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[Intervention Review]

Clinically-indicated replacement versus routine replacement of peripheral venous catheters

Joan Webster^{1,2,3}, Sonya Osborne⁴, Claire M Rickard^{2,5}, Karen New⁶

¹Centre for Clinical Nursing, Royal Brisbane and Women's Hospital, Brisbane, Australia. ²NHMRC Centre of Research Excellence in Nursing, Centre for Health Practice Innovation, Menzies Health Institute Queensland, Griffith University, Brisbane, Australia. ³School of Nursing and Midwifery, University of Queensland, Brisbane, Australia. ⁴School of Nursing, Queensland University of Technology, Kelvin Grove (Brisbane), Australia. ⁵Royal Brisbane and Women's Hospital, Brisbane, Australia. ⁶The University of Queensland, School of Nursing, Midwifery and Social Work, Brisbane, Australia

Contact address: Joan Webster, Centre for Clinical Nursing, Royal Brisbane and Women's Hospital, Level 2, Building 34, Butterfield Street, Brisbane, Queensland, 4029, Australia. joan_webster@health.qld.gov.au, wigan1943@bigpond.com.

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ABSTRACT

Background

US Centers for Disease Control guidelines recommend replacement of peripheral intravenous (IV) catheters no more frequently than every 72 to 96 hours. Routine replacement is thought to reduce the risk of phlebitis and bloodstream infection. Catheter insertion is an unpleasant experience for patients and replacement may be unnecessary if the catheter remains functional and there are no signs of inflammation. Costs associated with routine replacement may be considerable. This is an update of a review first published in 2010.

Objectives

To assess the effects of removing peripheral IV catheters when clinically indicated compared with removing and re-siting the catheter routinely.

Search methods

For this update the Cochrane Vascular Trials Search Co-ordinator searched the Cochrane Vascular Specialised Register (March 2015) and CENTRAL (2015, Issue 3). We also searched clinical trials registries (April 2015).

Selection criteria

Randomised controlled trials that compared routine removal of peripheral IV catheters with removal only when clinically indicated in hospitalised or community dwelling patients receiving continuous or intermittent infusions.

Data collection and analysis

Two review authors independently assessed trial quality and extracted data.

Main results

Seven trials with a total of 4895 patients were included in the review. The quality of the evidence was high for most outcomes but was downgraded to moderate for the outcome catheter-related bloodstream infection (CRBSI). The downgrade was due to wide confidence intervals, which created a high level of uncertainty around the effect estimate. CRBSI was assessed in five trials (4806 patients). There

was no significant between group difference in the CRBSI rate (clinically-indicated 1/2365; routine change 2/2441). The risk ratio (RR) was 0.61 (95% CI 0.08 to 4.68; $P = 0.64$). No difference in phlebitis rates was found whether catheters were changed according to clinical indications or routinely (clinically-indicated 186/2365; 3-day change 166/2441; RR 1.14, 95% CI 0.93 to 1.39). This result was unaffected by whether infusion through the catheter was continuous or intermittent. We also analysed the data by number of device days and again no differences between groups were observed (RR 1.03, 95% CI 0.84 to 1.27; $P = 0.75$). One trial assessed all-cause bloodstream infection. There was no difference in this outcome between the two groups (clinically-indicated 4/1593 (0.02%); routine change 9/1690 (0.05%); $P = 0.21$). Cannulation costs were lower by approximately AUD 7.00 in the clinically-indicated group (mean difference (MD) -6.96, 95% CI -9.05 to -4.86; $P \leq 0.00001$).

Authors' conclusions

The review found no evidence to support changing catheters every 72 to 96 hours. Consequently, healthcare organisations may consider changing to a policy whereby catheters are changed only if clinically indicated. This would provide significant cost savings and would spare patients the unnecessary pain of routine re-sites in the absence of clinical indications. To minimise peripheral catheter-related complications, the insertion site should be inspected at each shift change and the catheter removed if signs of inflammation, infiltration, or blockage are present.

PLAIN LANGUAGE SUMMARY

Replacing a peripheral venous catheter when clinically indicated versus routine replacement

Background

Most hospital patients receive fluids or medications via an intravenous catheter at some time during their hospital stay. An intravenous catheter (also called an IV drip or intravenous cannula) is a short, hollow tube placed in the vein to allow administration of medications, fluids or nutrients directly into the bloodstream. These catheters are often replaced every three to four days to try to prevent irritation of the vein or infection of the blood. However, the procedure may cause discomfort to patients and is quite costly.

Study characteristics and key results

This review included all of the randomised controlled trials (current up to March 2015), which have compared routine catheter changes with changing the catheter only if there were signs of inflammation or infection. We measured catheter-related blood stream infection, phlebitis and other problems associated with peripheral catheters, such as local infection and catheter blockage. There was no difference between the groups on any of these measures. However, we did find that it costs less, on average, when catheters were replaced when there was a clinical indication to do so, compared with routine changes.

Quality of the evidence

The overall quality of the evidence was rated as being high for most of the outcomes. There was some uncertainty for the outcome 'catheter related blood stream infection', so the evidence for that outcome was downgraded to moderate. We found no evidence of benefit to support current practice of changing catheters routinely every three to four days.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Clinically-indicated versus routine changes for peripheral venous catheter-related complications						
Patient or population: patients with peripheral venous catheter-related complications Settings: Hospitals and community settings Intervention: clinically-indicated versus routine changes						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Clinically indicated versus routine changes				
Catheter-related bloodstream infection Positive blood culture from a peripheral vein; clinical signs of infection; no other apparent source for the bloodstream infection except the intravenous catheter; and colonised intravenous catheter tip culture with the same organism as identified in the blood	Study population		RR 0.61 (0.08 to 4.68)	4806 (5 studies)	⊕⊕⊕⊕ moderate ^{1,2,3,4}	
	1 per 1000	1 per 1000 (0 to 5)				
	Moderate					
	0 per 1000	0 per 1000 (0 to 0)				
Phlebitis Any definition used by the author	Study population		RR 1.14 (0.93 to 1.39)	4806 (5 studies)	⊕⊕⊕⊕ high ^{1,3}	
	68 per 1000	78 per 1000 (63 to 95)				
	Moderate					

	68 per 1000	78 per 1000 (63 to 95)			
All-cause bloodstream infection	Study population		RR 0.47 (0.15 to 1.53)	3283 (1 study)	⊕⊕⊕⊕ high ^{1,3}
	5 per 1000	3 per 1000 (1 to 8)			
	Moderate				
	5 per 1000	2 per 1000 (1 to 8)			
Cost Estimated. Based on materials and staff costs ^{5,6}		The mean cost in the intervention groups was AUD \$6.96 lower (9.05 to 4.86 lower)		4244 (3 studies)	⊕⊕⊕⊕ high

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹ Although patients and those recording outcomes were aware of group allocation, it seems unlikely that this knowledge would have affected results. None of those recording outcomes were investigators and the diagnosis was based on verifiable data in patients medical records.

² In three of the five trials, no CRBSI occurred in either arm of the study. In the other two trials there was considerable overlap in the confidence intervals, consequently there was no statistical heterogeneity.

³ Participants, interventions and outcomes were similar across studies.

⁴ Confidence intervals were wide for this outcome, indicating a level of uncertainty around the effect size.

⁵ The overall cost for cannula replacement varies by cost of materials, time, solutions, additives to the solution.

⁶ Mean cost is reported in Australian dollars.

BACKGROUND

Among hospitalised patients, vascular access is the most common invasive procedure with 80% of hospital admissions involving an average of two vascular access devices per patient (Hadaway 2012). Peripheral intravenous access is associated with a phlebitis rate of between 1.5% (Malyon 2014) and 60% (Gupta 2007) and a peripheral intravenous catheter-related bacteraemia (CRBSI) rate of approximately 0.1% (Maki 2006). Current guidelines recommend that “there is no need to replace peripheral catheters more frequently than every 72 to 96 hours to reduce risk of infection and phlebitis in adults” (O’Grady 2011) but most hospitals interpret this to mean ‘change peripheral catheters every 72-96 hours’. The 2011 recommendation carries a category rating of 1B (strongly recommended for implementation and supported by some experimental, clinical or epidemiological studies). In support of the rating, the guideline cites two observational studies (Lai 1998; Tager 1983) and one RCT. The first observational study followed 3094 patients through their period of IV peripheral catheterisation and found that the phlebitis rate was 3.2% among those whose catheters remaining in situ for > seven days, compared with a rate of 4.1% and 3.9% for those whose dwell times were three and four days respectively (Tager 1983). The second observational study compared intravenous catheters left in place for 72 hours or 96 hours and found equivalent phlebitis rates (Lai 1998). The one RCT that was cited was designed to compare two types of catheter material, not dwell times (Maki 1991). The guideline also exempts children or patients with poor veins from the recommendation. In recent years, there have been improvements in catheter design and composition and more recent studies, including an earlier version of this review (Webster 2010), indicate that the recommendation may need to be revised. On the other hand, based on level 1 evidence, the most recent Infusion Nursing Standards of Practice and the epic3 National Evidence Based Guidelines recommend that short peripheral catheters should be replaced when clinically indicated, unless the patient is receiving parenteral nutrition peripherally (Infusion Nurses Society 2011; Loveday 2014). The projected 5-year savings from implementing clinically indicated peripheral intravenous catheter removal policies is US\$300 million and 1 million health-worker hours in the United States alone (Tuffaha 2014; Tuffaha 2014a).

Description of the condition

Peripheral vein infusion thrombophlebitis (PVT) is characterised by pain, erythema (redness of the skin), swelling, and palpable thrombosis of the cannulated vein (Monreal 1999). Diagnosis remains controversial and a number of grading systems have been proposed, although with limited validation testing performed (Ray-Barruel 2014). These include the Maddox scale (Maddox 1977) and the Baxter scale (Panadero 2002), which rank infusion thrombophlebitis according to the severity of clinical signs and

symptoms. The scales are limited because not all symptoms may be present, or they may not always be present in the clusters described in the scales. Consequently, many investigators define PVT based on two or more of pain, tenderness, warmth, erythema, swelling, and a palpable cord (Maki 1991; Monreal 1999), even though it may be difficult to distinguish between pain and tenderness. More recently, a new definition for phlebitis has been proposed, one based on a more objective assessment of the insertion site (Rickard 2012). Although the precise pathogenesis of thrombus formation remains unclear, it is thought to be related to inflammation of the vein wall. Studies have been unable to demonstrate a high correlation between phlebitis and catheter infection and Maki has suggested that phlebitis may primarily be a physical response (Maki 1991). This was supported by Catney and colleagues when investigating the aetiology of phlebitis; they found that drug irritation, size of catheter, and the person inserting the catheter were all predictors (Catney 2001). Ultrasonographic imaging has demonstrated thrombus formation in two thirds of catheterised veins studied and it has been suggested that catheter design may be implicated (Everitt 1997). Thus, possible causes of phlebitis are mechanical irritation from the catheter and the properties of the infusate or intravenously administered medications.

Description of the intervention

The intervention under consideration is replacing an intravenous peripheral catheter only if there are clinical indications to do so. Clinical indications include blockage, pain, redness, infiltration, swelling, leakage, and phlebitis.

How the intervention might work

Each time a catheter is inserted, the patient’s skin integrity is breached and a potential portal for pathogens is provided. For example, Uslusoy found a significant relationship between the number of times infusions were inserted and phlebitis (Uslusoy 2008). Consequently, it may be prudent to limit the frequency of peripheral catheter changes as long as there is no clinical reason to do so. There is some support for this approach from observational studies that have compared outcomes between catheters remaining in situ for varying periods. In an adequately powered observational study, which included patients from medical wards and intensive care units, the investigators were unable to demonstrate any increased risk of phlebitis beyond the second day (Bregenzer 1998). Similarly, in a retrospective study of 784 intravenous catheter starts the rate of phlebitis on days one and two was 11.5%, dropping to 3.9% by day four (Homer 1998). The authors concluded that “there appeared to be less risk in continuing therapy beyond the third day than re-starting the therapy” (pp 304). Catney 2001 also failed to demonstrate any increase in phlebitis rates with the passage of time, with failure rates being less at 144 hours (1.9%)

than at 72 hours (2.5%) (Catney 2001). Similarly, in a prospective investigation of 305 peripheral catheters there were 10 cases of infusion phlebitis amongst patients who had their catheter in situ for less than 72 hours whereas none were reported in patients where the dwell time was longer (White 2001). In the same study, there were three cases of post-infusion phlebitis; these all occurred amongst patients whose peripheral vein infusion catheter had been in place for less than 72 hours. Even among a high risk population of oncology and infectious diseases patients, phlebitis rates were no different when length of cannulation was dichotomised to three days or less and more than three days (Cornely 2002).

Why it is important to do this review

These observational studies create uncertainty around the US Centers for Disease Control (CDC) guidelines relating to peripheral intravenous catheter management. This uncertainty has led some hospitals to adopt the practice of re-siting only where there is evidence of inflammation or infiltration (personal communication). Included in the new CDC recommendations is a statement related to clinically-indicated (CI I) replacement in adults, advising that this was an “unresolved issue” and referencing the previous version of this review (Webster 2010), which showed ‘no difference’ between the two approaches to re-siting. Making the guidelines even more difficult to rationalise is the recommendation for peripheral catheter replacement in children, which states “replace peripheral catheters in children only when clinically indicated” (O’Grady 2011). References supporting the 2011 recommendation were unrelated to dwell times (Band 1980; Maki 1973) and may indicate a mistake in the CDC’s reference list (p61) (O’Grady 2011). Insertion of a peripheral intravenous catheter can be a painful and traumatic process and, if unnecessary, adds not only to a patient’s discomfort but also has significant cost implications for the institution. There is a clear need to provide direction for clinicians through systematically reviewing existing studies.

OBJECTIVES

To assess the effects of removing peripheral intravenous (IV) catheters when clinically indicated compared with removing and re-siting the catheters routinely.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs) comparing routine removal of peripheral IV catheters with removal only when clinically indicated were considered. Cross-over trials were not eligible for inclusion.

Types of participants

Any patient requiring a peripheral IV catheter to be in situ for at least three days for the administration of intermittent or continuous therapy (this may include patients in hospitals, nursing homes, or in community settings). Participants receiving parenteral fluids were excluded.

Types of interventions

Any duration of time before routine replacement versus clinically-indicated replacement will be included. Catheters made from any type of material (for example metal, plastic); non-coated or coated with any type of product (for example antibiotic, anticoagulant); or covered by any type of dressing (for example gauze, clear occlusive) were eligible.

Types of outcome measures

Primary outcomes

- Catheter-related blood stream infection (CRBSI) (defined as a positive blood culture from a peripheral vein; clinical signs of infection; no other apparent source for the bloodstream infection except the intravenous catheter; and colonised intravenous catheter tip culture with the same organism as identified in the blood)
 - Thrombophlebitis (using any definition identified by the trial author)
 - All-cause bloodstream infection (defined as a any positive blood culture drawn from a peripheral vein while an intravenous catheter is in situ or for 48 hours after removal)
 - Cost (in terms of materials and labour associated with IV catheter-related insertion)

Secondary outcomes

- Infiltration (defined as permeation of IV fluid into the interstitial compartment, causing swelling of the tissue around the site of the catheter)
- Catheter occlusion or blockage (identified by the inability to infuse fluids)
 - Number of catheter re-sites per patient
 - Local infection
 - Mortality
 - Pain
 - Satisfaction

Search methods for identification of studies

There was no restriction on language. If foreign language studies had been found, we intended to seek initial translation of abstracts for the application of the inclusion and exclusion criteria. Where necessary, the methods, results, and discussion sections would have been translated for inclusion in the review.

Electronic searches

For this update the Cochrane Vascular Trials Search Co-ordinator (TSC) searched the Cochrane Vascular Specialised Register (last searched March 2015) and the Cochrane Register of Studies (CRS) (<http://www.metaxis.com/CRSWeb/Index.asp>) (2015, Issue 2). See [Appendix 1](#) for details of the search strategy used to search the CRS. The Cochrane Vascular Specialised Register is maintained by the TSC and is constructed from weekly electronic searches of MEDLINE, EMBASE, CINAHL, AMED, and through hand-searching relevant journals. The full list of the databases, journals, and conference proceedings which have been searched, as well as the search strategies used, are described in the [Specialised Register](#) section of the Cochrane Vascular module in the *Cochrane Library* (www.cochranelibrary.com).

Searching other resources

We contacted researchers and manufacturers in order to obtain any unpublished data. Reference lists of potentially useful articles were also searched.

We also searched the following clinical trials registries;

- ClinicalTrials.gov (<http://clinicaltrials.gov/>) (10 April 2015) using the terms peripheral and catheter and routine
- World Health Organization International Clinical Trials Registry Platform (ICTRP) (<http://apps.who.int/trialsearch/>) (10 April 2015) using the terms peripheral and catheter

Data collection and analysis

Selection of studies

Titles and abstracts identified through the search process were independently reviewed by JW, SO, and CR. Full reports of all potentially relevant trials were retrieved for further assessment of eligibility based on the inclusion criteria. As the review authors were also the investigators on some of the included trials, assessment was allocated to a review author who was not an investigator. Differences of opinion were settled by consensus or referral to a third review author. There was no blinding of authorship.

Data extraction and management

Following Cochrane Vascular recommendations, two review authors independently extracted data to a pre-tested data extraction form. Disagreements were resolved by discussion and, where necessary, by a third review author. We contacted authors of published and unpublished trials for additional information.

We extracted the following main sets of data from each included study:

- lead author, date;
- study participant inclusion criteria;
- country where the research was conducted;
- participants' gender and age;
- study design, randomisation processes, allocation concealment;
- intervention descriptions;
- intervention setting (hospital, home, residential aged care facilities);
- numbers of participants in each trial arm, withdrawals and dropouts;
- outcome measures, time(s) at which outcomes were assessed.

The first review author entered the data into RevMan, with another review author checking the data entry accuracy.

Assessment of risk of bias in included studies

Two review authors independently assessed the included studies using the Cochrane Collaboration tool for assessing risk of bias ([Higgins 2011a](#)). This tool addresses six specific domains, namely sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other issues (for example extreme baseline imbalance). Disagreements between review authors were resolved by consensus or referral to a third review author. We contacted the investigators of included trials to resolve any ambiguities.

Measures of treatment effect

For individual trials, effect measures for categorical outcomes included risk ratio (RR) with its 95% confidence interval (CI). For statistically significant effects, the number needed to treat (NNT) or number needed to harm (NNH) was calculated. For continuous outcomes the effect measure we used was mean difference (MD) or, if the scale of measurement differed across trials, standardised mean difference (SMD), each with its 95% CI. For any meta-analyses (see below), for categorical outcomes the typical estimates of RR with their 95% CI were calculated; and for continuous outcomes the mean difference (MD) or a summary estimate for SMD, each with its 95% CI, were calculated. Data were analysed using the Cochrane Collaboration's Review Manager (RevMan) 5 software.

Summary of findings tables

To assess the overall body of evidence, we developed a 'Summary of findings' table for the four primary outcomes (catheter-related bloodstream infection; phlebitis; all-cause bloodstream infection; and cost) using GRADEprofiler. The quality of the body of evidence was assessed against five principle domains: 1) limitations in design and implementation; 2) indirectness of evidence or generalisability of findings; 3) inconsistency of results, for example unexplained heterogeneity and inconsistent findings; 4) imprecision of results where confidence intervals were wide; and 5) other potential biases, for example publication bias or high manufacturer involvement (Sch nemann 2011).

Unit of analysis issues

It is inadequate merely to compare longer and shorter dwell time intravenous devices (IVDs) on crude incidence of complications; this does not take into account the cumulative daily risk inherent with IVD use. There is clearly a 'per day risk' that is present, and grows with each day of IVD treatment, regardless of how many IVDs are used over the period of therapy. This cannot be extrapolated to mean that restricting (removing) individual IVDs will reduce overall risk. That is, an IVD in situ for seven days has seven days of exposure to risk compared with an IVD in use for only three days, but if the patient requires therapy for seven days in total then using multiple catheters over the period may not reduce risk but merely divide the same risk between multiple catheters. Appropriate time comparisons need to be made using statistics such as Kaplan-Meier analysis, logistic regression, or Cox proportional models. It is vital that the patient is used as the unit of measurement (denominator for comparison), not the IVD. If a patient requires therapy for example for five days, the patient may have one catheter used for the entire time or alternately multiple IVDs used over the five days. If the multiple catheters are viewed independently they may appear to have lower risk per catheter but the total risk for the patient over the five days may be the same. We dealt with this by only including studies where data were available per patient rather than per catheter. Where data were not originally analysed in this format we contacted the investigators (for example Van Donk 2009) to get these data. For comparison, we have also included an analysis of phlebitis per catheter days where this information was available.

Cross-over trials were not eligible. There were no cluster randomised trials.

Dealing with missing data

If any outcome data remained missing despite our attempts to obtain complete outcome data from authors, we assessed the risk of bias of the missing data and decided if the missing data were at 'low' or 'high' risk of bias according to our risk of bias criteria (Higgins 2011a). If data were considered to be missing at random,

we analysed the available information. If standard deviations were missing, we planned to impute them from other studies or, where possible, compute them from standard errors using the formula $SD = SE \times \sqrt{N}$ where these were available (Higgins 2008).

Assessment of heterogeneity

We explored clinical heterogeneity by examining potentially influential factors, for example intervention dwell time, care setting, or patient characteristics. We assessed statistical heterogeneity using the I^2 statistic (Higgins 2008). This examines the percentage of total variation across studies due to heterogeneity rather than to chance. Values of I^2 between 50% and 90% may represent substantial heterogeneity and values over 75% indicate a high level of heterogeneity. We carried out statistical pooling on groups of studies which were considered to be sufficiently similar. Where heterogeneity was absent or low ($I^2 = 0\%$ to 25%) we used a fixed-effect model; if there was evidence of heterogeneity ($I^2 > 25\%$) we used a random-effects model. If heterogeneity was high ($I^2 > 65\%$) we did not pool the data (Higgins 2003).

Assessment of reporting biases

Reporting bias was assessed using guidelines in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011a). Where sufficient study data were available for individual outcomes, funnel plots were developed and inspected for evidence of publication bias.

Data synthesis

Where appropriate, results of comparable trials were pooled using a fixed-effect model and the pooled estimate together with its 95% CI were reported. We conducted a narrative review of eligible studies where statistical synthesis of data from more than one study was not possible or considered not appropriate.

Subgroup analysis and investigation of heterogeneity

We planned to analyse potential sources of heterogeneity using the following subgroup analyses.

1. Type of randomisation (truly randomised versus not reported).
2. Concealment of allocation (adequate versus not reported).
3. Blinding (patients and clinicians blinded versus open-label).
4. Statement of withdrawals and losses to follow up in each group (stated versus not stated).
5. Intermittent versus continuous infusion.

Sensitivity analysis

We planned to perform sensitivity analyses to explore the effect of the following criteria.

1. Concealment of allocation.

2. Size of studies (< 100 patients versus at least 100 patients).
3. Duration of follow up.
4. Unpublished studies.

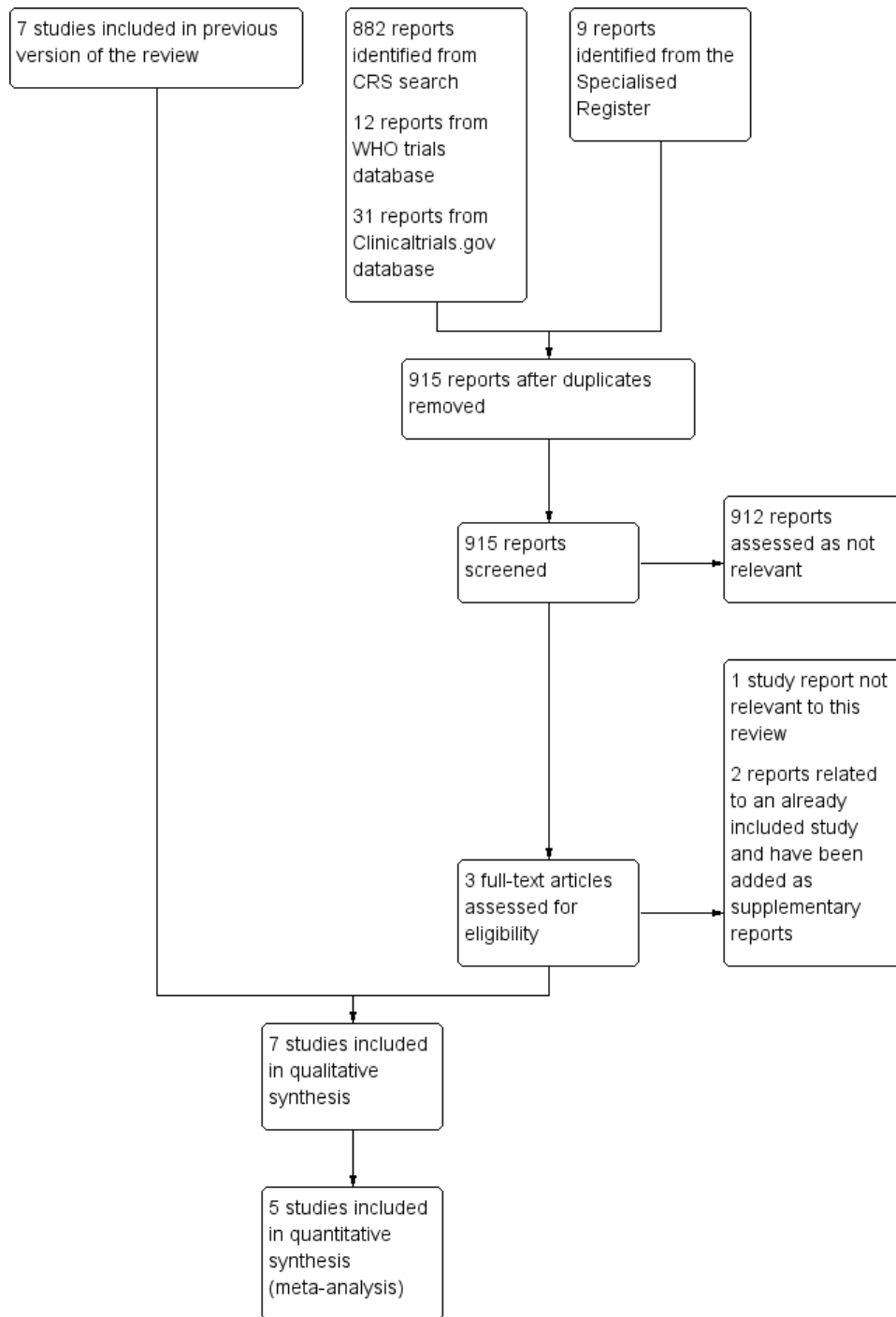
RESULTS

Description of studies

Results of the search

See [Figure 1](#).

Figure 1. Study flow diagram.



For this update, there were three additional citations which were considered potentially relevant following screening of the search results. Two of these were publications related to an already included study (Rickard 2012) and have been added as supplementary papers. The third was not relevant to this review. No additional trials were found in our search of trials registries.

Included studies

Because three of the authors of this review were also investigators in trials under consideration, we allocated the assessment of those trials to review authors who were not investigators for those particular studies.

Seven RCTs (Barker 2004; Nishanth 2009; Rickard 2010; Rickard 2012; Van Donk 2009; Webster 2007; Webster 2008) met the inclusion criteria (*see* table: Characteristics of included studies for details).

The seven trials involved a total of 4895 participants, with individual trial sizes ranging between 42 and 3283. One trial was carried out in England (Barker 2004), one in India (Nishanth 2009), the remaining five trials were Australian (Rickard 2010; Rickard 2012; Van Donk 2009; Webster 2007; Webster 2008). Five of the trials were conducted in single-centre, acute inpatient settings (Barker 2004; Nishanth 2009; Rickard 2010; Webster 2007; Webster 2008), one was a multi-centre trial in three Australian hospitals (Rickard 2012), and one was undertaken in a community setting (Van Donk 2009).

In six trials (Barker 2004; Nishanth 2009; Rickard 2010; Rickard 2012; Webster 2007; Webster 2008) patients were included if they were receiving either continuous infusions or intermittent infusions for medication therapy, whereas the catheters in the Van Donk 2009 trial were used for intermittent medication therapy only. In five trials (Rickard 2010; Rickard 2012; Van Donk 2009; Webster 2007; Webster 2008) the comparison was between routine care (planned three-day changes) and clinically-indicated changes. Barker 2004 and Nishanth 2009 compared 48-

hour changes with removal for clinical indications such as pain, catheter dislodgement, or phlebitis.

Five of the trials (Barker 2004; Rickard 2010; Rickard 2012; Webster 2007; Webster 2008) used a standard definition of two or more of the following: pain, warmth, erythema, swelling, or a palpable cord. Barker 2004 and Nishanth 2009 further classified phlebitis as either mild, moderate, or severe depending on the area of erythema (Barker 2004) or on the number of symptoms (Nishanth 2009). Van Donk 2009 included the same symptoms as other trials but scored them as either one or two depending on the severity. A score of two or more was classified as phlebitis, consequently a patient may have had only one symptom, for example pain, to receive a positive diagnosis.

Power calculations were reported by Nishanth 2009; Rickard 2010; Rickard 2012; Webster 2007; Webster 2008; and Van Donk 2009 but not by Barker 2004. All of the studies had institutional ethical approval.

Excluded studies

The table Characteristics of excluded studies contains the reasons for excluding nine trials. In summary, two were very small studies involving the administration of peripheral parenteral nutrition. Neither trial compared straightforward routine replacement with clinically-indicated removal (Kerin 1991; May 1996). One trial (Panadero 2002) compared one group that used the same catheter both intraoperatively and postoperatively with a group using two catheters, one during surgery and one postoperatively. The Haddad 2006 trial compared 72-hour changes with 96-hour changes, and the Cobb 1992; Eyer 1990; Nakae 2010; and Rijnders 2004 trials involved central venous catheters. The other excluded study was not an RCT (Arnold 1977).

Risk of bias in included studies

See individual 'Risk of bias' tables and Figure 2; Figure 3.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

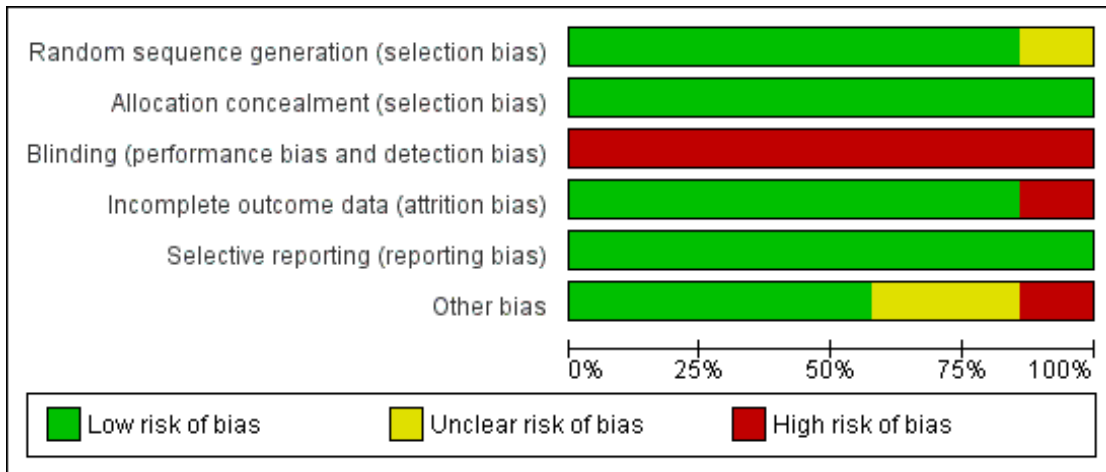


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding (performance bias and detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Barker 2004						
Nishanth 2009						
Rickard 2010						
Rickard 2012						
Van Donk 2009						
Webster 2007						
Webster 2008						

Allocation

Generation of random allocation sequence

All of the investigators reported that they used a computer-based sequence generator (Barker 2004; Nishanth 2009; Rickard 2010; Rickard 2012; Van Donk 2009; Webster 2007; Webster 2008).

Allocation concealment

Sealed envelopes were used for allocation concealment by Barker 2004; Nishanth 2009; and Van Donk 2009; the remaining four trials used a central telephone or computer-based service (Rickard 2010; Rickard 2012; Webster 2007; Webster 2008).

Blinding

It was not possible to blind either the participants or the healthcare providers in any of the trials.

Outcome assessment

The chief investigator assessed outcomes in the Barker 2004 and the Nishanth 2009 trial. In the Van Donk 2009; Webster 2007; and Webster 2008 trials, assessment was made by nurses caring for the patient or by a dedicated IV service nurse. None of the nurses were blinded to the group allocation but nor were any of them associated with the trial. In the Rickard 2010 and Rickard 2012 trials, outcome assessment was undertaken by a dedicated research nurse who was also aware of the allocation.

Incomplete outcome data

A flow chart was not provided by Barker 2004, so the numbers screened and eligible were unclear, nor were any dropouts reported. There was also an imbalance in the number of participants reported by group in this trial, which may indicate either a failure in the randomisation process in such a small trial or incomplete reporting. The number of protocol violations by group was not reported. There was complete reporting in the other six trials, all of which provided a flow of participants through each stage and used intention-to-treat analysis (Nishanth 2009; Rickard 2010; Rickard 2012; Van Donk 2009; Webster 2007; Webster 2008). In the Webster 2007; Webster 2008; and Van Donk 2009 trials,

approximately one third of the participants had protocol violations and in the Rickard 2012 trial, protocol violations occurred in 16% of the participants. Primarily these were in the routine replacement groups, where catheters were not replaced within the specified time period, reflecting day to day clinical practice.

Selective reporting

Study protocols were available for five trials (Rickard 2010; Rickard 2012; Van Donk 2009; Webster 2007; Webster 2008) and reporting followed pre-planned analyses. Barker 2004 and Nishanth 2009 reported on the expected primary outcomes.

Other potential sources of bias

In the Barker 2004 trial there were two definitions of phlebitis, one of which stated that two symptoms were necessary; yet it appears that erythema alone was diagnosed as phlebitis, with severity based on the area of inflammation. The extreme results in the Nishanth 2009 trial, where 100% of participants in the clinically-indicated group developed phlebitis compared with 9% in the two-day change group, suggests that chance or other unknown bias affected results in this small trial.

Effects of interventions

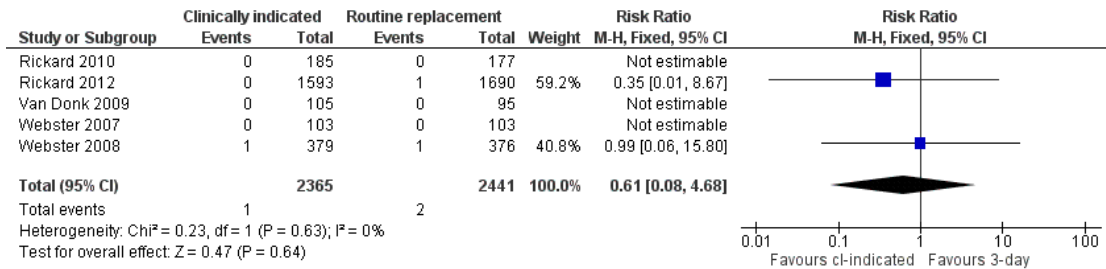
See: [Summary of findings for the main comparison Clinically-indicated versus routine changes for peripheral venous catheter-related complications](#)

Routine changes versus clinically-indicated changes

Catheter-related bloodstream infection (Analysis 1.1)

Catheter-related bloodstream infection was assessed in five trials (4806 patients) (Rickard 2010; Rickard 2012; Van Donk 2009; Webster 2007; Webster 2008). There were no reported CRBSIs in three of these trials (Rickard 2010; Van Donk 2009; Webster 2007). When results from the remaining two trials were combined there was a 39% reduction in the CRBSI rate favouring the clinically-indicated group (clinically-indicated 1/2365; routine change 2/2441). The RR was 0.61 but the confidence intervals were wide, creating uncertainty around the estimate (95% CI 0.08 to 4.68; P = 0.64) (Figure 4).

Figure 4. Forest plot of comparison: I Clinically-indicated versus routine change, outcome: I.1 Catheter-related bloodstream infection.

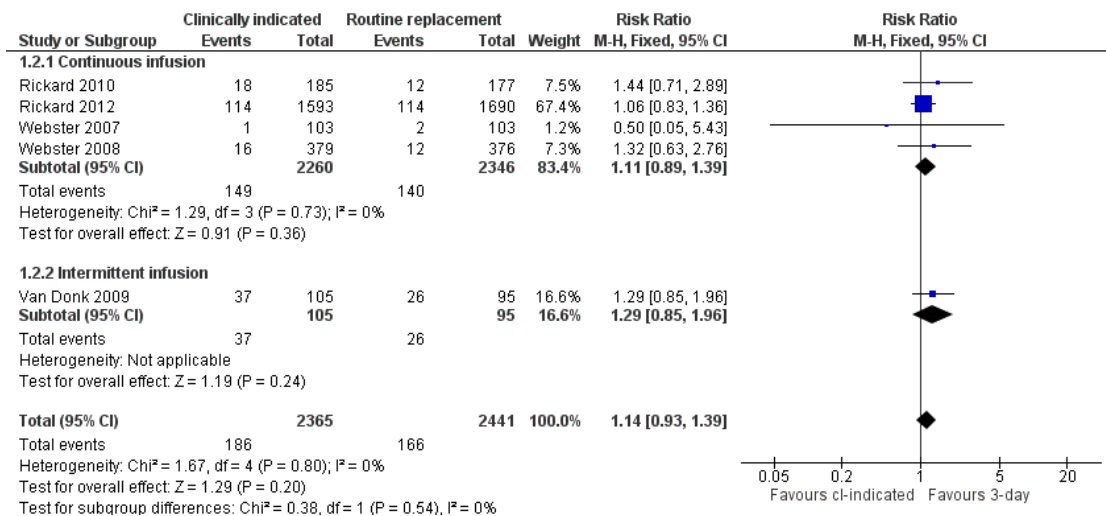


Phlebitis (Analysis 1.2 and Analysis 1.3)

All of the included studies reported incidence of phlebitis (4895 patients). When results of all trials were combined, heterogeneity was 65%. Consequently, we conducted a sensitivity analysis and removed the two trials with less than 100 participants, both of which used a two-day replacement schedule (Barker 2004; Nishanth 2009). Removing the two trials eliminated the heterogeneity ($I^2 = 0$).

Data from the remaining studies (4806 participants) were combined (Rickard 2010; Rickard 2012; Van Donk 2009; Webster 2007; Webster 2008). There was no difference in this outcome whether catheters were changed according to clinical indications or routinely (clinically-indicated 186/2365; 3-day change 166/2441; RR 1.14, 95% CI 0.93 to 1.39; P = 0.20). This result was unaffected by whether the infusion was continuous or intermittent (Figure 5).

Figure 5. Forest plot of comparison: I Clinically-indicated versus routine change, outcome: I.2 Phlebitis.

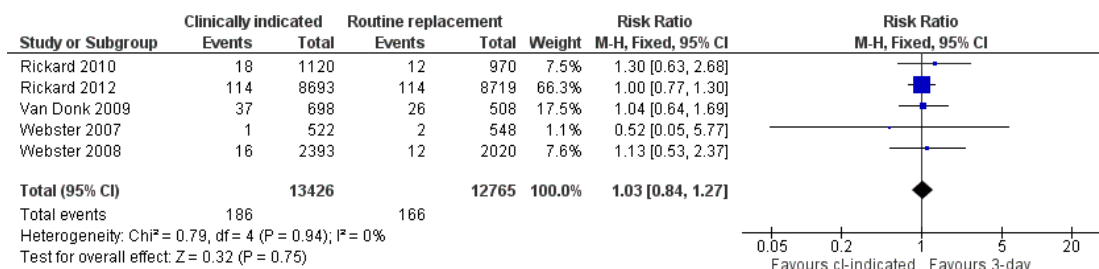


We also analysed the data by number of device days and, again, no differences between groups were observed (RR 1.03, 95% CI 0.84 to 1.27; P = 0.75) (Analysis 1.3; Figure 6). In the two trials using a two-day replacement schedule compared with clinically-indicated changes (Barker 2004; Nishanth 2009), heterogeneity was over 60% so results were not combined. In the first of these

two trials Barker 2004 reported that 11/26 (42.3%) participants in the clinically-indicated group developed phlebitis compared with 1/21 (4.8%) in the two-day change group. Nishanth 2009 diagnosed all of the participants in the clinically-indicated group (21/21; 100.0%) with phlebitis and 2/21 (9.5%) in the two-day

group.

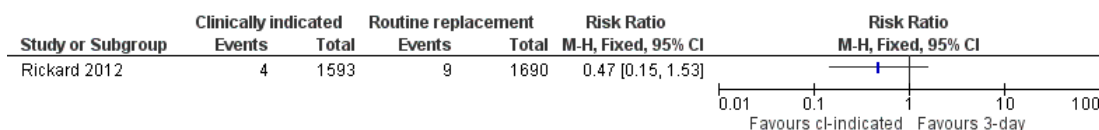
Figure 6. Forest plot of comparison: I Clinically-indicated versus routine change, outcome: I.3 Phlebitis per device days.



All-cause bloodstream infection (Analysis I.4)

One trial assessed this outcome (Rickard 2012). There was no difference in the all-cause bloodstream infection rate between the two groups (clinically-indicated: 4/1593 (0.02%); routine change 9/1690 (0.05%); P = 0.21) (Figure 7).

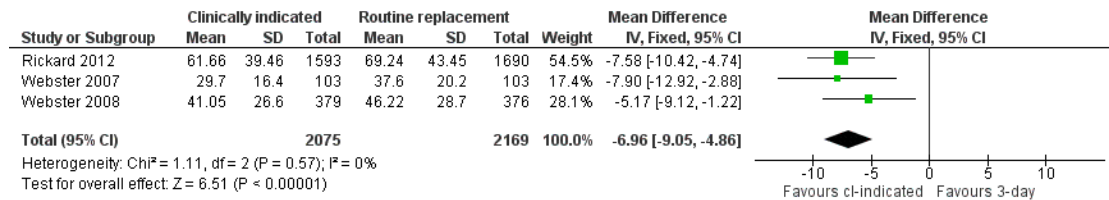
Figure 7. Forest plot of comparison: I Clinically-indicated versus routine change, outcome: I.4 All-cause bloodstream infection.



Cost (Analysis I.5)

In each of the three trials measuring this outcome (4244 participants) (Rickard 2012; Webster 2007; Webster 2008) cannulation costs, measured in Australian dollars (AUD), were lower by approximately AUD 7.00 in the clinically-indicated group (MD -6.96, 95% CI -9.05 to -4.86; P ≤ 0.00001) (Figure 8).

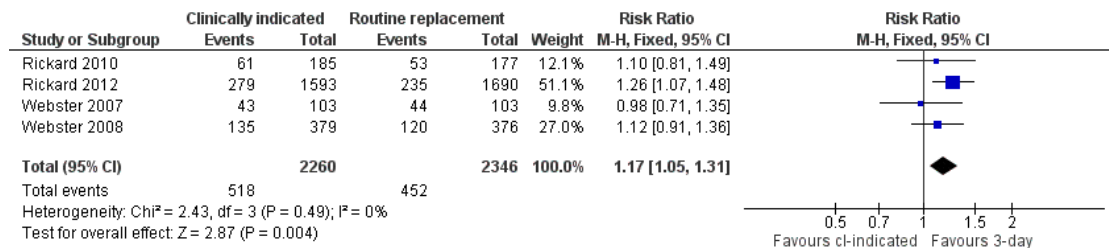
Figure 8. Forest plot of comparison: I Clinically-indicated versus routine change, outcome: 1.5 Cost.



Infiltration (Analysis 1.6)

A total of four trials assessed infiltration in 4606 participants (Rickard 2010; Rickard 2012; Webster 2007; Webster 2008). Infiltration of fluid into surrounding tissues was reported less often in the routine change group (452/2346; 19.3%) compared with the clinically-indicated group (518/2260; 22.9%). The RR was 1.17 (95% Ci 1.05 to 1.31; P = 0.004) (Figure 9).

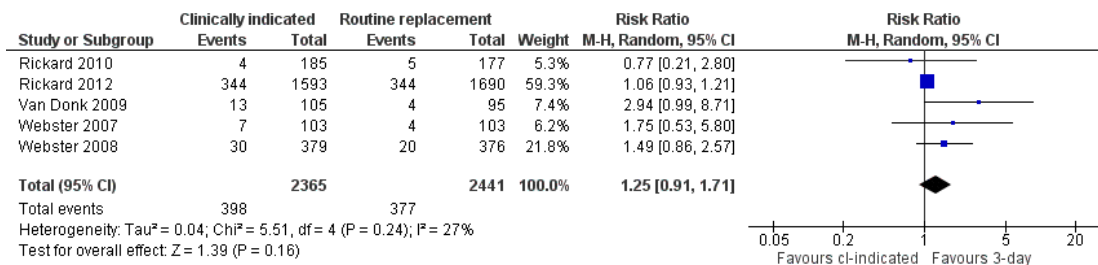
Figure 9. Forest plot of comparison: I Clinically-indicated versus routine change, outcome: 1.6 Infiltration.



Catheter occlusion/blockage (Analysis 1.7)

Five of the seven trials, reporting on 4806 participants, were included in this analysis (Rickard 2010; Rickard 2012; Van Donk 2009; Webster 2007; Webster 2008). Rates of catheter failure due to blockage were similar between groups (clinically-indicated 398/2395 (16.6%); routine replacement 377/2441 (15.40%); RR 1.25, 95% CI 0.91 to 1.71; P = 0.16) (Figure 10).

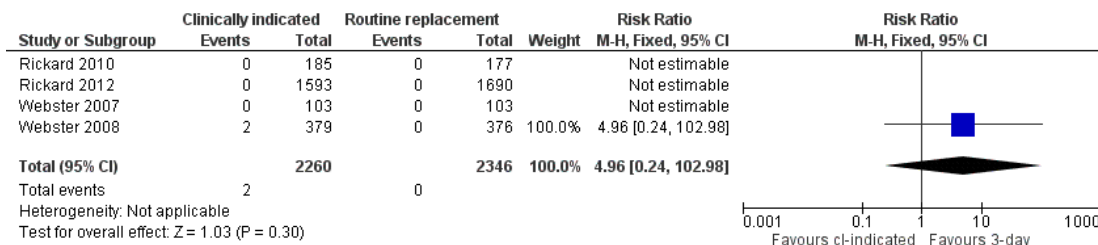
Figure 10. Forest plot of comparison: I Clinically-indicated versus routine change, outcome: I.7 Catheter blockage.



Local infection (Analysis I.8)

Among the four trials measuring local infection (Rickard 2010; Rickard 2012; Webster 2007; Webster 2008) no differences were found between groups (clinically-indicated 2/2260 (0.09%); routine replacement 0/2346 (0.0%); RR 4.96, 95% CI 0.24 to 102.98; P = 0.30) (Figure 11).

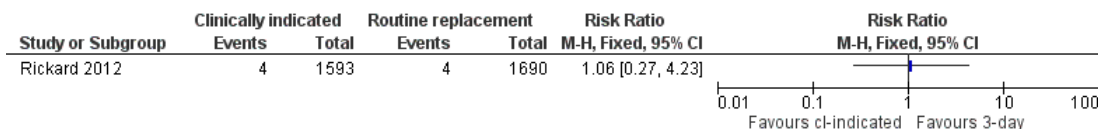
Figure 11. Forest plot of comparison: I Clinically-indicated versus routine change, outcome: I.8 Local infection.



Mortality (Analysis I.9)

Four deaths occurred in each group in the one trial (Rickard 2012) that assessed this outcome (RR 1.06, 95% CI 0.27 to 4.23; P = 0.93) (Figure 12).

Figure 12. Forest plot of comparison: I Clinically-indicated versus routine change, outcome: I.9 Mortality.



The pre-planned outcomes 'number of catheter re-sites per patient', 'pain' and 'satisfaction' were not reported by the studies included in the review.

Subgroup and sensitivity analysis

We planned to conduct subgroup analyses on 1) Type of randomisation (truly randomised versus not reported); 2) Concealment of allocation (adequate versus not reported) and; 3) Statement of withdrawals and losses to follow up in each group (stated versus not stated). However, there were too few studies in these subgroups to make any meaningful comparisons. Similarly, blinding was not possible in any of the studies. Nor did we conduct any of our pre-planned sensitivity analysis (except size of studies for the outcome 'phlebitis') for similar reasons.

DISCUSSION

Summary of main results

This systematic review analysed catheter-related bloodstream infection, phlebitis, other reasons for catheter failure, and cost with the intention of comparing routine catheter changes (at between two and four days) with replacing the catheter only if clinical signs were apparent.

The primary outcomes of this review suggest that patients are not adversely affected if the catheter is changed based on clinical indications rather than routinely, as recommended by the US Centers of Disease Control (O'Grady 2011). The rate of catheter-related bloodstream infection was similar in both groups, between 0.0% and 0.3%, and comparable to that previously reported in prospective studies (Maki 2006). A marginal but non-significant increase in the phlebitis rate in the clinically-indicated group was apparent when data were analysed by patient but became less perceptible when data were analysed per 1000 device days, which is a more clinically useful measure. In addition, most cases of phlebitis are mild in nature, requiring no treatment or removal of the catheter. There was no indication in our review that phlebitis was a precursor to bloodstream infection.

Catheter failure due to blockage was more frequent in the clinically-indicated group. This could be expected; all catheters will fail eventually and will need to be replaced if treatment is ongoing. The outcome is not clinically meaningful, it is simply an indicator of the longer dwell times in the clinically-indicated group. Since the 'treatment' for a blocked catheter is replacement of the catheter, it would not be of any benefit to the patient to replace the catheter earlier since it would not reduce the need for replacement, and would instead increase the chance of re-cannulation. Many catheters do not fail over the course of IV treatment, even with extended dwell times.

Cost was significantly less, around AUD 7, in the clinically-indicated group. This result was based on three studies and results were consistent and intuitively logical (fewer catheters, less clinician time and equipment). Although, this is a seemingly small amount, it corresponds to approximately 11% of catheter-related expenditure, which may represent a considerable saving to organisations with high use (Figure 8).

Overall completeness and applicability of evidence

Trials included in this systematic review directly addressed the review question and we were able to conduct a number of meta-analyses. Apart from the Barker 2004 and Nishanth 2009 trials, results from the other five trials were quite similar. Participants were representative of those usually managed in health care. They included patients in both acute and community settings and measured outcomes important to clinicians and patients, providing useful external validity. It has been suggested that insertion and management by an IV team may explain the inefficacy of routine replacement to prevent complications (Maki 2008), yet we saw no effect in trials that had significant numbers inserted by an IV team (Webster 2007; Webster 2008) or trials where insertion was by the general medical and nursing staff (Rickard 2010; Rickard 2012). In all of the trials except for Barker 2004 and Nishanth 2009 standard guidelines were followed for the control group, that is catheters were changed at between 72 and 96 hours, reflecting usual care. In the Barker 2004 and Nishanth 2009 trials, catheters were changed every 48 hours. None of the trials, except Rickard 2012, were powered to report on phlebitis alone, and some of the trials were very small. For example, the studies that showed statistically lower phlebitis rates in the clinically-indicated group (Barker 2004; Nishanth 2009) involved just 47 and 42 people respectively and showed differences between the control and intervention groups that were quite dissimilar to all of the other studies. Consequently, results of these two trials should be interpreted with caution, particularly results from the Nishanth 2009 trial where all patients in the clinically-indicated group developed phlebitis compared with none in the two-day change group. It seems unlikely that these results would have occurred by chance but correspondence with trial authors shed no further light on these extreme results. There are no other published papers showing phlebitis rates of 100%.

Five of the seven included trials were conducted in Australia; this imbalance is difficult to understand. It would be useful to see similar studies from other healthcare systems to test the robustness of results from this review.

Neither pain nor satisfaction were measured in any of the reviewed studies and would be a useful addition to any future trial.

Quality of the evidence

See [Summary of findings for the main comparison](#)

Limitations in study design and implementation

Risk of bias was assessed according to six components: sequence generation, allocation concealment, blinding, selective outcome reporting, incomplete follow up, and other potential biases. All of the studies avoided selection bias and ensured allocation concealment. The methodological quality of most of the RCTs was high with one exception. It was not possible to blind the primary outcome in any of the trials. Blinding was not possible because it was necessary to identify the catheter as either 'routine change' or 'clinically indicated', to prevent inadvertent routine replacement of catheters in the intervention group. It is unclear if this had any bearing on outcomes but the review authors argue that it is unlikely (Figure 2; Figure 3). In the Barker 2004 and Nishanth 2009 trials, the investigator was directly involved in diagnosing phlebitis; in all of the other studies either medical staff, ward nurses, IV therapy staff, or research nurses evaluated the outcomes. As one author noted, it is routine practice to record reasons for removal of an intravenous catheter in the medical record, and it is unlikely that such entries would be falsified based on group allocation (Webster 2008).

Indirectness of evidence

All of the trials compared routine changes with clinically-indicated changes. However, five trials used a three to four-day change schedule and two trials changed catheters every two days. Consequently, three to four-day results may provide indirect evidence for two-day changes, conversely two-day changes provide indirect evidence for a three to four-day change schedule. Additionally, only one study (Nishanth 2009) included patients who were from a developing country and who were "usually asthenic, many underhydrated/dehydrated on admission" (personal correspondence), so the evidence may be regarded as indirect for these types of patients.

Unexplained heterogeneity or inconsistency of results

When we combined results of studies that investigated the effect of different catheter replacement schedules on phlebitis, the heterogeneity was high. This was probably due to the different schedules for the routine catheter changes or population differences, or both. Small sample sizes may also have contributed to the extreme results, which caused the heterogeneity. We tested these assumptions by performing a sensitivity analysis, removing two of the seven studies. Results of the five trials are presented in the review text and the Summary of findings table (Summary of findings for the main comparison).

Imprecision of results

Confidence intervals were wide in the pooled outcomes of catheter-related bloodstream infection, local infection, and mortality (Figure 4; Figure 11; Figure 12) indicating a high level of

uncertainty around the effect size. Further research is therefore very likely to have an important impact on the confidence in the estimate of effect for these outcomes.

Publication bias

We feel confident that our comprehensive electronic searches identified all existing, published, randomised controlled trials addressing the review question.

Potential biases in the review process

Although the authors were investigators in one or more of the included trials, clearly described procedures were followed to prevent potential biases in the review process. A careful literature search was conducted and the methods we used are transparent and reproducible. None of the authors has any conflict of interests.

Agreements and disagreements with other studies or reviews

Our results concur with several prospective observational studies, which found no additional risk in extending IVD dwell times (Bregenzler 1998; Catney 2001; Homer 1998; White 2001). We believe the reason for this is the similarity in the mean dwell times between the intervention and control arms. Each of the included studies were pragmatic trials and, in real life, many catheters are not changed within the prescribed time frames. For example, in three-day protocols the 72-hour period may occur in the middle of the night; or a decision may be made to leave an existing catheter in place if the patient is due for discharge the following day or if they are thought to have poor veins. Conversely, the catheter may need to be removed early in any clinically-indicated group if the patient's catheter becomes blocked or infiltration or phlebitis occurs, or the patient is discharged within a couple of days of catheter insertion.

Our results also support the CDC guidelines for peripheral catheter replacement in children, which state "replace peripheral catheters in children only when clinically indicated" (O'Grady 2011). Similarly, in a guideline for timing peripheral intravenous replacement (Ho 2011) findings from the original version of this review were replicated (Webster 2010).

AUTHORS' CONCLUSIONS

Implications for practice

The review found no difference in catheter-related bloodstream infection or phlebitis rates whether peripheral intravenous catheters are changed routinely every 72 to 96 hours or when clinically

indicated. The consistency in these results, which include a very large multi-site study, indicate that healthcare organisations should adopt a clinically-indicated replacement policy. This would provide significant cost savings and would also be welcomed by patients, who would be spared the unnecessary pain of routine re-sites in the absence of clinical indications. Busy clinical staff would also reduce time spent on this intervention. To minimise peripheral catheter-related complications, the insertion site should be inspected at each shift change and the catheter removed if signs of inflammation, infiltration, or blockage are present.

Implications for research

Any future trial should use standard definitions for phlebitis and be sufficiently large to show true differences. Based on results from the meta-analysis in this review, at least 2500 participants would be required in each arm of any future trial to show a lowering of

phlebitis rates from 8% to 6% ($\alpha = 0.05$ and 80% power). Neither pain nor satisfaction were measured in any of the reviewed studies and would be a useful addition to any future trial. Although costs were estimated in some of the included trials, a careful economic analysis of routine versus clinically-indicated replacement would be helpful for healthcare administrators. There was also some evidence from this review that different results may occur when the population is drawn from a developing country. Consequently, trials conducted in a wider variety of healthcare systems would add to the external validity of the review's results.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Barker 2004

Methods	Study design: Single-centre RCT. Method of randomisation: Computer generated. Concealment of allocation: Sealed envelopes.	
Participants	Country: England. Number: 47 patients in general medical or surgical wards. Clinically indicated: 43 catheters were inserted in 26 patients. Routine replacement: 41 catheters were inserted in 21 patients Age: Clinically indicated 60.5 yrs (15.5); routine replacement 62.7 yrs (18.2) Sex (M/F): Clinically indicated 15/11; routine replacement 14/7. Inclusion criteria: Hospital inpatients receiving crystalloids and drugs. Exclusion criteria: Not stated.	
Interventions	Clinically indicated: Catheters were removed if the site became painful, the catheter dislodged or there were signs of PVT Routine replacement: Catheters were replaced every 48 hours.	
Outcomes	Primary: Incidence of PVT defined as “the development of two or more of the following: pain, erythema, swelling, excessive warmth or a palpable venous cord”	
Notes	<p>PVT was defined as “the development of two or more of the following: pain, erythema, swelling, excessive warmth or a palpable venous cord”. However, in the discussion, the author stated that “even a small area of erythema was recorded as phlebitis” (i.e., only one sign)</p> <p>It is unclear what proportion of patients were on continuous infusion Catheters were inserted “at the instruction of the principal investigator” “All patients were reviewed daily by the principal investigator, and examined for signs of PVT at the current and all previous infusion sites”</p>	
Risk of bias		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Comment: Computer generated (personal communication with author).
Allocation concealment (selection bias)	Low risk	Comment: Sealed envelopes (personal communication with author).
Blinding (performance bias and detection bias) All outcomes	High risk	Comment: Neither study personnel nor participants were blinded.

Barker 2004 (Continued)

Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: In this small sample, there were five fewer patients in the routine replacement group. No explanation was provided for the unequal sample size. No dropouts or loss to follow up were reported
Selective reporting (reporting bias)	Low risk	Comment: Phlebitis was the only outcome planned.
Other bias	High risk	Comment: The chief investigator allocated patients and was responsible for outcome evaluation No sample size calculation.

Nishanth 2009

Methods	Study design: Single-centre RCT. Method of randomisation: Not stated Concealment of allocation: Sequentially numbered sealed envelopes.	
Participants	Country: India. Number: 42 patients in surgical wards. Clinically indicated: 21. Routine replacement: 21 Age: Clinically indicated 40.2 yrs (15.0); routine replacement 42.9 yrs (15.0) Sex (M/F): Clinically indicated 17/4; routine replacement 16/5. Inclusion criteria: Hospital inpatients admitted for major abdominal surgery Exclusion criteria: Receiving total parenteral nutrition, duration of therapy expected to be < three days, if a cannula was already in situ, terminally ill patients	
Interventions	Clinically indicated: Catheters were removed if the site became painful, the catheter dislodged or there were signs of PVT Routine replacement: Catheters were replaced every 48 hours.	
Outcomes	Primary: Incidence of PVT defined as “the development of two or more of the following: pain, erythema, swelling, excessive warmth or a palpable venous cord”	
Notes		
Risk of bias		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated.
Allocation concealment (selection bias)	Low risk	Quote “group name was placed (on) an opaque serially numbered sealed envelope

Nishanth 2009 (Continued)

		(SNOSE).” Comment: Presumably the authors meant 'in' an opaque serially numbered sealed envelope - based on subsequent information
Blinding (performance bias and detection bias) All outcomes	High risk	Evidence for participants: Quote “unblinded study”. Evidence for personnel: As above. Evidence for outcomes: As above.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: Data for all patients were available.
Selective reporting (reporting bias)	Low risk	Comment: Stated outcomes were reported but original protocol not sighted
Other bias	Unclear risk	Extreme results: In this small trial, 100% of participants in the clinically indicated group developed phlebitis compared with 9% in the 2-day change group, which suggests that chance or other unknown bias affected results

Rickard 2010

Methods	Study design: Single-centre RCT. Method of randomisation: Computer generated. Concealment of allocation: Telephone service.
Participants	Country: Australia. Number: 362 patients requiring IV therapy in general medical or surgical wards. Clinically indicated: 280 catheters were inserted in 185 patients. Routine replacement: 323 catheters were inserted in 177 patients Age: Clinically indicated 62.7 yrs (15.5); routine replacement 65.1 yrs (17.3) Sex (M/F): Clinically indicated 82/103; routine replacement 81/91. Inclusion criteria: Patients in over 18 years, expected to have a peripheral intravenous device (IVD), requiring IV therapy for at least 4 days Exclusion criteria: Patients who were immunosuppressed, had an existing bloodstream infection or those in whom an IVD had been in place for > 48 hours
Interventions	Clinically indicated: Catheters were removed if there were signs of phlebitis, local infection, bacteraemia, infiltration or blockage Routine replacement: Catheters were replaced every 72 - 96 hours.
Outcomes	Primary: Phlebitis per person and per 1000 IVD days (defined as two or more of the following: pain, erythema, purulence, infiltration, palpable venous cord). IVD-related bacteraemia Secondary: Hours of catheterisation; number of IV devices; device-related bloodstream infection; infiltration; local infection

Rickard 2010 (Continued)

Notes	Approximately 75% of patients were receiving a continuous infusion	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Comment: Computer generated.
Allocation concealment (selection bias)	Low risk	Quote "assignment was concealed until randomisation by use of a telephone service"
Blinding (performance bias and detection bias) All outcomes	High risk	Comment: Neither study personnel nor participants were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: Results from all enrolled patients were reported.
Selective reporting (reporting bias)	Low risk	Comment: The protocol was available. All nominated outcomes were reported
Other bias	Unclear risk	Comment: Significantly more patients in the routine change group received IV antibiotics (73.1% versus 62.9%)

Rickard 2012

Methods	<p>Study design: Multi-centre RCT.</p> <p>Method of randomisation: Computer generated, stratified by site.</p> <p>Concealment of allocation: Allocation concealed until eligibility criteria was entered into a hand-held computer</p>
Participants	<p>Country: Australia.</p> <p>Number: 3283 patients requiring IV therapy in general medical or surgical wards. Clinically indicated: 1593 patients. Routine replacement: 1690 patients</p> <p>Age: Clinically indicated 55.1 yrs (18.6); routine replacement 55.0 yrs (18.4)</p> <p>Sex (M/F): Clinically indicated 1022/571; routine replacement 1034/656</p> <p>Inclusion criteria: Patients, or their representative able to provide written consent; over 18 years, expected to have a peripheral intravenous device (IVD) in situ, requiring IV therapy for at least 4 days</p> <p>Exclusion criteria: Patients who were immunosuppressed, had an existing blood stream infection or those in whom an IVD had been in place for > 48 hours or it was planned for the catheter to be removed < 24 hours</p>

Interventions	Clinically indicated: Catheters were removed if there were signs of phlebitis, local infection, bacteraemia, infiltration or blockage Routine replacement: Catheters were replaced every 72 - 96 hours.	
Outcomes	Primary: Phlebitis during catheterisation or within 48 hrs of removal (defined as two or more of the following: pain, erythema, swelling, purulent discharge, palpable venous cord) Secondary: Catheter-related bloodstream infection, all-cause bloodstream infection, local venous infection, colonisation of the catheter tip, infusion failure, number of catheters per patient, overall duration of intravenous therapy, cost, mortality	
Notes		
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Random allocations were computer-generated".
Allocation concealment (selection bias)	Low risk	Quote: "Random allocations were computer-generated on a hand-held device, at the point of each patient's entry, and thus were concealed to patients, clinical staff and research staff until this time"
Blinding (performance bias and detection bias) All outcomes	High risk	Evidence for participants: Quote "Patients and clinical staff could not be blinded". Evidence for personnel: Quote "Research nurses were similarly not masked". Evidence for outcomes: Quote "... laboratory staff were masked for rating of all microbiological end-points, and a masked, independent medical rater diagnosed catheter-related infections and all bloodstream infections"
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analysis reported.
Selective reporting (reporting bias)	Low risk	The protocol was available and all pre-defined outcomes were reported
Other bias	Low risk	No other known risks of bias.

Methods	<p>Study design: RCT. Method of randomisation: Computer generated. Concealment of allocation: Sealed envelopes.</p>	
Participants	<p>Country: Australia. Number: 200. Clinically indicated: 105 patients. Routine replacement: 95 patients Age: Clinically indicated 62.8 yrs (18.2); routine replacement 54.5 yrs (19.0) Sex (M/F): Not stated. Inclusion criteria: Adult patients who could be treated at home for an acute illness and had a 20, 22, or 24 gauge catheter inserted in an upper extremity Exclusion criteria: Not stated.</p>	
Interventions	<p>Clinically indicated: Catheters were removed if there were signs of phlebitis, local infection, bacteraemia, infiltration or blockage Routine replacement: Catheters were replaced every 72 - 96 hours.</p>	
Outcomes	<p>Primary: Phlebitis per patient and per 1000 device days (phlebitis was defined as a total score of 2 or more points from the following factors: pain (on a 10-point scale, 1 = 1 point, and 2 or more = 2 points; redness (less than 1cm = 1 point, and 1 or more cm = 2 points); swelling (as for redness); and discharge (haemoserous ooze under dressing = 1 point, and haemoserous ooze requiring dressing change or purulence = 2 points) Also reported on: Suspected IVD-related bacteraemia and occlusion/blockage.</p>	
Notes		
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Comment: Computer generated allocation (personal communication with author)
Allocation concealment (selection bias)	Low risk	Quote: "Randomization was concealed until treatment via sealed envelopes"
Blinding (performance bias and detection bias) All outcomes	High risk	Comment: Neither study personnel nor participants were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: Participant flow chart provided. Results from all enrolled patients were reported
Selective reporting (reporting bias)	Low risk	Comment: All planned outcomes were reported.
Other bias	Low risk	No other known risks of bias.

Methods	<p>Study design: Single-centre RCT.</p> <p>Method of randomisation: Computer generated.</p> <p>Concealment of allocation: Allocation concealed until telephone contact made with an independent person</p>	
Participants	<p>Country: Australia.</p> <p>Number: 206. Clinically indicated: 103 patients. Routine replacement: 103 patients</p> <p>Age: Clinically indicated 60.2 yrs (16.2); routine replacement 63.1 yrs (17.3)</p> <p>Sex (M/F): Clinically indicated 53/50; routine replacement 54/49.</p> <p>Inclusion criteria: At least 18 yrs of age, expected to have a peripheral intravenous device (IVD) in situ, requiring IV therapy for at least 4 days, catheter inserted by a member of the IV team</p> <p>Exclusion criteria: Immunosuppressed patients and those with an existing bloodstream infection</p>	
Interventions	<p>Clinically indicated: Catheters removed if there were signs of phlebitis, local infection, bacteraemia, infiltration or blockage</p> <p>Routine replacement: Catheters replaced every 3 days.</p>	
Outcomes	<p>Primary: Composite measure of any reason for an unplanned catheter removal</p> <p>Secondary: Cost (For intermittent infusion: 20 minutes nursing/medical time, a cannula, a 3 way tap, a basic dressing pack, gloves, a syringe, transparent adhesive dressing, skin disinfection and local anaesthetic per insertion. For patients receiving a continuous infusion: all the above costs plus the additional cost of replacing all associated lines, solutions and additives which are discarded when an IV catheter is changed (based on an intravenous administration set, 1 litre sodium chloride 0.09%)</p>	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization was by computer generated random number list, stratified by oncology status"
Allocation concealment (selection bias)	Low risk	Quote: "Allocation was made by phoning a person who was independent of the recruitment process"
Blinding (performance bias and detection bias) All outcomes	High risk	<p>Evidence for participants: Comment: Participants could not be blinded.</p> <p>Evidence for personnel: Quote "clinical staff were subsequently aware of the treatment group"</p> <p>Evidence for outcomes: Quote: "research staff had no involvement in nominating the reason for catheter removal or in diagnosing</p>

Webster 2007 (Continued)

		phlebitis” “Staff in the microbiological laboratory were blind to group assignment of catheters submitted for testing”
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: All recruited patients were accounted for in the results.
Selective reporting (reporting bias)	Low risk	Comment: Protocol was available. All planned outcomes were reported.
Other bias	Low risk	No other known risks of bias.

Webster 2008

Methods	Study design: Single-centre RCT. Method of randomisation: Computer generated. Concealment of allocation: Telephone randomisation.	
Participants	Country: Australia. Number: 755. Clinically indicated: 379 patients. Routine replacement: 376 patients Age: Clinically indicated 60.1 yrs (17.1); routine replacement 58.8 yrs (18.8) Sex (M/F): Clinically indicated 248/131; routine replacement 233/143. Inclusion criteria: At least 18 yrs of age, expected to have a IVD in situ, requiring IV therapy for at least 4 days Exclusion criteria: Immunosuppressed patients and those with an existing bloodstream infection	
Interventions	Clinically indicated: Catheter removed if there were signs of phlebitis, local infection, bacteraemia, infiltration or blockage Routine replacement: Catheter replaced every 3 days.	
Outcomes	Primary: A composite measure of phlebitis (defined as two or more of the following: pain, erythema, purulence, infiltration, palpable venous cord) and infiltration Secondary: Infusion-related costs. Cost (For intermittent infusion: 20-minutes nursing/medical time, a cannula, a 3-way tap, a basic dressing pack, gloves, a syringe, transparent adhesive dressing, skin disinfection and local anaesthetic per insertion. For patients receiving a continuous infusion: all the above costs plus the additional cost of replacing all associated lines, solutions and additives which are discarded when an IV catheter is changed (based on an intravenous administration set, 1 litre sodium chloride 0.09%) Individual reasons for catheter failure (occlusion/blockage, local infection) Also reported: Bacteraemia rate.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement

Webster 2008 (Continued)

Random sequence generation (selection bias)	Low risk	Quote: “Block randomisation was by a computer generated random number list”
Allocation concealment (selection bias)	Low risk	Quote: “... telephoned a contact who was independent of the recruitment process for allocation consignment”
Blinding (performance bias and detection bias) All outcomes	High risk	Neither study personnel nor participants were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All recruited patients were accounted for in the results.
Selective reporting (reporting bias)	Low risk	Protocol was available. All planned outcomes were reported.
Other bias	Low risk	No other known risks of bias.

IV: intravenous

IVD: peripheral intravenous device

PVT: peripheral vein infusion thrombophlebitis

RCT: randomised controlled trial

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Arnold 1977	Not a randomised controlled trial
Cobb 1992	Involved central, not peripheral lines
Eyer 1990	Involved pulmonary artery or arterial catheters, not peripheral catheters
Haddad 2006	End point was lymphangitis
Kerin 1991	Patients were receiving parenteral nutrition
May 1996	Patients were receiving parenteral nutrition
Nakae 2010	Involved central, not peripheral lines
Panadero 2002	Compared the use of a single intraoperative and postoperative catheters with two catheters, one used intraoperatively and a separate catheter for postoperative use

(Continued)

Rijnders 2004	Involved central, not peripheral lines
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DATA AND ANALYSES

Comparison 1. Clinically-indicated versus routine change

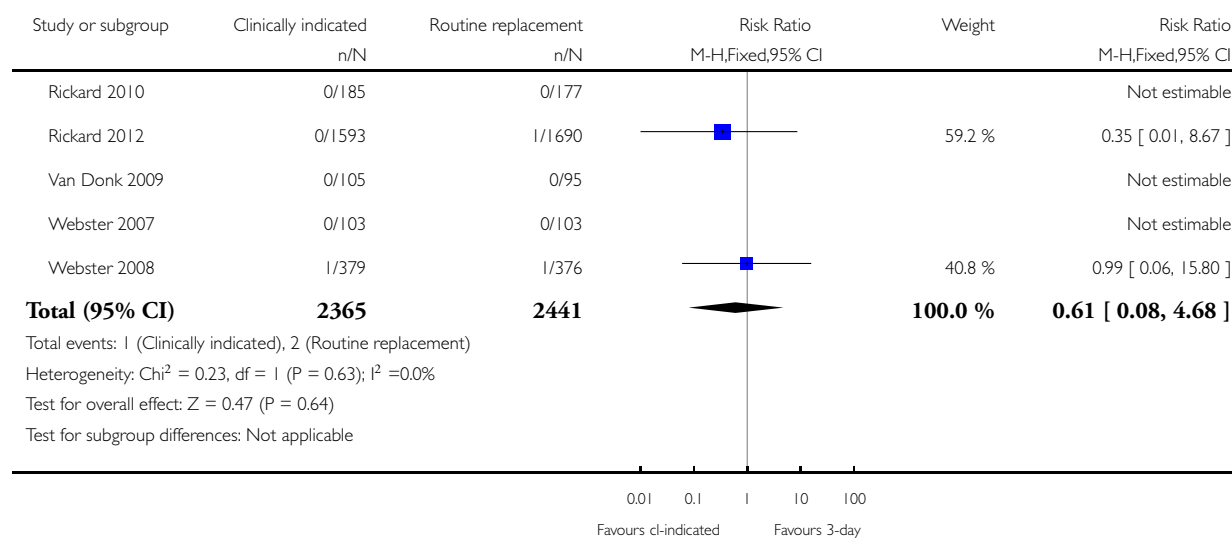
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Catheter-related blood stream infection	5	4806	Risk Ratio (M-H, Fixed, 95% CI)	0.61 [0.08, 4.68]
2 Phlebitis	5	4806	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.93, 1.39]
2.1 Continuous infusion	4	4606	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [0.89, 1.39]
2.2 Intermittent infusion	1	200	Risk Ratio (M-H, Fixed, 95% CI)	1.29 [0.85, 1.96]
3 Phlebitis per device days	5	26191	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.84, 1.27]
4 All-cause blood stream infection	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
5 Cost	3	4244	Mean Difference (IV, Fixed, 95% CI)	-6.96 [-9.05, -4.86]
6 Infiltration	4	4606	Risk Ratio (M-H, Fixed, 95% CI)	1.17 [1.05, 1.31]
7 Catheter blockage	5	4806	Risk Ratio (M-H, Random, 95% CI)	1.25 [0.91, 1.71]
8 Local infection	4	4606	Risk Ratio (M-H, Fixed, 95% CI)	4.96 [0.24, 102.98]
9 Mortality	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1 Clinically-indicated versus routine change, Outcome 1 Catheter-related blood stream infection.

Review: Clinically-indicated replacement versus routine replacement of peripheral venous catheters

Comparison: 1 Clinically-indicated versus routine change

Outcome: 1 Catheter-related blood stream infection

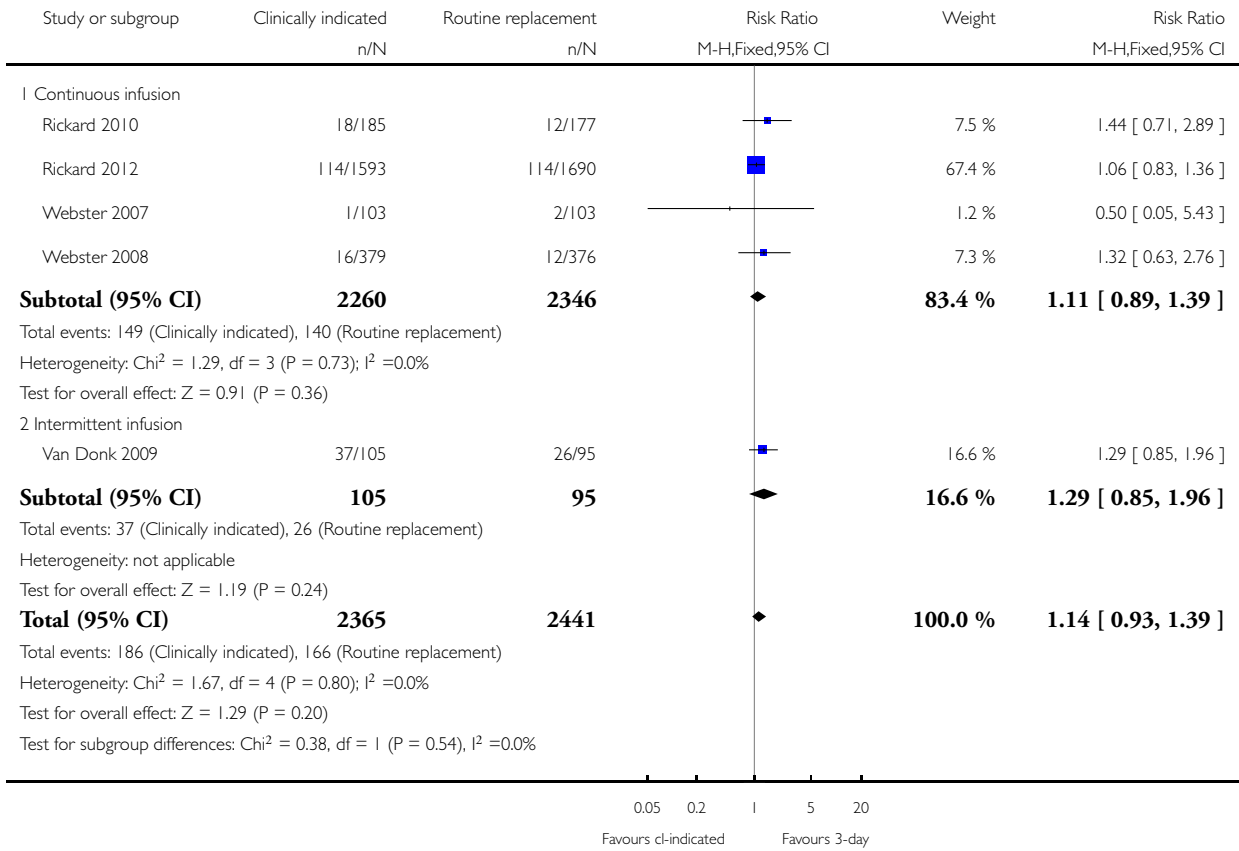


Analysis 1.2. Comparison 1 Clinically-indicated versus routine change, Outcome 2 Phlebitis.

Review: Clinically-indicated replacement versus routine replacement of peripheral venous catheters

Comparison: 1 Clinically-indicated versus routine change

Outcome: 2 Phlebitis

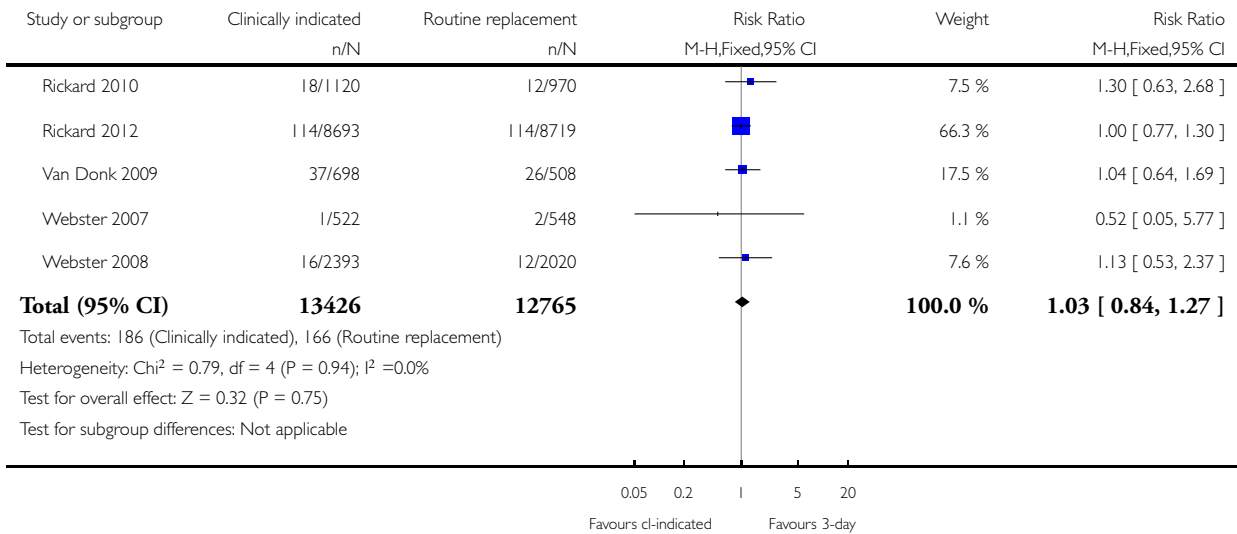


Analysis I.3. Comparison I Clinically-indicated versus routine change, Outcome 3 Phlebitis per device days.

Review: Clinically-indicated replacement versus routine replacement of peripheral venous catheters

Comparison: I Clinically-indicated versus routine change

Outcome: 3 Phlebitis per device days

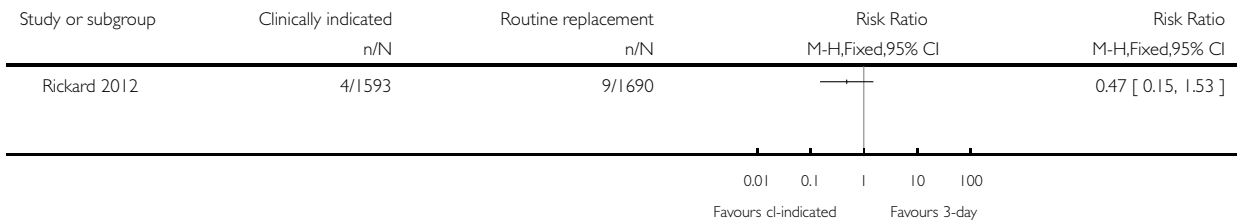


Analysis I.4. Comparison I Clinically-indicated versus routine change, Outcome 4 All-cause blood stream infection.

Review: Clinically-indicated replacement versus routine replacement of peripheral venous catheters

Comparison: I Clinically-indicated versus routine change

Outcome: 4 All-cause blood stream infection

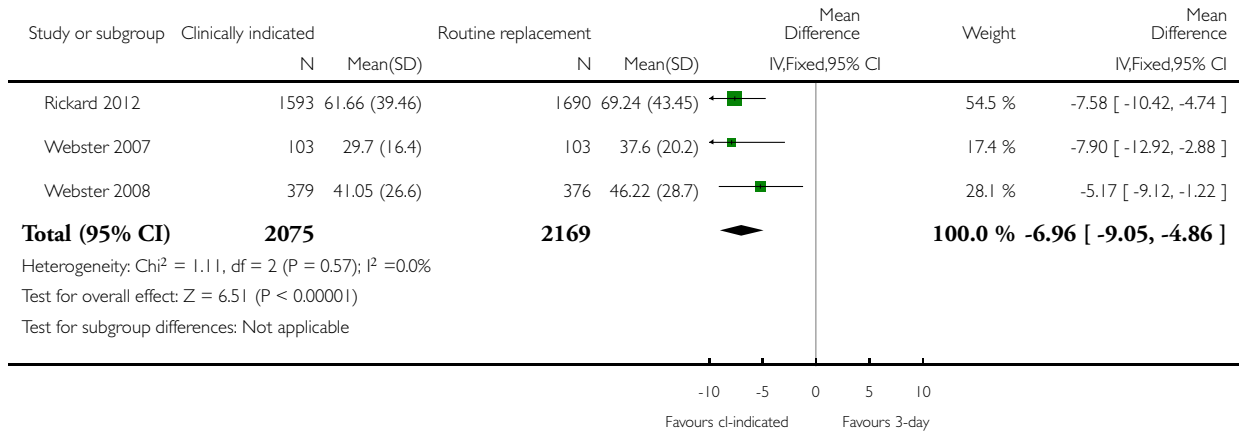


Analysis 1.5. Comparison 1 Clinically-indicated versus routine change, Outcome 5 Cost.

Review: Clinically-indicated replacement versus routine replacement of peripheral venous catheters

Comparison: 1 Clinically-indicated versus routine change

Outcome: 5 Cost

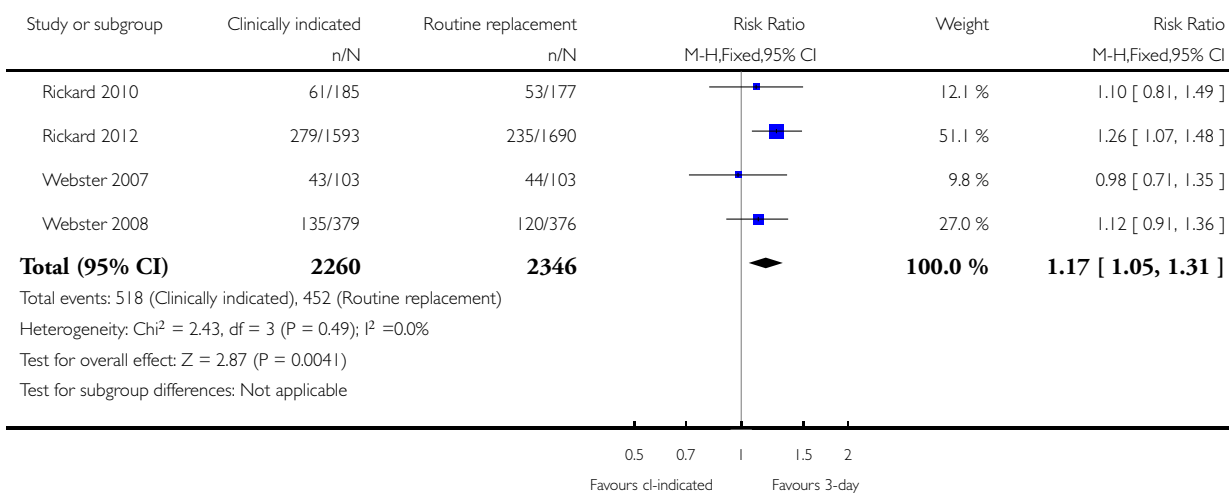


Analysis 1.6. Comparison 1 Clinically-indicated versus routine change, Outcome 6 Infiltration.

Review: Clinically-indicated replacement versus routine replacement of peripheral venous catheters

Comparison: 1 Clinically-indicated versus routine change

Outcome: 6 Infiltration

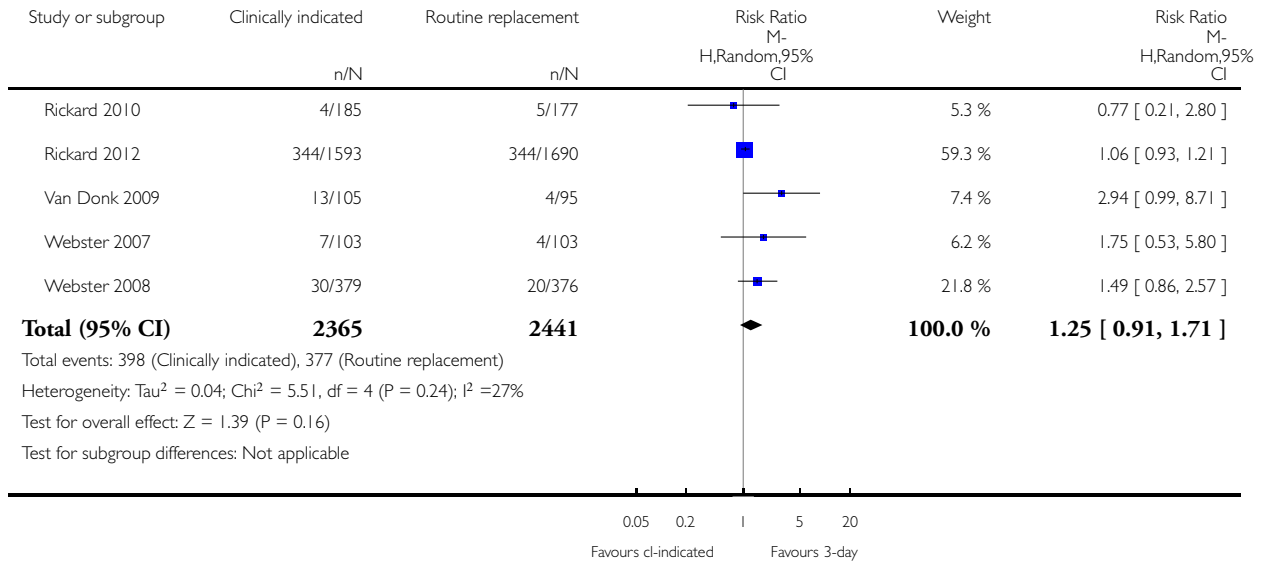


Analysis 1.7. Comparison 1 Clinically-indicated versus routine change, Outcome 7 Catheter blockage.

Review: Clinically-indicated replacement versus routine replacement of peripheral venous catheters

Comparison: 1 Clinically-indicated versus routine change

Outcome: 7 Catheter blockage

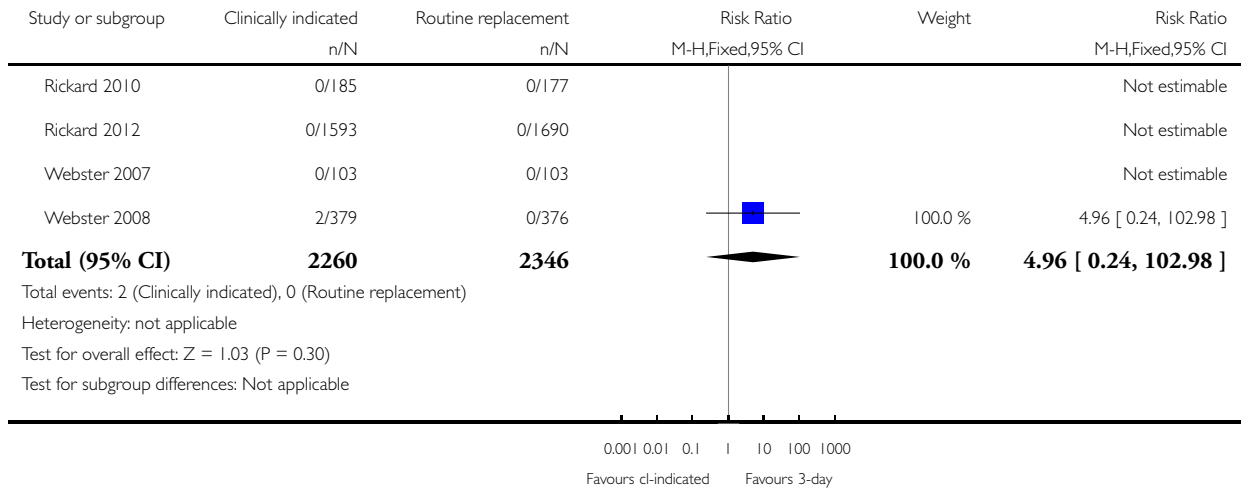


Analysis 1.8. Comparison 1 Clinically-indicated versus routine change, Outcome 8 Local infection.

Review: Clinically-indicated replacement versus routine replacement of peripheral venous catheters

Comparison: 1 Clinically-indicated versus routine change

Outcome: 8 Local infection

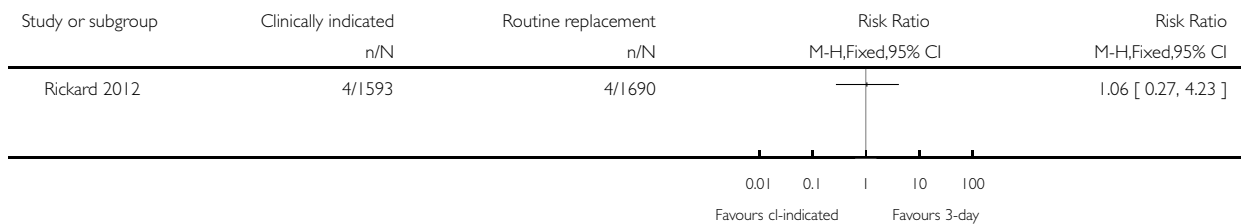


Analysis 1.9. Comparison 1 Clinically-indicated versus routine change, Outcome 9 Mortality.

Review: Clinically-indicated replacement versus routine replacement of peripheral venous catheters

Comparison: 1 Clinically-indicated versus routine change

Outcome: 9 Mortality



APPENDICES

Appendix I. CRS search strategy

#1	MESH DESCRIPTOR Infusions, Intravenous EXPLODE ALL TREES	8726
#2	MESH DESCRIPTOR Catheters, Indwelling EXPLODE ALL TREES	814
#3	MESH DESCRIPTOR Catheterization, Peripheral EXPLODE ALL TREES	635
#4	catheter*:TI,AB,KY	13341
#5	cannul*:TI,AB,KY	1778
#6	(iv near2 (therapy or treatment or device)):TI,AB,KY	530
#7	(intravenous near2 (therapy or treatment or device)):TI,AB, KY	2162
#8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	24589
#9	MESH DESCRIPTOR Device Removal EXPLODE ALL TREES	236
#10	change:TI,AB,KY	65511
#11	routine:TI,AB,KY	14417
#12	(resit* or re-sit*):TI,AB,KY	18
#13	replace* :TI,AB,KY	17180
#14	remov*:TI,AB,KY	13278
#15	#9 OR #10 OR #11 OR #12 OR #13 OR #14	104860
#16	#8 AND #15	4605
#17	* NOT SR-PVD:CC AND 12/12/2012 TO 31/03/2015:DL	170935
#18	#16 AND #17	882

WHAT'S NEW

Last assessed as up-to-date: 25 March 2015.

Date	Event	Description
25 March 2015	New citation required but conclusions have not changed	Searches re-run. No additional studies included or excluded. Minor changes to the text to adhere to current Cochrane standards
25 March 2015	New search has been performed	Searches re-run. No additional studies included or excluded.

CONTRIBUTIONS OF AUTHORS

JW conceived the idea for the review. JW and SO wrote the protocol. CR critically reviewed the protocol before final submission.

JW selected trials for inclusion, assessed methodological quality of trials and extracted data. JW entered the data, developed the analysis plan for the update and drafted the review update.

SO arbitrated on the selection of trials, assisted with data extraction, assessed methodological quality and assisted in drafting the final review.

CR selected trials for inclusion, assessed methodological quality of trials, extracted data, assisted with interpreting results and drafting of the final review.

KN assessed methodological quality of trials, extracted data, and commented on the review update.

DECLARATIONS OF INTEREST

JW: none known

SO: none known

CMR: CMR's employer has received unrestricted grants in aid from manufacturers of peripheral intravenous catheters and products, on her behalf for academic research projects. These sponsor had no involvement in the study design, execution, analysis or publication of these projects and they were unrelated to the topic of this review. CMR is an academic researcher and her employer has received funding on her behalf for her to provide expert advice, or educational lectures on her research at professional symposia and other events. CMR's employer has received payments on her behalf, for consultancy research projects which have been commissioned by manufacturers of vascular catheters and equipment, these were not on the topic of this review.

KN: KN, as Professional Officer of the Australian College of Neonatal Nurses, has received payment from Johnson and Johnson Consumer Companies and Johnson and Johnson Pacific to a conference to present on the experience of undertaking an educational road show and rollout of the AWHONN skin care guidelines around Australia; and to attend a baby advisory meeting.

Some of the review authors were also the investigators on several of the included trials, To eliminate any potential for a conflict of interest, assessment was allocated to a review author who was not an investigator.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- Chief Scientist Office, Scottish Government Health Directorates, The Scottish Government, UK. The Cochrane Vascular editorial base is supported by the Chief Scientist Office.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The primary outcome was changed to catheter-related bloodstream infection; all-cause bloodstream infection was added as a separate primary outcome. This was done to more closely differentiate between the two outcomes.

The methodological quality assessment of the included studies has been updated to the Cochrane Collaboration tool for assessing risk of bias ([Higgins 2011a](#)).

INDEX TERMS

Medical Subject Headings (MeSH)

Catheter-Related Infections [*prevention & control]; Catheterization, Peripheral [adverse effects; economics; *instrumentation]; Catheters, Indwelling [adverse effects]; Device Removal [*standards]; Guideline Adherence; Incidence; Phlebitis [epidemiology; etiology]; Randomized Controlled Trials as Topic; Time Factors

MeSH check words

Humans