Clinically-indicated replacement versus routine replacement of peripheral venous catheters (Review)

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[Intervention Review]

Clinically-indicated replacement versus routine replacement of peripheral venous catheters

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ABSTRACT

Background

Centers for Disease Control Guidelines recommend replacement of peripheral intravenous (IV) catheters every 72 to 96 hours. Routine replacement is thought to reduce the risk of phlebitis and bacteraemia. 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.

Objectives

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

Search strategy

The Cochrane Peripheral Vascular Diseases Group searched their Specialised Register (last searched October 2009) and the Cochrane Central Register of Controlled Trials (CENTRAL) (last searched Issue Issue 4, 2009). We also searched MEDLINE (last searched October 2009).

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

Three review authors independently assessed trial quality and extracted data.

Main results

In five trials (3408 participants) there was a 44% reduction in suspected catheter-related bacteraemia in the clinically-indicated group (0.2 versus 0.4%) but this was not statistically significant (odds ratio (OR) 0.57; 95% confidence interval (CI) 0.17 to 1.94; P = 0.37). Phlebitis was assessed in six trials (3455 patients); there was a non-significant increase in phlebitis in the clinically-indicated group (9% versus 7.2%); the OR was 1.24 (95% CI 0.97 to 1.60; P = 0.09). We also measured phlebitis per 1000 device days using data from five trials, (8779 device days). No statistical differences in the incidence of phlebitis per 1,000 device days was found (clinically indicated 1.6 cases per 1,000 catheter days versus 1.5 cases per 1,000 catheter days in the routine-replacement group).The combined OR was 1.04 (95% CI 0.81 to 1.32; P = 0.77). Cost was measured in two trials (961 patients). Cannulation costs were significantly reduced in the clinically-indicated group (mean difference (MD) -6.21; 95% CI -9.32 to -3.11; P = < 0.000).

Authors' conclusions

The review found no conclusive evidence of benefit in changing catheters every 72 to 96 hours. Consequently, health care organisations may consider changing to a policy whereby catheters are changed only if clinically indicated. 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.

PLAIN LANGUAGE SUMMARY

Replacing peripheral venous catheter when clinically indicated versus routine replacement

Most hospital patients receive fluids or medications via an intravenous catheter at some time during their hospital stay. An intravenous catheter is a short, hollow tube placed in the vein to allow administration of medications, fluids or nutrients directly into the bloodstream (also called a drip). These catheters are routinely replaced every three to four days, to try to prevent infection of the vein or of the blood. However, the evidence to support this practice is weak. Moreover, the procedure may cause considerable discomfort to patients and is quite costly. This review included all of the randomised controlled trials, which have compared routine catheter changes with changing the catheter only if there were signs of inflammation or infection. We found no evidence of benefit from these trials to support current practice of changing catheters every three to four days.

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

Routinely replaced peripheral intravenous catheters for preventing phlebitis and other intravenous catheter related complications

Patient or population: patients with peripheral IV therapy
Settings: hospitals and community settings
Intervention: Peripheral intravenous catheters replaced on clinical indication

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	Peripheral intravenous catheters replaced on clinical indication				
Catheter related bacteraemia Recording in patients medical record	**Low risk population**[1]		**OR 0.57** (0.17 to 1.94)	3408 (5 studies)	⊕⊕⊕⊕ **high**[2,3,4,5]	
	1 per 1000	**1 per 1000** (0 to 2)				
	High risk population[1]					
	7 per 1000	**4 per 1000** (1 to 13)				
Phlebitis	**Low risk population**[6]		**OR 1.24** (0.97 to 1.6)	3455 (6 studies)	⊕⊕⊕⊕ **high**[4,7,8,9]	
	25 per 1000	**31 per 1000** (24 to 39)				
	High risk population[6]					
	350 per 1000	**400 per 1000** (343 to 463)				

Cost Australian dollars[10]. Scale from: 30 to 100.	The mean cost in the control groups was **46.22 Dollars**[11]	The mean Cost in the intervention groups was **6.21 lower** (9.32 to 3.11 lower)		961 (2 studies)	⊕⊕⊕⊕ **high**[2]
Phlebitis per1000 device days Direct observation	**Low risk population**[6,12]		**OR 1.04** (0.81 to 1.32)	17201 (5 studies)	⊕⊕⊕⊕ **high**
	5 per 1000	**5 per 1000** (4 to 7)			
	High risk population[6,12]				
	13 per 1000	**14 per 1000** (11 to 17)			

*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; **OR:** Odds 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] Data extracted from a systematic review of 200 prospective studies (Maki 2006)
[2] Although patients and those recording outcomes were aware of group allocation, it seems unlikely that this would have affected results. None of those recording outcomes were investigators and the diagnosis was based on verifyable data in patients medical records.
[3] In three of the five trials, no bacteraemia occurred in either arm of the study. In the other two sudies there was considerable overlap in the confidence intervals and no statistically measured heterogeneity.
[4] Comparisons and outcomes were similar across all studies.
[5] Although over 3,400 patients were included in the meta-analyses, only 11 events occurred. When event rates are so low and confidence intervals around absolute effects are narrow, downgrading is not required.
[6] Rates depend on definitions used and populations studied.
[7] Patients and those recording outcomes were aware of group allocation. For five of the studies, it seems unlikely that this would have affected results. None of those recording outcomes were investigators and the diagnosis was based on verifyable data in patients

medical records. In one study (Barker 2004) the Chief investigator was also responsible for assessing outcomes, this may or may not have influenced results.

[8] Only one study showed a statistically significant effect favouring routine catheter changes (Barker 2004). This was a small study and had some limitations. Irrespective of this, confidence intervals of all of the studies overlapped and there was no staatistical evidence of heterogeneity between trials.

[9] Two unpublished trials have been included. One of the authors of this review is the chief investigator for both studies. She has a strong publication record and it is expected that results of both trials will be published during 2010.

[10] The overall cost for cannula replacement varies by cost of materials, time, solutions and drugs used in the infusion.

[11] Mean score is the final value amount in Australian dollars

[12] Data from this review

BACKGROUND

Among hospitalised patients, intravenous therapy is the most common invasive procedure. Intravenous therapy is associated with a phlebitis rate of between 2.3% (White 2001) and 60% (Gupta 2007) and an intravenous catheter-related bacteraemia (CRBSI) rate of approximately 0.8% (Maki 1991). Current guidelines recommend that peripheral intravenous (IV) catheters should be re-sited every 72 to 96 hours to restrict the potential of developing phlebitis (O,Grady 2002), and most hospitals follow this recommendation. The most recent guidelines state "replace peripheral venous catheters at least every 72 to 96 hours in adults to prevent phlebitis" (p.762) and carries a category rating of 1B (strongly recommended for implementation and supported by some experimental, clinical or epidemiological studies). However, the guideline cites only one observational study to support this recommendation. This was a paper published in 1998 and based on data collected in 1992, which compared IVs left in place for 72 hours or 96 hours with equivalent phlebitis rates (Lai 1998). 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 indicate that the recommendation may need to be revised.

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. 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 peripheral vein infusion thrombophlebitis based on two or more of the following: pain, tenderness, warmth, erythema, swelling, and a palpable cord (Maki 1991; Monreal 1999). 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 be primarily 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). Utrasonographic 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 intravenous 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 skin integrity is breached, a potential portal for pathogens is provided. For example, Uslusoy found a significant relationship between the number of times infusions were started and phlebitis (Uslusoy 2008). There is also some support for this relationship 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 for phlebitis beyond the second day (Bregenzer 1998). Similarly, in a retrospective study of 784 IV 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" (pp304). 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 CDC guidelines relating to peripheral intravenous catheter management. This has led some hospitals to adopt the practice of re-siting only where there is evidence of inflammation or infiltration (personal communication). Making the guidelines even more difficult to rationalise is the recommendation for peripheral catheter replacement in children, which states "do not replace peripheral catheters unless clinically indicated" (CDC,15; pp761) (O,Grady 2002). This recommendation was based on several studies using dwell times of intravenous catheters of greater than 72 hours (Catney 2001; Cornely 2002; Shimandle 1999). Insertion of a peripheral intravenous catheter can be a painful and traumatic pro-

cess and, if unneccessary, adds not only to 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 IV catheters when clinically indicated compared with removing and re-siting the catheter routinely.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials 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 are excluded.

Types of interventions

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

Types of outcome measures

Primary outcomes

- Suspected device-related bacteraemia (defined as a bacteraemia occurring while the IV is in situ or up to 48 hours post removal, where there are no other clinical or microbiological data to explain the source of the infection).
- Thrombophlebitis (using any definition identified by the trial author).
- Cost (in terms of materials and labour associated with IV catheter-related insertion). This may be unavailable in some reports so cost is not an inclusion criteria.

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 (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

Electronic searches

The Cochrane Peripheral Vascular Diseases (PVD) Group searched their Specialised Register (last searched October 2009) and the Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library* (last searched Issue 4, 2009) for publications describing randomised controlled trials of routine peripheral IV replacement compared with replacement based on clinical indications. See Appendix 1 for details of the search strategy used to search CENTRAL.

The Specialised Register is maintained by the Trials Search Co-ordinator 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 PVD Group module in *The Cochrane Library.*

The review authors searched the Cochrane Central Register of Controlled Trials (CENTRAL), (*The Cochrane Library*, issue 4, 2009) using the strategy described in Appendix 2 and MEDLINE (1950 to October 2009) using the search strategy described in Appendix 3.

Searching other resources

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

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 reviewer. There was no blinding of authorship.

Data extraction and management

Following PVD Group 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 quality of eligible trials, using the PVD quality assessment criteria outlined below. Disagreements between review authors was resolved by consensus or referral to a third reviewer. We contacted investigators of included trials to resolve any ambiguities.

Adequacy of the randomisation process

A - Adequate sequence generation is reported for example, using random number tables, computer random number generator, coin tossing or card shuffling.
B - did not specify on the adequate reported methods in (A) but mentioned randomisation method.
C - Other method of allocation that may not be random.

Adequacy of allocation concealment

A - Adequate: allocation concealment described that would not allow investigators /participants to know or influence intervention group before eligible participant entered in the study, for example central randomisation, serially numbered, opaque, sealed envelopes.
B - Unclear: unclearly concealed trials in which the author either did not report allocation concealment approach at all, or reported an approach that was not clearly adequate.
C - Inadequate: inadequately concealed trials in which the method of allocation is not concealed, such as alternation methods or unsealed envelopes; any information in the study that indicated that investigators or participants could influence intervention group.

Blinding

A - Blinding of treatment providers: Yes/No/Unclear.
B - Blinding of participants: Yes/No/Unclear.
C - Blinding of outcome assessor: Yes/No/Unclear.
D - Blinding of data analysis: Yes/No/Unclear.

Intention-to-treat (ITT) analysis

A - Yes: Specifically reported by authors that ITT analysis was undertaken and this was confirmed on study assessment, or not stated but evident form study assessment that ITT analysis was undertaken.
B - Unclear: Described as ITT analysis but unable to confirm on study assessment, or not reported and unable to confirm by study assessment.
C - No: Lack of ITT analysis confirmed on study assessment, for example patients who were randomised were not included in the analysis because they did not receive the study intervention, or they withdrew from the study, or were not included because of protocol violation, regardless of whether ITT reported or not.

Completeness of follow up

Percentage of participants for whom data were completed at defined study end-point.

Measures of treatment effect

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

Unit of analysis issues

It is inadequate merely to compare longer and shorter dwell 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 dwell, 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.

Cross-over trials were not eligible. Cluster randomised trials were not expected in this field.

Dealing with missing data

If any outcome data remained missing despite our attempts to obtain complete outcome data from authors, we planned to perform an available-case analysis, based on the numbers of patients for whom outcome data were known. 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 X $\sqrt{N}$, where these were available (Higgins 2008).

Assessment of heterogeneity

Heterogeneity was assessed visually and by using the chi-squared statistic with significance being set at $P < 0.10$. In addition, the degree of heterogeneity was investigated by calculating the I^2 statistic Higgins 2008. If evidence of significant heterogeneity was identified (> 50%), we explored potential causes and a random-effects approach to the analysis was used.

Assessment of reporting biases

Reporting bias was assessed using guidelines in Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2008). Where sufficient study data were available for individual outcomes, funnel plots were 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 is 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

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.

Results of the search

The electronic search identified 198 titles. Two further, unpublished trial were also considered. Of these, 13 were thought to be potentially useful after titles and abstracts were screened. Full texts of these papers were retrieved and reviewed against the inclusion criteria by two of the authors. Because three of the authors of this review were also investigators in trials under consideration, we allocated the assessment of those trials to reviewers who were not investigators for those particular studies. Seven of the 13 potentially useful trials did not meet our inclusion criteria and were excluded. Authors of all included trials were asked for additional information. Responses were received in all cases.

Included studies

Four published RCTs (Barker 2004; Van Donk 2009; Webster 2007; Webster 2008) and two unpublished trials (Rickard 2008; Rickard 2009) met the inclusion criteria (*see* Table: Characteristics of included studies) for details. Rickard 2009 is the interim analysis of the ongoing study Rickard 2010.

The six trials involved a total of 3,455 participants with individual trial sizes ranging between 47 and 1,885. One trial was carried out in England (Barker 2004) the remaining five trials were Australian (Rickard 2008; Rickard 2009; Van Donk 2009; Webster 2007; Webster 2008). Four of the trials were conducted in single-centre, acute inpatient settings (Barker 2004; Rickard 2008; Webster 2007; Webster 2008), one was a multi-centre trial of three Australian hospitals (Rickard 2009) and one was undertaken in a community setting (Van Donk 2009).

In five trials (Barker 2004; Rickard 2008; Rickard 2009; 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 two trials (Webster 2007; Webster 2008) the comparison was between routine care (planned three-day changes) and clinically-indicated changes. In the Rickard 2008; Rickard 2009; Van Donk 2009 trials, 72 to 96 hour catheter changes were compared with clinical indications and Barker 2004 compared 48 hour changes with removal for clinical indicators such as pain, catheter dislodgement or phlebitis.

Five of the trials (Barker 2004; Rickard 2008; Rickard 2009; 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 further classified phlebitis as either mild, moderate or severe, depending on the area of erythema. Van Donk 2009 included the same symptoms as other trials but scored them as either one or two depending on severity. A score of two or more was classified as phlebitis, consequently a patient may have had only one symptom, e.g. pain, to receive a positive diagnosis.

Power calculations were reported by Rickard 2008; Rickard 2009; 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 reasons for excluding seven 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 both the Cobb 1992; and Eyer 1990 trials involved central venous catheters. The other excluded study was not a randomised controlled trial (Arnold 1977).

Risk of bias in included studies

See individual *Risk of Bias* tables and (Figure 1; Figure 2).

Figure 1. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.

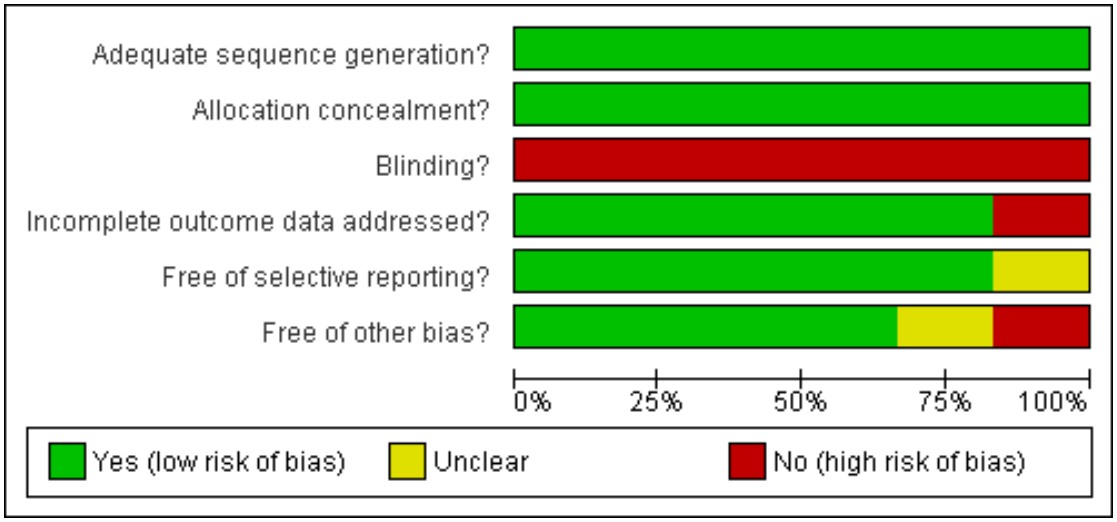
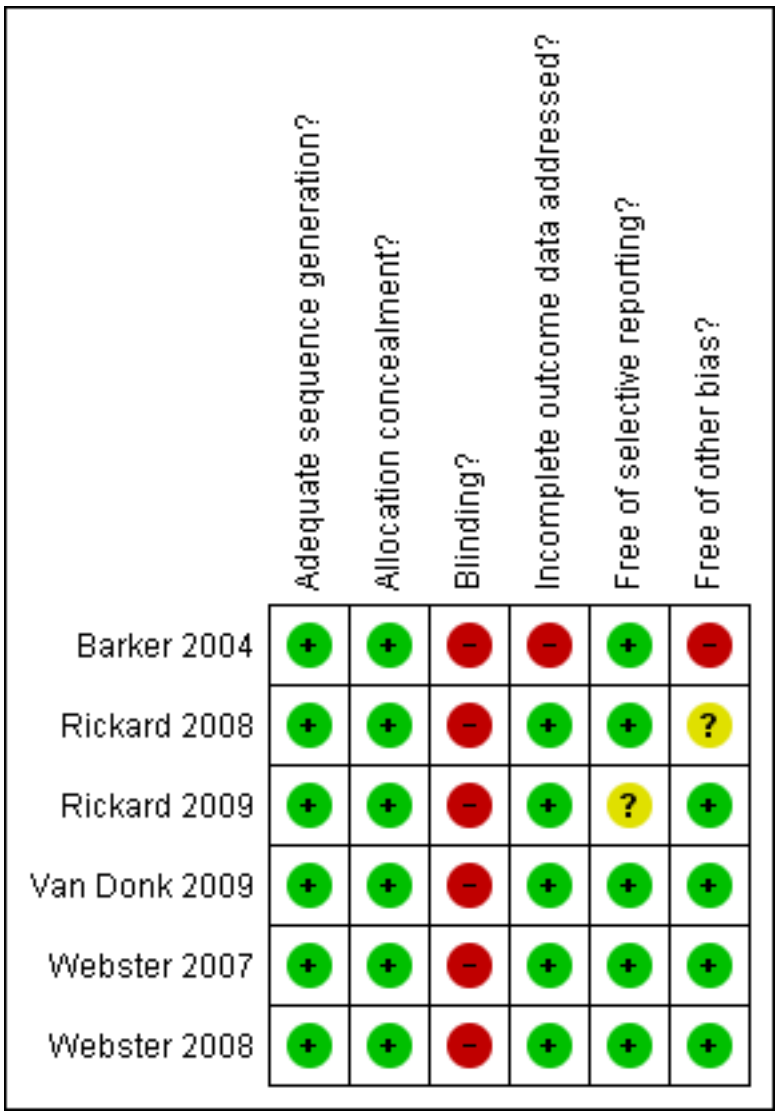


Figure 2. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.



Allocation

Generation of random allocation sequence

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

Allocation concealment

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

Blinding

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

Outcome assessment

The chief investigator assessed outcomes in the Barker 2004 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 2008 and the Rickard 2009 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 number screened and eligible is unclear, nor were any drop outs reported. There was an imbalance in the number of participants reported by group, 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 five trials, all of which provided a flow of participant through each stage and used intention-to-treat analysis (Rickard 2008; Rickard 2009; 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. Primarily, these were in the routine replacement groups, where catheters were not replaced within the specified time period.

Selective reporting

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

Other potential sources of bias

In the Barker 2004 trial, there are two definitions of phlebitis, one of which states that two symptoms are necessary; yet it appears that erythema alone was diagnosed as phlebitis, with severity based on the area of inflammation.

Effects of interventions

See: **Summary of findings for the main comparison** Routinely replaced peripheral intravenous catheters for preventing phlebitis and other intravenous catheter related complications

Routine changes versus clinically indicated (analysed per person)

Suspected catheter related bacteraemia was assessed in five trials (3408 patients) (Rickard 2008; Rickard 2009; Van Donk 2009; Webster 2007; Webster 2008); phlebitis in six trials (3455 patients) (Barker 2004; Rickard 2008; Rickard 2009; Van Donk 2009; Webster 2007; Webster 2008); cost in two trials (961 patients) (Webster 2007; Webster 2008); local infection in three trials (1323 patients) (Rickard 2008; Webster 2007; Webster 2008); catheter blockage in four trials (1523 patients) (Rickard 2008; Van Donk 2009; Webster 2007; Webster 2008) and infiltration in three trials (1323 patients) Rickard 2008; Webster 2007; Webster 2008).
Changing catheters when clinically indicated reduced the suspected device related bacteraemia rate by 43% but this was not statistically significant (odds ratio (OR) 0.57; 95% confidence interval (CI) 0.17 to 1.94; P = 0.37) (Figure 3). Conversely, there was a non-statistically significant increase in phlebitis of 24% in the clinically-indicated group (OR 1.24; 95% CI 0.97 to 1.60; P = 0.09) (Figure 4; Figure 5). This result was unaffected by whether the infusion was continuous or intermittent. Cannulation costs (measured in Australian dollars) were significantly reduced in the clinically-indicated group (mean difference (MD) -6.21; 95% CI -9.32 to -3.11; P = < 0.000) (Figure 6). The incidence of local infection was not statistically different between groups (OR 4.99; 95% CI 0.24 to 104.22; P = 0.30) (Figure 7) but catheter failure due to blockage was higher in the clinically-indicated group (OR 1.64; 95% CI 1.05 to 2.56; P = 0.03) (Figure 8). There was also a non-significant, 13% increase in the number of catheter failures due to infiltration in the clinically-indicated group (OR 1.13; 95% CI 0.90 to 1.42; P + 0.28) (Figure 9).

Figure 3. Forest plot of comparison: 1 Clinically indicated versus routine change, outcome: 1.1 Suspected catheter-related bacteraemia.

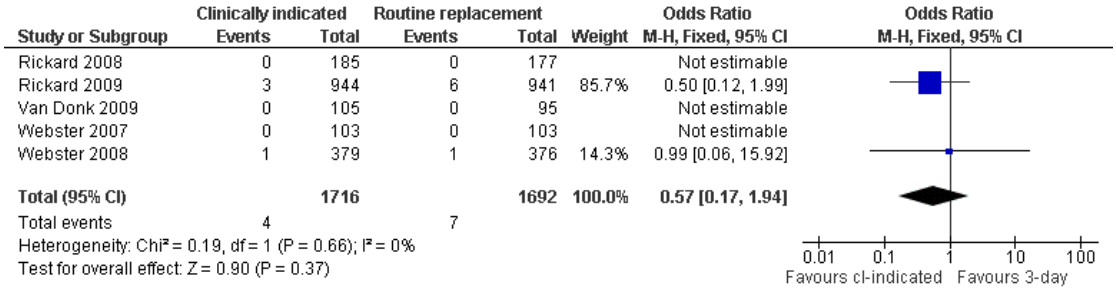


Figure 4. Forest plot of comparison: 1 Clinically indicated versus routine change, outcome: 1.2 Phlebitis all studies.

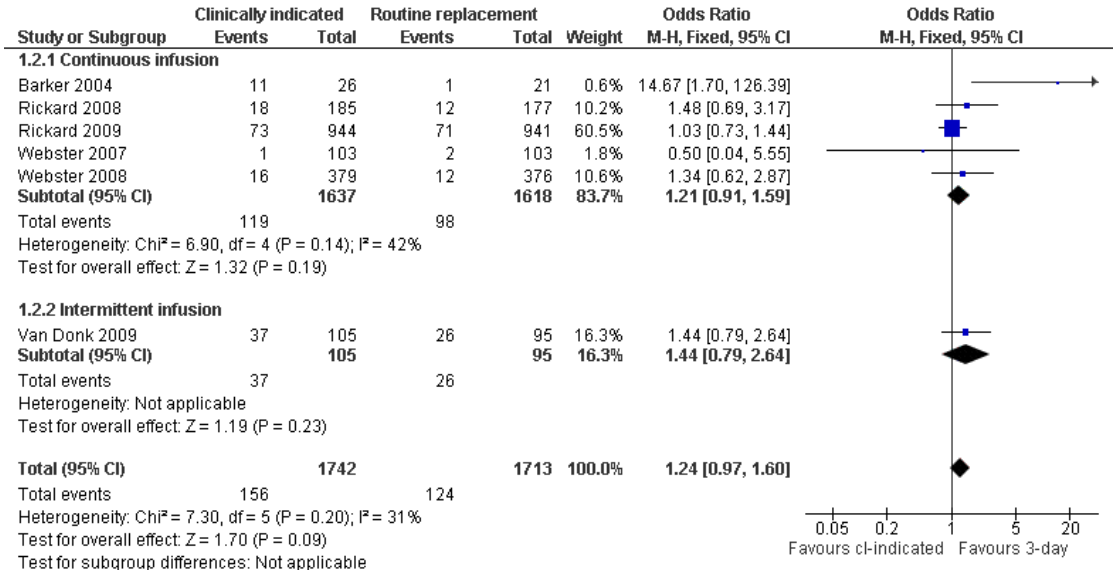


Figure 5. Funnel plot of comparison: 1 Clinically indicated versus routine change, outcome: 1.2 Phlebitis all studies.

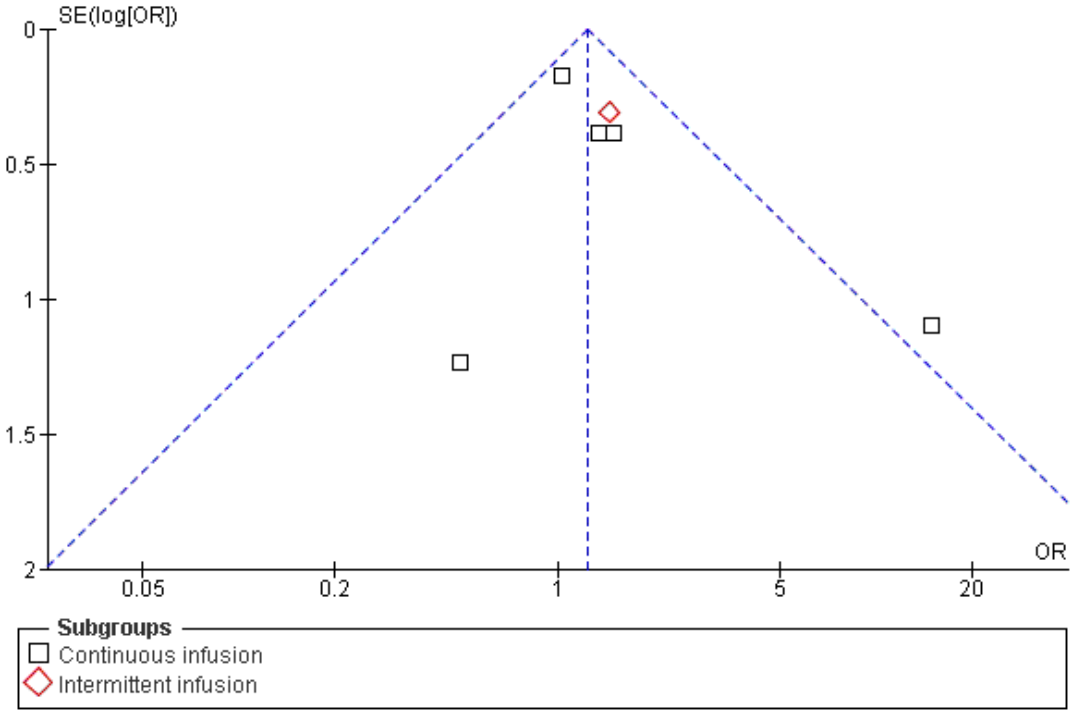


Figure 6. Forest plot of comparison: 1 Clinically indicated versus routine change, outcome: 1.3 Cost.

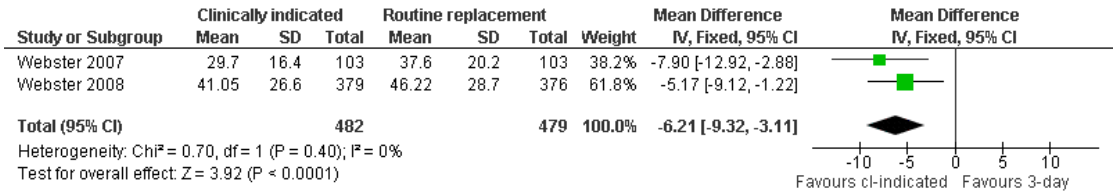


Figure 7. Forest plot of comparison: 1 Clinically indicated versus routine change, outcome: 1.5 Local infection.

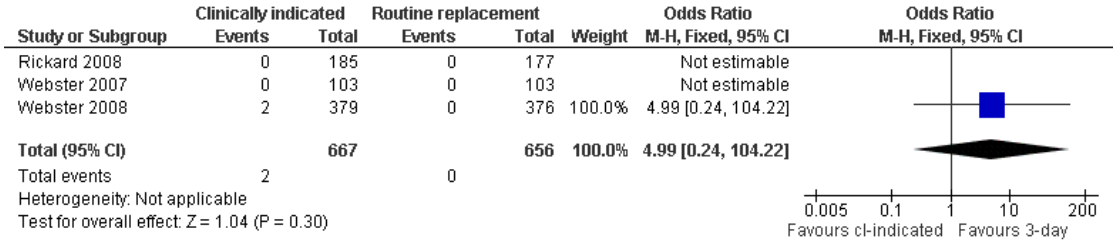


Figure 8. Forest plot of comparison: 1 Clinically indicated versus routine change, outcome: 1.6 Blockage.

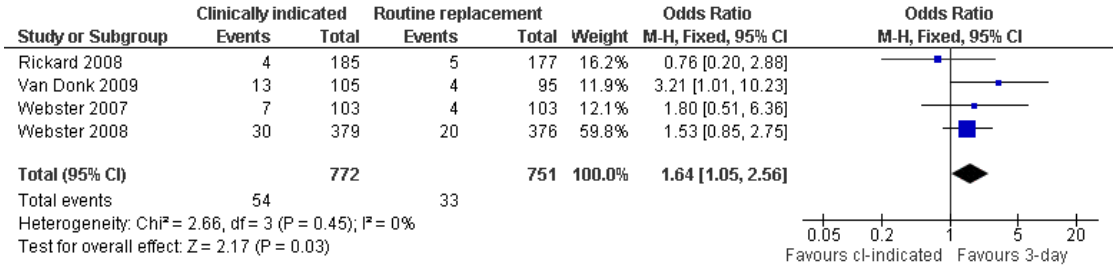
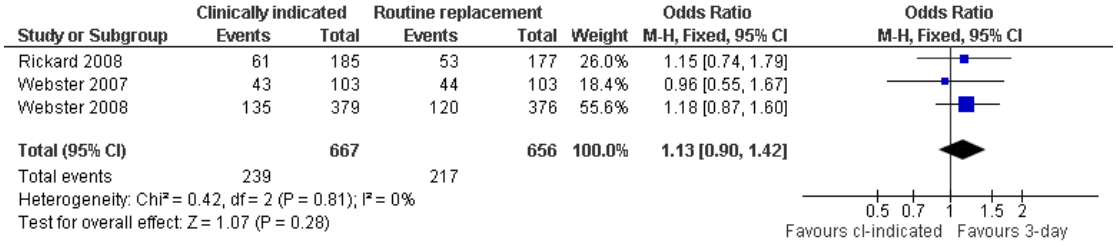


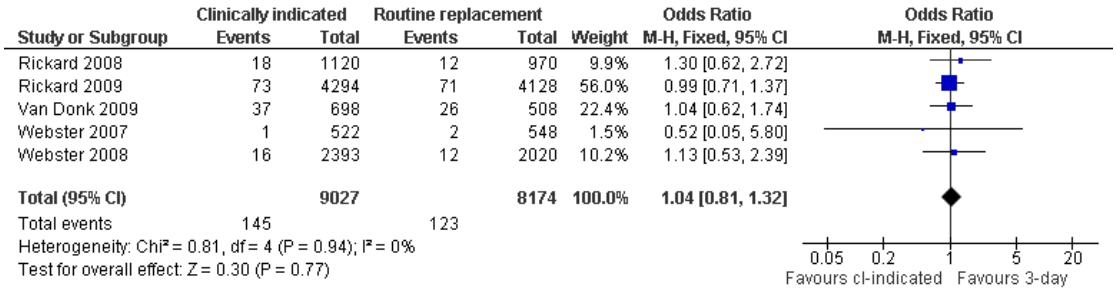
Figure 9. Forest plot of comparison: 1 Clinically indicated versus routine change, outcome: 1.7 Infiltration.



Routine changes versus clinically indicated (analysed per 1000 device days)

Data from five trials (Rickard 2008; Rickard 2009; Van Donk 2009; Webster 2007; Webster 2008), representing 8779 device days, were available for analysis. No statistical differences in the incidence of phlebitis per 1,000 device days was found in any of the trials. When results were combined the OR was 1.04 (95% CI 0.81 to 1.32 P = 0.77) (Figure 10).

Figure 10. Forest plot of comparison: 1 Clinically indicated versus routine change, outcome: 1.3 Phlebitis per 1000 device days.



Routine changes versus clinically indicated (sensitivity analyses)

Only two of the planned sensitivity analyses were possible. Five of the six included trials recruited over 100 participants Rickard 2008; Rickard 2009; Van Donk 2009; Webster 2007; Webster 2008); the five trials included a total of 3410 patients. The phlebitis rate was 17% higher in the clinically-indicated group but this was not statistically significant (OR 1.17; 95% CI 0.90 to 1.51; P = 0.24) Figure 11. Four of the six trials were published (Barker 2004; Van Donk 2009; Webster 2007; Webster 2008). When results from these trials were combined (1208 participants), there was a statistically significant increase in the phlebitis rate in the clinically-indicated group (OR 1.61; 95% CI 1.04 to 2.50; P = 0.03) Figure 12. We conducted one post hoc sensitivity analysis using phlebitis as an outcome. Four trials of 3210 were included (Rickard 2008; Rickard 2009; Webster 2007; Webster 2008). There was an 11% increase in the rate of phlebitis in the clinically-indicated group when two or more signs or symptoms were used to define phlebitis (OR 1.11; 95% CI 0.84 to 1.48; P = 0.47) but this was not statistically significant Figure 13.

Figure 11. Forest plot of comparison: 1 Clinically indicated versus routine change, outcome: 1.4 Phlebitis: excluding studies with less than 100 participants.

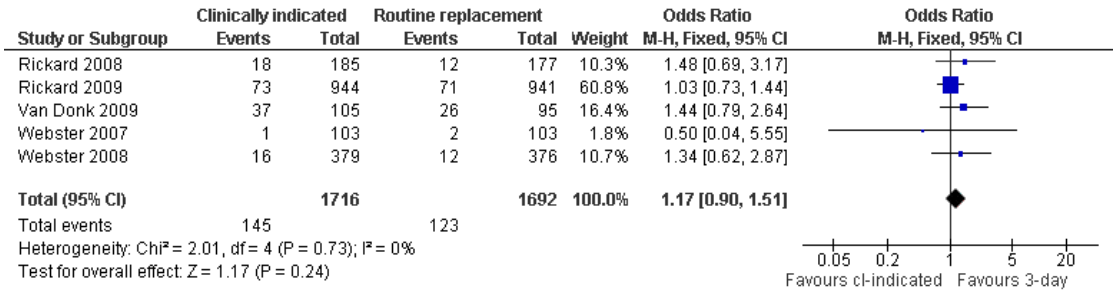


Figure 12. Forest plot of comparison: 1 Clinically indicated versus routine change, outcome: 1.5 Plebitis: excluding unpublished studies.

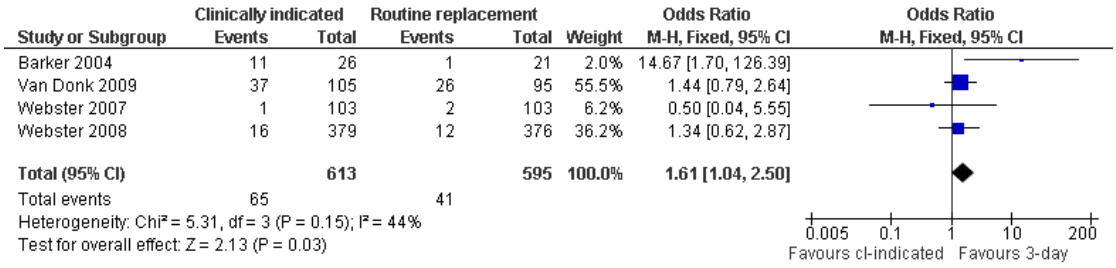
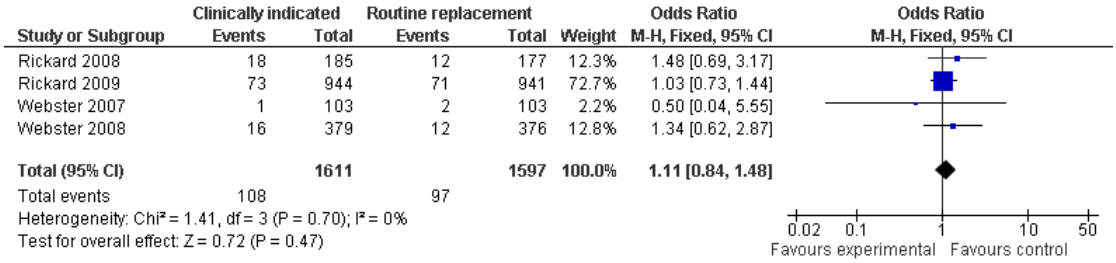


Figure 13. Forest plot of comparison: 1 Clinically indicated versus routine change, outcome: 1.10 Phlebitis: excluding studies using only one sign or symptom to define phlebitis.



DISCUSSION

Summary of main results

This systematic review analysed bacteraemia, phlebitis, other reasons for catheter failure and cost, with the intention of comparing routine catheter changes (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 on clinical indications rather than routinely, as recommended by Centers of Disease Control (O,Grady 2002). The rate of device-related bacteraemia was similar in both groups, between 0.0% and 0.6%, and comparable to that previously reported in observational studies (Maki 1991). 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 1,000 device days, which is a more clinically useful measure. This was also true when we undertook a sensitivity analysis, which included only those trials which diagnosed phlebitis using the well accepted definition of two or more signs or symptoms (Maki 1991). In addition, most cases of phlebitis are mild in nature, requiring either no treatment or removal of the catheter. There was no indication in our review that phlebitis was a precursor to bacteraemia.

Catheter failure due to blockage was significantly greater 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 important, 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, since many catheters do not fail over the course of IV treatment, even with extended dwell times.

Cost was significantly less, around AUD $6, in the clinically-indicated group. This result was based on only two studies but re-

sults 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.

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 trial, 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 2008; Rickard 2009). In all of the trials, except for Barker 2004, standard guidelines were followed for the control group, that is, catheters were changed between 72 and 96 hours, reflecting usual care. In the Barker 2004 trial, catheters were changed every 48 hours. None of the trials, except the Rickard 2009 unpublished study, were powered to report on phlebitis alone, and some of the trials were very small. For example, the only study that showed statistically lower phlebitis rates in the clinically-indicated group (Barker 2004) involved just 47 people and showed differences between the control and intervention groups that were quite dissimilar to all of the other studies.

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

Quality of the evidence

All of the studies avoided selection bias and ensured allocation concealment. The main difficulty with all of the trials was that the outcome was not able to be blinded. This is 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 authors argue that it is unlikely. Barker 2004 was the only investigator who 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).

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 (Bregenzer 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 guidelines for peripheral catheter replacement in children, which states "do not replace peripheral catheters unless clinically indicated" (CDC,15; pp761) (O,Grady 2002).

AUTHORS' CONCLUSIONS

Implications for practice

The review found no conclusive evidence of benefit for 72 to 96 hour catheter changes. Consequently, health care organisations may consider changing to a policy whereby catheters are changed only if clinically indicated. 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.

Implications for research

Any future trial should use standard definitions for phlebitis and be sufficiently large enough to show true differences. Based on results from the meta-analysis in this review, at least 3,000 subjects would be required in each arm of any future trial to show a lowering

of phlebitis rates from 9% to 7% (α = 0.05 and 80% power). It would also be useful to include patient satisfaction as an outcome measure and for trials to be conducted in a variety of health care systems.

ACKNOWLEDGEMENTS

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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 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	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). 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".

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Computer generated (personal communication with author).
Allocation concealment?	Yes	Sealed envelopes (personal communication with author).
Blinding? All outcomes	No	Neither study personnel nor participant were blinded.
Incomplete outcome data addressed? All outcomes	No	In this small sample, there were five fewer patients in the routine replacement group. No explanation was provided for the un-

Barker 2004 (*Continued*)

		equal sample size. No drop outs or loss to follow-up were reported.
Free of selective reporting?	Yes	Phlebitis was the only outcome planned.
Free of other bias?	No	The Chief Investigator allocated patients and was responsible for outcome evaluation. No sample size calculation.

Rickard 2008

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 blood stream 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 catheterization; number of IV devices; device related blood stream infection; infiltration; local infection.
Notes	Approximately 75% of patients were receiving a continuous infusion.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computer generated.
Allocation concealment?	Yes	Quote "assignment was concealed until randomisation by use of a telephone service".

Rickard 2008 (*Continued*)

Blinding? All outcomes	No	Neither study personnel nor participant were blinded.
Incomplete outcome data addressed? All outcomes	Yes	Results from all enrolled patients were reported.
Free of selective reporting?	Yes	The protocol was available. All nominated outcomes were reported.
Free of other bias?	Unclear	Significantly more patients in the routine change group received IV antibiotics (73.1% versus 62.9%).

Rickard 2009

Methods	**Study design:** Multi-centre RCT. **Method of randomisation:** Computer generated, stratified by site. **Concealment of allocation:** Allocation concealed until eligibility criteria was entered into a hand-held computer.
Participants	**Country:** Australia. **Number:** 1855 patients requiring IV therapy in general medical or surgical wards. Clinically indicated: 944 patients. Routine replacement: 941 patients. **Age:** Not provided (interim analysis). **Sex (M/F):** Not provided (interim analysis). **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. **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.
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:** IVD related bacteraemia. Phlebitis per patient (defined as two or more of the following: pain, erythema, purulence, infiltration, palpable venous cord).
Notes	This was an interim analysis conducted by a blinded independent data monitor. Projected total recruits from all sites is 3,300 patients.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computer generated.

Rickard 2009 (*Continued*)

Allocation concealment?	Yes	Allocation concealed until eligibility criteria was entered into a hand held computer.
Blinding? All outcomes	No	Neither study personnel nor participant were blinded.
Incomplete outcome data addressed? All outcomes	Yes	This was an interim analysis. data from all enrolled patients was reported.
Free of selective reporting?	Unclear	The protocol was available. The interim analysis reported only on suspected IVD related bacteraemia and phlebitis.
Free of other bias?	Yes	

Van Donk 2009

Methods	**Study design:** RCT. **Method of randomisation:** Computer generated. **Concealment of allocation:** Sealed envelopes.
Participants	**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.
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 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 mor cm = 2 points); swelling (as for redness); and discharge (hemoserous ooze under dressing = 1 point, and hemoserous ooze requiring dressing change or purulence = 2 points). **Also reported on:** Suspected IVD related bacteraemia and occlusion/blockage.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computer generated allocation (personal communication with author).

Van Donk 2009 (*Continued*)

Allocation concealment?	Yes	Quote "Randomization was concealed until treatment via sealed envelopes".
Blinding? All outcomes	No	Neither study personnel nor participant were blinded.
Incomplete outcome data addressed? All outcomes	Yes	Participant flow chart provided. Results from all enrolled patients were reported.
Free of selective reporting?	Yes	All planned outcomes were reported.
Free of other bias?	Yes	

Webster 2007

Methods	**Study design:** Single centre RCT **Method of randomisation:** Computer generated **Concealment of allocation:** Allocation concealed until telephone contact made with an independent person
Participants	**Country:** Australia. **Number:** 206. Clinically indicated: 103 patients. Routine replacement: 103 patients. **Age:** Clinically indicated 60.2 yrs (16.2); routine replacement 63.1 yrs (17.3). **Sex (M/F):** Clinically indicated 53/50; routine replacement 54/49. **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 fo the IV team. **Exclusion criteria:** Immunosuppressed patients and those with an existing blood stream infection.
Interventions	**Clinically indicated:** Catheters removed if there were signs of phlebitis, local infection, bacteraemia, infiltration or blockage. **Routine replacement:** Catheters replaced every 3 days.
Outcomes	**Primary:** Composite measure of any reason for an unplanned catheter removal. **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%).
Notes	

Risk of bias

Item	Authors' judgement	Description

Webster 2007 (*Continued*)

Adequate sequence generation?	Yes	Quote "randomization was by computer generated random number list, stratified by oncology status".
Allocation concealment?	Yes	Quote "Allocation was was made by phoning a person who was independent of the recruitment process".
Blinding? All outcomes	No	Neither study personnel nor participant were blinded.
Incomplete outcome data addressed? All outcomes	Yes	All recruited patients were accounted for in the results.
Free of selective reporting?	Yes	Protocol was available. All planned outcomes were reported.
Free of other bias?	Yes	

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 blood stream 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.

Webster 2008 (*Continued*)

Notes		

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Computer generated.
Allocation concealment?	Yes	Phone randomisation.
Blinding? All outcomes	No	Neither study personnel nor participant were blinded.
Incomplete outcome data addressed? All outcomes	Yes	All recruited patients were accounted for in the results.
Free of selective reporting?	Yes	Protocol was available. All planned outcomes were reported.
Free of other bias?	Yes	

IV: intravenous
IVD: peripheral intravenous device
PVT: peripheral vein infusion thrombophlebitis
RCT: randomised controlled trial

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

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
Panadero 2002	Compared the use of a single intra-operative and post-operative catheters with two catheters, one used intra-operatively and a separate catheter for post-operative use.

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

Rickard 2010

Trial name or title	Rickard C, Webster J, Gowardman J, Wallis M, McCann D, Whitby M, McGrail M.
Methods	Multi-centre randomised controlled trial
Participants	Medical and surgical patients in acute tertiary centres
Interventions	The experimental group will have their intravenous catheter changed only if clinically indicated. The control group will have their catheter changed every 3 days.
Outcomes	**Primary Outcome** Phlebitis **Secondary Outcomes** Severe Phlebitis Time in situ Catheters per patient Catheter colonisation Catheter Related Bloodstream Infection (CRBSI) Venous infection Costs
Starting date	
Contact information	Professor Claire Rickard (e-mail c.rickard@griffith.edu.au)
Notes	Data collection is completed. Undergoing final analysis.

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 bacteraemia	5	3408	Odds Ratio (M-H, Fixed, 95% CI)	0.57 [0.17, 1.94]
2 Phlebitis all studies	6	3455	Odds Ratio (M-H, Fixed, 95% CI)	1.24 [0.97, 1.60]
2.1 Continuous infusion	5	3255	Odds Ratio (M-H, Fixed, 95% CI)	1.21 [0.91, 1.59]
2.2 Intermittent infusion	1	200	Odds Ratio (M-H, Fixed, 95% CI)	1.44 [0.79, 2.64]
3 Phlebitis per 1000 device days	5	17201	Odds Ratio (M-H, Fixed, 95% CI)	1.04 [0.81, 1.32]
4 Phlebitis: excluding studies with less than 100 participants	5	3408	Odds Ratio (M-H, Fixed, 95% CI)	1.17 [0.90, 1.51]
5 Plebitis: excluding unpublished studies	4	1208	Odds Ratio (M-H, Fixed, 95% CI)	1.61 [1.04, 2.50]
6 Phlebitis: excluding studies using only one sign or symptom to define phlebitis	4	3208	Odds Ratio (M-H, Fixed, 95% CI)	1.11 [0.84, 1.48]
7 Cost	2	961	Mean Difference (IV, Fixed, 95% CI)	-6.21 [-9.32, -3.11]
8 Local infection	3	1323	Odds Ratio (M-H, Fixed, 95% CI)	4.99 [0.24, 104.22]
9 Blockage	4	1523	Odds Ratio (M-H, Fixed, 95% CI)	1.64 [1.05, 2.56]
10 Infiltration	3	1323	Odds Ratio (M-H, Fixed, 95% CI)	1.13 [0.90, 1.42]

Analysis 1.1. Comparison 1 Clinically indicated versus routine change, Outcome 1 Catheter-related bacteraemia.

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

Comparison: 1 Clinically indicated versus routine change

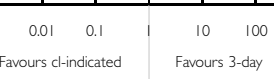
Outcome: 1 Catheter-related bacteraemia

Study or subgroup	Clinically indicated n/N	Routine replacement n/N	Odds Ratio M-H,Fixed,95% CI	Odds Ratio M-H,Fixed,95% CI
Rickard 2008	0/185	0/177		0.0 [0.0, 0.0]
Rickard 2009	3/944	6/941		0.50 [0.12, 1.99]
Van Donk 2009	0/105	0/95		0.0 [0.0, 0.0]
Webster 2007	0/103	0/103		0.0 [0.0, 0.0]
Webster 2008	1/379	1/376		0.99 [0.06, 15.92]
Total (95% CI)	**1716**	**1692**		**0.57 [0.17, 1.94]**

Total events: 4 (Clinically indicated), 7 (Routine replacement)

Heterogeneity: $Chi^2 = 0.19$, df = 1 (P = 0.66); $I^2 = 0.0\%$

Test for overall effect: Z = 0.90 (P = 0.37)

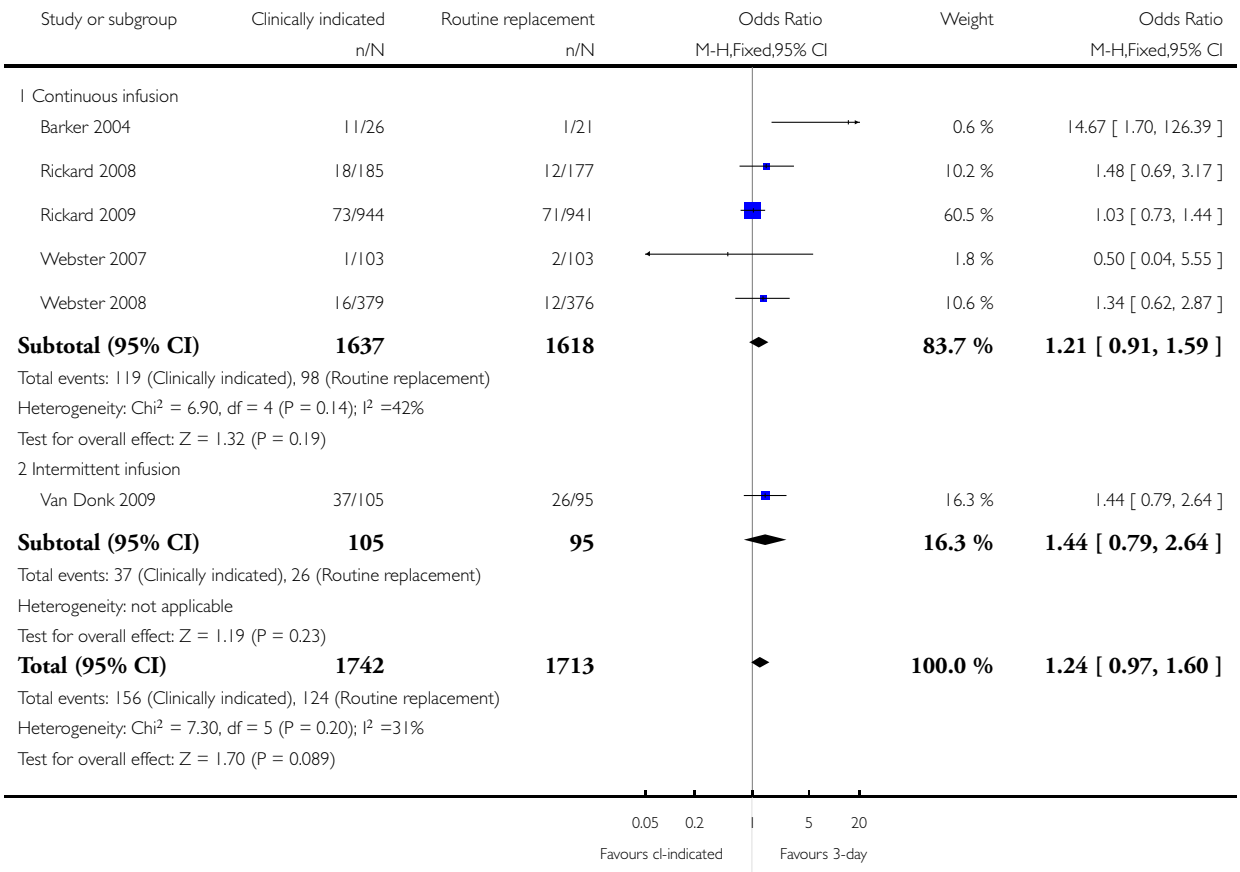


Analysis 1.2. Comparison 1 Clinically indicated versus routine change, Outcome 2 Phlebitis all studies.

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

Comparison: 1 Clinically indicated versus routine change

Outcome: 2 Phlebitis all studies



Analysis 1.3. Comparison 1 Clinically indicated versus routine change, Outcome 3 Phlebitis per 1000 device days.

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

Comparison: 1 Clinically indicated versus routine change

Outcome: 3 Phlebitis per 1000 device days

Study or subgroup	Clinically indicated n/N	Routine replacement n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Rickard 2008	18/1120	12/970		9.9 %	1.30 [0.62, 2.72]
Rickard 2009	73/4294	71/4128		56.0 %	0.99 [0.71, 1.37]
Van Donk 2009	37/698	26/508		22.4 %	1.04 [0.62, 1.74]
Webster 2007	1/522	2/548		1.5 %	0.52 [0.05, 5.80]
Webster 2008	16/2393	12/2020		10.2 %	1.13 [0.53, 2.39]
Total (95% CI)	**9027**	**8174**		**100.0 %**	**1.04 [0.81, 1.32]**

Total events: 145 (Clinically indicated), 123 (Routine replacement)

Heterogeneity: $Chi^2 = 0.81$, df = 4 (P = 0.94); $I^2 = 0.0\%$

Test for overall effect: Z = 0.30 (P = 0.77)

Analysis 1.4. Comparison 1 Clinically indicated versus routine change, Outcome 4 Phlebitis: excluding studies with less than 100 participants.

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

Comparison: 1 Clinically indicated versus routine change

Outcome: 4 Phlebitis: excluding studies with less than 100 participants

Study or subgroup	Clinically indicated n/N	Routine replacement n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Rickard 2008	18/185	12/177		10.3 %	1.48 [0.69, 3.17]
Rickard 2009	73/944	71/941		60.8 %	1.03 [0.73, 1.44]
Van Donk 2009	37/105	26/95		16.4 %	1.44 [0.79, 2.64]
Webster 2007	1/103	2/103		1.8 %	0.50 [0.04, 5.55]
Webster 2008	16/379	12/376		10.7 %	1.34 [0.62, 2.87]
Total (95% CI)	**1716**	**1692**		**100.0 %**	**1.17 [0.90, 1.51]**

Total events: 145 (Clinically indicated), 123 (Routine replacement)

Heterogeneity: Chi^2 = 2.01, df = 4 (P = 0.73); I^2 =0.0%

Test for overall effect: Z = 1.17 (P = 0.24)

Analysis 1.5. Comparison 1 Clinically indicated versus routine change, Outcome 5 Plebitis: excluding unpublished studies.

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

Comparison: 1 Clinically indicated versus routine change

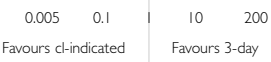
Outcome: 5 Plebitis: excluding unpublished studies

Study or subgroup	Clinically indicated n/N	Routine replacement n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Barker 2004	11/26	1/21		2.0 %	14.67 [1.70, 126.39]
Van Donk 2009	37/105	26/95		55.5 %	1.44 [0.79, 2.64]
Webster 2007	1/103	2/103		6.2 %	0.50 [0.04, 5.55]
Webster 2008	16/379	12/376		36.2 %	1.34 [0.62, 2.87]
Total (95% CI)	**613**	**595**		**100.0 %**	**1.61 [1.04, 2.50]**

Total events: 65 (Clinically indicated), 41 (Routine replacement)

Heterogeneity: $Chi^2 = 5.31$, df = 3 (P = 0.15); $I^2 = 44\%$

Test for overall effect: Z = 2.13 (P = 0.033)



Analysis 1.6. Comparison 1 Clinically indicated versus routine change, Outcome 6 Phlebitis: excluding studies using only one sign or symptom to define phlebitis.

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

Comparison: 1 Clinically indicated versus routine change

Outcome: 6 Phlebitis: excluding studies using only one sign or symptom to define phlebitis

Study or subgroup	Clinically indicated n/N	Routine replacement n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Rickard 2008	18/185	12/177		12.3 %	1.48 [0.69, 3.17]
Rickard 2009	73/944	71/941		72.7 %	1.03 [0.73, 1.44]
Webster 2007	1/103	2/103		2.2 %	0.50 [0.04, 5.55]
Webster 2008	16/379	12/376		12.8 %	1.34 [0.62, 2.87]
Total (95% CI)	**1611**	**1597**		**100.0 %**	**1.11 [0.84, 1.48]**

Total events: 108 (Clinically indicated), 97 (Routine replacement)

Heterogeneity: $Chi^2 = 1.41$, df = 3 (P = 0.70); $I^2 = 0.0\%$

Test for overall effect: Z = 0.72 (P = 0.47)

Analysis 1.7. Comparison 1 Clinically indicated versus routine change, Outcome 7 Cost.

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

Comparison: 1 Clinically indicated versus routine change

Outcome: 7 Cost

Study or subgroup	Clinically indicated N	Mean(SD)	Routine replacement N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Webster 2007	103	29.7 (16.4)	103	37.6 (20.2)		38.2 %	-7.90 [-12.92, -2.88]
Webster 2008	379	41.05 (26.6)	376	46.22 (28.7)		61.8 %	-5.17 [-9.12, -1.22]
Total (95% CI)	**482**		**479**			**100.0 %**	**-6.21 [-9.32, -3.11]**

Heterogeneity: Chi² = 0.70, df = 1 (P = 0.40); I² =0.0%

Test for overall effect: Z = 3.92 (P = 0.000088)

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

Study or subgroup	Clinically indicated n/N	Routine replacement n/N	Odds Ratio M-H,Fixed,95% CI	Odds Ratio M-H,Fixed,95% CI
Rickard 2008	0/185	0/177		0.0 [0.0, 0.0]
Webster 2007	0/103	0/103		0.0 [0.0, 0.0]
Webster 2008	2/379	0/376		4.99 [0.24, 104.22]
Total (95% CI)	**667**	**656**		**4.99 [0.24, 104.22]**

Total events: 2 (Clinically indicated), 0 (Routine replacement)

Heterogeneity: Chi² = 0.0, df = 0 (P = 1.00); I² =0.0%

Test for overall effect: Z = 1.04 (P = 0.30)

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

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

Comparison: 1 Clinically indicated versus routine change

Outcome: 9 Blockage

Study or subgroup	Clinically indicated n/N	Routine replacement n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Rickard 2008	4/185	5/177		16.2 %	0.76 [0.20, 2.88]
Van Donk 2009	13/105	4/95		11.9 %	3.21 [1.01, 10.23]
Webster 2007	7/103	4/103		12.1 %	1.80 [0.51, 6.36]
Webster 2008	30/379	20/376		59.8 %	1.53 [0.85, 2.75]
Total (95% CI)	**772**	**751**		**100.0 %**	**1.64 [1.05, 2.56]**

Total events: 54 (Clinically indicated), 33 (Routine replacement)

Heterogeneity: Chi^2 = 2.66, df = 3 (P = 0.45); I^2 =0.0%

Test for overall effect: Z = 2.17 (P = 0.030)

Analysis 1.10. Comparison 1 Clinically indicated versus routine change, Outcome 10 Infiltration.

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

Comparison: 1 Clinically indicated versus routine change

Outcome: 10 Infiltration

Study or subgroup	Clinically indicated n/N	Routine replacement n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Rickard 2008	61/185	53/177		26.0 %	1.15 [0.74, 1.79]
Webster 2007	43/103	44/103		18.4 %	0.96 [0.55, 1.67]
Webster 2008	135/379	120/376		55.6 %	1.18 [0.87, 1.60]
Total (95% CI)	**667**	**656**		**100.0 %**	**1.13 [0.90, 1.42]**

Total events: 239 (Clinically indicated), 217 (Routine replacement)

Heterogeneity: Chi^2 = 0.42, df = 2 (P = 0.81); I^2 =0.0%

Test for overall effect: Z = 1.07 (P = 0.28)

APPENDICES

Appendix 1. CENTRAL search strategy used by PVD Group

#1	MeSH descriptor Phlebitis explode all trees	1252
#2	*phlebitis	1793
#3	(#1 OR #2)	1821
#4	MeSH descriptor Infusions, Intravenous explode all trees	7676
#5	(*venous or peripheral) near3 infusion*	11196
#6	(peripheral near (cath* or can*))	982
#7	(PICs OR (peripheral near IV*))	127
#8	(ca* near indwelling)	1209
#9	MeSH descriptor Catheterization, Peripheral explode all trees	555
#10	MeSH descriptor Catheters, Indwelling explode all trees	799
#11	(#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10)	13300
#12	(#3 AND #11)	276

Appendix 2. Authors Central search strategy

#1 MeSH descriptor PHLEBITIS exp. trees 1and 2
#2 phlebitis in All Text
#3 thrombophlebitis in All Text
#4 (#1 OR #2 OR #3)
#5 MeSH descriptor INFUSIONS, intravenous
#6 MeSH descriptor Catheterization, Peripheral explode all trees
#7 MeSH descriptor Catheters, Indwelling explode all trees
#8 intravenous infusion* in All Text
#9 peripheral vein infusion* in All Text
#10 peripheral *venous catheter* OR PICs in All Text
#11 peripheral IVs in All Text
#12 catherization indwelling in All Text
#13 intravenous peripheral cannula* in All Text
#14 peripheral venous canula* in All Text
#15 (#5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #12 OR #13 OR #14)
#16 (#4 AND #15)

Appendix 3. Authors MEDLINE search strategy

#1 MeSH PHLEBITIS exp.
#2 phlebitis in All Fields
#3 periphlebitis in All Fields
#4 thrombophlebitis in All Fields
#5 (#1 OR #2 OR#3 OR #4 OR #5)
#6 MeSH INFUSIONS, intravenous
#7 MeSH Catheters, indwelling
#8 MeSH CATHERIZATION, peripheral
#9 intravenous infusion* in All Fields
#10 peripheral venous catheter* in All Fields
#11 peripheral intravenous catheter* OR PIC
#12 peripheral IVs in All Fields
#13 intravenous peripheral can* in All Fields
#14 peripheral venous can* in All Fields
#15 peripheral vein infusion* in All Fields Perhaps use (vein or ven*) to get venous
#16 (#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15)
#17 randomized controlled trial.pt.
#18 controlled clinical trial.pt.
#19 randomized.ab
#20 placebo.ab
#21 drug therapy.fs
#22 randomly.ab.
#23 trial.ab.
#24 groups.ab
#25 (#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24)
#26 (#6 AND #16 AND #25)

HISTORY

Protocol first published: Issue 2, 2009

Review first published: Issue 3, 2010

CONTRIBUTIONS OF AUTHORS

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

JW searched for and selected trials, assessed methodological quality of trials, extracted and entered data, analysed the results and drafted the final review.

SO arbitrated on the selection of trials, assisted with data extraction, assessing methodological quality, interpreting results and drafting the final review.

JH commented on the draft review.

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

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- Chief Scientist Office, Scottish Government Health Directorates, The Scottish Government, UK.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Suspected bacteraemia was included as a primary outcome. One additional sensitivity analysis was added.