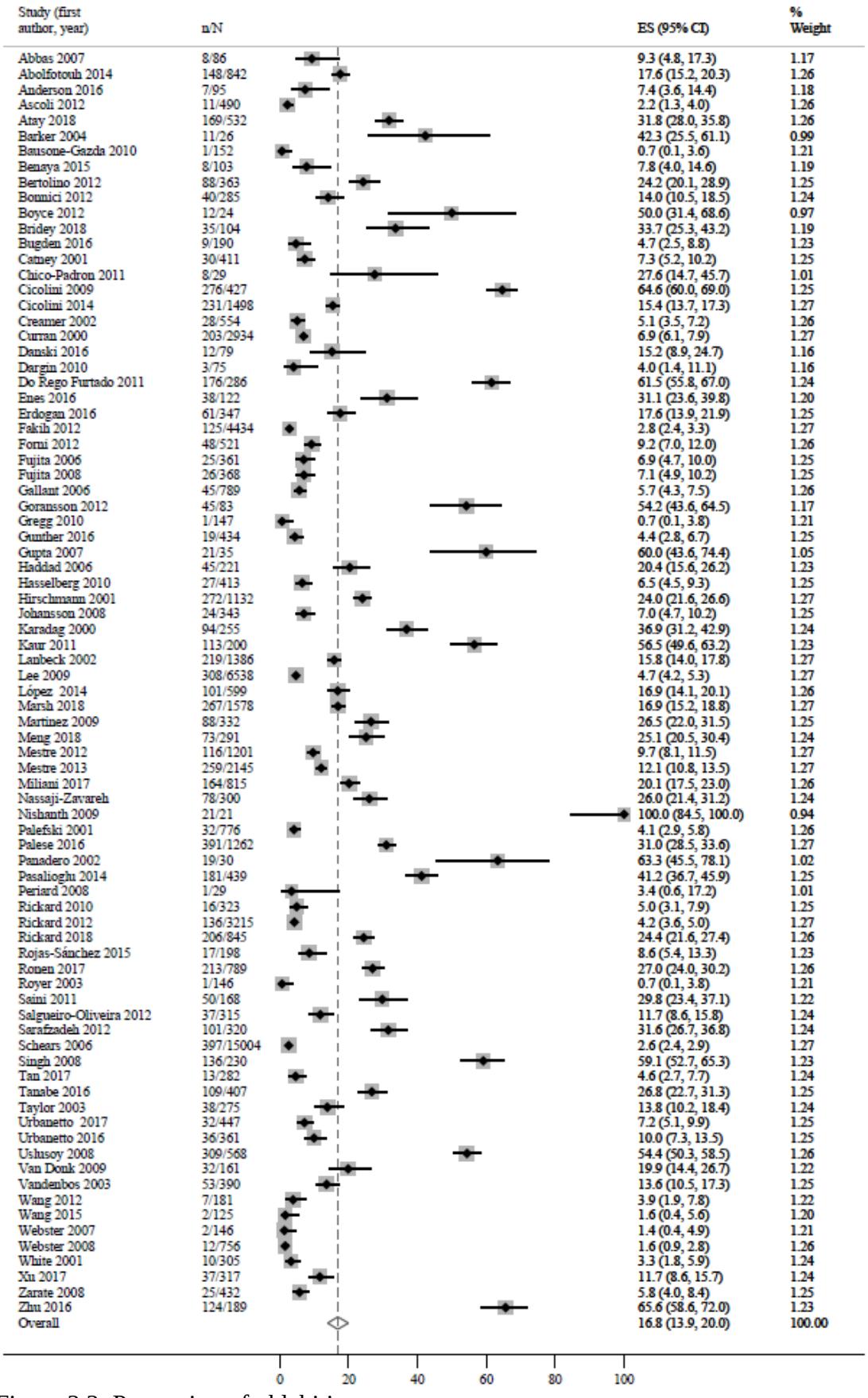

Figure 2.2: Proportion of phlebitis

Subgroup analyses are presented in Table 2.3. Due to unavailability of data, IR per 1000 days was not included in this analysis. The pooled proportion of infiltration for emergency department inserted PVCs (25.2%, [14.2%–38.2%]) was significantly higher ($p = 0.02$) than those inserted in other departments (12.2% [9.6%–15.1%]). However, no difference was detected in overall PVC failure in emergency department compared to other areas.

In developing economies, pooled phlebitis (26.2%, [18.4%–34.8%]; 27 studies) was significantly higher ($p = 0.001$) than in developed economies (12.9%, [10.1%–16.0%]; 52 studies). Overall PVC absolute failure was 4% higher in developing economies, but this was not statistically significant.

Table 2.3: Subgroup analysis: Proportion of PIV Failure and Complications across study populations and setting

Event	Proportion of events				
	Studies	PVCs	Outcomes	Pooled %	95% CI
PVC Failure					
Emergency	7	1,119	436	43.4[c,d]	30.4–56.8
Other	29	32,912	10,234	35.0 [c,d]	30.8–39.5
Pooled	36	34,031	10,670	36.5[c,d,g]	32.5–40.6
Phlebitis					
Emergency	10	3,190	793	20.0 [c,d]	9.7–32.8
Other	72	61,237	6,219	16.4[c,d]	13.4–19.5
Pooled	82	64,427	7,012	16.8 [c,d,g]	13.9–20.0
Occlusion					
Emergency	5	844	58	6.8 [b,d]	3.7–10.8
Other	29	18,118	1,467	8.0 [c,d]	5.6–10.8
Pooled	34	18,962	1,525	7.8 [c,d,g]	5.6–10.4
Infiltration					
Emergency	6	1,011	218	25.2 [c,d]	14.2–38.2
Other	38	24,717	2,879	12.2 [c,d]	9.6–15.0
Pooled	44	25,728	3,097	13.6 [c,d,f]	11.0–16.4
Dislodgement					
Emergency	6	1,033	99	7.8 [c,d]	4.0–12.8
Other	34	18,769	1,239	5.7 [c,d]	4.5–7.0
Pooled	40	19,802	1,338	5.9 [c,d,g]	4.8–7.2
Leakage					
Emergency	1	37	3	8.1[d]	2.8–21.3
Other	17	9,339	522	7.3 [c,d]	4.7–10.3
Pooled	18	9,376	525	7.3 [c,d,g]	4.7–10.3
CRBSI					
Emergency	1	391	0	<0.1[d]	< 0.1–0.1
Other	13	15,799	12	<0.1 [c,d]	< 0.1–< 0.1
Pooled	14	16,190	12	<0.1 [c,d,g]	< 0.1–< 0.1
Local Infection					
Emergency	2	1,154	14	1.1[d]	0.5–1.8
Other	10	13,575	201	0.5 [c,e]	< 0.–1.7

Pooled	12	14,729	215	0.6 [c,d,g]	< 0.1–1.7
Pain					
Emergency	4	768	78	7.7[c,d]	< 0.0–24.9
Other	22	17,834	997	6.2 [c,d]	4.6–7.9
Pooled	26	18,602	1,075	6.4 [c,d,g]	4.8–8.2
PVC Failure					
Developed	29	32,085	10,042	35.9[c,d]	31.8–40.0
Developing	7	1,946	628	39.6 [c,d]	22–58.7
Pooled	36	34,031	10,670	36.5[c,d,g]	32.5–40.6
Phlebitis					
Developed	55	50,218	4,638	12.9 [c,d]	10.1–16.0
Developing	27	14,209	2,374	26.2[c,d]	18.4–34.8
Pooled	82	64,427	7,012	16.8 [c,d,f]	13.9–20.0
Occlusion					
Developed	28	17,136	1410	7.9 [c,d]	5.5–10.6
Developing	6	1,826	115	7.6 [c,d]	1.9–16.6
Pooled	34	18,962	1,525	7.8 [c,d,g]	5.6–10.4
Infiltration					
Developed	36	23,384	2,799	13.3 [c,d]	10.7–16.0
Developing	8	2,344	298	15.2 [c,d]	5.2–29.0
Pooled	44	25,728	3,097	13.6 [c,d,g]	11.0–16.4
Dislodgement					
Developed	34	17,973	1,247	6.0 [c,d]	4.8–7.4
Developing	6	1,829	91	5.7 [c,d]	2.2–10.5
Pooled	40	19,802	1,338	5.9 [c,d,g]	4.8–7.2
Leakage					
Developed	14	7,946	422	6.7 [c,d]	3.8–10.2
Developing	4	1,430	103	9.6 [c,d]	4.3–16.5
Pooled	18	9,376	525	7.3 [c,d,g]	4.7–10.3
Suspected CRBSI					
Developed	7	2,821	15	<0.1 [b,d]	< 0.1–0.6
Developing	1	317	0	<0.1 [a,d]	< 0.1–1.2
Pooled	8	3,138	15	<0.1 [b,d,g]	< 0.1–< 0.1
Local Infection					
Developed	11	8,191	62	0.5 [c,d]	< 0.1–1.4
Developing	1	6,538	153	2.3 [a,d]	2.0–2.7

Pooled	12	14,729	215	0.6 [c,d,f]	< 0.1–1.6
Pain					
Developed	24	17,571	950	5.6 [c,d]	4.2–7.3
Developing	2	1,031	125	11.0 [a,d]	9.1–13.0
Pooled	26	18,602	1,075	6.4 [c,d,f]	4.8–8.2

Heterogeneity of studies: [a] low, [b] moderate, [c] high; effect-size test: [d] significant and [e] non-significant; Test for heterogeneity between subgroups [f] significant and [g] non-significant; Comparisons between emergency and other departments could not be calculated for suspected CRBSI; Comparisons between developed and developing economies could not be calculated for CRBSI

The sensitivity analysis between studies with < 100 PVCs (small studies) and studies with > 100 PVCs (large studies) did not find significantly different PVC failure or complication exception for phlebitis (Supplementary Table 2.2). Pooled phlebitis (32.5% [18.3%–48.6%]) from 13 small studies was significantly higher ($p = 0.01$) than the pooled proportion of phlebitis in 69 large studies (14.8% [12.0%–18.0%]).

Most studies (63%) in this review were prospective cohort studies, with only 6 retrospective studies (6%). Overall PVC failure was not significantly different between prospective (38.7% [32.8%–44.8%]) and retrospective cohort studies (31.8% [24.9%–39.6%]). Phlebitis incidence was significantly higher ($p < 0.001$) in 55 prospective compared to 2 retrospective studies. Overall, low and moderate heterogeneity existed for pooled PVC failure and a majority of PVC complications in the retrospective studies. However, infiltration ($I^2 = 95.9\%$) was an exception with high heterogeneity but no significant difference in complication rates between retrospective and prospective studies ($p = 0.95$).

Supplementary Table 2.2: Sensitivity analysis: Proportion of PIV Failure and Complications reported in small studies (< 100) and large studies (> 100); Prospective and Retrospective Studies.

Event	Proportion of events				
	Studies	PVCs	Outcomes	Pooled %	95% CI
PVC Failure					
Small Study	11	742	285	37.5 [c,d]	27.8–47.7
Large Study	25	33,289	10,385	36.1 [c,d]	31.6–40.6
Pooled	36	34,031	10,670	36.5 [c,d,g]	32.5–40.6
Phlebitis					
Small Study	13	773	200	32.5 [c,d]	18.3–48.6
Large Study	69	63,654	6,812	14.8 [c,d]	12.0–18.0
Pooled	82	64,427	7,012	16.8 [c,d,f]	13.9–20.0
Occlusion					
Small Study	7	451	41	10.2 [c,d]	4.6–17.5
Large Study	27	17,238	1,288	7.4 [c,d]	5.1–10.2
Pooled	34	18,962	1,525	7.8 [c,d,g]	5.6–10.4
Infiltration					
Small Study	6	395	60	15.1 [c,d]	6.9–25.7
Large Study	38	25,333	3,037	13.4 [c,d]	10.7–16.4
Pooled	44	25,728	3,097	13.6 [c,d,g]	11.0–16.4
Dislodgement					
Small Study	8	577	31	4.9 [b,d]	2.0–8.7
Large Study	32	19,225	1,307	6.2 [c,d]	4.9–7.6
Pooled	40	19,802	1,338	5.9 [c,d,g]	4.8–7.2
Leakage					
Small Study	5	394	26	6.1 [,d]	3.7–8.9
Large Study	13	8,982	499	7.5 [c,d]	4.6–11.1
Pooled	18	9,376	525	7.3 [c,d,g]	4.7–10.3
CRBSI					
Small Study	1	21	0	0.0 [e]	0.0–15.5
Large Study	13	16,169	12	< 0.1 [a,e]	< 0.1–< 0.1
Pooled	14	16,190	12	< 0.1 [a,d,g]	< 0.1–< 0.1
Suspected CRBSI					
Small Study	2	182	0	< 0.1 [e]	< 0.0–0.4
Large Study	6	2,956	15	0.2 [b,e]	< 0.1–0.8

Pooled	8	3,138	15	< 0.1 [b,e,g]	< 0.1–< 0.1
Local infection					
Small Study	1	21	0	< 0.0 [e]	< 0.0–15.5
Large Study	11	14,708	215	0.8 [c,d]	0.1–1.8
Pooled	12	14,729	215	0.6 [c,d,g]	< 0.1–1.6
Pain					
Small Study	6	378	45	6.5 [c,e]	0.1–19.0
Large Study	20	18,224	1,030	6.5 [c,d]	4.8–8.3
Pooled	26	18,602	1,075	6.4 [c,d,g]	4.8–8.2
PVC Failure					
Prospective	18	26,808	8,292	38.7 [c,d]	32.8–44.8
Retrospective	1	151	48	31.8 [a,d]	24.9–39.6
Pooled	17	26,959	8,340	38.3 [c,d,g]	32.6–44.22
Phlebitis					
Prospective	55	54,556	6,023	18.0 [c,d]	14.3–21.9
Retrospective	2	637	12	1.8 [a,d]	0.8–3.0
Pooled	57	55,193	6,035	17.1 [c,d,f]	13.6–21.0
Occlusion					
Prospective	13	9,641	463	5.4 [c,d]	2.9–8.5
Retrospective	2	641	27	3.6 [a,d]	2.3–5.2
Pooled	15	10,282	490	5.4 [c,d,g]	3.10–8.2
Infiltration					
Prospective	25	16,893	1,695	11.7 [c,d]	8.8–14.9
Retrospective	5	2,065	464	12.1 [c,d]	2.4–27.6
Pooled	30	18,958	2159	11.8 [c,d,g]	8.7–15.2
Dislodgement					
Prospective	18	10,083	716	6.2 [c,d]	4.2–8.6
Retrospective	3	1,298	98	6.2 [a,d]	3.2–9.9
Pooled	21	11,381	814	6.2 [c,d,g]	4.4–8.3
Leaking					
Prospective	9	4,238	377	8.6 [c,d]	6.1–11.5
Retrospective	1	490	21	4.3 [a,d]	2.8–6.5
Pooled	10	4,728	398	8.1 [c,d,f]	5.7–10.8
Local Infection					
Prospective	6	9,415	209	1.8 [c,d]	0.8–3.0
Retrospective	1	764	5	0.7 [a,d]	0.2–1.5

Pooled	7	10,179	214	1.6 [c,d,g]	0.7–2.7
Pain					
Prospective	13	12,693	704	7.1 [c,d]	4.7–10.1
Retrospective	1	151	1	0.7 [a,e]	0.1–3.7
Pooled	14	12,844	705	6.5 [c,d,f]	4.2–9.3

Heterogeneity of studies: [a] low, [b] moderate, [c] high; effect-size test: [d] significant and [e] non-significant; Test for heterogeneity between subgroups [f] significant and [g] non-significant; comparisons between prospective and retrospective studies could not be calculated for CRBSI and suspected CRBSI

Discussion

PVCs are the most ubiquitous but necessary invasive clinical device, yet they carry risk. Ideally, PVCs should remain complication free for the duration of therapy, yet the findings of this meta-analysis are that 36.5% currently fail from complications. Our systematic review provides the first, large scale understanding of how often and in what way PVCs fail. With more than two billion PVCs used globally each year, our results should trigger attention to, and action targeting, the hitherto unrecognised scale of this problem. Government guidelines on the prevention of PVC complications are currently limited to an infection focus (Loveday et al., 2014; O'Grady et al., 2011), but urgently need expansion to focus on all complications, similar to the Infusion Therapy Standards of Practice, produced and currently only available to members of one professional society (Infusion Nurses Society, 2016).

Phlebitis was the most frequently measured outcome and the most prevalent complication, affecting 16.8% of catheters, although phlebitis definitions were unclear in many studies. It is known that at least 71 different phlebitis scales exist, with highly disparate criteria and minimal validation testing (Ray-Barruel et al., 2014). It has also been suggested that variable phlebitis rates could reflect overlapping complications, such as occlusion, infiltration and early signs of infection (Helm et al., 2015). This may explain

why phlebitis in our included studies varied widely from less than 1% (Bausone-Gazda et al., 2010; Gregg et al., 2010; Royer, 2003) up to 100% (Nishanth et al., 2009). Phlebitis is perhaps an unhelpful term, and future studies should instead focus on individual signs/symptoms such as pain (Rickard & Ray-Barruel, 2017).

Catheter related bloodstream infection was measured in 14 studies making it one of the least frequently studied complications. This is a concern given this is the most serious potential PVC complication. The diagnosed CRBSI incident rate was < 0.1 per 1000 catheter days, substantially lower than an earlier review of 10 studies which found a rate of 0.5 per 1000 catheter days (Maki et al., 2006). This may reflect our focus on studies published between 2000 and 2018, whereas the earlier review covered 1970 to 2002 since which time PVC materials and infection prevention practices changed substantially. A more recent review, with dissimilar methods, also reported infection at 0.5 per 1000 days, with the majority of data from one French surveillance report (Mermel, 2017). Catheter related bloodstream infections increase the length of hospital stay, healthcare costs, morbidity and mortality (Pujol et al., 2007), and there is concern that these are under reported in PVCs (Hadaway, 2012). While we identified a low incidence rate of < 0.1 per 1000 catheter days, we concur with other authors that the high-volume use of these catheters, estimated at 2 billion purchased globally per year, means many millions of such infections likely occur each year, and a higher focus on prevention and monitoring is warranted (Rickard & Ray-Barruel, 2017).

Peripheral intravenous catheter failure from infiltration was an absolute 13% higher in PVCs inserted in the emergency department compared with other departments. This may reflect patients with difficult vascular access and urgent need for a PVC to administer resuscitation fluids, medications, or contrast for medical imaging (Sebbane et al., 2013).

Higher infiltration rates could also be related to the common emergency department practices, of using PVCs to draw blood samples (Fry, Romero, & Berry, 2016; Hawkins et al., 2018) and placement in the antecubital fossa, an area of flexion (Bugden et al., 2016; Zarate et al., 2008).

Countries with developing economies had more than twice the phlebitis of countries with developed economies ($p = 0.001$). Little is known about how PVCs are managed and what infection prevention practices are in place in countries with developing economies (Alexandrou et al., 2015). A recent systematic review found higher health-care-associated infections (HCAI) rates in developing countries at 15.5 per 100 patients, compared with developed countries [USA (4.5 per 100 patients); Europe (7.1 per 100 patients)] (Allegranzi et al., 2011). Our findings can aid key stakeholders in developing economies to lobby for investment in PVC related initiatives to reduce the current waste caused by PVC failure.

This comprehensive literature search, critique and synthesis of PVC failure rates in adults has identified an extensive problem, with a substantial proportion—one in three—of PVCs failing before the completion of IV treatment. In both the USA and UK, there has been an increased focus on preserving patients' vessel health, and recommending individual patient assessment to ensure the most appropriate VAD is inserted (Hallam et al., 2016; Moureau et al., 2012). The results of this review support the need for a more systematic and planned approach to not only insertion but also post-insertion management of this important medical device.

Our quality assessment was hampered by poor reporting by authors. Overall, over 40% of categories in the risk of bias table for RCTs were 'unclear' because information

was not included in the publication. These omissions emphasise the importance of using Consort Guidelines when reporting outcomes from RCTs.

Although we conducted a comprehensive literature search in four databases, the possibility of having missed a relevant study cannot be excluded. Furthermore, we were unable to obtain the number of catheter days for all included studies, which impacted our meta-analysis per 1000 catheter days. The heterogeneity of the study populations may preclude generalisability to specific patient subgroups, but does provide a good reflection of PVC issues at the system level, and subgroup analyses explored potential at risk subgroups. Limiting our search to English language and studies since the year 2000 may have impacted our findings. Nonetheless we believe this review reflects modern PVC materials and practices, provides the most comprehensive review to date of PVC complications and failure, and sets a new benchmark for CRBSI in PVCs.

In conclusion, this rigorous, comprehensive review shows that PVC failure is a significant worldwide problem which until now appears unacknowledged and unaddressed. These results should provoke an urgent response and have highlighted many areas for potential improvement. Phlebitis and infiltration as the most prevalent complications should be the most urgent priority, in addition to CRBSI which although rare per catheter, is prevalent at the system level. Given the multitude of phlebitis definitions, it may be more useful for future studies to focus instead on the frequency of individual complications. Developing standardised definitions and self-monitoring health systems via PVC registries and/or benchmarks for complications is a quality and safety challenge that will require inter-disciplinary efforts. The potential benefits for patients and health services are substantial if PVC failure can be reduced.

Part 2 — Vascular Access Specialist Insertion of PVCs: A Literature Critique

Introduction

The high global PVC failure and complication rate reported in the systematic review of this chapter highlighted a need to understand the effect of inserter skill on PVC complications and failure. The skill and training for clinical staff to successfully place PVCs is often underestimated with up to 50% of insertions requiring multiple attempts prior to successful placement (López et al., 2014; Rickard & Ray-Barruel, 2017). Previous literature has suggested that a VAS with advanced inserter knowledge and skill may improve patients' PVC-related outcomes (Alexandrou et al., 2014; Carr, Higgins, et al., 2018; A. Jackson, 2012; Wallis et al., 2014). Nevertheless, there is a paucity of clinical trials conducted to support the benefit of VAS PVC insertions. A recent published Cochrane systematic review that examined VAS team insertions for any vascular access device type for the prevention of failure found no RCTs had been conducted in this area (Carr, Higgins, et al., 2018). However, a review of studies using other research designs to compare VAS insertion of PVCs, either as part of an infusion team or within a current hospital framework, has not been conducted.

Description of a VAS

A VAS is typically defined as a clinician who has advanced knowledge and skills to place and manage vascular access devices (Carr, Higgins, et al., 2018). These specialists have advanced patient assessment skills and advanced knowledge of vascular access, technology including catheter design, insertion assistive devices such as ultrasound, and vascular access device related products including dressings and securement devices.

Different VAS insertion models are employed by hospitals and can include VAS teams, often referred to as infusion therapy or intravenous therapy teams (Carr, Higgins, et al., 2018). These teams are centrally structured within a health care facility and advocate that by providing specialised nurses, freed from other responsibilities, it allows them to focus on providing accurate PVC insertion, eliminates or reduces waiting lists, and provides consistency and safe delivery of all infusion services (Dougherty, 1996; Hadaway, Dalton, & Mercanti-Erieg, 2013; Kelly, Buchan, Brown, Tehrani, & Cowan, 2009).

Other health care models incorporate VAS as part of their existing nursing workforce (Palefski & Stoddard, 2001). These nurses have extensive training and education about PVC insertion and care. They assist with PVC placements and trouble shoot any infusion-related concerns or PVC complications within their clinical setting (Palefski & Stoddard, 2001). This model is thought to improve patient outcomes by reducing PVC-related complications, as well as offer cost savings benefits for the healthcare institution, as an additional labour force is not required (Palefski & Stoddard, 2001).

Description of the intervention

The intervention under consideration is placing PVCs by a VAS to reduce the incidence of PVC failure and complications.

Search methods for identification of studies

A detailed literature search was conducted in the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, and EMBASE, and last updated on the 11th of November 2018 (Appendix F) to identify the benefit of a VAS for PVC insertion. MESH terms and

descriptors included: catheterization, peripheral; catheters, indwelling; team; clinician; specialist. There were no date or language barriers for this search, which identified 708 potential papers for inclusion. Titles and abstracts were searched for relevant papers; once duplicates were removed, four papers (Carr et al., 2010; Hunter, 2003; Scalley, Van, & Cochran, 1992; Tomford, Hershey, McLaren, Porter, & Cohen, 1984) included information about expert PVC inserters.

Searching other resources

The reference lists of included papers were searched, and an additional six papers were retrieved (Bosma & Jewesson, 2002; da Silva, Priebe, & Dias, 2010; Meier, Fredrickson, Catney, & Nettleman, 1998; Miller, Goetz, Squier, & Muder, 1996; Palefski & Stoddard, 2001; Soifer, Borzak, Edlin, & Weinstein, 1998).

Types of included research

The research reported in this review included a quasi-randomised controlled trial (Soifer et al., 1998) and descriptive observational studies (Bosma & Jewesson, 2002; Carr et al., 2010; da Silva et al., 2010; Hunter, 2003; Meier et al., 1998; Miller et al., 1996; Palefski & Stoddard, 2001; Scalley et al., 1992; Tomford et al., 1984).

Outcomes

Studies included in this review reported on various outcomes such as first-time insertion success (Carr et al., 2010), PVC-related complications (Palefski & Stoddard, 2001; Soifer et al., 1998), and/or the number of PVC insertions per month (da Silva et al., 2010). Although the methodology and outcomes varied in the included studies, all reported a benefit with the use of a VAS.

Soifer et al. (1998) compared PVC insertions by a VAS team (Monday to Friday in business hours) with insertions by junior medical officers (week days between 5 pm and 9 am, and weekends) in relation to PVC complication rates. Patients with an even last digit in their medical record number were assigned to the VAS team, and those with an odd number to a junior medical officer. Although such allocation in principle may result in similar groups, allocation concealment is impossible. In other words, the recruiter had advanced knowledge of the intervention, therefore introducing the chance of selection bias.

This quasi-randomised controlled trial reported an almost 12% lower occurrence of local complications (tenderness, warmth, erythema, swelling, and palpable cord) with VAS-inserted catheters (VAS, *n* = 58/737, 7.9%; junior medical staff, *n* = 30/138, 21.7%). However, this lower rate may be a result of the trained outcome assessor inspecting all PVC sites for the VAS team but less than half of the PVCs inserted by the medical officers. This study also reported no PVC-related bacteraemia in the VAS group compared to three cases out of 138 PVCs (2%) inserted by junior medical staff (Soifer et al., 1998). Although these results appeared to favour VAS insertions, during analysis, 318 PVCs that had been inserted by junior medical staff were attributed to the VAS team, as they maintained these catheters post-insertion, making these results questionable.

Tomford et al. (1984) conducted a prospective observational study where four clinical units introduced PVC insertion by a VAS team. The researchers staggered each unit's commencement date by 10 days; the controls were patients from units awaiting introduction of the VAS team. Phlebitis decreased 17% (p = < 0.001) with VAS-inserted PVCs (*n* = 63/433, 15%) compared with the control which was medical staff (house officer) inserted PVCs (*n* =136/427, 32%) (Tomford et al., 1984). The VAS team, after introduction, only inserted PVCs Monday to Friday during the first shift of the day. It appears that PVCs inserted after hours were included as VAS inserted catheters because

they were maintained by the VAS team. The results of this study are therefore unclear as to the benefit of a VAS-inserted PVC for reducing the incidence of phlebitis.

Palefski and Stoddard (2001) compared PVC insertions by a VAS within an existing nursing framework, with a generalist nurse. They reported a 16% (p = < 0.001) lower PVC failure rate with VAS-inserted catheters (VAS, n = 126/639, 19.7%; generalist nurse, n = 49/137, 35.8%), and for a patient's first PVC per hospital admission there was a lower incidence of pain on infusion (VAS, n = 5/319, 1.6%; generalist nurse, n = 4/123, 3.3%), phlebitis (VAS n = 8/319, 2.5%; generalist nurse n = 6/123,4.9%), and a longer PVC dwell time (VAS 2.2 days; generalist nurse 2.0 days) (Palefski & Stoddard, 2001). However, a limitation to this study was that the classification of a VAS was made by the nurse placing the PVC or their nurse unit manager. The outcome data was collected by the nurse caring for the patient at the time the device was removed, regardless of whether they had inserted the catheter. These nurses were not blinded to the inserter, therefore introducing the potential for biased reporting.

In a descriptive study by Scalley et al. (1992), members of the VAS team, as part of their usual practice, inspected the PVC sites of hospitalised patients daily. In clinical areas PVCs were inserted by members of the VAS team, ward nurses, anaesthesiologists, nurse anaesthetists, paramedics and medical staff. As this was a descriptive study, patients were not allocated to have their PVC placed by a particular health professional. If an incidence of phlebitis was identified, the VAS team member graded the phlebitis severity. Phlebitis was reported as 3% lower (p = 0.05%) for VAS-inserted catheters (8.8%) compared to those inserted by other health professionals (11.8%) (Scalley et al., 1992). This study included 31,115 PVCs but did not identify the number of PVCs inserted by the VAS team compared to other health professionals, making it difficult to determine the benefit of VAS-inserted PVCs. A further limitation to this study was that the outcome measure of

phlebitis was recorded by the VAS team, who were un-blinded to the inserting health professional. This therefore created a potential for ascertainment bias favouring the VAS team, with the potential of under- or over-reporting of phlebitis.

PVC-related infection is a serious and sometimes life-threatening complication (Maki et al., 2006; Mermel, 2017). A descriptive study by Miller et al (1996) reported a 3-fold decrease (29 cases) of PVC-related infection in the first year of a VAS team in their hospital. Similarly, Meier et al. (1998) reported a decrease in primary bloodstream infections of 35% (1.1 per 1000 patient-days reduced to 0.7 per 1000 patient-days) with the introduction of a VAS team. They also reported a 51% reduction in primary nosocomial bloodstream infections with *Staphylococcus aureus* bacteraemia (0.33 infections per 1000 patients days reduced to 0.16% infections per 1000 patient days) (Meier et al., 1998). However, both studies had a pre-post design, and Miller (1996) acknowledged the limitations of their research and the need for an RCT to confirm their outcomes.

Two descriptive studies identified the benefits of the introduction of a VAS team but did not compare data with another insertion model (Carr et al., 2010; da Silva et al., 2010). Carr et.al. (2010) reported that during the first five months of establishing a VAS team, there was an improvement in first-attempt PVC insertion success from 49% to 97%. However, insertion attempts were self-reported, introducing the risk of reporting bias. Da Silvia et.al. (2010) reported a 5% increase in the use of smaller 24-gauge catheters (16.5% to 21.6%) and an overall decrease in the number of PVCs insertions (2.12 catheters per patient to 1.57 catheter per patient) with the introduction of a VAS team. A limitation of this study was that data was collected via hospital management software which observed pharmaceutical dispensing of catheter products. It is unclear whether this decrease of purchasing was only for the wards that had introduced a VAS or a reflection of hospital-wide purchasing. Furthermore, no consideration was given to other confounding factors

that may have influenced PVC usage during these time periods, such as different patient acuity.

Bosma and Jewesson (2002) randomly selected 250 patients who had PVC placements by their VAS team to describe the characteristics of their VAS service. This study reported that most of their consults were for surgical patients and that 39% of patients were graded as having poor vein status (Bosma & Jewesson, 2002). This study was purely descriptive, so the effectiveness of the service was not established.

In a descriptive study by Hunter (2003), 12 surveys were sent to similar sized hospitals inquiring about their PVC insertion practices, with nine surveys returned. No information was provided about who responded to the survey and if they were the most appropriate person. Based on the responses, a VAS service was established at the study hospital. This new VAS service reportedly led to a reduction in the number of PVC insertion attempts (from six to a maximum of two) and PVC complications (phlebitis rates dropped 2%) (Hunter, 2003), compared to PVC insertions by ward nurses. However, there was limited information about how the data was collected and its veracity.

Limitations of included studies

Five of the 10 studies included in this review were conducted before the year 2000 (Meier et al., 1998; Miller et al., 1996; Scalley et al., 1992; Soifer et al., 1998; Tomford et al., 1984), making it difficult to determine whether advancements in infusion therapy, such as new catheter materials and designs (Castillo et al., 2018; López et al., 2014), dressings and securements (Marsh, Larsen, et al., 2018; Marsh, Webster, Mihala, et al., 2015; Rickard et al., 2018), or the use of insertion assistance devices such as ultrasound (Holder et al., 2017; Joing et al., 2012), would impact PVC failure rates. Over the last 10 years, there has also been increased use of different vascular access devices such as midlines and peripherally

inserted central catheters (PICCs) (Anderson, 2004; Chopra et al., 2015; Deutsch, Sathyanarayana, Singh, & Nicastro, 2014; López et al., 2014). These devices are often used for patients with IV treatment expected to last for greater than one week or for patients with difficult vascular access. Therefore, the increased use of such devices may have impacted upon the incidence of PVC failure reported in recent studies compared with their older counterparts.

Further limitations to three studies included in this review was the unclear allocation of PVC insertion to the VAS team. This made it difficult to ascertain the true benefit of VAS-inserted PVCs for preventing failure. Tomford et al. (1984) and Soifer et al. (1998) included patients whose devices had been inserted by other health professionals to the VAS group if the patient's PVC had been maintained by the VAS team. Palefski et al. (2001) allowed nurses to self-evaluate their skill level and nominate themselves as a VAS.

Four studies included in this review were at risk of reporting bias, as outcome data was collected by members of the VAS team (Carr et al., 2010; Scalley et al., 1992), recorded by the bedside nurse who may have been the clinician who placed the catheter (Palefski & Stoddard, 2001), or collected by the study investigators who were aware of study allocation (Tomford et al., 1984). Soifer et al. (1998) used an independent observer to collect PVC-related outcome data. However, the observer inspected all PVC sites for the VAS team but only two in five of the medically inserted PVCs, creating uncertainty about the accuracy of the outcome data for this trial.

Summary

This literature review of VAS has established that although a promising intervention to reduce PVC failure, there is a knowledge gap in high-quality evidence to support the use of

a VAS for PVC insertion. It has identified a need for high-quality RCTs to compare VAS with the generalist PVC insertion model.

Chapter 2 Conclusion

The systematic review in Part 1 of this chapter revealed the global challenges being faced in healthcare, with greater than one in three PVCs failing before the completion of IV treatment. Until now, there has not been a clear understanding of why these catheters are failing, and this systematic review highlights not only the frequency, but the complications causing PVC failure. Part 2 of this chapter identified that the benefit of a VAS inserting PVCs has yet to be firmly established. The results from this chapter informed the prioritisation of PVC complications for both the analysis of cohort study data (Phase 1) and the pilot RCT comparing a VAS with generalist insertion (Phase 2). It also established the need to conduct an RCT to establish whether there is a benefit of VAS-placement of PVCs. The following chapter presents the modifiable and non-modifiable risk factors associated with PVC failure (Phase 1).

Chapter 3 — Methods

Introduction

This chapter outlines the methods used to achieve the aim and objectives for this research. Included in the chapter are the research designs and a description of methods including study participants, ethical considerations, methods to promote validity and reliability, study procedures, data collection, and data analysis. As an initial step, in Phase 1, existing data from a recently completed cohort study was analysed to identify risk factors to inform the design of a subsequent pilot RCT. Methods for the pilot RCT in Phase 2 are presented as a research protocol, published in the journal *Vascular Access,* prior to trial commencement.

Phase 1: Identifying Risk Factors Associated with PVC Failure

An analysis of data from a prospective cohort study of 1,000 patients admitted to the surgical and medical wards of the Royal Brisbane and Women's Hospital was undertaken. The study had been completed before the student started the PhD program but had not yet been analysed. As such, the methods for the cohort study are presented briefly, with in-depth methods on the multivariable analysis. The analysis was designed to identify risk factors associated with PVC failure and focused on insertion and maintenance risk factors. An investigation of both modifiable and non-modifiable risks associated with failure of PVCs, including patient and clinician factors, was planned.

Aims

The aims of the analysis were to answer the following research questions:

1. What are the risk factors associated with PVC failure in the adult in-patient population?

2. What are the potentially modifiable risk factors associated with PVC failure in the adult in-patient population to inform insertion knowledge and practices?

Design

Data from the cohort study, which was designed to identify risk factors associated with PVC failure (defined as an unplanned catheter removal not associated with termination of treatment), was interrogated. The advantage of exploring data from a prospective cohort study is that this design overcomes the problems of a retrospective or cross-sectional study; that is, the design: 1) avoids sampling bias (all eligible patients are included); 2) avoids length of time bias (patients followed until hospital discharge, so catheter failure at any time during hospitalisation will be identified); and 3) identifies the temporal sequence of exposure and outcome (none of the patients will have catheter failure at recruitment) (Sedgwick, 2013b; Song & Chung, 2010). In addition, a prospective cohort study allows the examination of multiple outcomes of risk factors (such as length of stay and cost) (Song & Chung, 2010).

Sample size

Sample size was determined as per the "10 events per variable" rule (Mallett, Royston, Dutton, Waters, & Altman, 2010; Vittinghoff & McCulloch, 2007) to estimate that with an average of 1.5 PVCs per patient and an expected PVC failure rate of 30%, a sample size of 1000 patients would be required.

Recruitment for the original cohort study

Patients were eligible for study participation if they met the following inclusion criteria, with no exclusions:

Inclusion criteria

- Patients requiring an intravenous device and able to provide informed consent
- Catheter inserted within 24 hours of recruitment

Exclusion criteria

- Patients admitted for palliative treatment or who are on a care of the dying pathway
- Patients under the age of 18 years

Data collection methods used in original cohort study

Patients whose PVC had been inserted within the preceding 24-hour period were identified prospectively. Permission to approach potentially eligible patients was obtained from the treating clinician, and written informed consent was attained.

Baseline data were founded on data points identified in the cohort and randomised controlled trials included in the systematic review in Chapter 2. Data were collected for all PVCs that the participant had had inserted during their hospital admission, until hospital discharge or insertion of a central venous access device. Participants were reviewed second daily and other risk factors were recorded. Examples of the data collected are presented in Table 3.1.

Table 3.1: Example of data collected for the Cohort Study

Patient Demographics • Age • Gender • Body mass index • Dominant side • Skin type (Fitzpatrick, 1988)) • Co-morbidities • Reason for admission • History of PVCs or CVAD on a previous admission
PVC characteristics • Date and time of insertion • Inserted where (e.g. ward, procedure room) • Insertion by (e.g. paramedic, anaesthetist, nurse) • Size/gauge • IV placement (e.g. cephalic vein) • Side of Insertion • Number of Insertion attempts • What type of dressing is in place
Second daily check • PVC use (e.g. IV medication/fluids) • Medications has the patient received (e.g. IV fluids, IV flucloxacillin) • Number of times the device been accessed • Number of dressing changes • Additional securements • Is the dressing clean, dry and intact?
Complication site check • Leaking • Pain • Tenderness • Erythema • Swelling • Palpable cord

PVC removal

- Date and time of removal
- Reason for removal (e.g. completed treatment – complications, treatment incomplete complications)
- Complication present (e.g. occlusion, infiltration)

Complication site check (as above)

- Mobility status (e.g. independent, unable to mobilise)
- Cognitive status at PVC removal (e.g. confused, drowsy)
- Highest temperature whilst PVC in place

Pathology results

- Infection present during time on trial (e.g. urine, respiratory)
- PVC tip sent for culture
- PVC swab of insertion sign sent for culture
- Blood culture collected

Outcomes included in the original cohort study

PVC failure was considered to have occurred if the removal of the catheter was unplanned from any cause (including infiltration, occlusion, phlebitis, accidental removal, or suspected infection).

PVC failure was grouped into one of three types:

(1) Occlusion or infiltration, defined as blockage, IV fluids moving into surrounding tissue, induration, or swelling greater than 1 cm from the insertion site at or within 24 hours of removal (Dychter et al., 2012; Gabriel, 2010; Helm et al., 2015). Occlusion and infiltration were combined as one outcome as these terms are often used interchangeably by clinicians, and this combination has been used previously in literature (Wallis et al., 2014).

(2) Phlebitis, defined as per the clinicians' definitions, or one or more of the following signs and symptoms at the time of, or within 24 hours of, PVC removal: pain or tenderness (scored at 2 or more on a 1–10 increasing severity pain scale); erythema; or a palpable cord (greater than 1 cm in length from the insertion site) (Rickard et al., 2018)

(3) Dislodgement, either partially or completely from the vein (Campbell & Bowden, 2011).

If patients had multiple complications, all were recorded.

PVC insertion and management

The insertion and care of all PVCs was as per the standard hospital policy (Royal Brisbane and Women's Hospital, 000259: Peripheral Intravenous Cannulation and Infusion Management – Adult and Paediatrics). As per this policy, PVC inserters were required to complete a learning module, attend a practical cannulation workshop with simulated insertion, and have supervised insertions until both confidence and independence were demonstrated. Each clinician was allowed a maximum of two insertion attempts; skin decontamination was 3M SoluPrep™ Antiseptic Swab (2% chlorhexidine gluconate in 70% isopropyl alcohol (3M, St Paul); PVCs were Becton Dickinson Insyte™ Autoguard™ Blood Control (non-winged) catheters with a Smart-Site™ Needle-Free Valve (BD, Salt Lake City); PVCs were dressed with a sterile transparent, semi-permeable, self-adhesive dressing or, if this was contraindicated, a gauze dressing; and PVCs were required to be removed as soon as they were no longer required or replaced every 72 hours, unless the clinician chose to extend the dwell time due to a clinical indication.

Data management

Data were documented for each patient in an electronic case report form (eCRF) supported by the electronic data platform, REDCap™ (Research Electronic Data Capture) (REDCap Software Version 6.10.6 © 2016 Vanderbilt University) (Harris et al., 2009). Data were de-identified prior to entry into the eCRF to maintain patient confidentiality. A master screening log of patients, with unit record numbers and sequential allocation of study numbers, was created (Appendix G). It was necessary to have data in a re-identifiable format to enable microbiology endpoints, such as CRBSI, to be accurately collected. The paper screening log was stored in a lockable filing cabinet, in the Principal Investigator's locked office. Following trial completion, these were housed in a secure archival unit, based at the recruiting site, under the guardianship of the Principal Investigator.

Data analysis

Data from eCRF was downloaded to Stata 14.2 (StataCorp, 2015) for data management and analysis (Stata commands provided in parentheses with the customary Courier New font for information). Observations were separated into patient-specific variables (unit of analysis: patient) and device-specific variables (unit of analysis: device). Text observations such as comorbidities or medications were converted to numeric data for analysis, where necessary. Missing data were not imputed. Observations collected during bi-daily checks were collapsed into single observations per device. Categorical variables (e.g. reason for admission) were recoded as necessary, by combining categories with $n < 20$ into 'other' for descriptive statistics. As a general rule, the largest category was selected as referent category for regression analyses. Considering the results of univariable regression analyses and categories with a similar effect on the outcome were combined in preparation for the multivariable analyses (e.g. *catheter gauge*). Variables such as device dwell time, device-

days, failure modes, body mass index (BMI) category, and pressure pattern were generated from observed data. Variables observed over time, for example, medications administered, device utilisation, dressing securement, etc. were collapsed into single observations per device as necessary. Data was set up for survival analyses considering censored devices. The terminology for regression analyses recommended by Hidalgo and Goodman (2013) was used.

Descriptive statistics of the collected data and outcome variables were presented using frequencies, proportions, means and standard deviations, medians and inter-quartile range, by patient or device as necessary. Failure incidence rates were calculated (`strate`), and the Kaplan-Meier survivor function was plotted (sts graph). In general, Cox proportional hazards models were fitted using the Efron method to handle tied failures (`stcox [varlist], cluster(id) efron`). Variable selection for multivariable models focused on identifying the important independent predictors of the outcome (Vittinghoff, Glidden, Shiboski, & McCulloch, 2005). Considering the relatively large number of variables observed during data collection, the variables entered into the multivariable regression models were selected based on the results of univariable exploratory analyses (eligible at an overall *p*-value of < 0.20) (Maldonado & Greenland, 1993) and clinical judgement. Correlations between selected variables were checked using Spearman's rank correlation (Sedgwick, 2014) between two binary variables (`ci2 varname1 varname2, spearman`), the R-squared (Sedgwick, 2013a) value of linear regressions between continuous and categorical variables, and between two continuous variables. Correlations between ordinal and categorical variables were calculated using Somer's D (Newson, 2002). Correlations were considered significant at $r > 0.5$ and the lower bound of the 95% confidence interval of r was also > 0.5 (where calculated).

Correlated covariates were not entered in multivariable models together. Interactions between covariates were also explored but ignored (due to the large number of possible pairings) unless the inclusion of an interaction term substantially changed the main covariate effects. These correlations and interactions were considered during multivariable model building. The multivariable models were constructed in two steps: using baseline covariates only, then using treatment covariates only. The final models were derived using the manual stepwise backward method (Vittinghoff et al., 2005), where covariates were dropped at $p \geq 0.05$. The baseline and treatment models were combined to derive the final multivariable models. The final models were tested using the global proportional-hazards assumption test (`estat phtest`), the concordance probability (`estat concordance`) to calculate agreement between predictions and outcomes, and Nelson-Aalen cumulative hazard function plotted against the Cox-Snell residuals (Cleves, Gould, & Marchenko, 2016). Since the purpose of the study was exploratory in nature, violations of the proportional-hazards assumption were tolerated as long as the hazard function vs residuals curve showed a reasonable fit.

Summary

The methods for the multivariable analysis have been described above. In the following section the methods for the pilot RCT will be presented in the form of a publication.

Phase 2: Pilot Study – RELIABLE Trial (RELiable Intravenous Access By Line Experts) [Publication 2]

Phase 2 of this research is a pilot RCT of patients admitted to the surgical and medical wards of the Royal Brisbane and Women's Hospital. The study compared insertion of a PVC by a VAS with insertion by a generalist model.

Aims

The aims of this phase were to answer the following research questions:

3. Is it feasible to conduct a full-scale randomised control trial to compare the effectiveness of PVC insertion by a vascular access expert versus insertion by usual practice on the incidence of PVC failure in the adult population?

The methods for Phase 2 are reported as a co-authored published protocol in the peer-reviewed journal *Vascular Access*. There were no variations to this protocol in the conduct of the pilot RCT.

Statement of contribution to co-authored published paper

The bibliographic details of the co-authored paper, including all authors, are:

Marsh, N., Webster, J., Cooke, M., Rickard, C. M. (2017). The RELIABLE trial (RELiable Intravenous Access By Line Experts): A pilot randomised controlled trial protocol of expert versus generalist peripheral intravenous catheter insertion. *Vascular Access,* 3(2), 3–7.

My contribution to the paper included: Critical review of the literature to inform the design of the study, conceptualising and designing the study, preparation of manuscript, and final responsibility for the decision to submit publication.

(Signed) (Date) 22/01/2019

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The RELIABLE trial: comparing peripheral intravenous catheter insertion by experts with a generalist insertion approach. A pilot randomised control trial protocol

Abstract

Introduction

A peripheral intravenous catheter (PVC) is essential for administration of intravenous fluids and medications. Successful PVC insertion and the decrease of catheter-related complications are important clinical objectives and patient outcomes. PVCs inserted by vascular access specialists (VAS) are believed to preserve veins, improve the experience for patients, decrease infusion complications and ultimately save costs associated with clinician time, materials and length of hospital stay. However, there is a lack of robust randomised controlled trials (RCT) that have tested skill level on successful PVC insertion and prevention of PVC failure.

Methods and analysis

This is a single centre, parallel group, pilot RCT. It will compare the effectiveness of PVC insertion by a VAS with insertion by any clinician (generalist model) on clinical and economic outcomes. This trial will be conducted in the Royal Brisbane and Women's Hospital, Australia. It has a recruitment target of 50 participants per group (n = 100). The primary outcome is to test the feasibility of conducting an adequately powered RCT as established by predetermined criteria for eligibility, recruitment, retention and attrition, protocol adherence, missing data, effect size and patient satisfaction. PVC failure defined as premature device removal before the end of therapy caused by: phlebitis, infiltration, occlusion, accidental removal, local infection or catheter related blood stream infection will be reported. Feasibility outcomes will be reported descriptively and analysed against

pre-determined acceptability criteria. As a pilot study, statistical comparison methods will be tested. Cox regression will assess the effect of patients and treatment differences.

Ethics and trial commencement

This pilot trial has ethical approval from Queensland Health (HREC/16/QRBW/386) and Griffith University (2016/782).

Trial registration: ACTRN12616001675415

Keywords

Intravenous, Vascular Access Devices, randomised controlled trial, Phlebitis

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Introduction

Peripheral intravenous catheters (PVCs) are essential for the administration of intravenous fluids and medications for the treatment of hospitalised patients. They are the most commonly used of all vascular access devices (VADS) with annual sales of 330 million per year in the USA and 14 million in Australia (Rickard et al., 2015; Zingg & Pittet, 2009). Yet for such an important device their failure rate remains unacceptably high, with reported resites required for up to 69% of PVCs (Bolton, 2010; Rickard et al., 2010; Royer, 2003; Smith, 2006).

In the past, hospitals often employed intravenous therapy teams (IVTT) to insert a majority of PVCs (Bosma & Jewesson, 2002; Carr et al., 2010). Increasing pressure on healthcare budgets has resulted in the disbanding of many IVTT (Hadaway et al., 2013). Now, many hospitals have PVC insertions performed by generalist clinicians (nursing and medical) at the unit level, who while assessed as competent are typically not expert inserters. Unit level inserters may provide superior continuity of care since clinical staff are

familiar with the patient's diagnosis and medical history, and there is a belief that their lesser expertise rarely has negative outcomes (Robertson, 1995). This model of care focuses on the procedural skill of PVC insertion, rather than the broader approach of the discipline of infusion therapy, such as selecting the right catheter and site for a specific patient and therapy (Hawes, 2007). Other models advocate the benefit of vascular access specialist (VAS) inserters, either through an IVTT (Carr et al., 2014) or within existing nursing infrastructure (Palefski & Stoddard, 2001) for PVC insertion and clinician education. The definition of a VAS for this research is a clinician with advanced knowledge of vascular access including catheter technology, insertion assistive devices, dressings and securement, modalities of catheter access, IV therapy management (Carr et al., 2014), in combination with expert inserter skills. It is argued that this expertise preserves veins, enhances the patient experience, decreases the incidence of infusion complications and ultimately saves costs associated with clinician time, materials and length of hospital stay (Palefski & Stoddard, 2001).The use of a VAS for PVC insertion exists in part due to an ongoing concern that a generalist approach results in multiple needlesticks (multiple insertion attempts) that cause great discomfort to patients and irreversible damage to the venous system, limiting current and future vascular access (Hawes, 2007).

Successful PVC insertion and prevention of resultant catheter-related complications and device failure are important clinical objectives and patient outcomes (Carr et al., 2014). The level of inserter skill has been identified as a risk factor for catheter failure (Carr et al., 2010; Wallis et al., 2014). However, there have been no high-quality randomised controlled trials (RCTs) investigating the benefit of a VAS. Observational studies and audits have found VAS-inserted PVCs to have longer functional dwell time (Bai et al., 2013); fewer insertion attempts (Carr et al., 2010; Hunter, 2003); and less

phlebitis (Scalley et al., 1992; Tomford et al., 1984), inflammation and catheter-related sepsis (Soifer et al., 1998). A number of these observational studies were conducted before the year 2000 (Miller et al., 1996; Scalley et al., 1992; Tomford et al., 1984), so there is little contemporary information about the impact of VAS inserters in the context of modern PVC materials, dressings and securement and the trend to older, more obese patient populations. Some studies identified a benefit of VAS inserters in hospital settings but their outcomes were not compared against a control group of generalist PVC inserters and thus have been adequately assessed (Bosma & Jewesson, 2002; Carr et al., 2010). Previous studies in this area have only measured the immediate success of the PVC insertion procedure and not the resultant impact on complications or device failure (Carr et al., 2010). In addition, data has been collected retrospectively risking recall bias (Bosma & Jewesson, 2002), or clinical staff have assessed their own PVC insertion skill level which may introduce detection bias (Palefski & Stoddard, 2001).

Current local (Department of Health, 2015) and international guidelines (Infusion Nurses Society, 2011; Intravenous Nursing New Zealand, 2011; O'Grady et al., 2011) provide limited direction on PVC insertion and maintenance, often referring to local health institutions requirements. In Australia there is no national credentialing for a minimum level of knowledge, expertise and decision-making skill for clinicians inserting a PVC. This results in a variation of knowledge, skill, experience and expertise for PVC inserters across healthcare settings (Vizcarra et al., 2014). The challenge for local and international guiding bodies is the lack of robust RCTs that have tested the effectiveness of different knowledge and skill level on successful PVC insertion and prevention of device failure and complications. Consequently, in the absence of evidence from high-quality RCTs it is impossible to produce comprehensive clinical practice guidelines for best PVC insertion model of care. The objective of this pilot randomised controlled trial is to test the

feasibility of conducting a suitably powered RCT by assessing both the methodology and rigour of methods planned for the larger study (Arnold et al., 2009; Polit & Beck, 2008).

Methods and analysis

Design

We will conduct a single centre, parallel group, pilot randomised controlled trial to compare PVC insertion by a VAS with the insertion by any clinician (generalist model, standard practice).

Hypothesis

Primary hypothesis

The feasibility of conducting a future large RCT with adequate statistical power to test hypotheses will be established by meeting targets formulated *a priori.* These are based on results from previous PVC pilot trials (Keogh et al., 2015; Marsh, Webster, Flynn, et al., 2015). Targets are as follows:

- Eligibility: over 90% of patients screened will be eligible
- Recruitment: over 90% of eligible participants will agree to enrol
- Retention and attrition: fewer than 5% of patients will be lost to attrition
- Protocol adherence: over 90% of participants in the intervention groups will receive their allocated treatment
- Missing data: less than 5% (primary endpoint)
- Patients and clinical staff will report greater than 80% satisfaction and acceptability with the vascular access expert.

Secondary hypothesis

Hypothesis 1

Patients whose PVC was inserted by a VAS will have fewer episodes of device failure (composite of phlebitis, infiltration, occlusion, accidental removal or dislodgement and local or CRBSI) than those whose PVC is inserted by standard practice (generalist approach).

Hypothesis 2

Patients whose PVC was inserted by a VAS will have fewer insertion attempts and associated patient reported pain.

Hypothesis 3

Patients whose PVC was inserted by a VAS will have longer device dwell time compared to those whose PVC is inserted by standard practice (generalist approach).

Setting

The trial will be conducted in a single-centre, 929-bed referral teaching hospital, the largest provider of healthcare services in Queensland, Australia, with more than 90,000 patients admitted every year.

Ethics

The study has received approval from the RBWH Human Research Ethics Committee (HREC/16/QRBW/386) and the Griffith University Human Research Ethics committee (2016/782). Written consent will be obtained from participants and serious adverse events will be monitored and reported to both HRECs, although these are not expected. In accordance with the National Health and Medical Research Council all data will be stored securely in a password-protected database or paper copies in a locked filing cabinet, and

participants' confidentiality will be maintained with only aggregate data published (NHMRC, 2015).

Participants

Participants for this study will be patients admitted to general medical and surgical wards, over the age of 18 and expected to require their PVC for greater than 24 hours. They will be excluded from recruitment if they have a current blood stream infection or have previously been in the study. Eligible patients will be advised of the study, provided with written information and consent to participate will be sought by a Research Nurse (ReN).

Sample size

Approximately 160 patients are discharged each month from medical and surgical wards of the hospital. For this pilot study, the recruitment target is 50 participants per group. The study will not be powered to detect statistical significance between groups, but rather to assess the feasibility of the methods to be used in a larger study. The sample size is recommended in the literature as adequate for the purposes of feasibility assessment (Hertzog, 2008; Julious, 2005).

Interventions

The control group of this trial will have PVCs inserted as per hospital policy by an accredited PVC inserter. This is a generalist approach. The access site, type of device and method of PVC securement will be at the inserting clinician's discretion.

For the intervention group the PVC will be inserted by a VAS who is a Registered Nurse with advanced knowledge of vascular access including catheter technology, insertion assistive devices, dressings, modalities of catheter access and intravenous therapy management, selecting the right VAD for the right patient in combination with expert insertion skills. The insertion will also follow the hospital's policy.

Outcome measures and definitions

Primary outcomes

The feasibility of conducting a definitive RCT will be assessed against the following criteria: 1. *Eligibility* (percentage of eligible screened patients), 2. *Recruitment* (percentage of eligible patients who consent to trial participation), 3. *Retention and attrition* (percentage of participants lost to follow up who withdraw consent), 4. *Protocol adherence* (percentage of participants who receive their randomised intervention), 5. *Missing data* (percentage of missing data), 6. *Patient satisfaction* (of PVC at insertion and removal, scored on an 11 point scale of 0 = very dissatisfied to 10 = very satisfied).

Secondary outcomes

PVC failure defined as premature device removal before the end of therapy because of:

- Phlebitis was considered to have occurred if or one or more of the following signs and symptoms: pain or tenderness scored at 2 or more on an increasing pain increment scale, or redness or a palpable cord (all extending greater than 1cm from the insertion site) or purulence (from site, with ulceration).
- Leakage (yes/no)
- Infiltration (the movement of IV fluids into the surrounding tissue, (Doellman et al., 2009; Dougherty, 2008a) swelling greater than 1cm from the insertion site)
- Occlusion (the PVC will not flush or leaks when flushed) (Helm et al., 2015)
- Accidental removal (partial or complete dislodgement of the PVC from the vein)
- Infection (laboratory confirmed local or catheter-associated bloodstream infection) (O'Grady et al., 2011): PVC skin swabs, PVC tip and blood cultures may be collected as per usual clinical practice if clinical suspicion of local infection or systemic infection.

PVC dwell time: from the time of PVC insertion until removal from either device failure, routine replacement or the completion of IV therapy.

PVC insertion: successful insertion and number of insertion attempts for 24 hours post randomisation.

Cost effectiveness: estimates of costs of staff resources, equipment and PVC failure resource usage with previously developed cost estimations (Tuffaha et al., 2014). Detailed resources used for a PVC insertion and removal will be recorded for a subset of 15 patients per study group.

Study procedures

Randomisation

Once the ReN obtains written consent, a web-based central randomisation service provided by the Griffith University Clinical Trials Randomisation Service, will be used to obtain group allocation. This process will provide a computer-generated ratio between groups of 1:1 and randomly varied small block sizes. Allocation will be concealed prior to randomisation.

Blinding

This trial is blinded for the secondary endpoint of PVC failure. This will be achieved as there are two ReN for this study. The first will be responsible for recruitment and randomisation. The second ReN will collect daily PVC site and device failure information and will be blinded to the treatment group. The endpoint CRBSI will also be allocated by a blinded infectious disease expert using a pre-determined definition. Due to the nature of the study, blinding of patients and treating clinicians to the intervention received will not

be possible. However, we have no reason to believe that clinicians and patient responses will be influenced to favour a particular intervention.

Other aspects of PVC care

PVCs will be inserted by hospital accredited clinicians. Subsequently, PVCs will be managed by clinical staff using the standard hospital policies. If required, PVCs will be re-sited every 72 hours, following hospital policy.

Strategies to promote protocol adherence

To promote adherence to the study protocol, any clinical staff inserting PVCs or caring for study participants will be provided with education about the study protocol prior to, and during the trial. The researcher will be available to answer queries from clinicians during the course of the study.

Data collection

Data will be collected and entered directly into an electronic data platform supported by REDCap™ (Research Electronic Data Capture) (REDCap Software Version 6.10.6 © 2016 Vanderbilt University) (P. A. Harris et al., 2009). The feasibility outcomes (eligibility, recruitment, retention and attrition, protocol adherence and sample size estimates) will be collected from enrolment screening logs (held at the study site) and the data entered into an electronic clinical research form on RedCap™. The screening log will have the patient's unique hospital number, eligibility and randomisation allocation.

At the time of recruitment the ReN who is a VAS will assess all patients and collect the following patient demographic and clinical characteristics: age, gender, diagnosis, possible insertion sites and vein quality as per the *peripheral vein assessment tool* (Hallam et al., 2016) (Appendix H: Permission from C Hallam to use peripheral vein assessment tool) . They will ask the patient about their preferred PVC insertion site, and decide based

on patient assessment and the planned IV therapy whether a PVC is the appropriate VAD choice for the patient and discuss this with the treating team if necessary (Chopra et al., 2015; Hallam et al., 2016). After PVC insertion, data will be collected on the gauge size, inserter, number of insertion attempts, place of insertion and type of securement/dressing will be collected. A convenience sample of 15 patients per intervention group will have the insertion procedure timed and data collected about the type of clinician (medical or nursing) and products used (e.g. dressing type). The patient will be asked about the number of insertion attempts and the pain level, as well as data extracted from the medical record. Inserters will be asked why they chose the insertion site and gauge of PVC, and to rate the difficulty of the insertion (0= difficult and 10 = easy).

All participants will be visited daily by a second ReN blinded to the intervention group. They will ask patients to rate their satisfaction with the insertion procedure. They will perform daily assessments for PVC complications based on an inspection the insertion site and patient-reported symptoms. On the day of PVC removal, the ReN (blinded to treatment group) will record the date, time and reason for PVC removal (device failure, routine resite, completion of treatment) as well as perform the daily site inspection. At removal the participant's overall satisfaction with the PVC (11-point scale, with 0= dissatisfied and 10 = satisfied) will be recorded.

Statistical analysis

Data related to the feasibility outcomes will be tabulated as percentages and means, reported descriptively and analysed against pre-determined acceptability criteria, e.g. <5% missing data. To pilot the inferential statistics, data will be exported into IBM SPSS Statistics version 22 (SPSS) for analysis. An intention-to-treat analysis framework will be used; the unit of analysis will be one PVC per patient. Proportions (%) will be reported for

categorical data. Mean values and standard deviations (*SD*) will be reported for normally distributed continuous data; with median values and $25^{th}/75^{th}$ percentiles reported otherwise. Cox regression will be used to assess the effect of patients and treatment differences as well as for group comparisons. A graph of the Kaplan-Meier survival function by group will be generated, and the proportional hazards assumption checked with the log-log plot of survival, and log-rank test performed.

A cost analysis for the subset of 30 patients (15 patients per group), will calculate the mean and median values for the total cost of each IV insertion. Total cost = clinician (directly measured time x estimated hourly salary) + fixed cost (supplies).

Validity and reliability

Internal validity will be maintained by adhering to the study protocol and by using accepted definitions published in the literature for measuring PVC outcomes. Daily PVC site inspections and assessment of outcome measures will be performed in a standardised manner by clinically appropriate staff (e.g. infectious Diseases expert will allocate the outcome CRBSI).

To promote external validity, the characteristics of the target population and the inclusion and exclusion criteria are clearly defined (Rothwell, 2006). The study will identify the type of clinician and level of experience of PVC inserters, and take pragmatic approach of usual clinical PVC care to ensure results are clinically relevant.

Reliability will be assessed by conduction of inter-rater reliability testing for 10% of PVC site daily inspections and outcome assessments, between the daily assessor and an independent VAS. Ten percent of the patient's data entry will also be cross checked, with missing data and implausible values also queried and corrected where possible.

Dissemination of results:

Study results will be presented locally and at relevant international meetings. Participants will be informed at recruitment about how to access results. Results will be published in a peer-reviewed nursing or vascular access journal.

Trial status

Recruitment is planned to commence in June 2017 and will take approximately 12 weeks.

Discussion

This study will be the first pilot RCT to investigate the potential benefits of employing a VAS for PVC insertions in an acute care setting. It will provide preliminary data to inform protocol development and funding applications to allow a larger definitive RCT to be undertaken. The study will aid in the development of PVC education as well as provide guidance for local and international clinical guidelines about the skill level required for PVC insertion. Currently, clinical guideline authors have limited high-quality research to inform their recommendations. This trial will also allow us to establish the adequacy and appropriateness of the study protocol, therefore ensuring the feasibility of conducting a large, multicentre RCT.

Chapter 3 Conclusion

This methods chapter has outlined the processes used to inform the two research phases. In line with the described research methods, data were collected, and analysed using the appropriate statistical methods. For Phase 1, the outlined multivariable analysis informed by the results of univariable regression analysis allowed the identification of both modifiable and non-modifiable risk factors associated with PVC failure. Phase 1 informed

Phase 2, a pilot RCT to establish the feasibility of conducting a larger, multi-centre RCT to compare a VAS with the generalist model for PVC insertion. This approach identified feasibility by addressing 1. Patient eligibility; 2. Recruitment; 3. Retention and attrition; 4. Protocol adherence; 5. Missing data; and 6. patient satisfaction. The next chapter presents the results of Phase 1 and contains a published manuscript that describes the findings of the multivariable analysis of a prospective cohort study.

Chapter 4 — Results of Phase 1

Introduction

This chapter presents the results from Phase 1 of the research and contains one co-authored publication, published in the peer-reviewed *Journal of Hospital Medicine*. Phase 1 presents a unique contribution to understanding PVC failure and associated risk factors. The publication presented in this chapter identified specific modifiable and non-modifiable risk factors associated with different PVC complications (phlebitis, infiltration/occlusion, and dislodgement).

Note: In the following publication, a peripheral intravenous catheter is abbreviated to PIV, rather than PVC. These terms are interchangeable in the literature.

Observational study of peripheral intravenous catheter outcomes in adult hospitalised patients — a multivariable analysis of peripheral catheter failure [Publication 3]

Statement of contribution to co-authored published paper

The bibliographic details of the co-authored paper, including all authors, are:

Marsh, N., Webster, J., Larsen, E., Mihala, G., Cooke, M., Rickard, C. M. (2018). Observational study of peripheral intravenous catheter outcomes in adult hospitalised patients – a multivariable analysis of peripheral catheter failure. *Journal of Hospital Medicine*, 13(2), 83–89.

My contribution to the paper included: Critical review of the literature to inform the design of the study, conceptualising and designing the study, data collection, data analyses,

data interpretation, writing of the manuscript, revision of the manuscript for important intellectual content, and approval of the final version.

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Observational study of peripheral intravenous catheter outcomes in adult hospitalised patients – a multivariable analysis of peripheral intravenous catheter failure

Abstract

Background

Almost 70% of hospitalised patients require a peripheral intravenous catheter (PIV), yet up to 69% fail prior to completion of therapy.

Objective

To identify risk factors associated with PIV failure.

Design

Single centre, prospective, cohort study.

Setting

Medical/surgical wards of a Queensland tertiary-hospital.

Participants

Adult patients requiring a PIV.

Measurements

Demographic, clinical, and potential PIV risk factors were collected. Failure occurred if the catheter had complications at removal.

Result

We recruited 1000 patients. Catheter failure occurred in 512 (32%) of 1578 PIVs. Occlusion/infiltration risk factors were: IV flucloxacillin (Hazard Ratio (HR) 1.98, 95% confidence interval (CI) 1.19-3.31), 22-gauge PIVs (HR 1.43, 95% CI 1.02-2.00), and female patients (HR 1.48, 95% CI 1.10-2.00). Phlebitis was associated with: female patients (HR 1.81, 95% CI 1.40-2.35), bruised insertion sites (HR 2.16, 95% CI 1.26-3.71), IV flucloxacillin (HR 2.01, 95% CI 1.26-3.21), and dominant side insertion (HR 1.39, 95% CI 1.09-1.77). Dislodgement risks were a paramedic insertion (HR 1.78, 95% CI 1.03-3.06). Each increase by 1 in the average number of daily PIV accesses was associated (HR 1.1, 95% CI 1.03-1.20)–(HR 1.14, 95% CI 1.08-1.21) with occlusion/infiltration, phlebitis and dislodgement. Additional securement products were associated with less (HR 0.32, 95% CI 0.22-0.46)–(HR 0.63, 95% CI 0.48-0.82) occlusion/infiltration, phlebitis and dislodgement.

Conclusion

Modifiable risk factors should inform education and inserter skill development to reduce currently high rate of PIV failure.

Keywords: Intravenous, Vascular Access Devices, Cohort studies, Phlebitis

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Introduction

Peripheral intravenous catheter (PIV) insertion is the fastest, simplest and most cost-effective method to gain vascular access, and is used for short-term intravenous fluids, medications, blood products and contrast media (Sabri et al., 2012). It is the most common invasive device in hospitalised patients (Webster et al., 2015), with up to 70% of hospital patients receiving a PIV (Zingg & Pittet, 2009). Unacceptable PIV failure rates have been reported, as high as 69% (Bausone-Gazda et al., 2010; Dillon et al., 2008; Rickard et al., 2012; Webster et al., 2008). Failure is most frequently phlebitis (vein wall irritation/inflammation), occlusion (blockage), infiltration/extravasation (intravenous fluids/vesicant therapy entering surrounding tissue), partial dislodgement or accidental removal, leakage and infection (Bolton, 2010; Rickard et al., 2012; Webster et al., 2008). These failures have important implications for patients, who endure the discomfort of PIV complications and catheter replacements, and healthcare staff and budgets.

To reduce the incidence of catheter failure and avoid preventable PIV replacements, a clear understanding of why catheters fail is required. Previous research has identified that catheter gauge (Abolfotouh et al., 2014; Catney et al., 2001; Wallis et al., 2014), insertion site (Barbut et al., 2003; Cicolini et al., 2009; Saini et al., 2011) and inserter skill (Palefski & Stoddard, 2001; Wallis et al., 2014) impact on PIV failure. Limitations of existing research are small study sizes (Bai et al., 2013; Goransson & Johansson, 2012; Karadeniz et al., 2003), retrospective design (Fields et al., 2012) or secondary analysis of an existing data set; all potentially introducing sampling bias (McNeill et al., 2009; Wallis et al., 2014).

To overcome these potential biases, we developed a data collection instrument based on catheter-associated risk factors described in the literature (Abolfotouh et al.,

2014; Catney et al., 2001; Cicolini et al., 2009; Wallis et al., 2014), and other potential insertion and maintenance risks for PIV failure (e.g. multiple insertion attempts, medications administered) with data collected prospectively. The study aim was to improve patient outcomes by identifying PIV insertion and maintenance risk factors amenable to modification through education or alternative clinical interventions, e.g. catheter gauge selection or insertion site.

Methods

Study design and participants

We conducted this prospective cohort study in a large tertiary hospital in Queensland, Australia. Ethics committee approval was obtained from the hospital (HREC/14/QRBW/76) [Appendix I] and Griffith University (NRS/26/14/HREC) [Appendix J]. The study was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12615000738527). Patients in medical and surgical wards were screened Monday, Wednesday and Friday between October 2014 and December 2015. Patients over 18 years with a PIV (Insyte ™ Autoguard™ BC; Becton Dickinson, standard care) inserted within 24 hours and able to provide written informed consent (Appendix K: Cohort study participant information sheet and participant consent form) were eligible and recruited sequentially. Patients classified as palliative by the treating clinical team were excluded.

Sample size calculation

The 'ten events per variable' rule was used to determine the sample size required to study 50 potential risk factors (Mallett et al., 2010; Vittinghoff & McCulloch, 2007). This determined that 1000 patients with an average of 1.5 PIVs each and expected PIV failure of 30% (500 events) were required.

Data collection

At recruitment, baseline patient information was collected by a Research Nurse (ReNs) (demographics, admitting diagnosis, co-morbidities, skin type (Fitzpatrick, 1988) and vein condition) and entered into an electronic data platform supported by REDCap (Research Electronic Data Capture) (P. A. Harris et al., 2009). Baseline data also included catheter variables (e.g. gauge, insertion site, catheterised vein) and insertion details (e.g. department of insertion, inserting clinician, number of insertion attempts). We included every PIV the participant had during their admission, until hospital discharge or insertion of a central venous access device. PIV sites were reviewed Monday, Wednesday and Friday by ReNs for site complications (e.g. redness, pain, swelling, palpable cord). Potential risk factors for failure were also recorded (e.g. infusates and additives, antibiotic type and dosage, flushing regimen, number of times the PIV was accessed each day for administration of intravenous medications of fluids, dressing type and condition, securement method for the catheter and tubing, presence of extension tubing or 3-way taps, patient mobility status, delirium). A project manager trained and supervised ReNs for protocol compliance, and audited study data quality. We considered PIV failure to have occurred if the catheter had complications at removal, identified by the ReNs assessment, from medical charts or by speaking to the patient and beside nurse. We grouped failure as one of three: 1) occlusion or infiltration, defined as blockage, intravenous fluids moving into surrounding tissue, induration, or swelling greater than 1 cm from the insertion site at or within 24 hours of removal; 2) phlebitis, defined as per clinicians' definitions or one or more of the following signs and symptoms: pain or tenderness scored at 2 or more on a 1 to 10 increasing severity pain scale, or redness or a palpable cord (either extending greater than 1 cm from the insertion site) – at or within 24 hours of PIV removal; and 3)

dislodgement (partial or complete). If multiple complications were present, all were recorded.

Statistical analysis

Data were downloaded from REDCap to Stata 14.2 for data management and analysis. Missing data were not imputed. Nominal data observations were collapsed into a single observation per device. Patient and device variables were described as frequencies and proportions, means and standard deviations, or medians and inter-quartile ranges. Failure incidence rates were calculated, and a Kaplan-Meier survival curve plotted. In general, Cox proportional hazards models were fitted (Efron method) to handle tied failures (clustering by patient). Variables significant at $p < 0.20$ on univariable analyses were subjected to multivariable regression. Generally, the largest category was set as referent. Correlations between variables were checked (Spearman's rank for binary variables, R-squared value of linear regressions for continuous/categorical or continuous/continuous variables. Correlations were considered significant if $r > 0.5$ and the lower bound of the 95% confidence interval was > 0.5 (where calculated). Covariate interactions were explored, and effects at $p < 0.05$ noted. The four steps of multivariable model building were: (1) baseline covariates only with manual stepwise removal of covariates at $p \geq 0.05$; (2) treatment covariates only with manual stepwise removal of covariates at $p \geq 0.05$; (3) combined the derived models from (1) and (2), and manual stepwise removal of covariates at $p \geq 0.05$; and (4) manual stepwise addition and removal (at $p \geq 0.05$) of variables dropped during the previous steps, and interaction testing. Final models were checked as follows: global proportional-hazards assumption test, concordance probability (that predictions and outcomes were in agreement), and Nelson-Aalen cumulative hazard function plotted against the Cox-Snell residuals.

Results

Patient characteristics

In total, 1000 patients with 1578 PIVs were recruited. The average age was 54 years and the majority were surgical patients (673; 67%). Almost half of patients (455; 46%) had two or more co-morbidities, and 334 (33%) were obese (body mass index greater than 30). Sample characteristics are shown by the type of catheter failure in Table 4.1.

Table 4.1: Participant characteristics at recruitment by failure type

Characteristic	Complication class			
	Total [a]	Occlusion/ Infiltration type [b]	Phlebitis type [b]	Dislodgement type [b]
Group size	1000 (100)	169 (17)	209 (21)	137 (14)
Age (years, mean and *SD*)	54 (19)	57 (17)	52 (19)	59 (19)
Sex (male)	546 (55)	80 (15)	99 (18)	80 (15)
BMI (WHO I. C.):				
- normal or underweight (BMI < 25)	301 (30)	43 (14)	65 (22)	50 (17)
- pre-obese (25 ≤ BMI < 30)	358 (36)	66 (18)	71 (20)	45 (13)
- obese class I (30 ≤ BMI < 35)	182 (18)	25 (14)	37 (20)	23 (13)
- obese class II-III (BMI ≥ 35)	152 (15)	35 (23)	33 (22)	18 (12)
Skin type: white *	857 (86)	146 (17)	25 (17)	14 (10)
Skin integrity:**				
- good	606 (61)	96 (16)	135 (22)	66 (11)
- fair	322 (32)	62 (19)	63 (20)	54 (17)
- poor	72 (7)	11 (15)	11 (15)	17 (24)
Co-morbidities:***				
- none	259 (26)	30 (12)	52 (20)	24 (9)
- one	286 (29)	49 (17)	66 (23)	34 (12)
- two	181 (18)	38 (21)	37 (20)	28 (15)
- three	136 (14)	26 (19)	26 (19)	25 (18)
- four or more	138 (14)	26 (19)	28 (20)	26 (19)
History of tobacco/nicotine use	578 (58)	98 (17)	116 (20)	88 (15)
Reason for admission:				
- gastrointestinal surgery	212 (21)	46 (22)	53 (25)	27 (13)
- orthopaedic surgery	199 (20)	30 (15)	49 (25)	31 (16)
- vascular surgery	64 (6)	12 (19)	13 (20)	12 (19)
- renal surgery	31 (3)	2 (6)	2 (6)	1 (3)
- other surgery	167 (17)	23 (14)	19 (11)	15 (9)
- gastrointestinal (medical)	86 (9)	17 (20)	19 (22)	13 (15)
- neurology (medical)	42 (4)	9 (21)	11 (26)	7 (17)
- other medical	99 (10)	19 (19)	28 (28)	24 (24)
- other than medical/surgical	100 (10)	11 (11)	15 (15)	7 (7)
Infection (any type)	107 (11)	34 (32)	43 (40)	17 (16)

Wound	502 (50)	83 (17)	99 (20)	68 (14)
Drain or IDC	266 (27)	49 (18)	53 (20)	38 (14)
No dietary/fluid restrictions	631 (63)	121 (19)	147 (23)	101 (16)

n (%) shown unless otherwise noted; [a] column percentages shown, where applicable; [b] row percentages shown, where applicable; occlusion type = occlusion or infiltration at removal, induration or swelling (> 1 cm) at or within ± 24 hours of removal; phlebitis type = phlebitis or pain at removal, pain, tenderness, erythema or palpable cord (> 1 cm) at or within ± 24 hours of removal; dislodgement type = accidental removal or dislodgement at removal; *SD* = standard deviation; BMI = body mass index; WHO I. C. = World Health Organization International Classification; proportions calculated using the number of non-missing values in the denominator; IDC = indwelling catheter; *skin type 2 as per the Fitzpatrick scale; **Good (healthy, well hydrated, elastic), Fair (intact, mildly dehydrated – reduced elasticity), Poor (paper, dehydrated-small amount or no elasticity); Co-morbidities were as per medical diagnosis documented in patient's medical chart

Peripheral intravenous catheter characteristics

All 1578 PIVs were followed until removal, with only 7 PIVs (0.44%) having missing data for the three outcomes of interest (these were coded as non-failures for analysis). Sixty percent of participants had more than one PIV followed in the study. Doctors/Physicians inserted 1278 (83%) catheters. A total of 550 (35%) were placed in the ward, with 428 (28%) inserted in the emergency department or ambulance. A third of catheters (540; 34%) were 18-gauge or larger diameter, and 1000 (64%) were located in the cubital-fossa or hand. Multiple insertion attempts were required to place 315 (23%) PIVs. No PIVs were inserted with ultrasound as this is rarely used in this hospital. The flushing policy was 0.9% sodium chloride eight hourly if no IV medications/fluids had been administered. Table 4.2 contains further details of device-related characteristics. Although the hospital policy was for catheter removal by 72 hours; dwell time ranged from < 1 to 14 days with an average of 2.4 days.

Peripheral intravenous catheter complications

Catheter failure (any cause) occurred in 512 (32%) catheters - a failure rate of 136 per 1000 catheter days (95% CI 125 to 148). A total of 346 patients of 1,000 (35%) had at

least one failed PIV during the study. Failures were phlebitis 267 (17%), occlusion/infiltration 228 (14%), and/or dislodgement 154 (10%) (Figure 1), with some PIVs exhibiting multiple concurrent complications (Table 4.2).

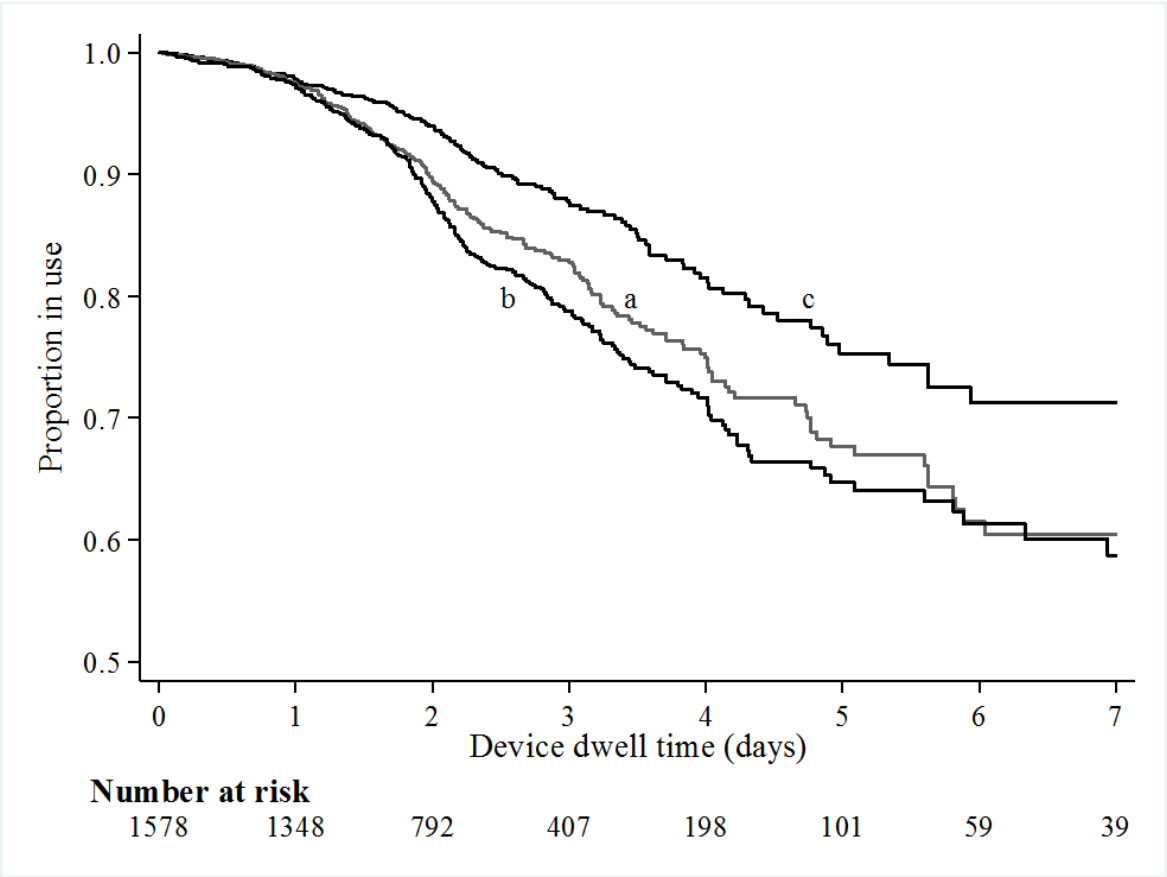

Figure 4.1: Kaplan-Meier curve of (a) occlusion or infiltration at removal, (b) phlebitis or pain at removal, and (c) accidental removal or dislodgement

Table 4.2: Peripheral intravenous catheter characteristics at insertion by failure type

Characteristic	Complication class			
	Total [a]	Occlusion type [b]	Phlebitis type [b]	Dislodgement type [b]
Group size	1578 (100)	228 (14)	267 (17)	154 (10)
First device for patient	1000 (63)	121 (12)	153 (15)	95 (10)
Inserted by:				
- doctor	1,278 (83)	177 (14)	218 (17)	118 (9)
- nurse	170 (11)	35 (21)	29 (17)	14 (8)
- paramedic	92 (6)	14 (15)	11 (12)	16 (17)
Inserted at:				
- ward	550 (35)	106 (19)	113 (21)	61 (11)
- operating theatre	481 (30)	42 (9)	57 (12)	31 (6)
- emergency department	340 (22)	51 (15)	67 (20)	33 (10)
- ambulant care	88 (6)	14 (16)	10 (11)	16 (18)
- other	119 (8)	15 (13)	20 (17)	13 (11)
Size (gauge):				
- 16 or lower	194 (13)	15 (8)	24 (12)	19 (10)
- 18	346 (23)	40 (12)	58 (17)	27 (8)
- 20	733 (49)	104 (14)	127 (17)	61 (8)
- 22	217 (15)	50 (23)	43 (20)	32 (15)
Location:				
- hand	582 (37)	85 (15)	84 (14)	59 (10)
- cubital fossa	418 (27)	61 (15)	75 (20)	41 (10)
- lower forearm	264 (17)	38 (14)	44 (17)	23 (9)
- wrist	190 (12)	21 (11)	35 (18)	21 (11)
- upper forearm	106 (7)	22 (21)	27 (25)	8 (8)
Inserted on dominant side	738 (47)	114 (15)	151 (20)	76 (10)
Difficult insertion [d]	315 (23)	47 (15)	60 (19)	39 (12)
Pain (range: 0–10) [e]	1.9 (2.0)	1.8 (1.9)	2.1 (1.9)	1.7 (1.8)
Bruising due to insertion	63 (4)	6 (10)	19 (30)	5 (8)
Hair unclipped at insertion	609 (39)	75 (12)	73 (12)	58 (10)
Dressing type:				
- bordered transparent dressing	742 (47)	128 (17)	143 (19)	86 (12)
- simple transparent dressing	592 (38)	71 (12)	87 (15)	48 (8)
- adhesive gauze dressing	134 (9)	13 (10)	17 (13)	8 (6)
- other	97 (6)	12 (12)	19 (20)	11 (11)

n (%) shown unless otherwise noted; [a] column percentages shown, where applicable; [b] row percentages shown, where applicable; occlusion type = occlusion or infiltration at removal, induration or swelling (> 1 cm) at or within ± 24 hours of removal; phlebitis type = phlebitis or pain at removal, pain, tenderness, erythema or palpable cord (> 1 cm) at or within ± 24 hours of removal; dislodgement type = accidental removal or dislodgement at removal; [d] including multiple insertion attempts; [e] mean and standard deviation; proportions calculated using the number of non-missing values in the denominator

Multivariable analysis

Occlusion/infiltration

The multivariable analysis (Table 4.3), showed occlusion or infiltration was statistically significantly associated with female patients (HR 1.48, 95% CI 1.10-2.00), with a 22-gauge catheter (HR 1.43, 95% CI 1.02-2.00), IV flucloxacillin (HR 1.98, 95% CI 1.19-3.31) and with frequent PIV access (HR 1.12, 95% CI 1.04-1.21 i.e. with each increase of 1 in the mean medications/fluids administrations per day, relative PIV failure increased 112%). Less occlusion/infiltration were statistically significantly associated with securement using additional non-sterile tape (HR 0.46, 95% CI 0.33-0.63), elasticised tubular bandage (HR 0.49, 95% CI0.35-0.70), or other types of additional securement for the PIV (HR 0.35, 95% CI 0.26-0.47).

Table 4.3: Cox multivariable regression, by failure mode

Predictors	Hazard Ratios (95% CI) by complication class		
	Occlusion/infiltration type *n* = 1,488	Phlebitis type *n* = 1,565	Dislodgement type *n* = 1,533
Age (one year increase)	^	0.99 (0.98–0.99)**	^
Female gender	1.48 (1.10–2.00)*	1.81 (1.40–2.35)**	^
Inserted by paramedic (ref. doctor or nurse)	^	^	1.78 (1.03–3.06)*
22-gauge device	1.43 (1.02–2.00)*	^	^
Inserted on dominant side	^	1.39 (1.09–1.77)*	^
Bruising due to insertion	^	2.16 (1.26–3.71)*	^
Non-sterile tape applied (ever)	0.46 (0.33–0.63)**	0.63 (0.48–0.82)*	0.44 (0.31–0.63)**
Elasticised tubular bandage applied (ever)	0.49 (0.35–0.70)**	^	^
Other securement applied (ever)	0.35 (0.26–0.47)**	0.53 (0.39–0.70)**	0.32 (0.22–0.46)**
Number of accesses (mean per day)	1.12 (1.04–1.21)*	1.14 (1.08–1.21)**	1.11 (1.03–1.20)*
Medications administered (at any time during trial):			
- IV cephazolin	^	0.63 (0.44–0.89)*	^
- IV flucloxacillin	1.98 (1.19–3.31)*	2.01 (1.26–3.21)*	^

Occlusion type = occlusion or infiltration at removal, induration or swelling (> 1 cm) at or within ± 24 hours of removal; phlebitis type = phlebitis or pain at removal, pain, tenderness, erythema or palpable cord (> 1 cm) at or within ± 24 hours of removal; dislodgement type = accidental removal or dislodgement at removal; IV = intravenous; [d] proportion of observations; * $p < 0.05$; ** $p < 0.001$; ref. = referent category; ^ not part of the multivariable model as the results did not reach significance.

Phlebitis

Phlebitis was statistically significantly associated with female patients (HR 1.81, 95% CI 1.40–2.35), bruising at the insertion site (HR 2.16, 95% CI 1.26–3.71), insertion in patients' dominant side (HR 1.39, 95% CI 1.09-1.77), IV flucloxacillin (HR 2.01, 95% CI 1.26–3.21), or with frequent PIV access (HR 1.14, 95% CI 1.08–1.21). Older age, (HR 0.99, 95% CI 0.98–0.99; i.e. each year older was associated with 1% less phlebitis) securement with additional non-sterile tape (HR 0.63, 95% CI 0.48–0.82), with any other additional securement (HR 0.53, 95% CI 0.39–0.70), or the administration of IV cephazolin (HR 0.63, 95% CI 0.44–0.89) were associated with lower phlebitis risk.

Dislodgement

Statistically significant predictors associated with an increased risk of PIV dislodgement included paramedic insertion (HR 1.78, 95% CI 1.03–3.06) and frequent PIV access (HR 1.14, 95% CI 1.08–1.21). Decreased risk was associated with additional securement of the PIV including non-sterile tape (HR 0.44, 95% CI 0.31–0.63) or other forms of additional securement (HR 0.32, 95% CI 0.22–0.46).

Discussion

One in three PIVs failed in this study, with phlebitis the most common cause of PIV failure. The 17% phlebitis rate reflected clinician reported phlebitis; or phlebitis observed by research staff using a 1-criteria definition since any sign/symptom can trigger PIV removal, e.g. pain, even if other signs/symptoms are not present. Reported phlebitis rates are lower if definitions require two signs/symptoms (Rickard et al., 2012; Webster et al., 2008). With over 71 different phlebitis assessment scales in use, and none well validated, the best method for diagnosing phlebitis remains unclear and explains variation in reported

rates (Ray-Barruel et al., 2014). Occlusion/infiltration and dislodgement were also highly prevalent forms of PIV failure at 14% and 10% respectively. Occlusion and infiltration were combined since clinical staff use these terms interchangeably, and differential diagnostic tools are not used in practice. Both result in the same outcome (therapy interruption and PIV removal), and this combination of outcomes has been used previously (Rickard et al., 2012). No PIV-associated bloodstream infections occurred, despite the heightened awareness of these infections in the literature (Zingg & Pittet, 2009).

Females had significantly more occlusion/infiltration and phlebitis than males, in keeping with previous studies (Abolfotouh et al., 2014; Dillon et al., 2008; Wallis et al., 2014). This could be due to females' smaller vein calibre although the effect remained after adjustment for PIV gauge (Dillon et al., 2008; Jacobson & Winslow, 2005). The effect of aging on vascular endothelium and structural integrity may explain the observed decrease in phlebitis of 1% with each older year of age (Schelper, 2003). However, gender and age effects could be explained by psychosocial factors (e.g. older people may be less likely to admit pain, or we may question them less sympathetically), but regardless, women and younger patients should be monitored more closely.

We found 22-gauge catheters were more likely to fail from occlusion/infiltration than other sizes. This confirms similar findings from Abolfotouh et.al (Abolfotouh et al., 2014). PIV gauge selection for this study was made at the inserter's discretion and may be confounded by smaller vein size, which was not measured. In addition, risk may be due to smaller gauge alone or also influenced by shorter length of the studied 22-gauge (25mm) than < 20-gauge catheters (30 mm). These results question international guidelines which currently recommend the smallest gauge peripheral catheter possible (Infusion Nurses Society, 2016; Intravenous Nursing New Zealand, 2011) and randomised trials are needed.

Although practice varies between inserters, some preferentially cannulate the non-dominant limb. We are not aware of previous studies on this practice; however, our results support this approach.

Flucloxacillin was associated with a two-fold increase in occlusion/infiltration and phlebitis. Although multiple studies have reported IV medications (Abolfotouh et al., 2014; Catney et al., 2001) and IV antibiotics (do Rego Furtado, 2011b; Infusion Nurses Society, 2016; Wallis et al., 2014) as risk factors for PIV failure, none have identified flucloxacillin as an independent risk factor. IV flucloxacillin is recommended for reconstitution as 1 gram in 15-20 ml sterile water, and injection over 3–4 minutes, although this may not be adhered to in practice. Alternative administration regimes, or improved adherence to current policy may be needed. An exception to the relationship between IV antibiotics and catheter failure was IV cephazolin; associated with 40% relatively less phlebitis. This may be a spurious finding since the administration, Ph and osmolality of cephazolin is similar to other IV antibiotics.

The more PIVs were accessed per day, whether for infusions or medications, the more failure occurred from occlusion/infiltration, phlebitis and dislodgement. This suggests that peripheral veins are easily damaged and/or inflamed by the influx of fluids/medications. Lower injection pressures or timely transfer to oral medications may limit this problem. Flushing regimens may also assist, since practice varies greatly, and questions on whether slow continuous flush infusion or intermittent manual flushing is more vein-protective, and the optimal flush volume, frequency and technique (e.g. pulsatile) remain (Keogh et al., 2015; Schreiber et al., 2015). Manual handling for frequent access may loosen dressings and securement, thus explaining the observed association between frequent access and catheter dislodgement. Finally, the association between use

and failure may indicate many of these patients were not suitable for a PIV, and different approaches (e.g. ultrasound-guided insertion) or a mid-line may have been superior. There is growing emphasis on the need for better pre-insertion assessment and selection of the most appropriate device for the patient and IV treatment required (Chopra et al., 2015).

Suboptimal dressings/securements are not unusual in hospitals (New, Webster, Marsh, & Hewer, 2014). Despite our policy of PIV securement with bordered transparent dressings, we found four dressing types in use. In addition, we found almost 50% of PIVs had an additional (secondary) securement and this was associated with significantly less PIV failure of all three types. This suggests one or more of non-sterile tape, elasticised tubular bandages, or other securement (e.g. bandage or second transparent dressing) can reduce PIV failure, although a randomised trial is lacking (Marsh, Webster, Mihala, et al., 2015). Whether the dressing was failing and required reinforcement or hospital staff lacked confidence in the dressing and placed additional securement preventatively is unclear. Both PIV failure and PIV dressing failure are common, and further research into superior PIV products and practices is urgently needed. Paramedic insertions had higher risk of dislodgement suggesting the increased emphasis on securement should start in the pre-hospital setting.

While multiple/difficult insertion attempts were not associated with PIV failure, insertions were not directly observed, and clinicians may have underreported attempts. In contrast, insertion-related bruising (a surrogate for difficult insertion) was associated with more than double the incidence of phlebitis. The long-term implications of multiple insertion attempts on patients' vasculature are unclear, but we believe first-time PIV insertion is important to patients and of interest to clinicians. A recent systematic review of strategies associated with first attempt PIV insertion success in an emergency department,

found little evidence for effective strategies and recommended further research (Parker, Benzies, Hayden, & Lang, 2017).

The overall PIV failure rate in our study was 32%, lower than the 35%–40% failure observed in our previous randomised controlled trials which had more stringent inclusion and exclusion criteria, e.g. longer predicted duration of therapy (Rickard et al., 2012; Webster et al., 2007). The implications for patients and costs to the organisation of frequent catheter replacement demonstrate urgent need for further research in this area of practice (Helm et al., 2015). A strength of this study is that all PIVs, regardless of expected length of dwell time or reason for insertion were eligible for inclusion, providing more generalizable results. The PIV failure rate of 32% is concerning, since these trigger treatment delays and replacement insertions, with significant increased labour and equipment costs. The mean cost of PIV replacement has been costed at AU$69.30 or US$51.92 (2010$) per episode of IV treatment (Tuffaha et al., 2014). For our hospital, using 200,000 PIVs per year, the current level of PIV failure suggests almost AU$5.5 (US $4.1) million in waste annually at this site alone.

Additional strengths of this study include the extensive information collected prospectively about PIV insertion and maintenance, including information on who inserted the PIV, IV medications administered, and PIV dressings used. Limitations were the population of surgical and medical patients in one tertiary hospital, which may not be generalizable to other settings.

Conclusion

Our study confirms the high rate of catheter failure in acute care hospitals, validates existing evidence related to PIV failure, and identifies new, potentially modifiable risk

factors to improve PIV insertion and management. Implications for future research were also identified.

Acknowledgements

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Chapter 4 Conclusion

Phase 1 has reported the findings of a multivariate analysis of data from a prospective cohort study undertaken in a large tertiary hospital in Queensland, Australia, contributing to the understanding of why PVCs fail. The multivariate analysis identified modifiable risk factors including a 22-gauge catheter, insertion in the dominant arm, and inadequate dressing or securement. This knowledge informed the design of the VAS intervention for Phase 2 of this research, whereby the VAS avoided these factors if possible, based on patient assessment. Strategies to address these factors were incorporated into the intervention protocol to ensure appropriate clinical knowledge and practice of the VAS in relation to PVC insertion. The following chapter presents the results of a pilot RCT comparing insertion of a PVC by a VAS with insertion by a generalist clinician.

Chapter 5 — Results of Phase 2

Introduction

The systematic review and meta-analysis (Chapter 2) reported that over one-third of PVCs fail prior to the completion of IV therapy, and the results of Phase 1 (Chapter 4) identified both modifiable and non-modifiable risk factors associated with PVC failure. This chapter presents the results from the pilot RCT in Phase 2 and contains one co-authored publication, published in the peer-reviewed journal *Trials*.

This pilot RCT is an important contribution to PVC-related research because it is the first RCT to compare different PVC insertion models. The publication of the pilot RCT presents an insertion model that potentially will reduce these alarmingly high failure rates with superior insertion skills and by addressing the modifiable insertion risk factors identified in Phase 1 of this thesis. This pilot RCT meets the feasibility and piloting stage of the Medical Research Council's framework for the evaluation of complex interventions, which underpins this PhD research (Craig et al., 2008). This framework highlights that the best evidence-base comes from carefully planned feasibility and pilot testing, which includes testing interventions and estimating study recruitment, and retention (Craig et al., 2008).

Expert versus generalist peripheral intravenous catheter insertion: A pilot randomised controlled trial [Publication 4]

Statement of contribution to co-authored published paper

The bibliographic details of the co-authored paper, including all authors, are:

Marsh, N., Webster, J., Larsen, E., Genzel, J., Cooke, M., Mihala, G., Cadigan, S., Rickard, C. M. (2018). Expert versus generalist peripheral intravenous catheter insertion: A pilot randomised controlled trial. *Trials*, 19, 564. doi.org/10.1186/s13063-018-2946-3

My contribution to the paper included: Critical review of the literature to inform the design of the study, conceptualising and designing the study, enrolment of participants, data collection, data analyses, data interpretation, writing of the manuscript, revision of the manuscript for important intellectual content, and approval of the final version.

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Expert versus generalist peripheral intravenous catheter insertion: A pilot randomised controlled trial (the RELIABLE Trial)

Abstract

Background

Peripheral intravenous catheters (PVCs) are essential invasive devices, with 2 billion PVCs sold each year. The comparative efficacy of expert versus generalist inserter models for successful PVC insertion and subsequent reliable vascular access is unknown.

Methods

A single centre, parallel group, pilot randomised controlled trial (RCT) of 138 medical/surgical patients was conducted in a large tertiary hospital in Australia, to compare PVC insertion by: I) a vascular access specialist (VAS); or, II) any nursing or medical clinician (generalist model). The primary outcome was the feasibility of a larger RCT as established by predetermined criteria (eligibility, recruitment, retention, protocol adherence). Secondary outcomes were PVC failure: phlebitis, infiltration/extravasation, occlusion, accidental removal or partial dislodgement, local infection or catheter-related bloodstream infection; dwell time; insertion success, insertion attempts; patient satisfaction; and procedural cost effectiveness.

Results

Feasibility outcomes were achieved: 92% of screened patients were eligible; 2 patients refused participation; there was no attrition or missing outcome data. PVC failure was higher with generalists 27/50 (54%) than for VAS 33/69 (48%) (228 vs 217 per 1000 PVC days; Incidence Rate Ratio 1.05, 95% CI 0.61–1.80). There were no local or PVC-related infections in either group. All PVCs (n = 69) were successfully inserted in the VAS group.

In the generalist group, 19 (28%) patients did not have a PVC inserted. There was inadequate data available for the cost-effectiveness analysis, but the mean insertion procedure time was 2 minutes in the VAS group and 11 minutes in the generalist group. Overall satisfaction with the PVC was measured on an 11-point scale (0 = not satisfied and 10 = satisfied) and higher in the VAS group (n = 43; median = 7) compared to the generalist group (n = 20; median = 4.5). The multivariable model identified medical diagnosis and bed bound status were significantly associated with higher PVC failure, and securement with additional non-sterile tape was significantly associated with lower PVC failure.

Conclusion

This pilot trial confirmed the feasibility and need for a large, multi-centre RCT to test these PVC insertion models.

Trial registration: Australian New Zealand Clinical Trials Registry (ACTRN12616001675415). Registered 6 December 2016, https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=371162&isReview=true

Keywords: Intravenous, Vascular Access Devices, randomised controlled trial, Phlebitis

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Background

Peripheral intravenous catheter (PVC) insertion is the most commonly performed invasive procedure in hospitalised patients. Worldwide, it is estimated that 2 billion PVCs are sold each year (Rickard & Ray-Barruel, 2017) and used for the short-term delivery of intravenous (IV) medications and fluids (Chopra et al., 2015). However, multiple insertion attempts are common, and post-insertion failures from complications such as occlusion are as high as 69%, triggering the insertion of subsequent catheters (Rickard et al., 2010; Royer, 2003; Smith, 2006).

PVC inserter models vary. Traditionally intravenous therapy teams (IVTT) were used for the majority of PVC insertions (Bosma & Jewesson, 2002; Carr et al., 2010). These teams were made up of nurses with advanced skills in insertion and maintenance (Bosma & Jewesson, 2002; Carr, Higgins, et al., 2018). More recently, many IVTTs have been discontinued due health care budget cuts, leaving PVC insertion to generalist nursing and medical staff (Hadaway et al., 2013). Data supporting cost savings associated with disbanding IVTTs are yet to be reported in literature (Hadaway et al., 2013).

The generalist model involves nurses and medical staff at the clinical unit level (Carr, Higgins, et al., 2018), which ideally enables continuity of care if they are aware of the patient's diagnosis and clinical history. A belief exists that even though generalists may have minimal PVC insertion skills, this rarely leads to negative outcomes (Robertson, 1995). This belief likely stems from a focus on PVC insertion success alone, but there is an ongoing concern that the varying skill level of generalist inserters leads to multiple needle-sticks, patient discomfort and irreversible damage to the venous system, limiting current and future vascular access options (Hadaway et al., 2013; Hawes, 2007).

Other workforce models for PVC insertion include vascular access specialist (VAS), who are practitioners with advanced assessment as well as technical skills for all vascular access devices. These practitioners may work within an IVTT, (Carr, Higgins, et al., 2018) or within a specific unit or nursing framework (Palefski & Stoddard, 2001) for device insertion, surveillance, research and education.

For the purpose of this trial, a VAS was defined as a clinician with advanced knowledge of vascular access, including: catheter technology (materials and design); insertion assistive devices (such as ultrasound); dressings; processes of catheter access; and management of IV therapy. This advanced level of expertise and knowledge is believed to preserve veins, enhance the patient experience, decrease the incidence of infusion complications and ultimately save on costs associated with clinician time, PVC related products and length of hospital stay (Palefski & Stoddard, 2001).

Effective PVC placement and the prevention of PVC related complications are not only important clinical objectives but also essential for patient satisfaction (Carr et al., 2010). A recent international survey exploring patients' perspectives on PVC insertion found that consumers wanted standards implemented for inserters in order to feel safe and trust their health care professionals (Cooke et al., 2018). The level of skill of the PVC inserter is a risk factor for catheter failure (Carr et al., 2010; Wallis et al., 2014). However, limited high-quality research exists exploring the efficacy of a VAS. Observational studies and audits report VAS inserted PVCs have fewer first-time insertion attempts (Carr et al., 2010; Hunter, 2003), less phlebitis (Scalley et al., 1992; Tomford et al., 1984), less inflammation and catheter related sepsis (Soifer et al., 1998), and higher patient satisfaction (Bai et al., 2013). As some of these studies were conducted before the year 2000 (Miller et al., 1996; Scalley et al., 1992; Tomford et al., 1984), it is unclear what

impact more advanced PVC materials, dressings and other IV supportive equipment have had on PVC failure. Other observational studies have reported on the success of PVC insertion but not the subsequent catheter failure rate (Carr et al., 2010), or the benefit of a VAS within a hospital but not compared to a generalist inserter (Bosma & Jewesson, 2002; Carr et al., 2010). Limitations of previous research include data collected retrospectively (Bosma & Jewesson, 2002), secondary analysis of existing datasets (Wallis et al., 2014) or clinical staff assigning their own level of insertion skill (Palefski & Stoddard, 2001).

There is a paucity of evidence from high-quality randomised control trials (RCTs) assessing inserter skill levels required for successful PVC insertion and prevention of device failure and complications. This makes it impossible for local and international guideline writers to produce comprehensive clinical practice guidelines for the best PVC insertion model of care. Therefore, it is important to examine the efficacy of different models for PVC insertion used in hospitals.

The Study

We compared standard care (generalist model: PVCs inserted in line with hospital policy by an accredited PVC inserter) with insertion by a VAS. The VAS for this pilot trial was a member of an intravenous therapy team for over 20 years, and an educator training clinician to place PVCs in both a hospital and university program. The aim of this trial was to test the feasibility of conducting a suitably powered RCT by assessing both the methodology and rigour of methods planned for the larger study.

Methods

Study design and participants

We undertook a single centre, parallel group, pilot randomised controlled trial in a large government, teaching hospital in Queensland, Australia. Human research ethics committee approval was obtained from the hospital ethics committee (HREC/16/QRBW/386) (Appendix L) and Griffith University (2016/782) (Appendix M). The trial was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12616001675415), and the protocol was published (Marsh, Webster, Cooke, & Rickard, 2017).

We recruited patients admitted to general medical and surgical wards between July and November 2017. A research nurse (ReN) screened for patients over the age of 18, who were expected to have a PVC for greater than 24 hours and able to provide written and informed consent (Appendix N: participant information sheet and participant consent form). We excluded patients who had a current blood stream infection or who had previously been enrolled in the study.

Sample size calculation

The recruitment target for this pilot RCT was 69 participants per group. This trial was not designed to have adequate power to detect statistical significances between groups, but rather to assess the feasibility of the methods to be used in a larger study. The sample size is considered appropriate for the purposes of feasibility assessment (Hertzog, 2008; Julious, 2005).

Randomisation and masking

The ReN obtained written informed consent and then, using a web-based central randomisation service (Griffith University Clinical Trials Randomisation Service), obtained group allocation, which was 1:1 with randomly varied small block sizes. Allocation was concealed prior to randomisation.

Two ReNs collected data for this trial. The first was responsible for recruitment and randomisation. The second ReN was masked to the study intervention and responsible for the daily PVC site inspections and device failure information. The endpoint of catheter related blood stream infection (CRBSI) was assessed by an Infectious Diseases Physician who, along with the study statistician, was masked to group allocation. However, due to the nature of the study, blinding of patients and treating clinicians to the intervention received was not possible.

PVC care and maintenance

All PVCs were inserted by hospital accredited clinicians using local hospital policies. Skin decontamination for all insertions was with a 3M (St Paul) SoluPrep™ Antiseptic Swab (2% chlorhexidine gluconate [CHG] in 70% isopropyl alcohol [IPA]). All PVCs were Becton Dickinson (Utah) Insyte™ Autoguard™ Blood Control (non-winged) catheters with a Smart-Site™ Needle-Free Valve (BD) and a 10cm extension tubing with a bonded 3-way connector (Connecta™, BD). As per hospital policy PVCs were to be re-sited every 72 hours, unless the clinician chose to extend dwell time in response to a clinical indication.

Outcome measure

The primary outcome was to establish the feasibility of an adequately powered RCT using the following criteria: > 90% of patients screened would be eligible; > 90% of eligible patients would agree to enrol; > 90% of eligible patients would receive the allocated intervention, < 5% of enrolled patients would be lost to follow up and < 5% missing data.

Secondary outcomes

The secondary outcomes included i) PVC failure, i.e. catheter removal before the end of therapy due to: phlebitis (two or more of pain, erythema, swelling, palpable cord or purulent discharge), infiltration (the movement of IV fluids into the surrounding tissue), occlusion (the PVC will not flush or leaks when flushed), accidental removal (partial or complete dislodgement of the PVC from the vein), infection (laboratory confirmed local or PVC-related bloodstream infection (O'Grady et al., 2011), PVC positive skin swabs and/or positive PVC tip culture (Maki, Weise, & Sarafin, 1977) (as per usual clinical practice); ii) PVC dwell time (from insertion until removal from either PVC failure, routine replacement or the completion of IV therapy); iii) insertion success; iv) insertion attempts; and, v) cost effectiveness (a sub-set of PVC insertions were observed and timed to establish estimates of staff costs and equipment).

Data collection

Data for this study were collected by a ReN and entered into an electronic data platform supported by REDCap™ (Research Electronic Data Capture 6.10.6 © 2016 Vanderbilt University) (P. A. Harris et al., 2009). Feasibility outcomes (eligibility, recruitment, retention and attrition, protocol adherence and sample size estimates) were collected from enrolment screening logs (Appendix O).

At participant recruitment the ReN, who was also a VAS, collected patient demographic and clinical characteristics such as age, gender and vein quality as per the *peripheral vein assessment tool* (Hallam et al., 2016). From this assessment, taking into consideration the planned IV treatment and patient preference, the ReN/VAS documented their recommendation for VAD choice and site selection. Participants were then randomised. Post PVC insertion, the ReN documented the gauge, profession of inserting clinician, number of insertion attempts, place of insertion and type of securement/dressing applied.

Trial participants were visited daily by the second ReN who was masked to the intervention group. They assessed patient satisfaction with the insertion procedure on an 11-point scale (0 = not satisfied and 10 = satisfied). They inspected the PVC site for: redness, swelling and palpable cord (measured in centimetres from insertion site); patient reported pain/tenderness (0 = no pain and 10 = maximum pain); leakage (yes/no); purulence (none, from site, with ulceration). At PVC removal, the ReN recorded the date and time, and reason for removal. The participant was then asked to rate their overall satisfaction with the catheter on an 11-point scale (0 = not satisfied and 10 = satisfied).

Statistical analysis

Feasibility outcomes were reported descriptively and analysed against pre-determined acceptability criteria. Statistical analysis was performed using Stata 15 (Stata Corp, College Station, Texas, USA). An intention-to-treat analysis framework was used; the unit of analysis was one PVC per patient. Missing data were not imputed. Frequencies and proportions were reported for categorical data. Mean values and standard deviations (*SD*) were reported for normally distributed data; median values and $25^{th}/75^{th}$ percentiles reported otherwise. Covariates were re-categorised to suit the regression analyses as

necessary, and were not analysed in regression models if they had fewer than 20 cases. A graph of the Kaplan-Meier survival function was generated, and log-rank test performed. Univariable and multivariable Cox regression was used to assess the effect of patient and treatment differences as well as for group comparisons. Covariates were deemed eligible for multivariable analysis at $p < 0.20$ and were dropped from the multivariable model during manual backward model building at $p \geq 0.05$. The proportional-hazards assumption was checked. *P* values < 0.05 were considered significant.

Results

Primary Outcome

Between July and November 2017, 150 patients were screened and 92% were eligible for trial recruitment. Willingness for study involvement was high with only two patients declining trial participation. No patients were lost to follow up, none received the incorrect study allocation, and there were no missing outcome events, therefore all predetermined feasibility criteria (Figure 1) were met as per the trial protocol (Marsh et al., 2017).

Patient and PVC Characteristics

At recruitment, patients had similar demographic characteristics between groups (Table 5.1). They were predominantly male, overweight or obese and admitted to a surgical ward. The 22-gauge PVC was more frequently used by VAS (67%) in comparison to generalists (50%). Generalists inserted more PVCs into the hand or wrist (46%) than the forearm (34%), whereas the VAS placed more catheters in the forearm (70%) than the hand or wrist (24%). The generalist inserters were medical staff (82%), anaesthetists (4%) and nurses (14%). The VAS inserter used ultrasound assistance with three insertions.

Ultrasound was not used by the generalist group. Multiple insertion attempts occurred more often in the generalist (35%) than the VAS group (19%).

The initial masked vein assessment identified a higher number of participants with fair or poor veins randomised to the VAS insertion group (54%) compared with 36% in the generalist group. The ideal site and vein for PVC placement assessed by the VAS prior to randomisation was achieved for 81% of PVCs placed by the VAS, compared with 26% of the generalist inserters.

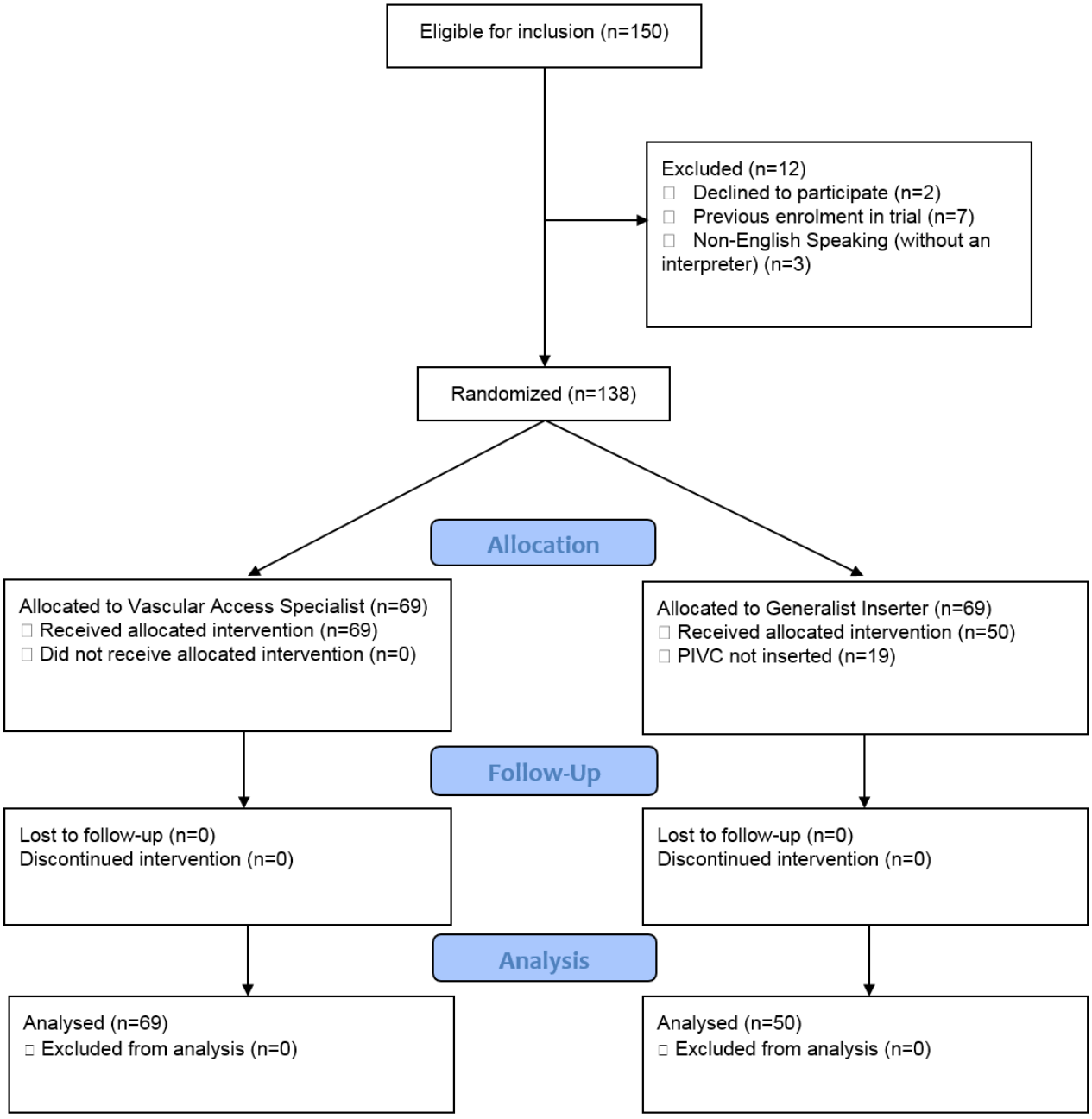


Figure 5.1: Consolidated Standards of Reporting Trials (CONSORT) flow chart

Table 5.1: Descriptive statistics by study groups

	n	Vascular Access Specialist	*n*	Generalist	Total
Group size[a]		69 (50)		69 (50)	138 (100)
Age (years)[b]	69	64.0 (47.0–73.0)	69	62.0 (47.0–71.0)	62.0 (47.0–73.0)
Sex: males	69	43 (62)	69	43 (62)	86 (62)
Weight category: overweight/obese	69	37 (54)	69	33 (48)	70 (51)
Skin integrity: good	69	41 (59)	69	36 (52)	77 (56)
Mobility at insertion:	69		69		
- independent		35 (51)		53 (77)	88 (64)
- required assistance to mobilise		21 (30)		9 (13)	30 (22)
- bedbound		13 (19)		7 (10)	20 (14)
Reason for admission:	69		69		
- medical		19 (28)		19 (28)	38 (28)
- surgical emergent		14 (20)		21 (30)	35 (25)
- surgical elective		36 (52)		29 (42)	65 (47)
Infection at recruitment	69	21 (30)	69	21 (30)	42 (30)
Number of comorbidities:	69		69		
- zero		12 (17)		10 (14)	22 (16)
- one		17 (25)		15 (22)	32 (23)
- two		11 (16)		17 (25)	28 (20)
- three		8 (12)		9 (13)	17 (12)
- four or more		21 (30)		18 (26)	39 (28)
Wound	69	42 (61)	69	40 (58)	82 (59)
Vein assessment:	69		69		
- excellent		18 (26)		25 (36)	43 (31)
- good		14 (20)		19 (28)	33 (24)
- fair or poor		37 (54)		25 (36)	62 (45)

	n	Vascular Access Specialist	*n*	Generalist	Total
Vein first choice for insertion:	69		69		
- cephalic		38 (55)		45 (65)	83 (60)
- medial antebrachial		15 (22)		6 (9)	21 (15)
- accessory cephalic		8 (12)		8 (12)	16 (16)
- other		8 (12)		10 (14)	18 (13)
Location first choice for ins.:	69		69		
- posterior lower forearm		32 (46)		45 (65)	77 (56)
- upper anterior forearm		20 (29)		7 (10)	27 (20)
- wrist		12 (17)		10 (14)	22 (16)
- other		5 (7)		7 (10)	12 (9)
Device sequence:	69		69		
- initial		3 (4)		0 (0)	3 (2)
- subsequent		66 (96)		69 (100)	135 (98)
Reason for insertion:	69		69		
- IV medications only		20 (29)		20 (29)	40 (29)
- IV medications and/or fluids		49 (71)		49 (71)	98 (71)
PVC is the appropriate device	69	58 (84)	69	55 (80)	113 (82)
Ins. difficulty (0 = easy 10 = diff.)[b]	69	2.0 (0.0–5.0)	11	2.0 (1.0–5.0)	2.0 (0.5–5.0)
Pain at ins. (0 = none 10 = max.)[b]	69	2.0 (1.0–3.0)	44	3.0 (1.0–4.0)	2.0 (1.0–3.0)
Device size (gauge):	69		50		
- 22		46 (67)		25 (50)	71 (60)
- 20		21 (30)		19 (38)	40 (34)
- other		2 (3)		2 (4)	4 (3)
- not documented		0 (0)		4 (8)	4 (3)
Reason for choosing size[c]:	69		11		
- clinician preference		41 (59)		10 (90)	51 (64)
- patient has limited vein size		33 (48)		2 (18)	35 (44)

	n	Vascular Access Specialist	*n*	Generalist	Total
- other		13 (19)		1 (9)	14 (18)
IV placement:	69		50		
- cephalic		31 (45)		20 (40)	51 (43)
- medial antebrachial		16 (23)		3 (6)	19 (16)
- accessory cephalic		10 (14)		3 (6)	13 (11)
- metacarpal		3 (4)		10 (20)	13 (11)
- other		9 (13)		14 (28)	23 (19)
IV location:	69		50		
- posterior lower forearm		26 (38)		13 (26)	39 (33)
- upper anterior forearm		22 (32)		4 (8)	26 (22)
- wrist		14 (20		9 (18)	23 (19)
- hand		3 (4)		14 (28)	17 (14)
- other		4 (6)		10 (20)	14 (12)
Side of insertion: right	69	38 (55)	50	23 (46)	61 (51)
Skin hair before ins.:	69		50		
- none present		31 (45)		31 (62)	62 (52)
- clipped		38 (55)		3 (6)	41 (34)
- unclipped		0 (0)		16 (32)	16 (13)

Frequencies and column percentages shown, unless otherwise noted; [a] Row percentage shown; [b] Median and 25^{th}–75^{th} percentiles shown; [c] multiple responses allowed; *n* number of non-missing observations, VAS vascular access specialist, IV intravenous, PVC peripheral intravenous catheter, max maximum

Secondary Outcomes

All PVCs (n = 69) were successfully inserted in the VAS group. In the generalist group, 19 (28%) patients did not have a PVC inserted and, in response, were changed to oral medication (n = 8); had a pre-existing PVC left in place (n = 6); had a peripherally inserted peripheral catheter inserted (n = 2); or remained waiting for a PVC insertion for at least 24 hours (n = 3).

PVC insertion timings and procedural resource usage were collected for 16 VAS and 4 generalist insertions. The mean PVC insertion procedure time was 2 minutes in the VAS group and 11 minutes in the generalist group. A full cost-effectiveness analysis was not able to be undertaken due to limited generalist group data collected as a result of (1) long delays from PVC request to insertion of the catheter; (2) many patients in the generalist group did not ultimately have a PVC inserted.

PVC post-insertion failure was 54% in the generalist group and 48% in the VAS group (Table 5.2). This equated to 217 and 228 failures per 1000 PIV days respectively (Incidence Rate Ratio 1.05, 95% CI 0.61–1.80, Table 5.2), which were not different on Kaplan Meier survival analysis (Figure 5.2; log-rank p = 0.92). The most common causes of failure were due to phlebitis and infiltration. Even though this study was not powered to show effect, phlebitis was 5% higher in VAS inserted catheters than for generalist insertions. Occlusion and partial or complete dislodgement were higher (absolute 8% and 5% respectively) in generalist inserted PVCs. There were no local or PVC-related bloodstream infections in either group.

Median satisfaction with PVC insertion was higher in the VAS group (9 versus 7) than the generalist group (Table 5.2). Overall median satisfaction with the PVC was also higher in the VAS group (7 vs 4.5, Table 5.2) than the generalist group.

Table 5.2: Study outcomes (*n* = 119)

	Vascular Access Specialist *n* = 69	Generalist *n* = 50	*p*-value
PVC successfully inserted	69 (100)	50 (70)	
Multiple insertion attempts [a]	13 (19)	16 (35)	
Number of insertion attempts [a,b]	1.22	1.74	
Reason for removal:			
- treatment complete without complications	29 (42)	19 (38)	
- treatment incomplete with complications	26 (38)	22 (44)	
- treatment completed with complications	7 (10)	5 (10)	
- routine re-site or theatre replacement	5 (7)	3 (6)	
- insertion of a CVAD	2 (3)	1 (2)	
Device failed	33 (48)	27 (54)	0.506 [c]
Positive blood count	0 (0)	2 (4)	
Complication [d]			
- phlebitis	19 (28)	10 20)	
- infiltration	13 (19)	9 (18)	
- occlusion	7 (10)	9 (18)	
- accidental removal	6 (9)	7 (14)	
- unknown	0 (0)	1 (2)	
Device-days	152	118	
Incidence Rate of failure [e,f]	217 (154–305)	228 (156–332)	
Incidence Rate Ratio	referent	1.05 (0.61–1.80)	0.924 [g]
Patient satisfaction [h,i]			
- insertion	9 (8–10)	7 (3.5–9)	
- overall	7 (6–9)	4.5 (1.5–6)	

Frequencies and column percentages shown, unless otherwise noted; [a] successfully inserted devices only; [b] average shown; [c] Chi-squared test; [d] multiple responses allowed; [e] Per 1,000 device-days log-rank test; [f] includes 95% confidence interval; [g] Log-rank test; [h] Median (25th/75th percentiles) shown; [i] 0 = not satisfied and 10 = satisfied; VAS vascular access specialist, *n* number of non-missing observations, PVC peripheral intravenous catheter, CVAD central venous access device

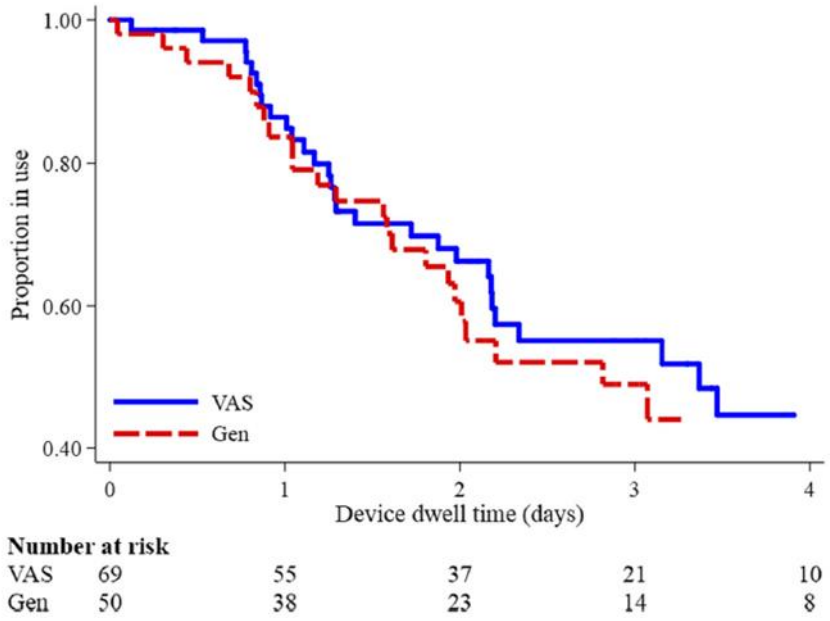


Figure 5.2: Kaplan-Meier curve of device failure

Multivariable modelling for PVC post-insertion failure

Although this study was not powered to show statistical significance between groups, in the multivariable model (Table 5.3), medical diagnosis ($p < 0.001$), or bed-bound status at insertion ($p < 0.05$) were associated with approximately two-fold higher incidence of PVC failure, and non-sterile tape securement remained associated with decreased PVC failure (HR 0.36, 95% CI 0.18–0.70, $p < 0.001$).

Table 5.3: Cox regression

	Univariable	Multivariable *n* = 119
Study group: red (ref. blue)	1.03 (0.61–1.73)	1.18 (0.70–2.00)
Sex: male (ref. female)	0.61 (0.35–1.05)*	#
Age (increment of 1 year)	1.00 (0.98–1.01)	^
Body Mass Index (increment of 1)	0.99 (0.94–1.03)	^
Comorbidities (nil / 1 / 2 / 3 / 4 or more)	0.96 (0.81–1.16)	^
Insertion on dominant side (ref. no)	1.03 (0.62–1.72)	^
Bed-bound at insertion (ref. no)	1.74 (0.93–3.24)*	2.17 (1.14–4.11)**
Medical reason for admission (ref. surgical)	2.08 (1.22–3.55)***	2.08 (1.21–3.57)***
Infection at recruitment (ref. no)	0.90 (0.52–1.55)	^
Vein assessment (ref. excellent):		^
- good	0.70 (0.32–1.52)	^
- fair/poor	0.34 (0.67–2.10)	^
Location selected was the location PVC was placed in (ref. no)	0.79 (0.47–1.34)	^
Difficulty with previous insertion (ref. no)	0.99 (0.56–1.74)	^
PIVC is the appropriate device (ref. no)	0.72 (0.39–1.32)	^
Device gauge: other (ref. 22)	0.64 (0.36–1.11)*	#
Location (ref. Posterior Lower Forearm):		^
- upper ant. forearm	1.49 (0.75–2.97)	
- wrist	1.31 (0.61–2.79)	
- hand	1.89 (0.87–4.14)*	
- other	0.73 (0.27–1.98)	
Multiple insertion attempts (ref. no)	0.95 (0.53–1.73)	^
Dressing: non-sterile tape [a] (ref. never)	0.38 (0.20–0.74)***	0.36 (0.18–0.70)***
Dressing: Tubi-grip [a] (ref. never)	0.81 (0.46–1.42)	^
Dressing dirty/wet/damaged [a] (ref. never)	0.89 (0.42–1.85)	^
Fluids [a] (ref. never)	1.00 (0.59–1.68)	^
Antibiotics [a, b] (ref. never)	1.35 (0.72–2.51)	^
Anaesthesia [a] (ref. never)	0.78 (0.42–1.46)	^
Cefazolin [a] (ref. never)	0.87 (0.47–1.62)	^
Pain relief [a] (ref. never)	0.97 (0.56–1.66)	^
Other IV medication [a, c] (ref. never)	0.71 (0.38–1.31)	^
Anti-emetic and anti-reflux [a] (ref. never)	0.93 (0.50–1.73)	^
Accesses (total, nil, 1 to 3, 4 to 6, 7 or more)	0.85 (0.69–1.05)*	#

Hazard Ratios and 95% confidence intervals shown; * p-value < 0.20; ** p-value < 0.05; *** p-value < 0.01; # dropped from multivariable model at $p \geq 0.05$; ^ ineligible for multivariable analysis at overall $p \geq 0.20$; [a] At any time during study; [b] Includes ampicillin, benzylpenicillin, gentamycin, vancomycin, ceftazidime, azithromycin, meropenem, cefepime, or Augmentin; [c] Includes frusemide, contrast, insulin, magnesium, or thiamine; VAS vascular access specialist, PVC peripheral intravenous catheter

Discussion

Improving the knowledge and skill of PVC inserters is likely to reduce the current situation where patients commonly experience multiple PVC insertion attempts and unacceptably high post-insertion catheter failure rates. In this pilot RCT, we compared two inserter workforce models for clinical, patient and feasibility outcomes. All pre-determined feasibility outcomes were met and thus we have established that tested methods are appropriate for an adequately powered, multi-centre randomised controlled trial. Overall PVC failure was higher in the generalist compared with VAS group and although pilot trials are not powered for statistical significance, this result is clinically meaningful and needs testing in a larger RCT. To compare 54% vs 48% post-insertion failure with 80% power ($p = 0.05$) would require 1084 patients per group (powerandsamplesize.com).

Under generalist models, establishment of vascular access is frequently left to junior medical and nursing staff who, with minimal knowledge about complications associated with IV medications, may choose a PVC as a default VAD (Hallam et al., 2016; T. Jackson, Hallam, Corner, & Hill, 2013). In our trial, 18% of PVCs were considered an inappropriate VAD by our blinded VAS assessor as they had IV therapy prescribed for greater than 5 days, and/or poor vascular access. Generalist models also lack standardization of knowledge and technique for clinicians inserting PVCs, meaning expertise and maintenance of competence cannot be guaranteed across and within healthcare settings (Vizcarra et al., 2014). Such deficiencies likely contributed to the lower first-time PVC insertion success in our generalist group, with multiple insertion attempts occurring almost twice as often with the generalist inserter (35%) than the VAS inserter (19%). An additional three patients allocated to the generalist group were still awaiting PVC placement after 24 hours and numerous unpleasant insertion attempts. This is not

only a poor patient experience but also has cost implications for clinician time, delayed treatment and potentially extended hospital stay.

More than a quarter of patients allocated to the generalist group in our trial did not receive a PVC, compared to 100% placement by the VAS group. The purpose of placing a PVC is to start or continue treatment and this was an unexpected result. It may indicate a lack of PVC insertion skill in the generalist group or lack of comprehensive assessment regarding the requirement for a PVC. Either way we consider this may be the more appropriate primary endpoint for a follow-on study. The most common reported reason in this study for non-placement was the change of antibiotic therapy from intravenous to oral. The decision to change antibiotic route should be based on three key factors: the antimicrobial agent, the patient, and the condition being treated, and careful consideration is necessary to provide the best care (Béïque & Zvonar, 2015). Within this trial it was unclear if these factors were the determining considerations, or if this change was due to the unavailability of staff to place the catheter or unsuccessful insertion attempts rather than the patient's clinical need.

Our multivariable model identified that patients admitted with a medical diagnosis and those who were non-ambulant (bed bound) were at higher risk of PVC failure. These patients may have a higher risk as they are likely to; have more co-morbidities; a history of greater VAD use than ambulant patients; and/or those with an acute surgical diagnosis. These patients should be the priority for efforts to improve PVC outcomes. We also found that patients whose PVC was secured with additional non-sterile tape had a significant association with decreased PVC failure. These results reflect a similar finding by a large cohort study at the same hospital that reported significantly lower occlusion/infiltration, phlebitis and dislodgement rates when non-sterile tape was used as an additional PVC

securement (Marsh, Webster, et al., 2018). This suggests that despite advances in dressings and securement devices PVC failure rates have remained high and even good quality insertion requires effective securement to maintain function.

Limitations

The main limitation of this study is that it is a pilot RCT and although results are clinically interesting, the study is not designed to provide definitive conclusions about the best model for PVC insertion. The use of the same VAS for the pre-randomisation assessment and to insert the PVCs in the VAS group was also a limitation of this study. However, the VAS was blinded to allocation at the time the assessment was conducted, and information was directly entered into an electronic platform at the bedside.

Conclusion

This study suggests less insertion failure and less post-insertion failure occur when catheters are placed by a VAS. This pilot trial has confirmed the feasibility and clinical need for a large, multi-centre RCT to test these PVC insertion models to provide evidence for health service delivery improvements.

Chapter 5 summary

This chapter contained a published manuscript reporting the pilot RCT undertaken in Phase 2 of this research. Feasibility and clinical endpoints were reported consistent with the published protocol. The study results indicated that PVCs inserted by a VAS had better first-time insertion success, less device failure, and greater patient satisfaction associated with their insertions. As per the underpinning conceptual framework for this research, this pilot RCT was an important step to clarify any shortcomings of a trial design and processes before conducting a definitive study (Craig et al., 2008).

Chapter 6 — Conclusion

Introduction

The final chapter of this thesis presents an overview of the research study methods and findings and discusses the contribution this body of work has made to the PVC knowledge base related to catheter insertion and failure. Finally, the conclusion for this PhD research will offer recommendations for clinical practice, education, healthcare policy, and future research.

Overview of Structure and Methods

The overall aim of this PhD was to identify effective methods to prevent PVC failure. This was achieved, firstly, by determining risk factors associated with PVC failure and complications and, secondly, by conducting a feasibility RCT of VAS versus a generalist PVC insertion model to prevent failure. Three research questions were posed and addressed during the two phases of this PhD research.

The research was underpinned by the Medical Research Council (MRC) Framework for the Evaluation of Complex Interventions (Craig et al., 2008). This Framework articulates the need to not only identify existing evidence before undertaking a substantial evaluation but to model complex interventions prior to a full-scale evaluation (Craig et al., 2008, 2013). Using this Framework as a guide, previous knowledge about PVC failure and VAS insertion models were synthesized by conducting a systematic review of PVC failure formatted for publication in *BMJ Open and* critiquing current evidence into prevention strategies. Subsequently, new knowledge was generated via analysis of data from an existing cohort study, and published in *Journal of Hospital Medicine*. Establishing this evidence base provided the underlying rationale to inform the

pilot testing of a PVC insertion intervention model, the results of which were published in *Trials*.

The systematic review and meta-analysis were conducted to understand the global incidence of PVC failure and complications within the adult population. Cohort studies and randomised controlled trials (control group data only) were included in this review. Using well established methods for the meta-analysis of observational studies, dichotomous outcomes for complications and failure were pooled and reported using the MOOSE guidelines (Meta-analysis Of Observation Studies in Epidemiology) (Stroup et al., 2000).

Next, a critique of literature was conducted to explore the potential benefits of a VAS approach to inserting PVCs, compared to standard generalist inserter models, to prevent the incidence of PVC failure and complications. All studies that involved the use of a VAS either as part of a team, or within an existing nursing framework, were eligible for inclusion. This systematic literature review and literature critique were conducted to describe the current evidence available to understand the effect of a VAS insertion model. The results were summarised, identifying a current knowledge gap in this area and highlighting the need for quality randomised controlled trials to test the benefit of VASs inserting PVCs. Together, the systematic review on PVC failure and the critique of evidence for insertion models justified and contextualised the need for the two PhD research phases.

In Phase 1, in order to identify risk factors associated with PVC failure as a result of phlebitis, infiltration and/or occlusion, or PVC dislodgement, a multivariate analysis was conducted of previously unanalysed data from a cohort study of 1000 patients admitted to the medical and surgical wards of the Royal Brisbane and Women's Hospital (Marsh, Webster, et al., 2018). This study addressed Research Questions 1 and 2: 'What

are the risk factors associated with PVC failure in the adult in-patient population?' and 'What are the potentially modifiable risk factors associated with PVC failure in the adult in-patient population to inform insertion knowledge and practices?' PVC insertion and maintenance risk factors amenable to modification were identified through building a multivariable model by: considering variables significant at $p < 0.20$ on univariable analyses and clinical judgement, for consideration in multivariable regression. Correlations were considered significant and covariate interactions were explored. The final models were derived using the manual stepwise backward method (Vittinghoff et al., 2005) with covariates dropped at $p \geq 0.05$.

Finally, in Phase 2 a pilot RCT was undertaken to assess the feasibility of conducting a randomised controlled, efficacy trial to test the effectiveness of a VAS insertion model to prevent PVC failure. The primary outcome was feasibility of an adequately powered RCT, assessed by *a priori* established criteria including participant eligibility, recruitment, retention and attrition, protocol adherence, missing data, patient and clinical staff satisfaction, and acceptability (Hertzog, 2008; Lancaster, Dodd, & Williamson, 2004). The sample size for this pilot RCT was consistent with recommendations for feasibility trials to assess the likelihood of success for a later definitive RCT (Hertzog, 2008; Thabane et al., 2010). This pilot trial answered Research Question 3: Is it feasible to conduct a full-scale RCT to compare the effectiveness of PVC insertion by a vascular access expert (VAS model) versus insertion by usual practice (generalist model) on the incidence of PVC failure within the adult population?

To ensure the reliability of the pilot RCT, the protocol was registered and published prior to trial commencement (Marsh et al., 2017). Further, inter-rater reliability was checked for 10% of PVC site daily inspections and outcome assessments, between the

daily assessor and an independent VAS. Ten percent of the data entry was also cross-checked, with missing data and implausible values queried and corrected if possible. Internal validity was maintained by: observance to the study protocol with monitoring of adherence by the researcher; the use of accepted published definitions in literature for measuring PVC outcomes; and ensuring that daily PVC site inspections and assessment of outcome measures were performed in a standardised manner by clinically appropriate staff. External validity was promoted by: clearly defining the characteristics of the target population; as well as the inclusion and exclusion criteria (Rothwell, 2006); and identification of the type of clinician (medical, nursing) inserting the PVC. A pragmatic approach of usual clinical PVC care ensured results were clinically relevant.

The pilot RCT conformed to best practice standards by ensuring randomisation concealment and computer generated random allocations. Due to the nature of the study, blinding of patients and treating clinicians to the intervention received was not possible. However, there is no reason to believe that clinicians' and patients' responses were influenced to favour a particular intervention. Trial findings were reported using the CONSORT guidelines (Schulz, Altman, & Moher, 2010).

The research presented in this thesis has consistently followed the MRC Framework for the Evaluation of Complex Interventions (Craig et al., 2008). This Framework provided a structured and systematic approach to the development and conduct of the research. To minimise potential bias and ensure the reliability and validity of the study results, well established and high-quality study methods were used. This research has provided several significant contributions to theory for PVC insertion and prevention of complications and failure, and has confirmed the feasibility of conducting a large, multi-centre RCT to determine the benefit of VAS insertion of PVCs.

Findings

Incidence of PVC failure and complications

The completed systematic review and meta-analysis demonstrated high PVC failure and complication rates within the adult population internationally. Over a third (36.5%) of PVCs were reported to fail prior to the completion of treatment (95% CI [32.5%–40.6%]), at an incident rate of 116.8 failures per 1000 catheter days (95% CI [74.2%–159.5%]). The work completed for this thesis encompassed PVC outcomes of 74,798 PVCs from 70 observational studies and 31 randomised controlled trials that met the study inclusion criteria.

The most frequently occurring individual complication was phlebitis, at 16·8% (13.9%–20.0%) of PVCs (82 studies), with an incident rate of 37.7 (27.4–48.0) per 1000 catheter days (14 studies). In countries with developing economies, pooled phlebitis (26.2%, [18.4%–34.8%]; 27 studies) was significantly higher ($p = 0{\cdot}001$) than in developed economies (12.9% [10.1%–16.0%]; 52 studies).

Rates of other complications for PVCs were unsatisfactorily high, with infiltration occurring in 13.6% (11.0%–16.4%); occlusion 7.8% (5.6%–10.4%); leakage 7.3% (4.7%–10.3%); pain 6.4% (4.8%–8.2%); and dislodgement 5.9% (4.8%–7.2%) of PVCs. Infection outcomes were the least frequently reported and least common complication when reported. CRBSI was only measured in 14 included studies; this is concerning as it is the most serious and potentially fatal PVC complication. The pooled proportion of confirmed CRBSI was < 0.1% PVCs (< 0.1%–< 0.1%) (14 studies) or < 0.1 per 1000 days (< 0.0–0.3) (6 studies). Pooled suspected CRBSI (8 studies) was < 0.1% of PVCs [< 0.1%–< 0.1%), with local infection in 12 studies being a pooled 0.6% (< 0.1%–1.6%).

These high rates of PVC failure and complication clearly have substantial negative impacts upon patients, staff, and healthcare budgets. PVC failure and the need for catheter replacement results in venous depletion, interrupted important IV treatments, and increased chance of prolonged hospital admission (Helm et al., 2015; Monreal et al., 1999). By synthesizing global studies, the systematic review demonstrated the burden PVC failure and complications place not only on patients but the international healthcare system.

This systematic review is the first of its kind to provide a comprehensive understanding of how often and in what way PVCs are failing. Given that over 2 billion PVCs are used globally each year (Rickard & Ray-Barruel, 2017), and many PVC complications are potentially avoidable with improved PVC care (Carr, Higgins, et al., 2018; Palefski & Stoddard, 2001; Rickard, Webster, & Playford, 2013; Wallis et al., 2014), this systematic review identified a need for evidence-based improvement for PVC care.

Risk factors for PVC failure

For Phase 1 of the research, in keeping with the first objective of this thesis regarding the determination of modifiable risk factors associated with PVC failure and complications, analysis was undertaken of a large prospective cohort study dataset. This identified that one in three (n = 512/1578, 32%) PVCs failed prior to the completion of IV treatment, a number consistent with the systematic review discussed above. Phlebitis was the most frequently occurring cause of failure (n = 267, 17%) followed by occlusion and/or infiltration (combined n = 228, 14%) and catheter dislodgement (n =154, 10%). Infection was confirmed as rare, with no cases occurring.

Suboptimal dressings or securements in hospitals are not unusual (Alexandrou et al., 2018; New et al., 2014) and over 50% of PVCs in this study had some form of

secondary securement, such as non-sterile tape, or a tubal bandage. These additional securements were associated with significantly less failure from phlebitis: nonsterile tape (HR 0.63, 95% CI 0.48–0.82), any other type of securement (HR 0.53, 95% CI 0.39–0.70); occlusion and infiltration: nonsterile tape (HR 0.46, 95% CI 0.33–0.63), elasticised tubular bandage (HR 0.49, 95% CI 0.35–0.70), any other type of securement (HR 0.35, 95% CI 0.26–0.47); dislodgement: nonsterile tape (HR 0.44, 95% CI 0.31–0.63), and any other securement (HR 0.32, 95% CI 0.22–0.46). Paramedic-inserted PVCs were associated with significantly more failure from dislodgement (HR 1.78, 95% CI 1.03–3.06), which may also be associated with poor PVC securement since these may become loosened as patients are transferred to and within the hospital.

Although other studies have found IV medications are risk factors for PVC failure (Lanbeck et al., 2002; Salgueiro-Oliveira et al., 2012; Wallis et al., 2014), this study was the first to identify IV flucloxacillin to have a significant association with phlebitis (HR 0.44, 95% CI 0.31–0.63) and occlusion and/or infiltration (HR 0.44, 95% CI 0.31–0.63). It has identified a need to ascertain whether new administration regimens or improved adherence to administration policies for dilution and speed of administration may be required.

Insertion site bruising—a surrogate for difficult PVC insertion—was significantly associated with more than double the incidence of phlebitis (HR 1.98, 95% CI 1.26–3.71). This highlighted the importance of optimal PVC insertion, including first-time insertion success, and further supported the need to test an intervention of VAS insertion, since experts could be anticipated to take fewer attempts to insert, and to cause less tissue trauma.

Inserting a PVC into a patient's dominant side significantly increased the risk of PVC failure from phlebitis (HR 1.39, 95% CI 1.09–1.77), and placing a 22-gauge catheter compared to larger other gauge sizes significantly increased the patient's risk of PVC failure from occlusion and/or infiltration (HR 1.43, 95% CI 1.02–2.00). PVC insertion location and gauge are selection are at the inserting clinician's discretion. These results are important as both these risk factors are modifiable and amenable to practice change, particularly in the hands of a VAS, who may be expected to have superior assessment skills, and to identify more potentially suitable veins to cannulate with a 20-gauge or larger PVC.

Another modifiable risk factor for PVC failure was the frequency of PVC access. This study found that the more often the catheter was accessed for infusions or medications, the more likely it was to fail from phlebitis (HR 1.14, 95% CI 1.08–1.21), occlusion and/or infiltration (HR 1.12, 95% CI 1.04–1.21) and dislodgement (HR 1.11, 95% CI 1.03–1.20). This may be due to damage to the veins from the influx of fluids and intravenous medications, or high injection pressures. This identified a need for the inserting clinician to consider if a different approach to PVC insertion may be appropriate, such as the use of ultrasound to place the catheter, which would allow visualisation of deeper veins and avoidance of vessel valves and patient joints. In addition, the inserter should consider alternative vascular access devices such as midline catheters.

This multivariate regression identified a number of strategies that clinicians could adopt when inserting as well as caring for PVCs that would reduce PVC failure rates, and improve patient outcomes and healthcare budgets. By identifying these modifiable risk factors, it helps clinicians, policy makers, and researchers to prioritise education, resources, and research on areas that require improvement.

Models for PVC insertion

The high international PVC failure identified a need to understand whether the skill of the PVC inserter reduced the incidence of PVC failure and complications. A VAS is described as a clinician with advanced knowledge and skills to place and manage vascular access devices (Carr, Higgins, et al., 2018). In order to understand current evidence about the potential benefits of a VAS in the reduction of PVC failure and complications, a critique of literature was conducted.

A systematic search identified 10 studies for inclusion in this literature critique, including a quasi-randomised controlled trial (Soifer et al., 1998), and nine descriptive, observational studies (Bosma & Jewesson, 2002; Carr et al., 2010; da Silva et al., 2010; Hunter, 2003; Meier et al., 1998; Miller et al., 1996; Palefski & Stoddard, 2001; Scalley et al., 1992; Tomford et al., 1984). Although the methodologies and outcomes varied between the included studies, all found a benefit with PVC insertions performed by a VAS. These included lower PVC failure (VAS, *n* = 126/639, 19.7%; generalist nurse, *n* = 49/137, 35.8%) (Palefski & Stoddard, 2001); complications (VAS, *n* = 58/737, 7.9%; junior medical staff, *n* = 30/138, 21.7%) (Soifer et al., 1998); number of PVCs per patient (before VAS, 2.12 catheters per patient; after VAS team, 1.57 catheter per patient) (da Silva et al., 2010); and a relative decrease in primary bloodstream infections of 35% (1.1 per 1000 patient-days reduced to 0.7 per 1000 patient-days) with the introduction of a VAS-inserted PVC model of care (Meier et al., 1998).

However, there were limitations to previous studies. Half were conducted before the year 2000 (Meier et al., 1998; Miller et al., 1996; Scalley et al., 1992; Soifer et al., 1998; Tomford et al., 1984). This made it difficult to determine if factors such as newer catheter materials and designs, products such as dressings, or insertion assistance devices

including ultrasound would have had an impact PVC failure rates. Other limitations included a risk of reporting bias, as data was either collected by members of the VAS team (Carr et al., 2010; Scalley et al., 1992) or recorded by the clinician who placed the catheter (Palefski & Stoddard, 2001). Lastly, no study was randomised, thus allocation bias or confounding by time may have been present.

This critique of evidence found that VAS inserting PVCs was a promising intervention to reduce PVC failure, but there was a knowledge gap in high-quality evidence to support the use of a VAS. It identified a need for high-quality RCTs to establish whether there is a benefit to PVC placement by a VAS.

VAS vs generalist model

The second objective of this thesis was to evaluate the feasibility of large RCT of VAS versus a generalist PVC inserter model to prevent failure. The pilot RCT of 138 participants assessed *a priori* defined feasibility criteria, including: patient eligibility, consent, protocol adherence, and retention.

Eligibility for trial participation was high, with 150 patients screened and 138 (92%) recruited. Two patients declined trial participation, no patients were lost to follow-up, no patients received the incorrect study allocation, and there were no missing outcome events. All predetermined feasibility criteria were met in line with the trial protocol, suggesting that the tested methods are appropriate for a large, multi-centre RCT.

Patient satisfaction on a 11-point scale (0–10) was higher in the VAS group for PVC insertion (VAS, 9 [8–10]); generalist, 7 [3.5–9]) and overall satisfaction with their catheter (VAS, 7 [6–9]); generalist, 4.5 [1.5–6]). While the results of this trial were unable to be compared with other research (as these outcomes have not been assessed previously)

a patient satisfaction score such as this is important to enable comparison of provider performance, which in turn stimulates improvements in performance (Black, 2013).

The proportion of failure (54%) in the VAS group compared to the generalist inserter (48%) provided point estimates for future interventional studies. For a 6% absolute reduction (54% vs 48%) in PVC failure to be statistically tested in a future efficacy study (p = 0.05; 80% power), 1084 participants would be needed in each study group (powerandsamplesize.com). Although this pilot feasibility RCT was not designed to test statistical differences, the results are clinically meaningful as PVC complications associated with failure such as phlebitis (VAS 19/69, 28%; generalist 10/50, 20%), occlusion (VAS, n = 7/69, 10%; generalist, n = 9/50, 18%), and accidental removal or dislodgement (VAS, n = 6/69, 9%; generalist, n = 7/50, 14%) were generally lower in the VAS group.

At participant recruitment and prior to randomisation, the ReN (who was also a VAS) assessed all study participants' vasculature and prescribed IV treatment. They reported that for 18% (25/138) of patients, a PVC was an inappropriate vascular access device choice, and another device such as a midline or PICC was likely preferable. However, as the establishment of vascular access is often left to junior medical staff and nursing staff who have limited knowledge about the effect of IV medications on vessel health, or the assessment of patients' vasculature, they are more likely to select a PVC as the default vascular access device (Hallam et al., 2016; T. Jackson et al., 2013). This lack of expertise in the generalist group likely contributed to almost double the number of insertion attempts to place a PVC (n = 16, 35%) compared to the VAS group (n = 13, 19%). An unexpected outcome of this study was that a quarter of participants randomised to the generalist insertion group did not receive a PVC, compared to 100% successfully

placed catheters in the VAS group. As a result, an 'available case analysis' was conducted for PVCs successfully placed. The high number of PVCs not placed likely indicates a lack of PVC insertion skill or ability to conduct a comprehensive assessment regarding the appropriateness of the placement of a PVC. The most common reported reason for non-placement was the conversion of patients from IV to oral antibiotics. However, it was unclear if the decision for this change in treatment was due to the unavailability of skilled staff to place the catheter or unsuccessful insertion attempts, rather than patient need. As a pilot trial this raises an important challenge for a larger RCT and successful placement of a PVC may be a more appropriate primary outcome.

The use of generalist insertion models can result in a lack of standardised knowledge and techniques for clinicians placing PVCs, meaning that competence cannot be certain or consistent across and within health care settings (Vizcarra et al., 2014). The adoption of VAS into an existing nursing framework or as part of a VAS team are likely to be worthwhile if they can significantly reduce the number of failed insertion attempts, and post-insertion PVC failure. The pilot RCT has promising results for VAS models and has identified the need to conduct a large RCT to improve not only patient outcomes but health service delivery.

Contribution to Knowledge

By using rigorous and reliable methods, this PhD has identified current local and international PVC failure and complication rates in the adult population. The systematic review and meta-analysis included in this thesis will allow local and international healthcare settings to benchmark their PVC outcomes against other healthcare facilities. The review has shown that PVC failure is a significant worldwide problem which until now appeared unacknowledged and unaddressed. These results should provoke an urgent

response and have highlighted many areas for potential improvement. In conjunction with clearly identified PVC risk factors associated with failure ascertained from the comprehensive cohort study analysis included in this PhD research, clinicians, key stakeholders, and researchers can target local areas for improvement, plan education and practice change, as well as identify priority areas to focus future research.

Within hospital and healthcare settings, there is uncertainty about the best model of care for PVC insertion. Using a systematic approach, this PhD research has critiqued current evidence about the benefits of PVC insertion by a VAS to contextualise what is known in this area. The literature review confirmed a knowledge gap about optimal PVC insertion models and led to the world's first pilot RCT of PVC insertion models. The pilot RCT has established the feasibility of a larger RCT to test the benefit of a VAS insertion model, against standard, generalist insertion.

Theoretical Implications

The systematic review in this PhD research found that over one-third (*n* = 10,670; 36.5%) of PVCs fail prior to the completion of treatment. However, researchers over the last decade have focused their attention on CVAD-related research, producing more high-quality evidence to support CVAD products or practices compared with the more frequently used PVC. This is evident in the results of two recent scoping reviews conducted over similar time periods. The CVAD scoping review of RCTs was able to include 178 trials (January 2006 and December 2015) (Takashima, Ray-Barruel, Ullman, Keogh, & Rickard, 2017), compared to the PVC scoping review which included 94 PVC-related RCTs (January 2005 and June 2015) (Takashima, Ray-Barruel, Keogh, & Rickard, 2015). This has likely resulted in sub-optimal evidence to inform and improve PVC insertion and maintenance practices overall, and thereby clinical outcomes.

Additionally, the systematic review in this thesis found that phlebitis was the most frequently measured PVC outcome, therefore inferring that authors believe phlebitis is the main cause of PVC failure. Over 71 different phlebitis scales have been developed, with dissimilar criteria and minimal validation testing (Ray-Barruel et al., 2014), which likely explains the wide range of phlebitis rates (< 1% to 100%; mean 16.8%) in the systematic review. It has also been suggested that variable phlebitis rates could reflect overlapping complications, such as occlusion, infiltration, and early signs of infection (Helm et al., 2015). As this systematic review showed such variation in phlebitis rates, perhaps it is not the most useful term and these results may change thinking in this area and encourage future researchers to focus more attention on individual signs and symptoms of complications, such as pain and erythema.

While many clinical practice guidelines of PVC management (Department of Health, 2015; O'Grady et al., 2011) have a single focus on the prevention of CRBSI indicating they believe this is an important and common issue, the systematic review in this thesis demonstrated clinical trial investigators rarely report CRBSI (n = 14; 14% of studies; 16,190 PVCs). This perhaps indicates they do not see this as a high priority or high frequency area of concern. The meta-analysis results further demonstrated an extremely low overall CRBSI rate associated with PVCs (< 0.1 per 1000 catheter days). While current practice appears to be maintaining a low CRBSI rate, ongoing prevention is clearly important. However, clinical practice guidelines urgently need expansion to focus on all complications, not just on infection prevention, in an approach similar to the Infusion Therapy Standards of Practice (Infusion Nurses Society, 2016).

The theoretic premise that expert VAS have superior skills at PVC insertion, compared to generalist inserters, is sound. The evidence presented in this PhD research

supports the use of VAS insertion models in hospitals since the results suggest that this not only improves PVC insertion success and decreases PVC failure rates, but also prevents generalist inserters attempting some PVC insertions altogether. Reducing insertion attempts, particularly by unconfident inserters in difficult patients, would avoid irreversible damage to the venous system, which limits current and future vascular access options (Hadaway et al., 2013; Hawes, 2007). Although the economic benefit of different insertion models is yet to be established, consideration should be given to the fast and reliable access provided by VAS, compared to generalist inserters who, with less skill and knowledge about PVC access, are required to fit this procedure into their current workload. Of further consideration is the consumer experience. Recent research into patients' perspectives on PVC insertion found that consumers wanted standards implemented for inserters in order to feel safe and trust their health care professionals (Cooke et al., 2018); and they want the clinicians placing their catheters to demonstrate 'competence' (Larsen, 2017). This again supports the utilisation of highly skilled VAS in hospitals.

Limitations

Several limitations to this work should be noted.

Systematic review

A limitation of the systematic review included in this PhD research was that the quality assessment was hindered by the poor reporting by study authors. In the 70 cohort studies included in this review, 113 (18%) did not define their outcome measures and 59 studies (84%) did not provide a sample size justification. Of the 31 RCTs in this review, over 40% of categories in the risk of bias table for RCTs were 'unclear' because information was not included in the publication.

A further limitation to the systematic review was the inability to obtain the number of catheter days for all included studies, which impacted our meta-analysis per 1000 catheter days. The heterogeneity of the study populations may also preclude generalisability to specific patient subgroups. However, the subgroup analyses in the review did explore potential at-risk subgroups. Limiting our search to English language and studies since the year 2000 may have impacted our findings, although this was done to ensure the review reflects modern PVC materials and practices.

Phase 1 and 2

The primary limitation to the cohort study and pilot RCT in this PhD research were that the study populations were medical and surgical patients from one tertiary hospital, which may not be generalisable to other settings. However, worldwide, a large proportion of patients requiring PVCs would be medical-surgical patients, thus the results should have a reasonably wide application. Another limitation of Phase 1 was that observational studies can only identify association with PVC failure and complications, rather than causation (Sedgwick, 2013b). Randomised controlled trials would be needed to test if interventions based on the identified risk factors do indeed prevent complications.

In Phase 2, the main limitation is that, as a pilot RCT, this study was unable to provide definitive results supporting the best model for PVC insertion. A larger study would be needed to test statistical hypotheses with adequate power to avoid type II error. A further limitation to the study was that due to the nature of the intervention, nurses and the patient were unable to be blinded to the PVC inserter. However, to avoid outcome assessment bias, the ReN collecting outcome data was blinded to the study intervention.

Recommendations

From the results of the research included in this PhD, nine recommendations are presented to guide clinical practice, education, healthcare policy, and future research.

Clinical practice

Recommendation 1: *Audit and benchmark local PVC data to plan and implement appropriate education and clinical practices*

To improve the clinical practice of clinicians placing and maintaining PVCs, and to ensure that patients are receiving the best possible quality of care, it is important to benchmark local PVC failure and complication rates with other healthcare facilities. This can be achieved by comparing local PVC data with the international failure and complication rates presented in the systematic review included in this PhD research. Clinical auditing and subsequent external benchmarking are important quality improvement processes which make it possible to identify any shortcomings and plan education strategies and processes to ensure improvement of patient care (Ray-Barruel, Ullman, Rickard, & Cooke, 2018).

Recommendation 2: *Discontinue using phlebitis as a descriptor for PVC failure*

A recommendation from the body of research presented in this PhD is that clinicians should no longer use the term phlebitis to describe PVC failure. There are over 71 different phlebitis scales in use internationally, with varying inclusion criteria (Ray-Barruel et al., 2014) which could result in confusion and an overlap with other complications such as occlusion, infiltration, and early signs of infection (Helm et al., 2015). The systematic review in this PhD reported varied phlebitis rates from less than 1%

to 100%. To prevent confusion, clinicians should instead focus on individual signs and symptoms such as pain and erythema.

Recommendation 3: *Adopt the findings from the multivariable analysis to facilitate improved PVC insertion and maintenance.*

Through understanding the modifiable risk factors associated with PVC failure, clinicians can reframe the way they provide care to patients who are having a PVC inserted or maintained. Clinicians can no longer simply place a PVC and consider this alone to be a success. They need a broader understanding that how they insert and care for a PVC will impact the subsequent incidence of PVC complications and failure. This PhD research recommends that patients need comprehensive evaluation of their vasculature and prescribed IV treatment to ensure that the most appropriate vascular access device is chosen. For example, if a patient requires multiple daily access of their PVC for the delivery of IV treatment, or are prescribed IV flucloxacillin, an alternative vascular access device such as a midline or PICC should be considered. At insertion, clinicians must take into account factors such as: placing the PVC in the patient's non-dominant side; applying additional securement such as appropriate tapes or a tubular bandage; and not choosing a 22-gauge PVC without a vasculature assessment.

Recommendation 4: *Introduce a VAS to hospitals planning to standardise care*

A recommendation from this PhD research is to introduce VAS to hospitals where PVC insertion and maintenance education programs are already established but PVC failure and complication rates remain high. Results from Phase 2 of this PhD research found that VAS had fewer multiple insertion attempts, higher proportions of patients completing treatment without complications, greater patient satisfaction, and lower overall

PVC failure rates. Although further research is required to confirm these results, evidence to date supports that a VAS model would offer standardised care, competence, and knowledge of PVC insertion and maintenance across the hospital setting.

Education

Recommendation *5: Develop and deliver PVC education programs to health professionals, particularly at undergraduate and postgraduate levels that focus on comprehensive PVC insertion and maintenance care.*

To improve PVC insertion and maintenance care, there is a need for clinicians to have a comprehensive understanding of the potential sequelae associated with PVC complications and failure. In education sessions, the results of the systematic review will alert students to the extent of this worldwide problem and identify how preventing PVC failure is a high priority for healthcare. The results from the multivariable analysis can be used to ensure that risk factors amenable to modification through education or alternative clinical interventions are the focus of these education programs, which will improve the patient experience, preserve patients' vascular access, prevent delay in medical treatment, and reduce healthcare associated costs. These inclusive education programs would be best provided at undergraduate as well postgraduate level for nursing, medical staff and other health professionals. This would ensure that clinicians entering a healthcare setting would understand how to provide best care for PVCs, as well as offer professional development for experienced healthcare professionals.

Healthcare policy

Recommendation 6: *Update local and national PVC guidelines*

Health professionals continue to vary PVC insertion and management strategies based on individual knowledge, personal preference and availability of products rather than high-quality evidence. This perpetuates the inconsistency of PVC insertion and management guidelines and care provided in Australian healthcare settings. A recommendation from this research is that health professionals need to work collaboratively to examine the content of PVC clinical practice guidelines across Australian healthcare facilities. Future local and national guidelines should include factors identified as important from this PhD research, such as: inserter skill; the application of additional securement such as appropriate tapes or a tubular bandage; consideration of vascular access device selection particularly for patients with multiple IV accesses or receiving IV flucloxacillin; avoidance of insertion in the patient's dominant side; and careful gauge selection, avoiding a 22-gauge catheter where appropriate. This will ensure that guidelines are consistent and based upon the best available evidence, which will improve PVC outcomes for patients.

Recommendation 7: *Update international guidelines on the prevention of PVC failure to focus on all PVC complications*

The research included in this PhD has provided the first worldwide understanding of how often and in what way PVCs fail. Current government guidelines have an infection focus for the prevention of PVC failure, which is vitally important but not the only type of PVC failure (Loveday et al., 2014; O'Grady et al., 2011). The recommendation from this research is that government guidelines need to be updated and extended to include

strategies to prevent failure from other complications such as occlusion, infiltration, and dislodgement, which this research has found constitute a much higher proportion of PVC failure.

Future research

Recommendation 8*: High-quality research is needed regarding measures to prevent PVC failure*

This program of research has highlighted that more high-quality research is needed to explore many different measures to prevent PVC failure. While the insertion model is important, post-insertion care is also vital to prevent complications. Firstly, almost half of the patients included in the multivariable analysis in Phase 1 of this research had additional securement products supporting their primary PVC dressing, and various permutations of these were found statistically beneficial. Both PVC failure and dressing failure are common, and with new products frequently becoming available, researchers need to provide RCT evidence to inform clinical decision-making regarding the efficacy of new generation dressings and securements.

Secondly, this research found that 22-gauge catheters were more likely to fail than any larger diameter PVC. These results are in direct conflict to current international guidelines which recommend the use of the smallest PVC gauge possible for IV treatment (Infusion Nurses Society, 2016; Intravenous Nursing New Zealand, 2011). This highlights a need for high-quality RCTs to inform best practice for PVC gauge selection.

Finally, IV flucloxacillin was associated with a twofold increase in occlusion and/or infiltration and phlebitis. Future high-quality research is needed to test whether alternative administration regimes for the delivery of IV flucloxacillin will decrease PVC failure. In

addition, RCTs are needed to determine whether IV flucloxacillin would be better administered through an alternate vascular access device such as a midline to improve patient outcomes.

Recommendation 9: *Replication and extension of the pilot RCT of VAS compared to generalist PVC inserters in a larger, multi-centre study*

Local and international guiding bodies have been unable to provide comprehensive guidance on optimal skill levels required for successful PVC insertion and how this impacts subsequent device failure and complications, due to a lack of robust RCTs comparing PVC insertion models. Nevertheless, literature reviewed in this thesis consisting of observational studies was suggestive of benefits with the VAS model, and the results of this feasibility RCT, while preliminary, extended knowledge supportive of VAS insertions being superior to current approaches. A recommendation from this research is the need to replicate the pilot RCT in a larger multi-centre study, not only in Australia but internationally to provide the much-needed evidence to support the best PVC insertion model for clinical practice.

Finally, the high PVC failure rate reported in this research emphasises the possibility that not all patients are suitable for a PVC. Future research needs to focus on alternative approaches such as the use of midline catheters for patients with poor vascular access.

Final Summary

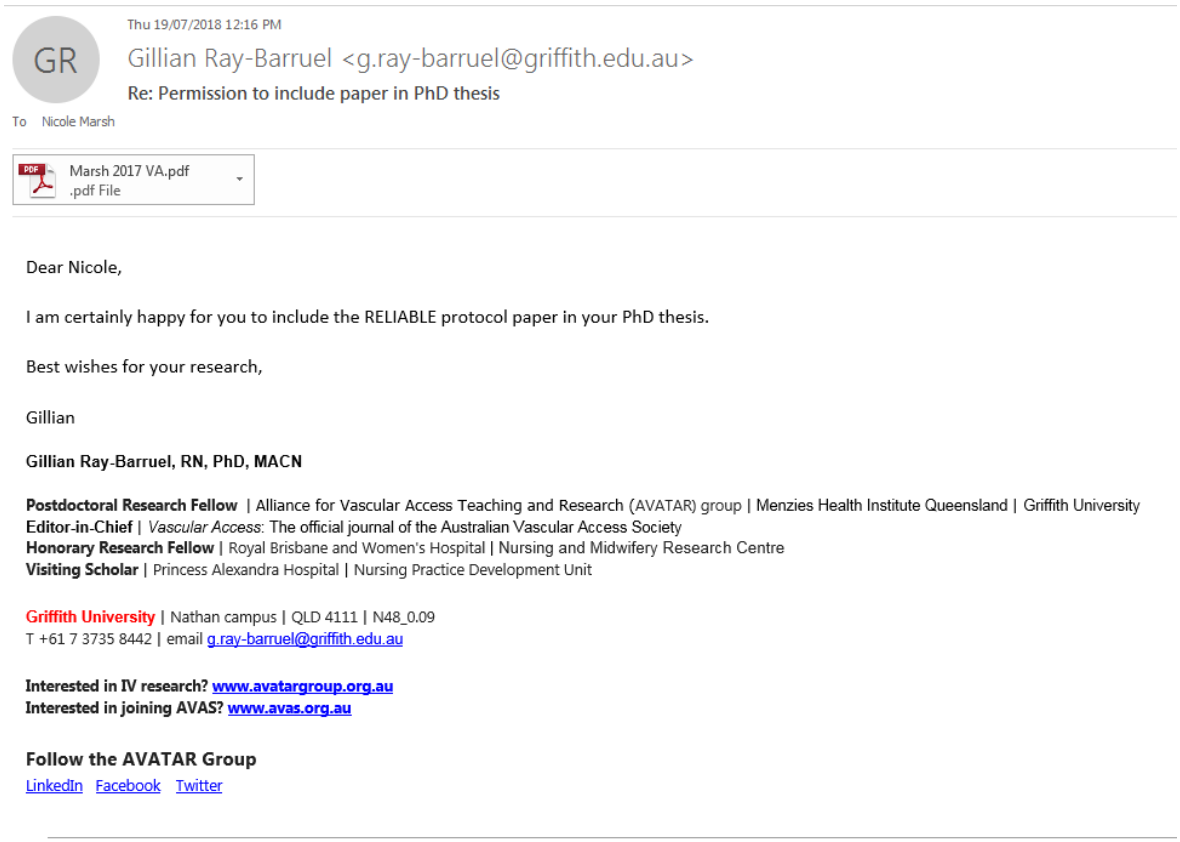
PVCs are important medical devices for patients. More than two billion are purchased globally each year for essential IV treatment across many healthcare settings. Improving

PVC outcomes is important and relevant to international nursing practice since nurses insert many of the PVCs and provide post-insertion care to all patients with PVCs. This program of research has provided evidence-based strategies that nurses and other clinicians can implement to reduce PVC failure—such as careful selection of gauge size and improved first-time PVC insertion success—and has supported the use of the VAS model as a worthy area for further exploration that likely will achieve better patient and system outcomes. This PhD research has shown that this important vascular access device is associated with high failure and complication rates, which require immediate attention and prioritisation from both clinicians, policy makers, and researchers.

Appendices

Appendix A: Copyright permission to reproduce Marsh et.al (2017)

Marsh, N., Webster, J., Cooke, M., & Rickard, C. M. (2017). The RELIABLE trial (RELiable Intravenous Access By Line Experts): A pilot randomised controlled trial protocol of expert versus generalist peripheral intravenous catheter insertion. *Vascular Access*, *3*(2), 3-7.



Thu 19/07/2018 12:16 PM

GR

Gillian Ray-Barruel <g.ray-barruel@griffith.edu.au>

Re: Permission to include paper in PhD thesis

To Nicole Marsh

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Dear Nicole,

I am certainly happy for you to include the RELIABLE protocol paper in your PhD thesis.

Best wishes for your research,

Gillian

Gillian Ray-Barruel, RN, PhD, MACN

Postdoctoral Research Fellow | Alliance for Vascular Access Teaching and Research (AVATAR) group | Menzies Health Institute Queensland | Griffith University
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Marsh, N., Webster, J., Larson, E., Cooke, M., Mihala, G., & Rickard, C. M. (2018). Observational study of peripheral intravenous catheter outcomes in adult hospitalized patients: A multivariable analysis of peripheral intravenous catheter failure. *Journal of Hospital Medicine*, *13*(2), 83-89. doi:10.12788/jhm.2867

Nicole Marsh

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Kind regards,
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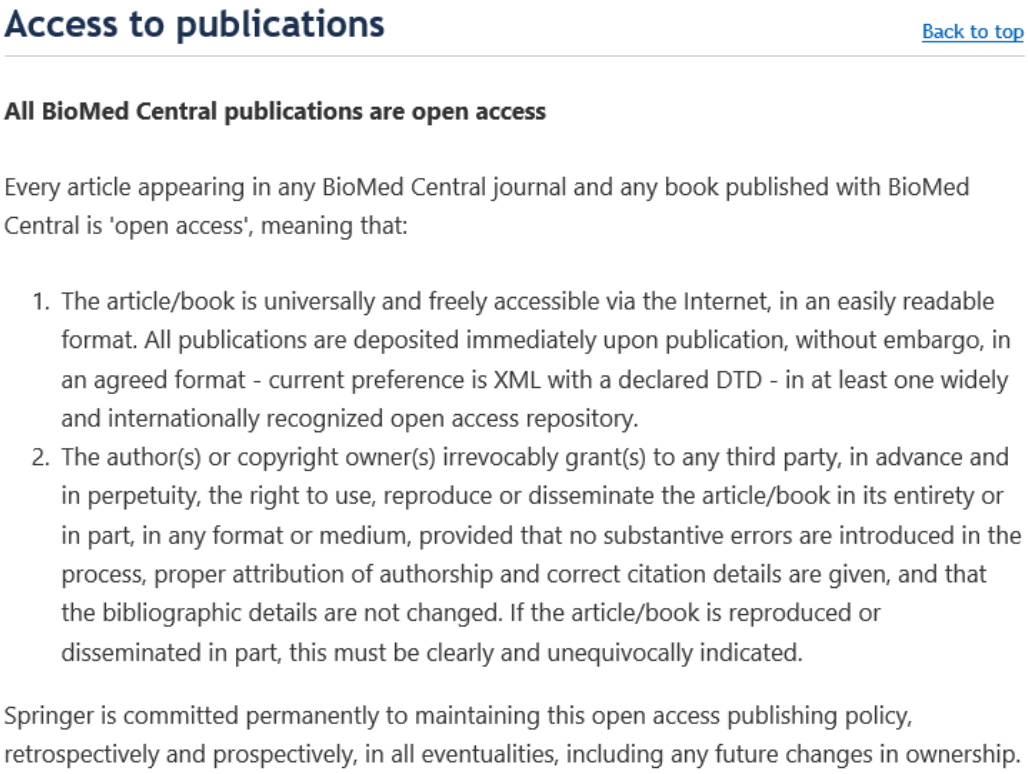

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Medical Research Council framework for developing and evaluating complex interventions in Figure 1.1

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Appendix E: PROSPERO registration of systematic review

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A systematic review and meta-analysis of the incidence of peripheral intravenous catheter failure and complications in the adult population

Nicole Marsh, Joan Webster, Marie Cooke, Claire Rickard

Citation

Nicole Marsh, Joan Webster, Marie Cooke, Claire Rickard. A systematic review and meta-analysis of the incidence of peripheral intravenous catheter failure and complications in the adult population. PROSPERO 2016:CRD42016043722 Available from http://www.crd.york.ac.uk/PROSPERO_REBRANDING/display_record.asp?ID=CRD42016043722

Review question(s)

What is the incidence of peripheral intravenous catheter failure and complications within the adult population?

Searches

Our search will be conducted in the Cochrane Central Register of Controlled Trials (CENTRAL; the Cochrane Library), US National Library of Medicine National Institutes of Health (PubMed), and Cumulative Index to Nursing and Allied Health (CINAHL) databases for all studies that report PVC failure or PVC-related complications. This review will be limited to studies written in English and conducted in a healthcare environment since the year 2000.

Types of study to be included

Studies will be eligible for inclusion if they are: cohort design (prospective or retrospective) or randomised controlled trials (RCTs). For RCTs, only results from the control group of the RCT will be included.

Condition or domain being studied

Peripheral intravenous catheter failure or complications at catheter removal.

Participants/ population

Inclusion criteria:

a) Adult participants with a PVC in any hospital/healthcare setting

b) Time period: published after the 1st of January 2000

b) Published in English

c) Cohort design (prospective or retrospective) or the control group of an RCT

Exclusion criteria:

a) Non peer reviewed

b) Case studies

c) Systematic review of cohort studies

d) Qualitative research

Intervention(s), exposure(s)

Not applicable

Comparator(s)/ control

None

Context
The rationale for including only the control group of an RCT is that this will reflect usual rates of failure or complications in the study setting.

Outcome(s)
Primary outcomes
PVC failure due to complications at catheter removal.

Secondary outcomes
Phlebitis: as defined by the study author.

Occlusion: as defined by the study author and including the inability to infuse intravenous therapy.

Infiltration/extravasation: as defined by the study author and including the permeation of intravenous fluids or medications into the surrounding tissue.

Dislodgement/accidental removal: as defined by the study author and including the partial or complete migration of the PVC from the vein.

Leakage: as defined by the study author and including the leakage of fluid from the insertion site.

CRBSI with laboratory confirmation of the catheter as the source of infection (O'Grady et al., 2011)

Suspected CRBSI: as defined by the study author.

Local infection: as defined by the study author and including purulent discharge from the insertion site.

Data extraction, (selection and coding)
Two review authors will independently assess titles and abstracts identified by the outlined search strategy. Full copies of relevant studies will be reviewed and independently assessed for their eligibility for inclusion in this review. A third author's judgment will be sought if differences of opinion cannot be resolved by unanimity.

One author will extract data from all the included studies using a data extraction form designed for this review. The extracted data will be checked for accuracy by the second reviewer. If information is unclear an attempt will be made to contact the study author for further clarification.

Where possible data will be extracted for the following items: author, study type, title, year, country, hospital/healthcare facility, characteristics of participants (e.g. age, sex, diagnosis), unit of measurement (PVC or participant), length of follow up, primary outcomes, secondary outcomes, limitations.

Risk of bias (quality) assessment
For the purposes of ensuring the quality, transparency and relevance of the studies included in this review, the STROBE (The strengthening the reporting of observational studies in epidemiology statement: Guidelines for reporting observational studies) checklist will be used.

Strategy for data synthesis
As cohort studies and RCT control groups are included in this review, descriptive statistics will be used to provide a summary of the study population results. Score confidence intervals (CI) with Freeman-Tukey double arcsine transformations will be calculated for individual studies with dichotomous (failure/no failure) outcomes. Pooled estimates for each outcome will be generated with random-effects meta-analysis. The resulting meta-analysis of the prevalence reported in the included studies will be grouped by a random-effects model and presented with 95% CI (Joanna Briggs Institute, 2014). Heterogeneity between studies will be assessed using the I-squared statistic (<25% suggests low heterogeneity, <50% suggests moderate heterogeneity and >75% suggests high heterogeneity).

Analysis of subgroups or subsets
Given the predicted heterogeneity of the study populations, the following subgroup analyses are planned:

• Emergency department inserted PVCs compared with insertion in the general medical/surgical wards.

• Studies with fewer than 100 participants compared to those with greater than 100 participants.

• Characteristics of country (e.g. developed countries compared to developing countries).

Dissemination plans
Results from this systematic literature review and meta-analysis will be presented locally and at relevant international meetings. It is planned to publish these results in a peer reviewed nursing or vascular access journal.

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Professor Claire Rickard, Alliance for Vascular Access Teachng and Research Group, Menzies Health Institute Queensland, Griffith University;

Anticipated or actual start date
29 August 2016

Anticipated completion date
28 August 2017

Funding sources/sponsors
No funding was received for this project.

Conflicts of interest
None known

Language

English

Country
Australia

Subject index terms status
Subject indexing assigned by CRD

Subject index terms
Adult; Catheterization, Peripheral; Humans; Incidence; Infusions, Intravenous

Stage of review
Ongoing

Date of registration in PROSPERO
02 August 2016

Date of publication of this revision
02 August 2016

Stage of review at time of this submission	Started	Completed
Preliminary searches	No	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

Appendix F: Critique of literature about Vascular Access Specialist Insertion of PVCs search strategy

The Cochrane Library

The Cochrane library

#1 MeSH descriptor: [Catheterization, Peripheral] explode all trees

#2 MeSH descriptor: [Catheters, Indwelling] explode all trees

#3 MeSH descriptor: [Catheterization] explode all trees

#6 (#1 or #2 or #3) and (team* or clinician* or specialist*infusion nurse)

Medline (OVID)

((Catheterization, Peripheral/ or Catheters, Indwelling/ or Catheterization) and (team* or clinician* or specialist*). And ((randomized controlled trial or controlled clinical trial or observational study or cohort study)

Embase

((indwelling catheter/ or catheterization /) and (team* or clinician* or specialist*or inserter infusion nurse OR intravenous therap*) and (randomized-controlled-trial/ or controlled-study/ or multicenter-study/ or cohort study OR observational study

Appendix G: Cohort study screening Log

REPLACE

Screening Log (enter all patients that are screened)

Inclusion criteria

1. Informed consent
2. First IVC inserted within 24 hours of recruitment

Exclusion criteria:

1. Non-English speaking without interpreter
2. Patients admitted for palliative treatment or who are on care of the dying pathway
3. Age under 18 years
4. Absence of cannula

Patient Initials (first/last)	UR Number	Date of Admission (dd/mm/yyyy)	Date of Screening (dd/mm/yyyy)	Inclusion Criteria Met (Y or N) If yes Study No.	Exclusion criteria Met (If yes provide reason from list)	Allocated Study no. (if yes)

Appendix H: Permission from C Hallam to use peripheral vein assessment tool

HC

HALLAM, Carole (CALDERDALE AND HUDDERSFIELD NHS FOUNDATION TRUST) <carole.hallam@nhs.net>

Wed 15/03/2017, 6:22 AM

Hi Nicole

I am happy for you to use the vein assessment tool and hope your research goes well, is sound very interesting. I will look forward to seeing your published work.

Kind regards

Carole

Carole Hallam
IPS Secretary
Infection Prevention Society
Mobile: 07766905562
Twitter: @hallamcarole

www.ips.uk.net

NM

Nicole Marsh
Tue 14/03/2017, 1:26 PM

Dear Dr Hallam,

I am currently a PhD student at Griffith University in Queensland, Australia. My research topic is preventing peripheral intravenous catheter failure. As part of my research I will be conducting a pilot randomised controlled trial comparing a generalist approach to PVC insertion (currently used in my hospital) with insertion by a vascular access specialist. I seek your permission to use the 'peripheral vein assessment tool' outlined in your publication titled *Development of the UK Vessel Health and Preservation (VHP) framework; a multi-organizational collaborative* as part of our initial patient assessment. I will of course reference your teams work.

Kind regards
Nicole Marsh

Appendix I: Royal Brisbane and Women's Hospital HREC approval Phase 1

Queensland Government

Royal Brisbane & Women's Hospital
Human Research Ethics Committee

Metro North
Hospital and Health Service

Enquiries to: Ann-Maree Gordon
A/Coordinator
Telephone: 07 3646 5490
Facsimile: 07 3646 5849
File Ref: HREC/14/QRBW/76
Email: RBWH-Ethics@health.qld.gov.au

Professor Joan Webster
Centre for Clinical Nursing
Level 2, Building 34
Royal Brisbane & Women's Hospital
Herston Q 4029

Dear Professor Webster,

Re: Ref N^{o}: HREC/14/QRBW/76: REplacing PeripheraL intrAvenous CathEters: The REPLACE Study

Thank you for submitting the above research project for single ethical review. This project was considered by the Royal Brisbane & Women's Hospital Human Research Ethics Committee (RBWH HREC) **(EC00172)** at its meeting held on 10 March, 2014.

I am pleased to advise that the RBWH Human Research Ethics Committee has granted ethical approval of this research project.

The nominated participating site for this project is:

- Royal Brisbane & Women's Hospital, Qld

This letter constitutes ethical approval only. This project cannot proceed until separate research governance authorisation has been obtained from the CEO or Delegate of the Royal Brisbane & Women's Hospital under whose auspices the research will be conducted.

The approved documents include:

Document	*Version*	*Date*
Covering Letter		13 January 2014
Application: NEAF *(Submission Code: AU/1/F7C613)*	2.1 (2013)	12 February 2014
Curriculum Vitae of Emily Nicole Larsen		

Document	*Version*	*Date*
Response to Request for Further Information		24 March 2014
REPLACE Trial Protocol	1.2	07 April 2014
RBWH Participant Information Sheet & Consent Form	1.1	24 March 2014

Approval of this project from the RBWH HREC is valid from **09.04.2014** to **09.04.2017** subject to the following conditions being met:

- The Coordinating Principal Investigator will immediately report anything that might warrant review of ethical approval of the project.
- The Coordinating Principal Investigator will notify the RBWH HREC of any event that requires a modification to the protocol or other project documents and submit any required amendments in accordance with the instructions provided by the HREC. These instructions can be found at http://www.health.qld.gov.au/rbwh/research/hrec.asp.
- The Coordinating Principal Investigator will submit any necessary reports related to the safety of research participants in accordance with the RBWH HREC policy and procedures. These instructions can be found at http://www.health.qld.gov.au/rbwh/research/hrec.asp.
- In accordance with Section 3.3.22 (b) of the National Statement the Coordinating Principal Investigator will report to the RBWH HREC annually in the specified format, the first report being due on **09.04.2015** and a final report is to be submitted on completion of the study. These instructions can be found at http://www.health.qld.gov.au/ohmr/html/regu/reporting_templates.asp.
- The Coordinating Principal Investigator will notify the RBWH HREC if the project is discontinued before the expected completion date, with reasons provided.
- The Coordinating Principal Investigator will notify the RBWH HREC of any plan to extend the duration of the project past the approval period listed above and will submit any associated required documentation. Instructions for obtaining an extension of approval can be found at http://www.health.qld.gov.au/rbwh/research/hrec.asp.
- The Coordinating Principal Investigator will notify the RBWH HREC of his or her inability to continue as Coordinating Principal Investigator including the name of and contact information for a replacement.
- A copy of this ethical approval letter together with completed Site Specific Assessment (SSA) and any other requirements must be submitted by the Coordinating Principal Investigator to the Research Governance Office at the Royal Brisbane & Women's Hospital in a timely manner to enable the institution to authorise the commencement of the project at its site.

- Should you have any queries about the RBWH HREC's consideration of your project please contact the HREC Coordinator on 07 3646 5490. The RBWH HREC's Terms of Reference, Standard Operating Procedures, membership and standard forms are available from http://www.health.qld.gov.au/rbwh/research/hrec.asp.

The RBWH HREC wishes you every success in your research.

Yours sincerely,

Dr Conor Brophy
Chairperson RBWH Human Research Ethics Committee
Metro North Hospital and Health Service
09.04.2014

This HREC is constituted and operates in accordance with the National Health and Medical Research Council's (NHMRC) *National Statement on Ethical Conduct in Human Research (2007)*. The processes used by this HREC to review research proposals have been certified by the National Health and Medical Research Council.

Appendix J: Griffith University HREC approval Phase 2

Correspondence 28 April 2014 Griffith Ethics Approval - Notepad

File Edit Format View Help

GRIFFITH UNIVERSITY HUMAN RESEARCH ETHICS COMMITTEE

28-Apr-2014

Dear Ms Ullman

I write further to the additional information provided in relation to the conditional approval granted to your application for ethical clearance for your project "PR: REplacing PeripheraL intrAvenous CathEters: The REPLACE Study" (GU Ref No: NRS/26/14/HREC).

This is to confirm receipt of the remaining required information, assurances or amendments to this protocol.

Consequently, I reconfirm my earlier advice that you are authorised to immediately commence this research on this basis.

The standard conditions of approval attached to our previous correspondence about this protocol continue to apply.

Regards

Dr Kristie Westerlaken
Policy Officer
Office for Research
Bray Centre, Nathan Campus
Griffith University
ph: +61 (0)7 373 58043
fax: +61 (07) 373 57994
email: k.westerlaken@griffith.edu.au
web:

Cc:

Researchers are reminded that the Griffith University Code for the Responsible Conduct of Research provides guidance to researchers in areas such as conflict of interest, authorship, storage of data, & the training of research students. You can find further information, resources and a link to the University's Code by visiting http://policies.griffith.edu.au/pdf/Code%20for%20the%20Responsible%20Conduct%20of%20Research.pdf

Appendix K: Cohort study participant information sheet and participant consent form

The REPLACE Study

REplacing PeripheraL intrAvenous CathEters

REPLACE Study.

Queensland Government

PARTICIPANT INFORMATION SHEET

Royal Brisbane and Women's Hospital

Royal Brisbane and Women's Hospital Principal Researcher/s: Professor Joan Webster (07) 3646 8590, Nicole Marsh (07) 3646 8740
Royal Brisbane and Women's Research Nurses: Jodie Genzel, Alyson Eastgate, and Emily Larsen

This information sheet has been provided to you to allow you to give fully informed consent. You should keep a copy of this sheet for your future reference.

Description of Research Study

A majority of patients at the Royal Brisbane and Women's Hospital need an intravascular device ('IV drip') as part of their medical treatment. These are small plastic tubes which are placed in a vein to administer fluid, nutrients, medicines and blood products.

The rate of peripheral intravenous catheter failure at the RBWH is high (around 40%). When a catheter fails, before treatment has been completed, a new catheter is generally required, causing discomfort to the patient and considerable cost to the organisation. There are a number of reasons for catheter failure, some of which may be preventable with appropriate intervention. At present we do not have a clear idea of the causes of catheter failure at the RBWH.

This study will follow patients from admission to discharge and closely monitor any IV access events associated with their stay. We are doing this research to improve practice in the hospital and find out ways to reduce catheter failure. Patients with catheter failure will be compared to a group who do not have catheter failure, to identify opportunities for intervention.

Why you have been chosen

You are invited to participate in this important study because your doctor/nurse believes that you will require one or more IV drips during your treatment at the Royal Brisbane and Women's Hospital.

What we will ask you to do

a) Information about your IV drip/s, your medical condition, and any complications associated with your drip, will be recorded from your hospital chart by a research nurse or assistant.
b) Multiple IV drips may be followed up on during your occupancy in the hospital, from admission to discharge.
c) Research nurses will inspect your IV drip daily to assess any complications arising over time and you may be questioned on levels of pain, discomfort and/or tenderness.
d) After your IV drip/s is/are no longer needed, it may be examined in the research laboratory for signs of infection risk.
e) You are also asked to consider allowing the collected information to be kept in an anonymous manner for other research into infection control and IV drips that may occur in the future.
f) Photographs/video-footage may be taken of the IV drip (including insertion/removal) during your participation in this study. ***These images may be taken if time permits and suitable equipment is available.*** These photographs/video-tapes are for research purposes and may be used in conference/seminar presentations to demonstrate causes of catheter failure. These will not include images of your face/identifying features and will be kept anonymous.

Risks to you
There are no foreseeable risks associated with participation in this study. This study will evaluate IV access events already taking place as part of your care and medical treatment will continue as per normal practice.

Benefits to you
We do not expect you to get any direct benefit by participating in the study. We do think that your participation will benefit patients, nurses, doctors and hospitals in the future, and you may feel satisfaction at your contribution to improving health care through research. You will be able to receive a report on the results of the research study by ticking the box on this form.

Confidentiality
Data collected during this study will be treated confidentially. The research nurse and assistants will store your data using a unique research number. The information will be safely stored at the hospital and within Griffith University. Combined patient results of this study will be presented in scientific journals and conferences. However, you will not be referred to by name and your personal identity will not be revealed in any publication or presentation. Research records will be destroyed 15 years after the study.

Choosing to participate or not
Your participation is entirely voluntary and if you decide not to participate this will not affect your medical care, or treatment by hospital staff in any way. If you choose to participate, you are free to withdraw your consent and to discontinue participation later, by telling the research nurse. A decision not to participate or to withdraw your participation will not affect your treatment in any way.

If you have any questions
If you have any questions now, or at a later time, we hope and expect that you will ask us. Please contact Professor Joan Webster or a research nurse, and we will be happy to answer your questions. Contact details are at the top of the form or ask the ward nurses/receptionist to contact us.

Other issues
This document in no way limits your rights at law from any damage that might arise from negligence on the part of investigators.

You should keep a copy of this form.

This information has been provided to allow you to give informed consent.

This study has been reviewed and approved by the Royal Brisbane and Women's Hospital Human Research Ethics Committee (EC00172) which was designated by the Queensland Health Office of Health and Medical Research for this study. Should you wish to discuss the study with someone not directly involved, in particular in relation to matters concerning policies, information about the conduct of the study or your rights as a participant, or should you wish to make an independent complaint, please contact the Coordinator or Chairperson, Human Research Ethics Committee, Royal Brisbane & Women's Hospital, Herston, Qld, 4029 or telephone (07) 3646 5490, email: RBWH-Ethics@health.qld.gov.au or the Royal Brisbane & Women's Hospital Patient Liaison Officer on (07) 3646 8216.

The REPLACE Study

REplacing PeripheraL intrAvenous CathEters

REPLACE Study.

Queensland Government

PARTICIPANT CONSENT FORM

Royal Brisbane and Women's Hospital

Thank you for agreeing to participate in this important research study. Although you may not benefit personally, you will help provide valuable information to help us to deliver safe and effective care.
I have had the contents of this information sheet explained to me and I have been provided with a copy. I agree to be enrolled in the project and understand that this will involve a research nurse collecting information about my IV drip/s and medical condition, including infection results, recorded from my hospital chart as outlined on the information sheet. I agree that my IV drip/s may be examined in the research laboratory once they are no longer needed for my treatment, as well as skin swabs (if taken).

Please read the following carefully, and sign below if you agree with these statements and are happy to participate in the study:

1. I have read and understood the information sheet and this consent form.
2. I have had the opportunity to ask questions about the study and these have been answered to my satisfaction.
3. I understand that this project is for research and that I may not benefit directly.
4. I have been informed that the information collected about me in this study will remain confidential and will be adequately safeguarded, and that when results are published, they will be presented in such a way that I cannot be identified.
5. I understand that if I do participate, I am free to withdraw my consent and to discontinue participation at any time without comment, and with no effect on my treatment or my relations with the Hospital in any way, but that I do need to tell the research staff if I wish to withdraw.
6. If I have any questions or comments about the study at any time I am free to contact Professor Joan Webster (07) 3646 8590 and the research nurses.
7. If I have any complaints about the ethical conduct of the study, I may direct these to the Human Research Ethics Committee, Royal Brisbane & Women's Hospital, Herston, Qld, 4029 on (07) 3646 5490, or email: RBWH-Ethics@health.qld.gov.au. Alternatively I may contact Griffith University Human Research Ethics Committee on (07) 3735 4375, or email research-ethics@griffith.edu.au.
8. I agree to have a skin swab taken around the IV drip site at removal

I agree to participate in the study and I give permission for authorised study personnel to extract details that pertain to this study from my hospital medical record.

I also agree for the information and IV drip/s collected to be kept in an anonymous format for future research studies by the investigators on infection control topics : ☐*Yes* ☐*No*

I agree that my IV Drip/Cannula may be photographed/video-taped during the insertion and removal of my IV drip/s by one of the members of the research team. These images may be taken if time permits and suitable equipment is available. This may be used in future conference/seminar presentations for research purposes. I understand that although the image will be shown, names will not be used:

☐*Yes* ☐*No*

I would like a copy of the research results to be sent to me at the end of the trial: ☐*Yes* ☐*No*

Email/address for report to be sent:.....

*Name of Participant:*_____

*Signature:*_____

*Date:*_____

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

*Name of Researcher:*_____

*Signature:*_____

*Date:*_____/

Appendix L: Royal Brisbane and Women's Hospital HREC approval Phase 2

Queensland Government

Metro North Hospital and Health Service

Royal Brisbane & Women's Hospital
Human Research Ethics Committee

Enquiries to: Ann-Maree Gordon
Coordinator
Telephone: 07 3646 5490
Facsimile: 07 3646 5849
File Ref: HREC/16/QRBW/386
Email: RBWH-Ethics@health.qld.gov.au

Ms Nicole Marsh
Nursing and Midwifery Research Centre
Centre for Clinical Nursing
Level 2, Building 34
Royal Brisbane & Women's Hospital
Herston Qld 4029

Dear Ms Marsh,

Re: Ref N^{o}: HREC/16/QRBW/386: Intravenous Access by Line Experts

Thank you for submitting the above research project for single ethical review. This project was considered by the Royal Brisbane & Women's Hospital Human Research Ethics Committee (RBWH HREC) **(EC00172)** at its meeting held on 12 September 2016. The research project meets the requirements of the National Health and Medical Research Council's (NHMRC) *National Statement on Ethical Conduct in Human Research (2007).*

I am pleased to advise that the RBWH Human Research Ethics Committee has granted ethical approval of this research project.

The nominated participating site for this project is:

- Royal Brisbane & Women's Hospital, Qld

This letter constitutes ethical approval only. This project cannot proceed until separate research governance authorisation has been obtained from the CEO or Delegate of the Royal Brisbane & Women's Hospital under whose auspices the research will be conducted.

The approved documents include:

Document	*Version*	*Date*
Covering Letter		26 August 2016
Application: NEAF *(Submission Code: AU/1/653829)*	2.2 (2014)	18 August 2016

Document	*Version*	*Date*
Email correspondence re: eCRF Data Collection Sheet		29 August 2016
Data Collection Sheet		
Response to Request for Further Information		26 August 2016 *(received - 15 September 2016)*
Response to Request for Further Information		19 September 2016
Protocol	1.2	19 September 2016
RBWH Participant Information Sheet & Consent Form	1.2	19 September 2016

Approval of this project from the RBWH HREC is valid from **22.09.2016** to **22.09.2019** subject to the following conditions being met:

- The Coordinating Principal Investigator will immediately report anything that might warrant review of ethical approval of the project.
- The Coordinating Principal Investigator will notify the RBWH HREC of any event that requires a modification to the protocol or other project documents and submit any required amendments in accordance with the instructions provided by the HREC. These instructions can be found at https://www.health.qld.gov.au/metronorth/research/ethics-governance/hrec-approval/default.asp.
- The Coordinating Principal Investigator will submit any necessary reports related to the safety of research participants in accordance with the RBWH HREC policy and procedures. These instructions can be found at https://www.health.qld.gov.au/metronorth/research/ethics-governance/post-approval-reporting/default.asp.
- In accordance with Section 3.3.22 (b) of the National Statement the Coordinating Principal Investigator will report to the RBWH HREC annually in the specified format, the first report being due on **22.09.2017** and a final report is to be submitted on completion of the study. These instructions can be found at https://www.health.qld.gov.au/metronorth/research/ethics-governance/post-approval-reporting/default.asp.
- The Coordinating Principal Investigator will notify the RBWH HREC if the project is discontinued before the expected completion date, with reasons provided.
- The Coordinating Principal Investigator will notify the RBWH HREC of any plan to extend the duration of the project past the approval period listed above and will submit any associated required documentation. Instructions for obtaining an extension of approval can be found at https://www.health.qld.gov.au/metronorth/research/ethics-governance/hrec-approval/default.asp.

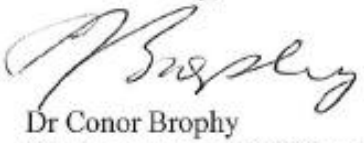
- The Coordinating Principal Investigator will notify the RBWH HREC of his or her inability to continue as Coordinating Principal Investigator including the name of and contact information for a replacement.

- A copy of this ethical approval letter together with completed Site Specific Assessment (SSA) and any other requirements must be submitted by the Coordinating Principal Investigator to the Research Governance Office at the Royal Brisbane & Women's Hospital in a timely manner to enable the institution to authorise the commencement of the project at its site.

- Should you have any queries about the RBWH HREC's consideration of your project please contact the HREC Coordinator on 07 3646 5490. The RBWH HREC's Terms of Reference, Standard Operating Procedures, membership and standard forms are available from https://www.health.qld.gov.au/metronorth/research/ethics-governance/hrec-approval/membership/default.asp.

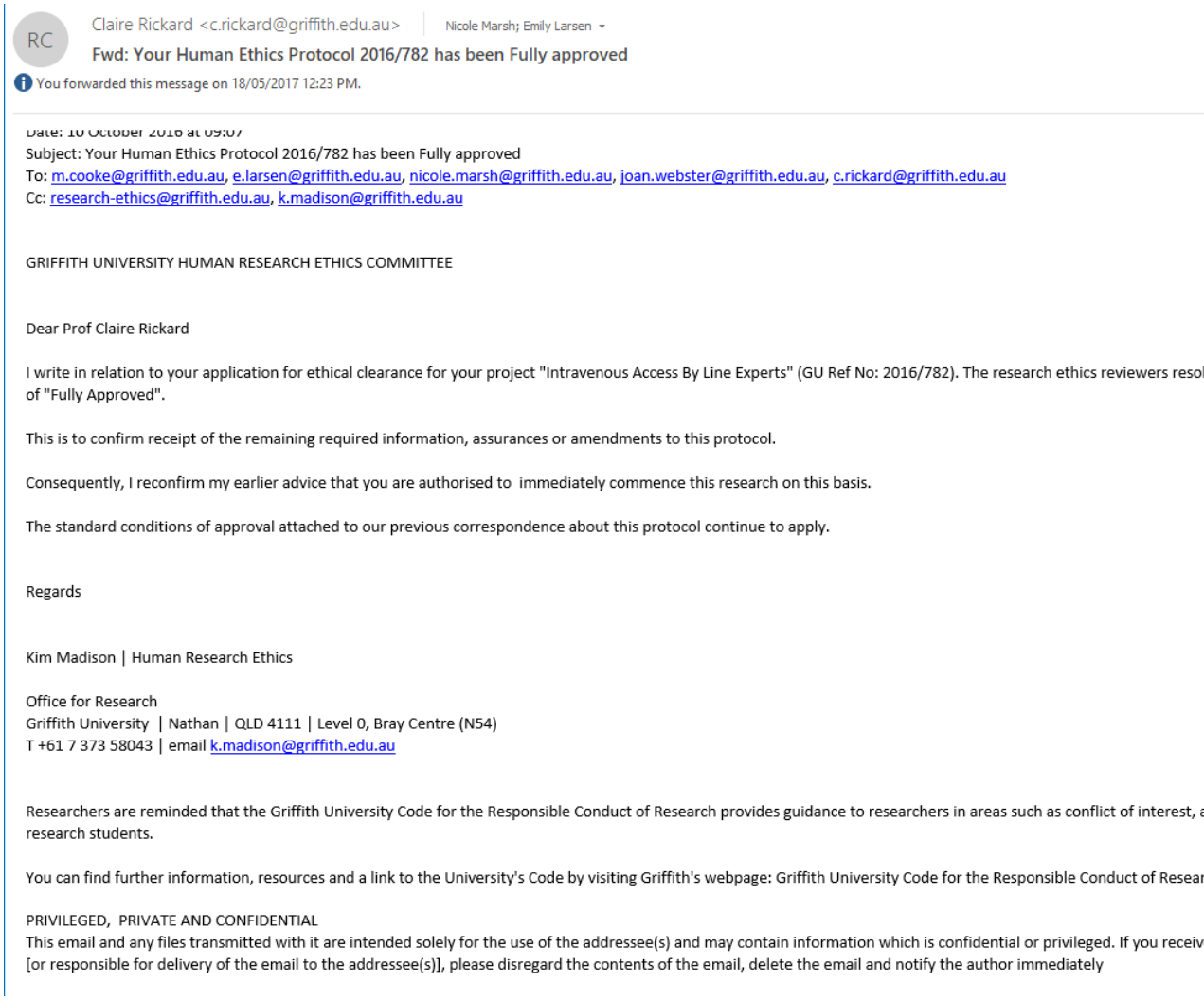
The RBWH HREC wishes you every success in your research.

Yours sincerely,



Dr Conor Brophy
Chairperson RBWH Human Research Ethics Committee
Metro North Hospital and Health Service
22.09.2016

Appendix M: Griffith University HREC approval Phase 2



RC

Claire Rickard <c.rickard@griffith.edu.au> Nicole Marsh; Emily Larsen

Fwd: Your Human Ethics Protocol 2016/782 has been Fully approved

You forwarded this message on 18/05/2017 12:23 PM.

Date: 10 October 2016 at 09:07
Subject: Your Human Ethics Protocol 2016/782 has been Fully approved
To: m.cooke@griffith.edu.au, e.larsen@griffith.edu.au, nicole.marsh@griffith.edu.au, joan.webster@griffith.edu.au, c.rickard@griffith.edu.au
Cc: research-ethics@griffith.edu.au, k.madison@griffith.edu.au

GRIFFITH UNIVERSITY HUMAN RESEARCH ETHICS COMMITTEE

Dear Prof Claire Rickard

I write in relation to your application for ethical clearance for your project "Intravenous Access By Line Experts" (GU Ref No: 2016/782). The research ethics reviewers resol
of "Fully Approved".

This is to confirm receipt of the remaining required information, assurances or amendments to this protocol.

Consequently, I reconfirm my earlier advice that you are authorised to immediately commence this research on this basis.

The standard conditions of approval attached to our previous correspondence about this protocol continue to apply.

Regards

Kim Madison | Human Research Ethics

Office for Research
Griffith University | Nathan | QLD 4111 | Level 0, Bray Centre (N54)
T +61 7 373 58043 | email k.madison@griffith.edu.au

Researchers are reminded that the Griffith University Code for the Responsible Conduct of Research provides guidance to researchers in areas such as conflict of interest, a
research students.

You can find further information, resources and a link to the University's Code by visiting Griffith's webpage: Griffith University Code for the Responsible Conduct of Resear

PRIVILEGED, PRIVATE AND CONFIDENTIAL
This email and any files transmitted with it are intended solely for the use of the addressee(s) and may contain information which is confidential or privileged. If you receiv
[or responsible for delivery of the email to the addressee(s)], please disregard the contents of the email, delete the email and notify the author immediately

Appendix N: Phase 2 participant information sheet and participant consent form

Royal Brisbane and Women's Hospital

Metro North Hospital and Health Service

Intravenous Access by Line Experts

PARTICIPANT INFORMATION SHEET

Royal Brisbane and Women's Hospital

Principal Researcher/s: Ms Nicole Marsh, Professor Joan Webster, Professor Claire Rickard, Professor Marie Cooke.
Associate Researcher/s: Ms Emily Larsen, Ms Sue Cadigan
Royal Brisbane and Women's Hospital Research Nurses/ Team: Ms Jodie Genzel, Ms Vicki Adermann (07) 3646 8725.

You are invited to take part in this research project, Intravenous Access by Line Experts. This is because you are currently receiving treatment in the Royal Brisbane and Women's Hospital and having a Peripheral Intravenous Catheter (PVC) inserted as part of your care. This pilot research project is aiming to explore the effectiveness of PVC insertion by a vascular access specialist compared with a generalist clinician (standard practice). Participation is completely voluntary and you may refuse/ withdraw your consent at any time.

This information sheet has been provided to you to allow you to give fully informed consent. You should keep a copy of this sheet for your future reference.

Description of Research Study
Peripheral intravenous catheters (PVC) are the world's most commonly used invasive medical device. They may be inserted by either a generalist inserter (a clinician who has been specifically trained and assessed by the hospital to insert catheters) or a Vascular Access Specialist (VAS) (a clinician whose primary role is to insert PVC). The failure of PVC remains unacceptably high, with reported re-insertions required for up to 69% of patients. When a catheter fails, before treatment has been completed, a new catheter is generally required, causing discomfort to the patient and considerable cost to the organisation. There are a number of reasons for catheter failure, some of which may be preventable with appropriate intervention. The skill of the PVC inserter may be a potential modifiable risk factor and this pilot randomised controlled trial will test the efficacy, cost effectiveness and acceptability to patients of a vascular access specialist. The results of this study may show that a larger study (with a greater number of patients) could be done later to explore the real (if any) difference of IV outcomes between vascular access specialist and generalist clinician insertions.

Why you have been chosen
You are invited to participate in this trial because nursing staff have identified you will be requiring a peripheral intravenous catheter for at least 24 hours and are receiving treatment within a Medical / Surgical inpatient setting.

What we will ask you to do

A. You will be asked to consent to participate in this trial.
B. If you agree to participate in this study, you will be randomised (like tossing a coin) to either having your peripheral intravenous catheter inserted by either (1) a vascular access specialist or (2) a generalist clinician (standard practice).
C. A research nurse will visit you every day to look at your device and check for any signs of complications, including infection, redness, irritation or swelling. This will continue until your intravenous catheter has been removed.
D. Information about your age, gender, medical condition, treatment and any factors that may put you at risk of a device failure will be recorded from you or your hospital medical record.
E. The Research Nurse/s may take photographs/video-footage of the PVC during your participation in this study. *These images may be taken if time permits and suitable equipment is available.* These photographs/video-tapes are for research purposes and may be used in conference/seminar presentations to demonstrate causes of catheter failure. These will not include images of your face/identifying features and will be kept anonymous.
F. Data, will be kept in an anonymous format and may be used for future research studies by the investigators on infection control topics, subject to further Royal Brisbane and Women's Hospital Ethics Committee approval.

Risks to you

Complications related to PVCs (inserted by either type of clinician) may include bruising, pain and swelling, leaking intravenous fluid, nerve damage or infection. Your device site will be monitored closely to ensure any emerging complications are identified quickly and brought to the attention of your treating nurse.

Benefits to you

We do not expect you to get any direct benefit by participating in the study. We do think that your participation may benefit patients, nurses, doctors and hospitals in the future, and you may feel satisfaction at your contribution to improving health care through research. You will be able to receive a report on the results of the research study by ticking the box on this form.

Confidentiality

Data collected during this study will be treated confidentially, and all identifiable information will be kept in a secure setting at the Royal Brisbane and Women's Hospital. The research nurse and assistants will store your data using a unique research number. Information entered into the database will not include any identifiable information (eg. your name, date of birth or hospital identification number). The de-identified information will be safely stored at the hospital and within Griffith University. Combined patient results of this study will be presented in scientific journals and conferences. However, you will not be referred to by name and your personal identity will not be revealed in any publication or presentation. Research records will be destroyed 15 years after the study.

Royal Brisbane and Women's Hospital

Metro North Hospital and Health Service

Choosing to participate or not

Your participation is entirely voluntary and if you decide not to participate this will not affect your medical care, or treatment by hospital staff in any way. If you choose to participate, you are free to withdraw your consent and to discontinue participation later, by telling the research nurse. A decision not to participate or to withdraw your participation will not affect your treatment in any way. If you choose to withdraw you will be given the opportunity to revoke the researcher's rights to keep any data collected, or otherwise consent to its use in the final results. This choice will not impact upon your treatment in any way.

Complaints and Compensation

If you suffer any injuries or complications as a result of this research project (including, but not limited to, the initial insertion of the device), you should contact the study team and notify your nurse/doctor as soon as possible and you will be assisted with arranging appropriate medical treatment. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital. In the event of loss or injury, the parties involved in this research have agreed to cover the costs associated with study harm arising from participation, if over and above what you are eligible for within Medicare. This document in no way limits your rights at law from any damage that might arise from negligence on the part of investigators.

If you have any questions

If you have any questions now, or at a later time, we hope and expect that you will ask us. Please contact Emily Larsen (07) 3646 8725 (emily.larsen@health.qld.gov.au) or Nicole Marsh on (07) 3646 8740 (nicole.marsh@health.qld.gov.au) or, and we will be happy to answer your questions. Contact details are at the top of the form or ask the ward nurses/receptionist to contact us.

You should keep a copy of this form.

This information has been provided to allow you to give informed consent.

This study has been reviewed and approved by the Royal Brisbane and Women's Hospital Human Research Ethics Committee (EC00172) which was designated by the Queensland Health Office of Health and Medical Research for this study, and the Griffith University Human Research Ethics Committee. Should you wish to discuss the study with someone not directly involved, in particular in relation to matters concerning policies, information about the conduct of the study or your rights as a participant, or should you wish to make an independent complaint, please contact the Coordinator or Chairperson, Human Research Ethics Committee, Royal Brisbane & Women's Hospital, Herston, Qld, 4029 or telephone (07) 3646 5490, email: RBWH-Ethics@health.qld.gov.au or the Royal Brisbane & Women's Hospital Patient Liaison Officer on (07) 3646 8216. Alternatively you may contact Griffith University Human Research Ethics Committee on (07) 3735 4375, or email research-ethics@griffith.edu.au. For any local research complaints, please also contact Mrs Jacqueline Robinson, Research Governance Officer for RBWH on 3646 8579 or RBWH-RGO@health.qld.gov.au .

Royal Brisbane and Women's Hospital

Metro North Hospital and Health Service

Intravenous Access by Line Experts

PARTICIPANT CONSENT FORM

Royal Brisbane and Women's Hospital

I have had the contents of this information sheet explained to me and I have been provided with a copy. I agree to be enrolled in the project and understand that this will involve a research nurse randomly allocating me to having my PVC inserted by either a vascular access specialist or a generalist clinician (standard practice). I also understand the project will involve the collection of information about my peripheral intravascular device and medical condition, including infection results, recorded from my hospital chart as outlined on the information sheet.

Please read the following carefully, and sign below if you agree with these statements and are happy to participate in the study:

1. I have read and understood the information sheet and this consent form.
2. I have had the opportunity to ask questions about the study and these have been answered to my satisfaction.
3. I understand that this project is for research and that I may not benefit directly.
4. I have been informed that the information collected about me in this study will remain confidential and will be adequately safeguarded, and that when results are published, they will be presented in such a way that I cannot be identified.
5. I understand that if I do participate, I am free to withdraw my consent and to discontinue participation at any time without comment, and with no effect on my treatment or my relations with the hospital in any way, but that I do need to tell the research staff if I wish to withdraw.
6. If I have any questions or comments about the study at any time I am free to contact Emily Larsen (07) 3646 8725 and the research nurses.

If I have any complaints about the ethical conduct of the study, I may direct these to the Human Research Ethics Committee, Royal Brisbane & Women's Hospital, Herston, Qld, 4029 on (07) 3646 5490, or email: RBWH-Ethics@health.qld.gov.au. Alternatively I may contact Griffith University Human Research Ethics Committee on (07) 3735 4375, or email research-ethics@griffith.edu.au and (for any local research complaints) Mrs Jacqueline Robinson, Research Governance Officer for RBWH on 3646 8579 or RBWH-RGO@health.qld.gov.au .

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I agree to participate in the study and I give permission for authorised study personnel to extract basic demographic details that pertain to this study from my hospital medical record. ☐

I also agree for the information collected to be kept in an anonymous format for future research studies by the investigators on infection control topics. ☐

I agree that my PVC may be photographed/video-taped by one of the members of the research team. These images may be taken if time permits and suitable equipment is available. This may be used in future conference/seminar presentations for research purposes. I understand that although the image will be shown, names will not be used. ☐

I would like a copy of the research results to be sent to me at the end of this study. ☐
*Email or postal address for report to be sent:*_____
_____

*Name of Participant:*_____
*Signature:*_____
*Date:*_____

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.
*Name of Researcher:*_____
*Signature:*_____
*Date:*_____

Appendix O: Phase 2 (Pilot trial) screening log

RELIABLE Trial

Screening Log (enter all patients that are screened)

Inclusion criteria:

1. Patient = or > 18 y/o
2. PVC required = or > 24 hours,
3. Able to provide informed consent*

**If eligible, but refused or missed, please still list in the table below under Allocated Study No.*

Exclusion criteria:

1. Current bloodstream infection (positive BC within 48 hours)
2. Non-English speaking without interpreter
3. Patients on a palliative care pathway and/or receiving critical care treatment.
4. Previous enrolment in the study.

Patient Initials *(first/last)*	UR Number	Date of Admission *(dd/mm/yyyy)*	Date of Screening *(dd/mm/yyyy)*	Exclusion criteria Met *(Y or N)* *(If yes provide reason from list)*	Allocated Study No. *(if eligible for randomisation on CTCC).*

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