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

Webster J, Osborne S, Rickard CM, Marsh N

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Clinically-indicated replacement versus routine replacement of peripheral venous catheters

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A B S T R A C T

Background

US Centers for Disease Control guidelines recommend replacement of peripheral intravenous catheters (PIVC) 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 or infection. Costs associated with routine replacement may be considerable. This is the third update of a review first published in 2010.

Objectives

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

Search methods

The Cochrane Vascular Information Specialist searched the Cochrane Vascular Specialised Register, CENTRAL, MEDLINE, Embase and CINAHL and World Health Organization International Clinical Trials Registry Platform and ClinicalTrials.gov trials registers to 18 April 2018. We also undertook reference checking, and contacted researchers and manufacturers to identify additional studies.

Selection criteria

We included randomised controlled trials that compared routine removal of PIVC 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 reviewed trials for inclusion, extracted data, and assessed risk of bias using Cochrane methods. We used GRADE to assess the overall evidence certainty.

Main results

This update contains two new trials, taking the total to nine included studies with 7412 participants. Eight trials were conducted in acute hospitals and one in a community setting. We rated the overall certainty of evidence as moderate for most outcomes, due to serious risk of bias for unblinded outcome assessment or imprecision, or both. Because outcome assessment was unblinded in all of the trials, none met our criteria for high methodological quality.

Primary outcomes

Seven trials (7323 participants), assessed catheter-related bloodstream infection (CRBSI). There is no clear difference in the incidence of CRBSI between the clinically indicated (1/3590) and routine change (2/3733) groups (risk ratio (RR) 0.61, 95% confidence interval (CI) 0.08 to 4.68), low-certainty evidence (downgraded twice for serious imprecision).

All trials reported incidence of thrombophlebitis and we combined the results from seven of these in the analysis (7323 participants). We excluded two studies in the meta-analysis because they contributed to high heterogeneity. There is no clear difference in the incidence of thrombophlebitis whether catheters were changed according to clinical indication or routinely (RR 1.07, 95% CI 0.93 to 1.25; clinically indicated 317/3590; 3-day change 307/3733, moderate-certainty evidence, downgraded once for serious risk of bias). The result was unaffected by whether the infusion was continuous or intermittent. Six trials provided thrombophlebitis rates by number of device days (32,709 device days). There is no clear difference between groups (RR 0.90, 95% CI 0.76 to 1.08; clinically indicated 248/17,251; 3-day change 236/15,458; moderate-certainty evidence, downgraded once for serious risk of bias).

One trial (3283 participants), assessed all-cause blood stream infection (BSI). We found no clear difference in the all-cause BSI rate between the two groups (RR 0.47, 95% CI 0.15 to 1.53; clinically indicated: 4/1593 (0.02%); routine change 9/1690 (0.05%); moderate-certainty evidence, downgraded one level for serious imprecision).

Three trials (4244 participants), investigated costs; clinically indicated removal probably reduces device-related costs by approximately AUD 7.00 compared with routine removal (MD −6.96, 95% CI −9.05 to −4.86; moderate-certainty evidence, downgraded once for serious risk of bias).

Secondary outcomes

Six trials assessed infiltration (7123 participants). Routine replacement probably reduces infiltration of fluid into surrounding tissues compared with a clinically indicated change (RR 1.16 (95% CI 1.06 to 1.26; routine replacement 747/3638 (20.5%); clinically indicated 834/3485 (23.9%); moderate-certainty evidence, downgraded once for serious risk of bias).

Meta-analysis of seven trials (7323 participants), found that rates of catheter failure due to blockage were probably lower in the routine-replacement group compared to the clinically indicated group (RR 1.14, 95% CI 1.01 to 1.29; routine-replacement 519/3733 (13.9%); clinically indicated 560/3590 (15.6%); moderate-certainty evidence, downgraded once for serious risk of bias).

Four studies (4606 participants), reported local infection rates. It is uncertain if there are differences between groups (RR 4.96, 95% CI 0.24 to 102.98; clinically indicated 2/2260 (0.09%); routine replacement 0/2346 (0.0%); very low-certainty evidence, downgraded one level for serious risk of bias and two levels for very serious imprecision).

One trial (3283 participants), found no clear difference in the incidence of mortality when clinically indicated removal was compared with routine removal (RR 1.06, 95% CI 0.27 to 4.23; low-certainty evidence, downgraded two levels for very serious imprecision).

One small trial (198 participants) reported no clear difference in device-related pain between clinically indicated and routine removal groups (MD −0.60, 95% CI −1.44 to 0.24; low-certainty evidence, downgraded one level for serious risk of bias and one level for serious imprecision).

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

Authors' conclusions

There is moderate-certainty evidence of no clear difference in rates of CRBSI, thrombophlebitis, all-cause BSI, mortality and pain between clinically indicated or routine replacement of PIVC. We are uncertain if local infection is reduced or increased when catheters are changed when clinically indicated. There is moderate-certainty evidence that infiltration and catheter blockage is probably lower when PIVC are changed routinely; and moderate-certainty evidence that clinically indicated removal probably reduces device-related costs. The addition of two new trials for this update found no further evidence to support changing catheters every 72 to 96 hours.

Healthcare organisations may consider changing to a policy whereby catheters are changed only if there is a clinical indication to do so, for example, if there were signs of infection, blockage or infiltration. This would provide significant cost savings, spare patients the unnecessary pain of routine re-sites in the absence of clinical indications and would reduce time spent by busy clinicians on this intervention. To minimise PIVC-related complications, staff should inspect the insertion site at each shift change and remove the catheter if signs of inflammation, infiltration, occlusion, infection or blockage are present, or if the catheter is no longer needed for therapy.

PLAIN LANGUAGE SUMMARY

Replacing a peripheral venous catheter when clinically indicated versus routine replacement

Review question

We reviewed the evidence about the effects of changing a catheter routinely (every three to four days) or changing the catheter only if there were signs or symptoms of a problem with the catheter remaining in place.

Background

Most hospital patients receive fluids or medications via a peripheral intravenous catheter at some time during their hospital stay. An intravenous catheter (also called an IV drip, an IV line 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, replacing the catheter may cause discomfort to patients and is quite costly. This is the third update of a review first published in 2010.

Study characteristics

In April 2018 we searched for randomised controlled trials (RCTs) that compared changing catheters every 72 to 96 hours (routine change) with changing the catheter only if there were complications or therapy was complete. We measured catheter-related blood stream infection, phlebitis and other problems associated with peripheral catheters, such as local infection and catheter blockage. We included two new studies for this update, bringing the total to nine studies with 7412 participants.

Key results

We found no clear difference in rates of catheter-related blood stream infection, phlebitis (inflammation of the vein), blood stream infection from any cause, local infection, mortality or pain. We are uncertain if local infection is reduced or increased when catheters are changed when clinically indicated. Infiltration (fluid seeping into the tissue around the catheter) and catheter blockage (an inability to infuse fluids or medication through the catheter), are probably reduced when catheters are changed routinely. Cost is reduced when catheters are replaced when there was a clinical indication to do so. The pre-planned outcomes 'number of catheter re-sites per patient', and 'satisfaction' were not reported by any studies included in the review.

Quality of the evidence

The overall quality of the evidence was judged to be moderate for most outcomes, which leaves us uncertain of our findings. The uncertainty is largely due to outcomes, such as phlebitis, being assessed by people who were aware of the group allocation, which may or may not affect their decision about whether a problem is present or absent.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Effects of clinically indicated replacement compared to routine change of peripheral intravenous catheters (PIVC)

Patient or population: any patient requiring a PIVC expected to remain in-situ for at least 3 days
Setting: hospital or community
Intervention: PIVC replaced if a clinical indication is present
Comparison: changing the PIVC routinely, according to a set time frame (usually between 72-96 hours)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with routine change	**Risk with clinically indicated**				
Catheter-related blood stream infection (during hospitalisation)	Study population		RR 0.61 (0.08 to 4.68)	7323 (7 RCTs)	⊕⊕◯◯ Low[1]	There is no clear difference in the incidence of catheter-related blood stream infection. The wide CI includes the possibility of both increased and decreased infection. The true effect could range from a 92% reduction to a 4.68 times increase in the clinically indicated group
	1 per 1000	0 per 1000 (0 to 3)				
Thrombophlebitis (during hospitalisation)	Study population		RR 1.07 (0.93 to 1.25)	7323 (7 RCTs)	⊕⊕⊕◯ Moderate[2]	There is no clear difference in the incidence of phlebitis between the clinically indicated and routine-change groups. Although the outcome assessment for laboratory-based outcomes,

					such as blood stream infection was blinded; only 2 trials reported these outcomes. Most outcomes were assessed by clinicians or researchers who were aware of the group to which the participant belonged
	82 per 1000	88 per 1000 (76 to 103)			
Thrombophlebitis (per device days) (during hospitalisation)	Study population		RR 0.90 (0.76 to 1.08)	32,709 device days (6 RCTs)	⊕⊕⊕◯ Moderate[2]	There is no clear difference in the incidence of phlebitis when assessed correctly (incidence/1000 device days) between the clinically indicated and routine-change groups. The true effect could range from a 24% reduction to an 8% increase in the clinically indicated group
	15 per 1000	14 per 1000 (12 to 16)			
All-cause blood stream infection (during hospitalisation)	Study population		RR 0.47 (0.15 to 1.53)	3283 (1 RCT)	⊕⊕⊕◯ Moderate[3]	There is no clear difference in all-cause blood stream infections between the clinically indicated and routine-change groups. Although a large trial, only Rickard 2012 assessed this outcome. The assessor was blinded for this outcome

	5 per 1000	3 per 1000 (1 to 8)				
Cost (during hospitalisation)	The mean cost in the control group was AUD 51.02	The mean cost in the intervention group was AUD 44.14 MD (AUD 9.05 lower to AUD 4.86 lower)	-	4244 (3 RCTs)	⊕⊕⊕◯ Moderate[2]	Clinically indicated peripheral catheter removal probably reduces the cost of catheter-related care by approximately AUD 7.00
Infiltration (during hospitalisation)	Study population		RR 1.16 (1.06 to 1.26)	7123 (6 RCTs)	⊕⊕⊕◯ Moderate[2]	Routine replacement probably leads to a slightly lower incidence of infiltration compared to a clinically indicated change
	205 per 1000	238 per 1000 (218 to 259)				
Catheter blockage (during hospitalisation)	Study population		RR 1.14 (1.01 to 1.29)	7323 (7 RCTs)	⊕⊕⊕◯ Moderate[2]	Routine replacement probably leads to a slightly lower incidence of blockage compared to a clinically indicated change
	139 per 1000	158 per 1000 (140 to 179)				

***The risk in the intervention group** (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; **MD**: mean difference; **PIVC**: peripheral intravenous catheter; **RR**: risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1] Downgraded two levels for very serious inconsistency.

[2] Downgraded one level for serious risk of bias (no blind outcome assessment).

[3] Downgraded one level for serious inconsistency.

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 (IV) access is associated with a pooled proportion for phlebitis of 36% (Marsh 2018a), and a pooled proportion catheter-related blood stream infection (CRBSI) rate of less than 0.1% (Marsh 2018a). A number of current guidelines have been updated to reflect findings from previous versions of this systematic review (Webster 2015), recommending changing short peripheral intravenous catheters (PIVC) when there is a clinical indication to do so (Infusion Nurses Society 2011; Loveday 2014). However, the influential Centers for Disease Control (CDC) guidelines state that, "no recommendation is made regarding replacement of peripheral catheters in adults only when clinically indicated" (p. 15, O'Grady 2011). In practice most hospitals already exempt patients with poor veins from routine changes and, for children, CDC guidelines have always recommended that PIVC be replaced only when clinically indicated (O'Grady 2011). In recent years, there have been improvements in catheter design and composition, and more recent studies, including an earlier version of this review (Webster 2015), indicate that the recommendation may need to be revised. Based on level 1 evidence, the most recent Infusion Nursing Standards of Practice in the USA and the epic3 National Evidence Based Guidelines in the UK recommend that short PIVC should be replaced when clinically indicated, unless the patient is receiving parenteral nutrition peripherally (Infusion Nurses Society 2011; Loveday 2014). The projected five-year savings from implementing clinically indicated PIVC removal policies is USD 300 million and 1 million health-worker hours in the USA alone (Tuffaha 2014a; Tuffaha 2014b).

Description of the condition

Catheter-related blood stream infection (CRBSI), defined as the presence of bacteraemia originating from an intravenous (IV) catheter, is a rare but severe outcome of IV catheterisation (Gahlot 2014). The infection occurs when bacteria track along the catheter and enter the bloodstream. The bacterial source may be the patient's own skin or that of a healthcare provider; CRBSI has an attributable mortality rate of 12% to 25% (Maki 2006). Peripheral vein infusion thrombophlebitis (phlebitis) 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 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). 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 suggestion 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 of phlebitis (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 IV-administered medications, particularly flucloxacillin, which is associated with a two-fold increase in phlebitis (Marsh 2018b).

Description of the intervention

The intervention under consideration is replacing an PIVC only if there are clinical indications to do so. Clinical indications include blockage, pain, redness, infiltration, swelling, leakage, and phlebitis, as well as when therapy is completed.

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, a significant relationship was found between the number of times PIVC were inserted and phlebitis in a study of 568 IV sites (Uslusoy 2008). Consequently, it may be prudent to limit the frequency of PIVC replacements if 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 participants 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 IV 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 PIVC there were 10 cases of infusion phlebitis amongst patients who had their catheter in situ for fewer 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 participants whose PIVC had been in place for fewer 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 fewer and more than three days (Cornely 2002).

Why it is important to do this review

These observational studies and previous versions of our Cochrane Review (Webster 2010; Webster 2013; Webster 2015), create uncertainty around the US Centers for Disease Control (CDC) guidelines relating to PIVC management, which states that clinically indicated replacement in adults is an "unresolved issue" (O'Grady 2011). The recommendation referenced an earlier version of this review (Webster 2010), which showed 'no difference' between the two approaches to PIVC replacement. As long as discrepancies exist between the CDC recommendations, often seen as the gold standard, and other international guidelines, updating this review with contemporary evidence is important. Particularly when 'choosing wisely' commentators find that "routine replacement should be considered a thing that we do for no reason" (Patel 2017). The review is also important because insertion of a PIVC may be painful, especially when placed in the hand or wrist, with an average score of 4.5 on a 10-point pain scale (Tan 2016), so preventing unnecessary replacements may reduce a potentially traumatic experience for patients. Additionally, routine replacement has significant cost implications for the facility. Routine replacement costs approximately AUD 7 more per patient compared with clinically indicated replacement (Tuffaha 2014a). With an estimated two billion PIVC used globally each year (Rickard 2018), there is a clear need to provide direction for clinicians and administrators by systematically searching for and appraising relevant studies to add to the review.

O B J E C T I V E S

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

M E T H O D S

Criteria for considering studies for this review

Types of studies

We considered all randomised controlled trials (RCTs) comparing routine removal of PIVC with removal only when clinically indicated. Cross-over trials were not eligible for inclusion.

Types of participants

We included any patient requiring a PIVC 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). We excluded participants receiving parenteral fluids.

Types of interventions

We included short PIVC 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). We included any duration of time before routine replacement versus clinically indicated replacement. We excluded midline catheters and long peripheral catheters.

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 IV catheter; and colonised IV 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 (BSI, defined as a any positive blood culture drawn from a peripheral vein while an IV 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 participant
- Local infection (using any definition identified by the trial author)

- Mortality
- Pain during infusion (measured by any validated pain assessment scale)
- Satisfaction (measured by any validated satisfaction scale)

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

The Cochrane Vascular Information Specialist (CIS) conducted systematic searches of the following databases for RCTs without language, publication year or publication status restrictions:

- the Cochrane Vascular Specialised Register via the Cochrane Register of Studies (CRS-Web searched on 18 April 2018);
- the Cochrane Central Register of Controlled Trials (CENTRAL; 2018, Issue 3) via Cochrane Register of Studies Online;
- MEDLINE (Ovid MEDLINE® Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE®) (searched from 1 January 2017 to 18 April 2018);
- Embase Ovid (searched from 1 January 2017 to 18 April 2018);
- CINAHL Ebsco (searched from 1 January 2017 to 18 April 2018);
- AMED Ovid (searched from 1 January 2017 to 18 April 2018).

The Information Specialist modelled search strategies for other databases on the search strategy designed for CENTRAL. Where appropriate, they were combined with adaptations of the highly sensitive search strategy designed by the Cochrane Collaboration for identifying RCTs and controlled clinical trials (as described

in the *Cochrane Handbook for Systematic Reviews of Interventions* Chapter 6, Lefebvre 2011). Search strategies for major databases are provided in Appendix 1.

The Information Specialist searched the following trials registries on 18 April 2018:

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

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 (clinicaltrials.gov/; 12 July 2018), using the terms peripheral and intravenous and catheter and routine;
- World Health Organization International Clinical Trials Registry Platform (ICTRP; apps.who.int/trialsearch/) (12 July 2018) using the terms peripheral and intravenous and catheter;
- Australian and New Zealand Clinical Trials Registry (ANZCTR; 12 July 2018), using the terms peripheral and intravenous and catheter.

Data collection and analysis

Selection of studies

Two review authors independently reviewed titles and abstracts identified through the search process (JW, NM). We retrieved full reports of all potentially relevant trials for further assessment of eligibility based on the inclusion criteria. If we excluded any full texts, we recorded the reasons. We completed a PRISMA flow chart (Liberati 2009; Figure 1), to summarise the selection process. As the review authors were also the investigators on some of the included trials, we allocated assessment to a review author who was not an investigator (former author KN). We settled differences of opinion by consensus or referral to a third review author. There was no blinding of authorship.

Figure 1. Study flow diagram
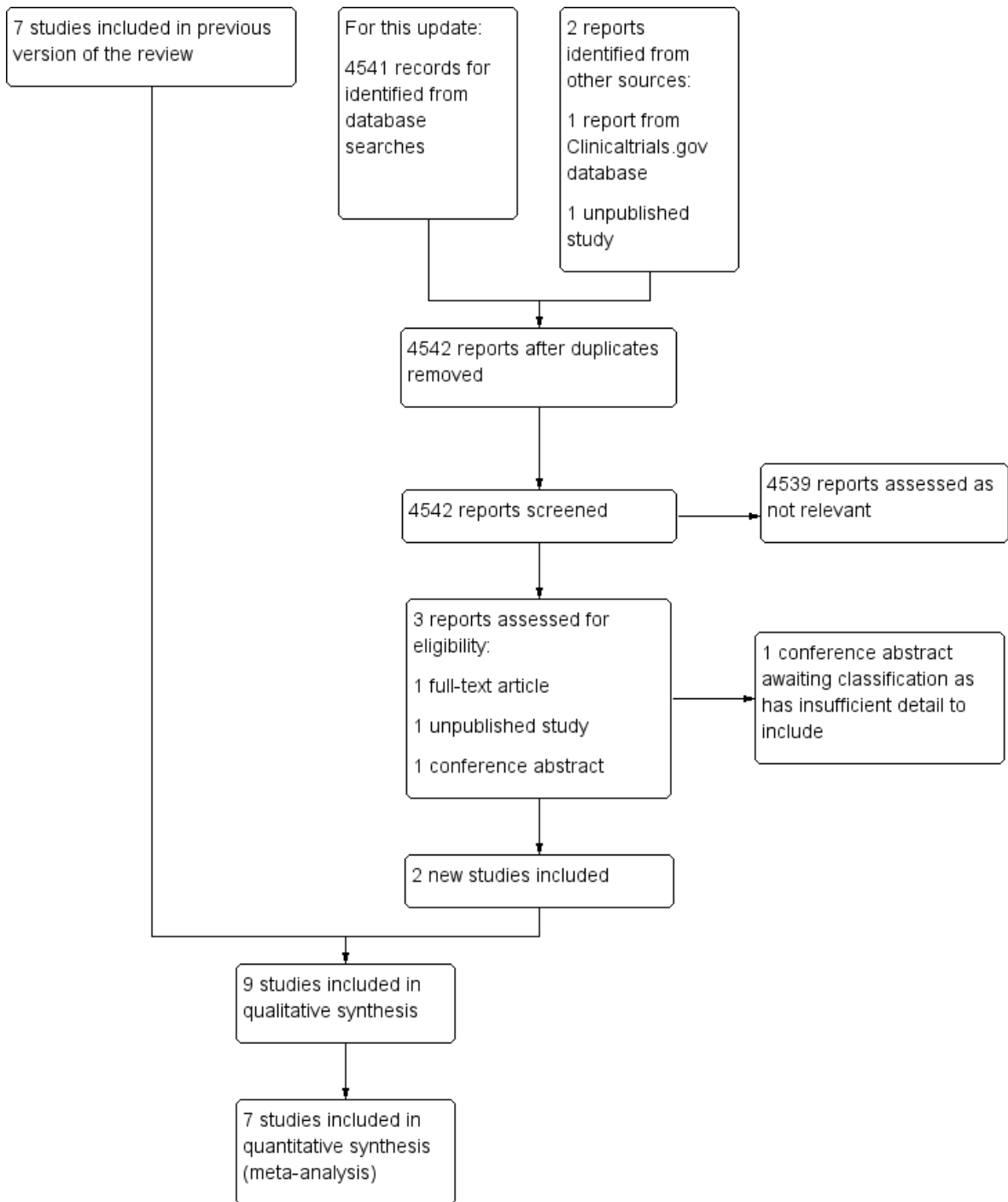
Data extraction and management

Following Cochrane Vascular recommendations, two review authors (two of JW, CR, or SO) independently extracted data to a pre-tested data extraction form. We resolved disagreements by discussion and, where necessary, by a involving 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;
- funding source;
- ethics approval and consent;
- prospective registration on a clinical trials registry.

The first review author (JW) entered the data into Review Manager 5, with another review author (NM) checking data entry accuracy (Review Manager 2014).

Assessment of risk of bias in included studies

Two review authors (two of JW, CR, SO, NM) independently assessed the included studies using the Cochrane Collaboration tool for assessing risk of bias (Higgins 2017). 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). We resolved any disagreements between review authors 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, we calculated the number needed to treat for an additional beneficial outcome (NNTB) or number needed to treat for an additional harmful outcome (NNTH).

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 we calculated the typical estimates of RR with their 95% CI; and for continuous outcomes we calculated the mean difference (MD) or a summary estimate for standardised mean difference (SMD), each with its 95% CI. We analysed data using the Cochrane Collaboration's Review Manager 5 software (Review Manager 2014).

'Summary of findings' tables

To assess the overall body of evidence, we developed 'Summary of findings' tables for the following outcomes, using GRADE approach.

- CRBSI
- Thrombophlebitis
- Thrombophlebitis per device days
- All-cause BSI
- Cost
- Infiltration
- Catheter blockage

We assessed the certainty of the body of evidence 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 (Schünemann 2017). We downgraded the evidence from 'high certainty' by one level for serious risk of bias or by two for very serious risk of bias.

Unit of analysis issues

Unit of analysis issues may arise in catheter trials when the participant is randomised but the number of outcomes are reported per catheter. We resolved this issue by using the participant as the unit of analysis if the number of catheters and number of participants were similar (assuming one catheter per individual). The more difficult challenge is where studies randomise at the participant level, use the allocated intervention on multiple catheters per participant, and then analyse outcomes per catheter. Such approaches should be treated as cluster trials. If a cluster trial had been correctly analysed, we planned to include effect estimates in any meta-analysis using the generic inverse methods in Review Manager 5 (Review Manager 2014).

Comparing longer and shorter PIVC dwell times on crude incidence of complications is also problematic; this does not take into

account the cumulative daily risk inherent with peripheral intravenous device (IVD) use. There is clearly a 'per day risk' that is present, and grows with each day of intravascular 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 participant is used as the unit of measurement (denominator for comparison), not the IVD. If a patient requires therapy, for example for five days, they 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 participant 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 also included an analysis of phlebitis per catheter days where this information was available.

Where a cluster-randomised trial had been included but incorrectly analysed, we planned to record the unit of analysis issue in our 'Risk of Bias' assessment. If possible, we planned to approximate the correct analyses based on guidance from the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011a). That is, we calculated the 'design effect' by using the formula 1+ (M-1) ICC where M is the average size of each cluster, We did identify one cluster-randomised trial, the results of which did not appear to have been adjusted (Xu 2017). For this trial, we were unable to identify an external intracluster correlation coefficient (ICC), so used an estimate of 0.02 and calculated the average cluster size to be 58.9.

Dealing with missing data

If any outcome data remained missing despite our attempts to obtain complete outcome data from trial 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 2017). If we considered data 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 2011b).

Assessment of heterogeneity

We explored clinical heterogeneity by examining potentially influential factors, for example, intervention dwell time, care setting, or participant characteristics. We assessed statistical heterogeneity using the Chi^2 test (considering $P < 0.10$ to represent significant heterogeneity), along with the I^2 statistic (Higgins 2003), which examines the percentage of total variation across studies due to heterogeneity rather than to chance. We planned to explore potential causes of moderate to significant heterogeneity ($I^2 > 30\%$) and use a random-effects approach to the analyses (Deeks 2017).

Assessment of reporting biases

We assessed reporting bias using guidelines in the *Cochrane Handbook for Systematic Reviews of Interventions* (Sterne 2017). Reporting bias occurs when reports of research results are affected by the type and direction of results. We assessed reporting bias in each study as part of our 'Risk of Bias' evaluation. If sufficient study data had been available for individual outcomes (> 10 trials), we would have developed funnel plots and inspected them for evidence of publication bias.

Data synthesis

Where clinical and statistical heterogeneity was low, we pooled results of comparable trials using a fixed-effect model, and reported the pooled estimate together with its 95% CI. Otherwise, we used a random-effects model for our meta-analytic approach. In cases where clinical heterogeneity between studies was similar but heterogeneity was high, we planned to meta-analyse results and attempt to provide an explanation for the heterogeneity. 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.

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

Sensitivity analysis

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

- Concealment of allocation

- Size of studies (< 100 participants versus at least 100 participants)
  - Duration of follow-up
  - Unpublished studies

RESULTS

Description of studies

Results of the search

See Figure 1.

For this update, we identified 4541 unique records through our electronic search. After reading titles and abstracts there were two additional citations which we considered potentially relevant (Chin 2018; Xu 2017). Chin 2018 was an abstract of an Australian trial in newborn infants with insufficient information in the report to consider inclusion. We contacted the author, asking for further study details but have had no response; we have placed a reference to the report in the Studies awaiting classification section of the review. We retrieved the full text of the second study and have included it in this update (Xu 2017). We have also included results from an unpublished study, which we were aware of through our network of intravascular device researchers (Vendramim 2018). We did not find any additional trials in our search of trials registries.

Included studies

Nine RCTs, involving a total of 7392 participants met the inclusion criteria (Barker 2004; Nishanth 2009; Rickard 2010; Rickard 2012; Van Donk 2009; Vendramim 2018; Webster 2007; Webster 2008; Xu 2017), see Characteristics of included studies for details. Individual trial sizes ranged between 42 and 3283 participants. Five trials were carried out in Australia (Rickard 2010; Rickard 2012; Van Donk 2009; Webster 2007; Webster 2008), and one each was carried out in Brazil (Vendramim 2018), China (Xu 2017), England (UK (Barker 2004)), and India (Nishanth 2009). Five of the trials were conducted in single-centre, acute inpatient settings (Barker 2004; Nishanth 2009; Rickard 2010; Webster 2007; Webster 2008), two were multicentred trials in large tertiary hospitals - one in Australia (Rickard 2012) and one in Brazil (Vendramim 2018); the Chinese trial was a cluster trial, which randomised 20 hospital wards (Xu 2017); and one trial was undertaken in a community setting (Van Donk 2009).

In eight trials (Barker 2004; Nishanth 2009; Rickard 2010; Rickard 2012; Vendramim 2018; Webster 2007; Webster 2008; Xu 2017), 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 seven trials (Rickard 2010; Rickard 2012; Van Donk 2009; Vendramim 2018; Webster 2007; Webster 2008; Xu 2017), the comparison was between routine care (planned 72- to 96-hour 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.

Xu 2017; Rickard 2010 and Rickard 2012 defined CRBSI by using the CDC definition: a positive blood culture from a peripheral vein; clinical signs of infection; no other apparent source for the bloodstream infection except the IV catheter (in situ within 48 hours of the bloodstream infection); and a colonised IV catheter tip with the same organism identified in the blood (O'Grady 2011). In the Webster 2007 and Webster 2008 trials CRBSI was based on the isolation of a phenotypically identical organism from a catheter segment and a blood culture. None of the other trials provided definitions of CRBSI. Seven of the trials used a standard definition of two or more of the following: pain, warmth, erythema, swelling, or a palpable cord to define phlebitis (Barker 2004; Rickard 2010; Rickard 2012; Vendramim 2018; Webster 2007; Webster 2008; Xu 2017). 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 participant may have had only one symptom, for example pain, to receive a positive diagnosis.

Nishanth 2009; Rickard 2010; Rickard 2012; Van Donk 2009; Vendramim 2018; Webster 2007; Webster 2008; and Xu 2017 reported power calculations but Barker 2004 did not. All of the studies had institutional ethical approval.

Excluded studies

We did not exclude any new studies in this update. The table Characteristics of excluded studies contains the reasons for excluding nine trials (Arnold 1977; Cobb 1992; Eyer 1990; Haddad 2006; Kerin 1991; May 1996; Nakae 2010; Panadero 2002; Rijnders 2004). 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). 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. Haddad 2006 compared 72-hour changes with 96-hour changes, and Cobb 1992; Eyer 1990; Nakae 2010; and Rijnders 2004 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
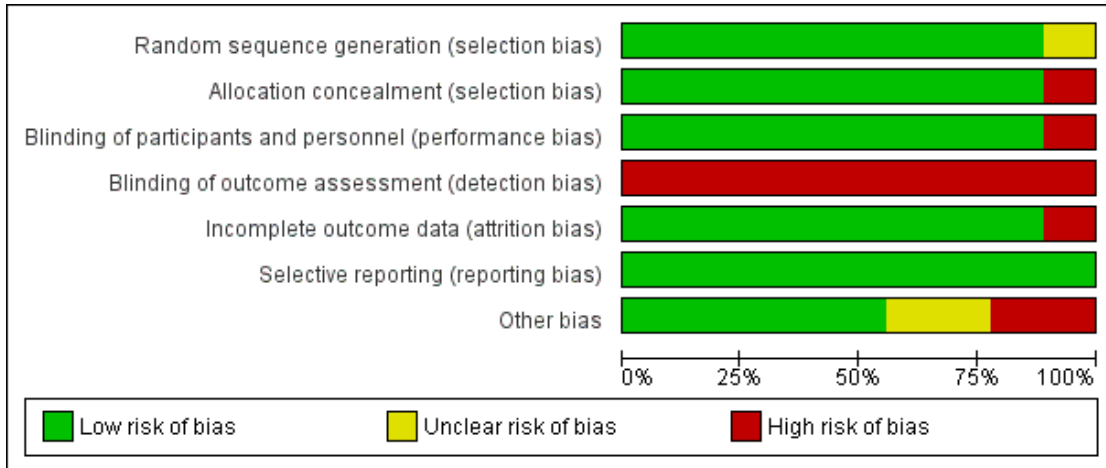
Figure 3. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study

Allocation

Generation of random allocation sequence

Eight of the nine investigators reported that they used a computer-based sequence generator (Barker 2004; Nishanth 2009; Rickard 2010; Rickard 2012; Van Donk 2009; Vendramim 2018; Webster 2007; Webster 2008). Xu 2017 used a 'coin toss' to generate the random sequence. All studies were at low risk of bias except for Nishanth 2009, where it was unclear how they had generated the sequence.

Allocation concealment

Barker 2004; Nishanth 2009 and Van Donk 2009 used sealed envelopes for allocation concealment. Vendramim 2018 provided each ward with a sequentially numbered, randomised list. A coin toss in the Xu 2017 trial concealed allocation until randomisation. The remaining four trials used a central telephone or computer-based service (Rickard 2010; Rickard 2012; Webster 2007; Webster 2008). All studies were at low risk of bias except for Nishanth 2009, which was at high risk due to the investigators being responsible for allocation.

Blinding

It was not possible to blind either the participants or the healthcare providers in any of the trials but we did not believe that outcomes would be affected by this knowledge so we judged all trials to be at low risk of performance bias, except for Barker 2004 which we considered to be at high risk of bias because the investigator was involved in all stages of the study.

Outcome assessment

The chief investigator was directly involved in assessing outcomes in Barker 2004 and Nishanth 2009. In the Van Donk 2009; Vendramim 2018; Webster 2007 and Webster 2008 trials, nurses caring for the participant or a dedicated IV service nurse made the assessment. None of the nurses were blinded to the group allocation but nor were any of them associated with the trial. In Rickard 2010; Rickard 2012 and Xu 2017, a dedicated research nurse, who was also aware of the allocation, undertook outcome assessment. Because outcome assessment could not be blinded (except for CRBSI), we classified all trials as high risk of bias.

Incomplete outcome data

Barker 2004 did not provide a flow chart, so the numbers screened and eligible were unclear, nor did they report any dropouts. 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. They did not report the number of protocol violations by group, and we judged Barker 2004 to be at high risk of attrition bias. The remaining eight studies were at low risk of bias as there was complete reporting and all provided a flow of participants through each stage and used intention-to-treat analysis (Nishanth 2009; Rickard 2010; Rickard 2012; Van Donk 2009; Vendramim 2018; Webster 2007; Webster 2008; Xu 2017). Nishanth 2009 did not report any protocol violations in the trial. In the Van Donk 2009; Vendramim 2018; Webster 2007; Webster 2008; and Xu 2017 trials, between 7% and approximately one third of the participants had protocol violations. Primarily, violations were in the routine replacement groups, where catheters were not replaced within the specified time period, reflecting day to day clinical practice.

Selective reporting

All studies were at low risk of reporting bias. Study protocols were available for seven trials and reporting followed pre-planned analyses (Rickard 2010; Rickard 2012; Van Donk 2009; Vendramim 2018; Webster 2007; Webster 2008; Xu 2017). Barker 2004 had only one outcome (phlebitis) and Nishanth 2009 reported on outcomes expected in this type of trial.

Other potential sources of bias

Five studies were at low risk of other bias (Rickard 2012; Van Donk 2009; Vendramim 2018; Webster 2007; Webster 2008). Barker 2004 used two definitions of phlebitis, one of which stated that two symptoms were necessary; yet it appears that they diagnosed erythema alone as phlebitis, with severity based on the area of inflammation; which leads to an assessment of high risk for other bias. The extreme results in Nishanth 2009, 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, to which we also gave a high-risk judgement. Two studies were at unclear risk of bias (Rickard 2010; Xu 2017). The Xu 2017 cluster-randomised trial analysed by individual not cluster; and significantly more participants in the routine-change group received IV antibiotics compared to the clinically indicated group in Rickard 2010.

Effects of interventions

See: **Summary of findings for the main comparison** Effects of clinically-indicated replacement compared to routine change of peripheral intravenous catheters

Routine changes versus clinically indicated changes

Catheter-related bloodstream infection (Analysis 1.1)

Seven trials (7323 participants) assessed catheter-related bloodstream infection (CRBSI; Rickard 2010; Rickard 2012; Van Donk 2009; Vendramim 2018; Webster 2007; Webster 2008; Xu 2017). There were no reported CRBSIs in five of these trials (Rickard 2010; Van Donk 2009; Vendramim 2018; Webster 2007; Xu 2017). There is no clear difference in the incidence of CRBSI between the clinically indicated (1/3590) and routine-change (2/3733) groups. The RR was 0.61 but the confidence intervals (CI) were wide, creating uncertainty around the estimate (95% CI 0.08 to 4.68; Figure 4; Analysis 1.1). We judged the evidence as low certainty, as we downgraded two levels for serious imprecision.

Figure 4. Forest plot of comparison 1, clinically indicated versus routine change, outcome: 1.1 Catheter-related bloodstream infection

Thrombophlebitis (Analysis 1.2 and Analysis 1.3)

All of the included studies reported incidence of phlebitis; the initial analysis was based on 7412 participants. When results of all trials were combined, heterogeneity was 65%. Consequently, we conducted a sensitivity analysis and removed the two trials with fewer than 100 participants (combined total n = 89), both of which used a two-day replacement schedule and reported extreme results (Barker 2004; Nishanth 2009). Removing the two trials eliminated the heterogeneity ($I^2 = 0$). We combined data from the remaining seven studies, with 7323 participants (Rickard 2010; Rickard 2012; Van Donk 2009; Vendramim 2018; Webster 2007; Webster 2008; Xu 2017). There was no clear difference in this outcome, whether catheters were changed according to clinical indications or routinely (RR 1.07, 95% CI 0.93 to 1.25; clinically indicated 317/3590; 3-day change 307/3733; moderate-certainty evidence, downgraded once for serious risk of bias (no blinding of outcome assessment in any of the trials)). The result was unaffected by whether the infusion was continuous or intermittent (Analysis 1.2; Figure 5).

Figure 5. Forest plot of comparison 1, clinically indicated versus routine change, outcome: 1.2 Phlebitis

Study or Subgroup	Clinically indicated Events	Total	Routine replacement Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
1.2.1 Continuous infusion							
Rickard 2010	18	185	12	177	4.1%	1.44 [0.71, 2.89]	
Rickard 2012	114	1593	114	1690	36.8%	1.06 [0.83, 1.36]	
Vendramim 2018	55	672	64	647	21.7%	0.83 [0.59, 1.17]	
Webster 2007	1	103	2	103	0.7%	0.50 [0.05, 5.43]	
Webster 2008	16	379	12	376	4.0%	1.32 [0.63, 2.76]	
Xu 2017	76	553	77	645	23.7%	1.15 [0.86, 1.55]	
Subtotal (95% CI)		3485		3638	90.9%	1.05 [0.90, 1.23]	
Total events	280		281				
Heterogeneity: Chi² = 3.74, df = 5 (P = 0.59); I² = 0%							
Test for overall effect: Z = 0.64 (P = 0.52)							
1.2.2 Intermittent infusion							
Van Donk 2009	37	105	26	95	9.1%	1.29 [0.85, 1.96]	
Subtotal (95% CI)		105		95	9.1%	1.29 [0.85, 1.96]	
Total events	37		26				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.19 (P = 0.24)							
Total (95% CI)		3590		3733	100.0%	1.07 [0.93, 1.25]	
Total events	317		307				
Heterogeneity: Chi² = 4.52, df = 6 (P = 0.61); I² = 0%							
Test for overall effect: Z = 0.95 (P = 0.34)							
Test for subgroup differences: Chi² = 0.78, df = 1 (P = 0.38), I² = 0%							

0.05 0.2 1 5 20
Favours cl-indicated   Favours 3-day

In the two trials using a two-day replacement schedule compared with clinically indicated changes (Barker 2004; Nishanth 2009), heterogeneity was over 60% so we did not combine results. 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. We judged the evidence from these two trials to be very low certainty, downgraded two levels for very

serious risk of bias and two levels for very serious imprecision.
Six of the trials provided phlebitis rates by number of device days (Rickard 2010; Rickard 2012; Van Donk 2009; Vendramim 2018; Webster 2007; Webster 2008), but again, there is no clear difference between groups for this outcome (RR 0.90, 95% CI 0.76 to 1.08; clinically indicated 248/17,251; 3-day change 236/15,458; moderate-certainty evidence, downgraded once for serious risk of bias (no blind outcome assessment in any of the trials); Analysis 1.3; Figure 6).

Figure 6. Forest plot of comparison 1 clinically indicated versus routine change, outcome: 1.3 Phlebitis per device days

Study or Subgroup	Clinically indicated Events	Total	Routine replacement Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Rickard 2010	18	1120	12	970	5.1%	1.30 [0.63, 2.68]	
Rickard 2012	114	8693	114	8719	44.8%	1.00 [0.77, 1.30]	
Van Donk 2009	37	698	26	508	11.9%	1.04 [0.64, 1.69]	
Vendramim 2018	62	3825	70	2693	32.4%	0.62 [0.44, 0.87]	
Webster 2007	1	522	2	548	0.8%	0.52 [0.05, 5.77]	
Webster 2008	16	2393	12	2020	5.1%	1.13 [0.53, 2.37]	
Total (95% CI)		17251		15458	100.0%	0.90 [0.76, 1.08]	
Total events	248		236				
Heterogeneity: Chi² = 7.04, df = 5 (P = 0.22); I² = 29%							
Test for overall effect: Z = 1.15 (P = 0.25)							

0.05 0.2 1 5 20
Favours cl-indicated   Favours 3-day

All-cause bloodstream infection (Analysis 1.4)

One trial assessed this outcome (Rickard 2012). We found no clear

difference in the all-cause bloodstream infection rate between the two groups (RR 0.47, 95% CI 0.15 to 1.53; clinically indicated: 4/1593 (0.02%); routine change 9/1690 (0.05%)). We judged the

evidence as moderate certainty, downgraded one level for serious imprecision (Analysis 1.4).

Cost (Analysis 1.5)

Three trials (4244 participants) measured this outcome (Rickard 2012; Webster 2007; Webster 2008). Device-related costs were measured in Australian dollars (AUD). Clinically indicated removal probably reduces device-related costs by approximately AUD 7.00 per participant compared with routine removal (MD −6.96, 95% CI −9.05 to −4.86; moderate-certainty evidence, downgraded once for serious risk of bias (no blind outcome assessment in any of the trials); Analysis 1.5).

Infiltration (Analysis 1.6)

A total of six trials assessed infiltration in 7123 participants (Rickard 2010; Rickard 2012; Vendramim 2018; Webster 2007; Webster 2008; Xu 2017). Routine replacement probably reduces infiltration of fluid into surrounding tissues (747/3638; 20.5%) compared with the clinically indicated group (834/3485; 23.9%). The RR was 1.16 (95% CI 1.06 to 1.26); moderate-certainty evidence, downgraded once for serious risk of bias (no blinding of outcome assessment in any of the trials; Analysis 1.6).

Catheter occlusion/blockage (Analysis 1.7)

We included seven of the nine trials, reporting on 7323 participants, in this analysis (Rickard 2010; Rickard 2012; Van Donk 2009; Vendramim 2018; Webster 2007; Webster 2008; Xu 2017). Rates of catheter failure due to blockage were probably lower in the routine-replacement group compared to the clinically indicated group (RR 1.14, 95% CI 1.02 to 1.27; routine-replacement group 519/3733 (13.9%); clinically indicated group 560/3590 (15.6%); Analysis 1.7). We judged the evidence as moderate certainty, as we downgraded once for serious risk of bias (no blinding of outcome assessment in any of the trials).

Local infection (Analysis 1.8)

Among the four trials measuring local infection (Rickard 2010; Rickard 2012; Webster 2007; Webster 2008), it is uncertain if there are differences in local infection rates between groups (RR 4.96, 95% CI 0.24 to 102.98; clinically indicated 2/2260 (0.09%); routine replacement 0/2346 (0.0%); very-low-certainty evidence, downgraded one level for serious risk of bias (no blinding of outcome assessment in any of the trials) and two levels for very serious imprecision (Analysis 1.8)).

Mortality (Analysis 1.9)

One trial reported this outcome (Rickard 2012). In the clinically indicated group 4/1593 (0.25%) died compared with 4/1690 (0.24%) in the routine-replacement group (RR 1.06, 95% CI 0.27 to 4.23). We judged the evidence as low certainty, downgraded two levels for very serious imprecision (Analysis 1.9).

Pain during infusion (Analysis 1.10)

Vendramim 2018 (198 participants), measured pain on an 11-point scale (0 to 10), where higher scores represented higher levels of pain. There was no clear difference in device-related pain between clinically indicated and routine-removal groups. The mean pain score in the clinically indicated group was 4.6 (SD 3.0), compared with 5.2 (SD 3.0), in the routine replacement group (MD −0.60, 95% CI −1.44 to 0.24; low-certainty evidence, downgraded one level for serious risk of bias (no blinding of outcome assessment in any of the trials) and one-level for serious imprecision; Analysis 1.10).

The pre-planned outcomes 'number of catheter re-sites per patient', and 'satisfaction' were not reported by 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. We did not conduct any of our pre-planned sensitivity analyses (except size of studies for the outcome 'phlebitis'), for similar reasons.

DISCUSSION

Summary of main results

This systematic review analysed catheter-related bloodstream infection (CRBSI), 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 warranting removal or replacement were apparent. This update, which added a further two trials, confirms findings from the previous version of this review (Webster 2015). The primary outcomes suggest that patients are not adversely affected if the catheter is changed based on clinical indications rather than routinely. The rate of catheter-related bloodstream infection was similar in both groups, between 0.03% and 0.05%, and comparable to that previously reported in prospective studies (Maki 2006).

Because the incidence of peripheral intravenous (IV) CRBSI is very low, mounting a trial with sufficient power to show differences in CRBSI between catheters removed routinely or by clinical indication would be prohibitive. There is no clear difference in the phlebitis rate between groups whether rates are reported by the incidence per participant or by 1000 device days, which is a more clinically useful measure. Most cases of phlebitis are mild in nature, requiring no treatment or only 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 less, around AUD 7.00 per participant, 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 of peripheral intravenous catheters (PIVC).

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 Barker 2004 and Nishanth 2009, results from the other seven trials were quite similar, providing useful external validity. For example, participants were representative of those usually managed in healthcare, including patients in both acute and community settings. Additionally, measured outcomes were those important to clinicians and patients. 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), and none of the trials involved research nurses or IV teams providing post-insertion care of catheters. 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. Barker 2004 and Nishanth 2009 changed catheters every 48 hours. Only Rickard 2012 was 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 participants 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 Nishanth 2009, where all participants 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 nine included trials were conducted in Australia; this imbalance is difficult to understand but the two additional studies, one from China (Xu 2017), and one from Brazil (Vendramim 2018), provide added diversity to the evidence and increase external validity. It would be useful to see similar studies from other healthcare settings to test the robustness of results from this review. Only Vendramim 2018 assessed levels of pain, and none of the trials measured device-related satisfaction or number of catheter re-sites per participant. These outcomes would be a useful addition to any future trial.

Quality of the evidence

See Summary of findings for the main comparison

Overall we found the quality of evidence for most outcomes to be of moderate to low quality, primarily due to risk of bias (particularly non-blinding of the outcome assessor), and imprecision. Imprecision was due in some cases, such as 'pain', to few participants but in other cases, such as mortality, to few events.

Limitations in study design and implementation

We assessed risk of bias according to six components: sequence generation, allocation concealment, blinding, selective outcome reporting, incomplete follow-up, and other potential biases. All of the studies (except Nishanth 2009), avoided selection bias and ensured allocation concealment. We rated the evidence for methodological quality of most of the outcomes as moderate. It was not possible to blind the intervention in any of the trials 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 we decided to downgrade one level for all outcomes except CRBSI, where a blinded microbiologist diagnosed the condition. However, as one trial author noted, it is routine practice to record reasons for removal of an IV catheter in the medical record, and it is unlikely that such entries would be falsified based on group allocation (Webster 2008). In Barker 2004 and Nishanth 2009, 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.

Indirectness of evidence

All of the trials compared routine changes with clinically indicated changes. However, seven 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 Nishanth 2009 included participants who were from a low-income 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 nine studies. Results of all trials are presented in the review text and of seven trials in the 'Summary of findings' table (Summary of findings for the main comparison).

Imprecision of results

Confidence intervals were wide in the pooled outcomes of CRBSI, all-cause blood stream infection, local infection, mortality and pain, 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, handsearching, and searches of large clinical trials databases, identified all existing, published, randomised controlled trials addressing the review question. We also have an established international network of researchers in the field of vascular access, who alert us to new trials. We would have developed a funnel plot to detect reporting bias, if we had included more than 10 studies in the review.

Potential biases in the review process

Although the review authors were investigators in one or more of the included trials, we followed clearly described procedures to prevent potential biases in the review process. We conducted a careful literature search and the methods we used were transparent and reproducible. None of the review 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 intravenous device (IVD) dwell times (Abolfotouh 2014; Catney 2001; White 2001). In addition, two implementation studies, which changed their policies to replacing PIVCs only if clinical indications were present, showed no increase in rates of PIVC-related infection (Bolton 2015; De Vries 2016). In addition, Bolton 2015 reported a significant cost saving with a 25% stock reduction. Similarly, in the De Vries 2016 study, peripheral line start kits were reduced by 48% in the year following the policy change. Two recently published reviews, assessing the effect of changing PIVCs only where a clinical indication exists also concurred with our results (Morrison 2015; Patel 2017). Importantly, international and other guidelines have been changed to reflect the results of this review (Gorski 2016; Ho 2011; Loveday 2014). One of our outcomes was catheter-related blood stream infection (CRBSI). We included seven RCTs (over 7000 participants), and found no evidence that dwell time had any effect on this outcome. In contrast, in another systematic review, Mermel 2017 suggested that longer dwell times resulted in higher CRBSI rates. The reason for the discrepancy between the two reviews is the inclusion criteria. We included only RCTs whereas Mermel 2017 included incidence studies, quality improvement studies, quasi-experimental designs and a number of RCTs where difference in dwell time was not the focus of the study. When participants are not randomised, or not randomised for the purpose of assessing the effect of dwell time on catheter-related outcomes, a potential for bias exists. For example, the sickest participants, those most likely to develop a CRBSI, are also those who would be expected to have their catheters in place for longer periods. Randomisation ensures risk factors that may affect the outcome, are equally distributed between groups.

AUTHORS' CONCLUSIONS

Implications for practice

This review update found moderate to low-certainty evidence of no clear difference in rates of catheter-related bloodstream infection (CRBSI), thrombophlebitis, all-cause bloodstream infection,

mortality or pain between clinically indicated or routine replacement of peripheral intravenous catheters. We are uncertain if local infection is reduced or increased when catheters are changed when clinically indicated. There is moderate-certainty evidence that infiltration and catheter blockage is probably lower when PIVC are changed routinely; and moderate-certainty evidence that clinically indicated removal probably reduces device-related costs. The consistency in these results, which include two very large multisite studies, indicate that healthcare organisations should consider changing to a policy whereby catheters are changed only if there is a clinical indication to do so, for example, if there were signs of infection, blockage or infiltration. 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. Time spent by busy clinical staff on this intervention would also be reduced. 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, or as soon as therapy is completed.

Implications for research

Based on results from the meta-analyses in this review, a sample size of greater than 25,000 participants would be required to show clear differences between groups for the most important outcomes in this review, that is CRBSI and phlebitis. Consequently, it is unlikely that such a trial is warranted, given the low event rate for CRBSI and the very high number needed to treat (almost 1700) for one patient to avoid phlebitis.

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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, UK **Number:** 47 patients in general medical or surgical wards. Clinically indicated: 43 catheters were inserted in 26 participants. Routine replacement: 41 catheters were inserted in 21 participants **Age:** clinically indicated 60.5 years (15.5); routine replacement 62.7 years (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 h
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 trial author stated that "even a small area of erythema was recorded as phlebitis" (i.e. only 1 sign) It is unclear what proportion of participants 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

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Comment:** computer-generated (personal communication with trial author)
Allocation concealment (selection bias)	Low risk	**Comment:** sealed envelopes (personal communication with trial author)
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Evidence:** "Forty-seven patients were included in this randomised, controlled, unblinded study" **Comment:** classified as high risk because the investigator was involved in all stages of

Barker 2004 (*Continued*)

		the study
Blinding of outcome assessment (detection bias) All outcomes	High risk	**Evidence:** "Forty-seven patients were included in this randomised, controlled, unblinded study"
Incomplete outcome data (attrition bias) All outcomes	High risk	**Comment:** in this small sample, there were five fewer participants 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 participants 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 years (15.0); routine replacement 42.9 years (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 < 3 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 h
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	**Evidence:** "The patients were allocated to either study or the control group using block randomisation method. The patients were divided into 6 blocks with block sizes of 8 or 10 or 12 arranged randomly" **Comment:** how the sequence was generated was not stated. With group sizes of 21 per group, that block sizes make no sense
Allocation concealment (selection bias)	High risk	**Evidence:** "Group name was placed (on) an opaque serially numbered sealed envelope (SNOSE)." **Comment:** presumably the trial authors meant 'in' an opaque serially numbered sealed envelope - based on subsequent information. The investigator was responsible for allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence:** "..unblinded study" **Comment:** neither participants nor clinical personnel were blinded but review authors do not believe this would introduce bias
Blinding of outcome assessment (detection bias) All outcomes	High risk	**Evidence:** "...unblinded study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** data for all participants were available
Selective reporting (reporting bias)	Low risk	**Comment:** stated outcomes were reported but original protocol not sighted
Other bias	High 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. Clin-

	ically indicated: 280 catheters were inserted in 185 participants. Routine replacement: 323 catheters were inserted in 177 participants **Age:** clinically indicated 62.7 years (15.5); routine replacement 65.1 years (17.3) **Sex (M/F):** clinically indicated 82/103; routine replacement 81/91 **Inclusion criteria:** > 18 years, expected to have an IVD, requiring IV therapy for $\geq$ 4 days **Exclusion criteria:** patients who were immunosuppressed, had an existing BSI or those in whom an IVD had been in place for > 48 h
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 h
Outcomes	**Primary:** phlebitis per person and per 1000 IVD days (defined as $\geq$ 2 of the following: pain, erythema, purulence, infiltration, palpable venous cord); IVD-related bacteraemia **Secondary:** hours of catheterisation; number of IV devices; device-related BSI; infiltration; local infection
Notes	Approximately 75% of participants were receiving a continuous infusion

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Evidence:** "Patients were randomly assigned (computer generated)"
Allocation concealment (selection bias)	Low risk	**Evidence:** "Assignment was concealed until randomisation by use of a telephone service"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence:** "Open (non-blinded) parallel group RCT" **Comment:** neither participants nor clinical personnel were blinded but review authors do not believe this would introduce bias
Blinding of outcome assessment (detection bias) All outcomes	High risk	**Comment:** although laboratory staff were blinded for microbiological outcomes, there were no BSIs; consequently, all other outcome assessment was at high risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** results from all enrolled participants were reported
Selective reporting (reporting bias)	Low risk	**Comment:** the protocol was available. All nominated outcomes were reported

Rickard 2010 *(Continued)*

Other bias	Unclear risk	**Comment:** significantly more participants in the routine-change group received IV antibiotics (73.1% versus 62.9%)

Rickard 2012

Methods	**Study design:** multicentre 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:** 3283 patients requiring IV therapy in general medical or surgical wards. Clinically indicated: 1593 participants. Routine replacement: 1690 participants **Age:** clinically indicated 55.1 years (18.6); routine replacement 55.0 years (18.4) **Sex (M/F):** clinically indicated 1022/571; routine replacement 1034/656 **Inclusion criteria:** patients, or their representative able to provide written consent; > 18 years, expected to have an IVD in situ, requiring IV therapy for ≥ 4 days **Exclusion criteria:** patients who were immunosuppressed, had an existing BSI or those in whom an IVD had been in place for > 48 h or it was planned for the catheter to be removed < 24 h
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 h
Outcomes	**Primary:** phlebitis during catheterisation or within 48 h of removal (defined as ≥ 2 of the following: pain, erythema, swelling, purulent discharge, palpable venous cord) **Secondary:** CRBSI, all-cause BSI, local venous infection, colonisation of the catheter tip, infusion failure, number of catheters per participant, overall duration of IV therapy, cost, mortality
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Evidence:** "Random allocations were computer-generated"
Allocation concealment (selection bias)	Low risk	**Evidence:** "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"

Rickard 2012 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence:** "Patients and clinical staff could not be blinded ....Research nurses were similarly not masked" **Comment:** neither participants nor clinical personnel were blinded but review authors do not believe this would introduce bias
Blinding of outcome assessment (detection bias) All outcomes	High risk	**Evidence:** "... 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" **Comment:** diagnosis of all other outcomes was unblinded
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

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 participants. Routine replacement: 95 participants **Age:** clinically indicated 62.8 years (18.2); routine replacement 54.5 years (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 h
Outcomes	**Primary:** phlebitis per participant and per 1000 device days (phlebitis was defined as a total score of $\geq$ 2 points from the following factors: pain (on a 10-point scale, 1 = 1 point, and $\geq$ 2 = 2 points); redness (< 1 cm = 1 point, and $\geq$ 1 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

Van Donk 2009 *(Continued)*

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Comment:** computer-generated allocation (personal communication with trial author)
Allocation concealment (selection bias)	Low risk	**Evidence:** "Randomization was concealed until treatment via sealed envelopes"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** neither participants nor clinical personnel were blinded but review authors do not believe this would introduce bias
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessment unable to be blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** participant flow chart provided. Results from all enrolled participants were reported
Selective reporting (reporting bias)	Low risk	**Comment:** all planned outcomes were reported
Other bias	Low risk	No other known risks of bias

Vendramim 2018

Methods	**Study design:** multicentre, non-inferiority, RCT **Method of randomisation:** computer-generated **Concealment of allocation:** sequentially numbered, sealed envelopes
Participants	**Country:** Brazil **Number:** 1319. Clinically indicated: 672 participants. Routine replacement: 647 participants **Age:** clinically indicated 59.7 (20.9); routine replacement 59.9 years (20.1) **Sex (M/F):** clinically indicated 339/333; routine replacement 318/329 **Inclusion criteria:** • "aged at least 18 years, expected use of PIVC for at least 96 hours, patients with PIVC inserted in data collection units (wards), intensive care units or surgical centres and accepted of the proposals expressed in the Informed Consent Form by the patient or by someone responsible for the patient. Patients aged eighteen and older, from two São Paulo City hospital" (personal communication) **Exclusion criteria:**

	• "blood stream infection and or sepsis, neutrophil less than or equal to 1000/mm^3 and simultaneous use of more than one PIVC" (personal communication)
Interventions	**Clinically indicated:** catheters were removed according to clinical signs **Routine replacement:** catheters were replaced systematically every 96 h
Outcomes	**Primary:** phlebitis **Secondary:** pain; infiltration; occlusion; accidental removal; extravasation
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Evidence:** "A computerized randomization program (random.org), a list prepared in blocks of six patients and stratified by ward and per hospital. Thus, each ward had its own randomization list, totaling 10 lists of randomization, six in Hospital A and four in Hospital B". (Personal communication)
Allocation concealment (selection bias)	Low risk	**Evidence:** "At the moment of the recruitment, that is, after the acceptance of the patient, the assistants have sent a message from a App (whatsApp) and I indicated the group" **Comment:** the person providing the allocation was unaware of the status of the potential participant and the person recruiting the participant was unaware of the allocation sequence
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Comment:** neither participants nor clinical personnel were blinded but review authors do not believe this would introduce bias
Blinding of outcome assessment (detection bias) All outcomes	High risk	Unblinded study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses in either group. ITT analysis available
Selective reporting (reporting bias)	Low risk	Expected outcomes reported. Consistent with ClinicalTrials.gov entry
Other bias	Low risk	None detected

Webster 2007 *(Continued)*

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 participants. Routine replacement: 103 participants **Age:** clinically indicated 60.2 years (16.2); routine replacement 63.1 years (17.3) **Sex (M/F):** clinically indicated 53/50; routine replacement 54/49 **Inclusion criteria:** ≥ 18 years of age, expected to have an IVD in situ, requiring IV therapy for ≥ 4 days, catheter inserted by a member of the IV team **Exclusion criteria:** immunosuppressed patients and those with an existing BSI
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 min 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 participants receiving a continuous infusion: all the above costs plus the additional cost of replacing all associated lines, solutions and additives that are discarded when an IV catheter is changed (based on an IV administration set, 1 L sodium chloride 0.09%)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Evidence:** "Randomization was by computer generated random number list, stratified by oncology status"
Allocation concealment (selection bias)	Low risk	**Evidence:** "Allocation was made by phoning a person who was independent of the recruitment process"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence:** "Clinical staff were subsequently aware of the treatment group" **Comment:** neither participants nor clinical personnel were blinded but reviewers do not believe this would introduce bias

Blinding of outcome assessment (detection bias) All outcomes	High risk	**Evidence:** "Research staff had no involvement in nominating the reason for catheter removal or in diagnosing phlebitis" **Comment:** diagnosis of all outcomes were unblinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** all recruited participants 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 participants. Routine replacement: 376 participants **Age:** clinically indicated 60.1 years (17.1); routine replacement 58.8 years (18.8) **Sex (M/F):** clinically indicated 248/131; routine replacement 233/143 **Inclusion criteria:** $\geq$ 18 years of age, expected to have a IVD in situ, requiring IV therapy for $\geq$ 4 days **Exclusion criteria:** immunosuppressed patients and those with an existing BSI
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 $\geq$ 2 of the following: pain, erythema, purulence, infiltration, palpable venous cord) and infiltration
	Secondary:
	• infusion-related costs.
	   ◦ for intermittent infusion: 20-min 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 continuous infusion: all the above costs plus the additional cost of replacing all associated lines, solutions and additives that are discarded when an IV catheter is changed (based on an IV administration set, 1 L sodium chloride 0.09%)
	• Individual reasons for catheter failure (occlusion/blockage, local infection)
	Also reported: bacteraemia rate

Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	**Evidence:** "Block randomisation was by a computer generated random number list"
Allocation concealment (selection bias)	Low risk	**Evidence:** "…. telephoned a contact who was independent of the recruitment process for allocation consignment"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence:** "Allocation concealment avoided selection bias but clinical staff were subsequently aware of the treatment group" **Comment:** neither participants nor clinical personnel were blinded but review authors do not believe this would introduce bias
Blinding of outcome assessment (detection bias) All outcomes	High risk	**Evidence:** "Staff in the microbiological laboratory were blind to group assignment of catheters submitted for testing" **Comment:** all other outcomes were unblinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	All recruited participants 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

Xu 2017

Methods	**Study design:** cluster-RCT of 20 wards in a tertiary referral hospital in China **Method of randomisation:** coin toss **Concealment of allocation:** coin toss
Participants	**Country:** China **Number:** clinically indicated: 553 patients. Routine replacement: 645 patients **Age:** clinically indicated 58.7 years (39.7); routine replacement 56.2 years (27.1) **Sex (M/F):** clinically indicated 325/208; routine replacement 335/310 **Inclusion criteria:** adult patients > 18 years of age who received catheter infusion; patients who were expected to use the indwelling catheter for ≥ 3 days; patients who used PIVCs for the first time during hospitalisation; and patients who agreed to participate in this study **Exclusion criteria:** patients with BSI or under immunosuppressive therapy; patients

	receiving parenteral nutrition infusion through PIVC; patients with indwelling catheters for > 72 h at study entry; and severe infection or hepatocellular failure and renal failure
Interventions	**Intervention:** PIVCs were removed/replaced if there was a clinical indication to do so **Control:** PIVCs were replaced every 3 days in the control group (the routine-replacement group) following hospital policy. The duration of '3 days' refers to the approximate 72 h (range: 48-96 h) from the time of insertion to removal of a catheter. They were also removed/replaced if there was a clinical indication to do so
Outcomes	**Primary:** incidence of phlebitis: defined as when ≥ 2 of the following signs occurred at the catheter access site: redness, swelling, fever, pain, or palpable cord-like veins **Secondary**: fluid infiltration (when the infused non-blister drug leaked into the surrounding tissue from the normal vascular access, causing tissue swelling around the catheter access site); catheter occlusion (when the drug fluid could not flow into the body or the fluid could not be withdrawn); accidental catheter removal; CRBSI (diagnosed when signs of infection (e.g. fever, chills, and hypotension), positive results, and the same type of bacteria were found in bacterial cultures of both peripheral venous blood and the PIVC tip, and no other apparent source of BSI other than the IV catheter was observed (including BSI within 48 hours of catheter indwelling); local venous infection, i.e. purulent discharge or bloodstream-related infection with no evidence at vein segment; and indwelling time
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Evidence:** "These 20 internal medicine and surgery ward patients were randomly assigned by a research assistant via a coin toss into 2 groups"
Allocation concealment (selection bias)	Low risk	**Evidence:** "These 20 internal medicine and surgery ward patients were randomly assigned by a research assistant via a coin toss into 2 groups" **Comment:** allocation remains concealed until the coin is tossed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** "All of the participating patients were not blinded in the groups" **Evidence for personnel:** "Because of the nature of the intervention in this study, the chief nurse in charge of the research wards and the clinical nurses were not blinded to the random grouping" **Comment:** neither participants nor clinical

Xu 2017 *(Continued)*

		personnel were blinded but review authors do not believe this would introduce bias
Blinding of outcome assessment (detection bias) All outcomes	High risk	**Evidence:** "The peripheral blood samples and the catheter tips of patients with suspected CRBSI were sent for laboratory examination, and the laboratory examiners were blinded" **Comment:** blinding not possible for other outcomes and there was no laboratory confirmed diagnosis
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** complete data reporting for all outcomes: after 235 people, who were potentially eligible by belonging to a ward that was randomised, were excluded. 1198 participants were included for the final analysis (flow chart included)
Selective reporting (reporting bias)	Low risk	**Comment:** expected outcomes reported
Other bias	Unclear risk	**Comment:** this was a cluster trial but analysed by individual not cluster

BSI: blood stream infection; **CRBSI:** catheter-related blood stream infection; **ITT:** intention-to-treat; **IV:** intravenous; **IVD:** peripheral intravenous device; **PIVC:** peripheral intravenous catheter; **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 RCT
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	Participants were receiving parenteral nutrition
May 1996	Participants were receiving parenteral nutrition

(Continued)

Nakae 2010	Involved central, not peripheral lines
Panadero 2002	Compared the use of a single intraoperative and postoperative catheters with 2 catheters, 1 used intraoperatively and a separate catheter for postoperative use
Rijnders 2004	Involved central, not peripheral lines

RCT: randomised controlled trial

Characteristics of studies awaiting assessment *[ordered by study ID]*

Chin 2018

Methods	RCT 1:1
Participants	113 neonates born at ≥ 32 weeks' gestation
Interventions	PIVC replaced every 72-96 h or replaced when clinically indicated
Outcomes	**Primary:** extravasation **Secondary:** phlebitis; leakage; accidental dislodgement
Notes	No response to request for additional data as yet

PIVC: peripheral intravenous catheter; **RCT:** randomised controlled trial

D A T A   A N D   A N A L Y S E S

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	7	7323	Risk Ratio (M-H, Fixed, 95% CI)	0.61 [0.08, 4.68]
2 Phlebitis	7	7323	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.93, 1.25]
2.1 Continuous infusion	6	7123	Risk Ratio (M-H, Fixed, 95% CI)	1.05 [0.90, 1.23]
2.2 Intermittent infusion	1	200	Risk Ratio (M-H, Fixed, 95% CI)	1.29 [0.85, 1.96]
3 Phlebitis per device days	6	32709	Risk Ratio (M-H, Fixed, 95% CI)	0.90 [0.76, 1.08]
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	6	7123	Risk Ratio (M-H, Fixed, 95% CI)	1.16 [1.06, 1.26]
7 Catheter blockage	7	7323	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [1.02, 1.27]
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
10 Pain during infusion	1		Mean Difference (IV, 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

Study or subgroup	Clinically indicated n/N	Routine replacement n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Rickard 2010	0/185	0/177			Not estimable
Rickard 2012	0/1593	1/1690		59.2 %	0.35 [0.01, 8.67]
Van Donk 2009	0/105	0/95			Not estimable
Vendramim 2018	0/672	0/647			Not estimable
Webster 2007	0/103	0/103			Not estimable
Webster 2008	1/379	1/376		40.8 %	0.99 [0.06, 15.80]
Xu 2017	0/553	0/645			Not estimable
Total (95% CI)	**3590**	**3733**		**100.0 %**	**0.61 [0.08, 4.68]**

0.01   0.1   1   10   100

Favours cl-indicated   Favours 3-day

(*Continued* . . .)

Study or subgroup	Clinically indicated	Routine replacement	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H,Fixed,95% CI		M-H,Fixed,95% CI

Total events: 1 (Clinically indicated), 2 (Routine replacement)

Heterogeneity: Chi² = 0.23, df = 1 (P = 0.63); I² =0.0%

Test for overall effect: Z = 0.47 (P = 0.64)

Test for subgroup differences: Not applicable

```
          0.01   0.1    1    10   100
       Favours cl-indicated   Favours 3-day
```

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

Study or subgroup	Clinically indicated	Routine replacement	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H,Fixed,95% CI		M-H,Fixed,95% CI
1 Continuous infusion					
Rickard 2010	18/185	12/177		4.1 %	1.44 [0.71, 2.89]
Rickard 2012	114/1593	114/1690		36.8 %	1.06 [0.83, 1.36]
Vendramim 2018	55/672	64/647		21.7 %	0.83 [0.59, 1.17]
Webster 2007	1/103	2/103		0.7 %	0.50 [0.05, 5.43]
Webster 2008	16/379	12/376		4.0 %	1.32 [0.63, 2.76]
Xu 2017	76/553	77/645		23.7 %	1.15 [0.86, 1.55]
Subtotal (95% CI)	**3485**	**3638**		**90.9 %**	**1.05 [0.90, 1.23]**

Total events: 280 (Clinically indicated), 281 (Routine replacement)

Heterogeneity: Chi² = 3.74, df = 5 (P = 0.59); I² =0.0%

Test for overall effect: Z = 0.64 (P = 0.52)

2 Intermittent infusion					
Van Donk 2009	37/105	26/95		9.1 %	1.29 [0.85, 1.96]
Subtotal (95% CI)	**105**	**95**		**9.1 %**	**1.29 [0.85, 1.96]**

Total events: 37 (Clinically indicated), 26 (Routine replacement)

Heterogeneity: not applicable

```
          0.05   0.2    1     5    20
       Favours cl-indicated   Favours 3-day
```

(*Continued* . . .)

Study or subgroup	Clinically indicated	Routine replacement	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H,Fixed,95% CI		M-H,Fixed,95% CI

Test for overall effect: Z = 1.19 (P = 0.24)

Total (95% CI)   **3590**   **3733**   **100.0 %**   **1.07 [0.93, 1.25]**

Total events: 317 (Clinically indicated), 307 (Routine replacement)

Heterogeneity: Chi² = 4.52, df = 6 (P = 0.61); I² =0.0%

Test for overall effect: Z = 0.95 (P = 0.34)

Test for subgroup differences: Chi² = 0.78, df = 1 (P = 0.38), I² =0.0%

0.05   0.2   1   5   20

Favours cl-indicated   Favours 3-day

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

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

Comparison: 1 Clinically-indicated versus routine change

Outcome: 3 Phlebitis per device days

Study or subgroup	Clinically indicated	Routine replacement	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H,Fixed,95% CI		M-H,Fixed,95% CI
Rickard 2010	18/1120	12/970		5.1 %	1.30 [0.63, 2.68]
Rickard 2012	114/8693	114/8719		44.8 %	1.00 [0.77, 1.30]
Van Donk 2009	37/698	26/508		11.9 %	1.04 [0.64, 1.69]
Vendramim 2018	62/3825	70/2693		32.4 %	0.62 [0.44, 0.87]
Webster 2007	1/522	2/548		0.8 %	0.52 [0.05, 5.77]
Webster 2008	16/2393	12/2020		5.1 %	1.13 [0.53, 2.37]
Total (95% CI)	**17251**	**15458**		**100.0 %**	**0.90 [0.76, 1.08]**

Total events: 248 (Clinically indicated), 236 (Routine replacement)

Heterogeneity: Chi² = 7.04, df = 5 (P = 0.22); I² =29%

Test for overall effect: Z = 1.15 (P = 0.25)

Test for subgroup differences: Not applicable

0.05   0.2   1   5   20

Favours cl-indicated   Favours 3-day

Analysis 1.4. Comparison 1 Clinically-indicated versus routine change, Outcome 4 All-cause blood stream infection.

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

Comparison: 1 Clinically-indicated versus routine change

Outcome: 4 All-cause blood stream infection

Study or subgroup	Clinically indicated n/N	Routine replacement n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Rickard 2012	4/1593	9/1690		0.47 [0.15, 1.53]

```
          0.01   0.1    1    10   100
        Favours cl-indicated  Favours 3-day
```

Analysis 1.5. Comparison 1 Clinically-indicated versus routine change, Outcome 5 Cost.
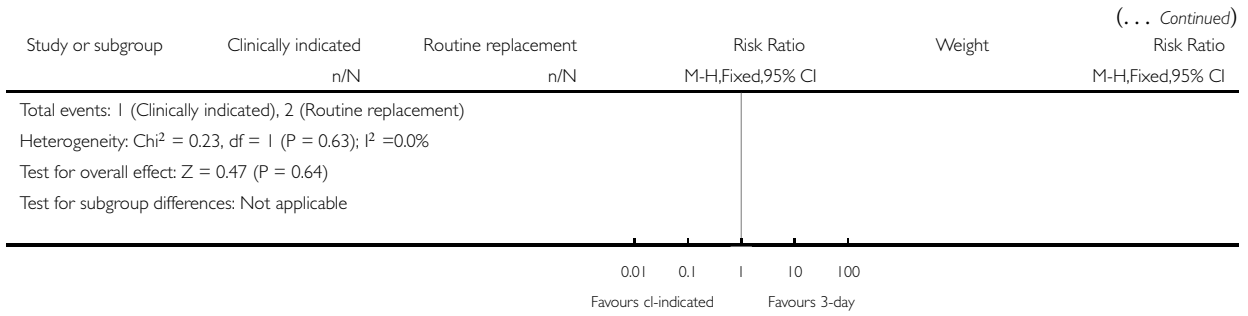
Review: Clinically-indicated replacement versus routine replacement of peripheral venous catheters

Comparison: 1 Clinically-indicated versus routine change

Outcome: 5 Cost

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
Rickard 2012	1593	61.66 (39.46)	1690	69.24 (43.45)		54.5 %	-7.58 [-10.42, -4.74]
Webster 2007	103	29.7 (16.4)	103	37.6 (20.2)		17.4 %	-7.90 [-12.92, -2.88]
Webster 2008	379	41.05 (26.6)	376	46.22 (28.7)		28.1 %	-5.17 [-9.12, -1.22]
Total (95% CI)	**2075**		**2169**			**100.0 %**	**-6.96 [-9.05, -4.86]**

Heterogeneity: Chi^2 = 1.11, df = 2 (P = 0.57); I^2 =0.0%

Test for overall effect: Z = 6.51 (P < 0.00001)

Test for subgroup differences: Not applicable

```
         -10    -5     0     5     10
       Favours cl-indicated   Favours 3-day
```
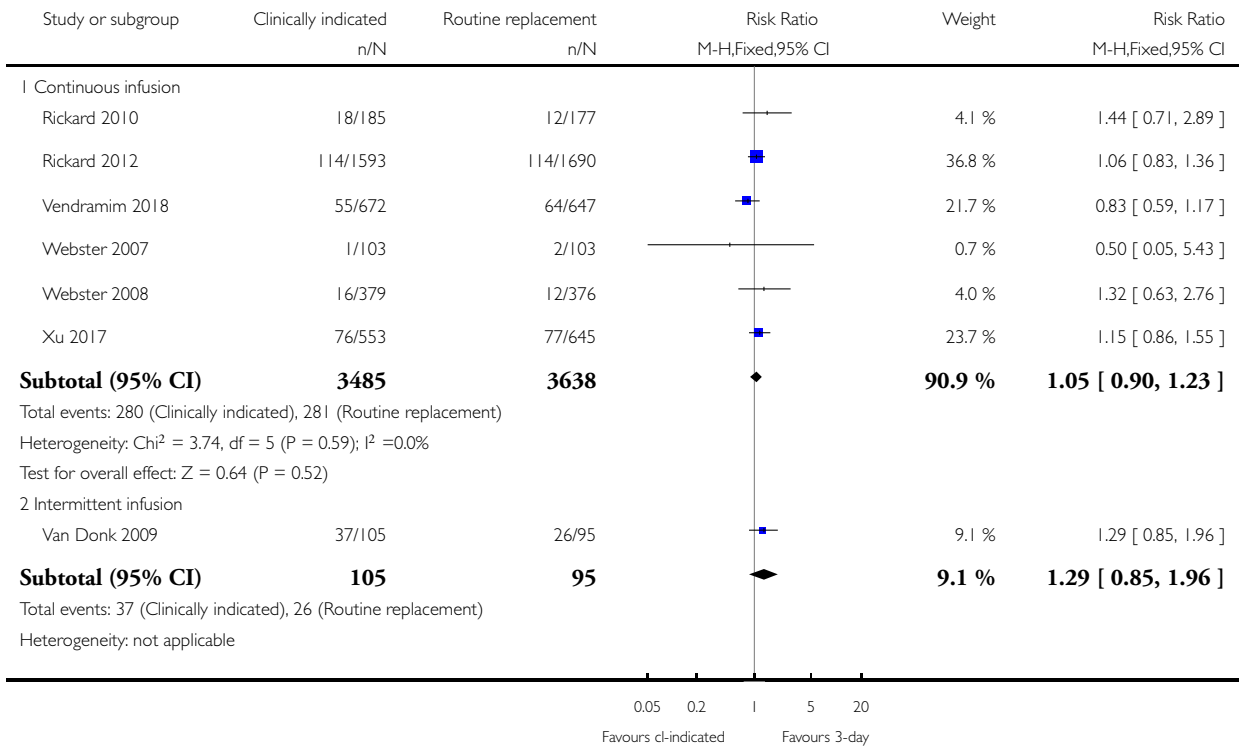
Analysis 1.6. Comparison 1 Clinically-indicated versus routine change, Outcome 6 Infiltration.
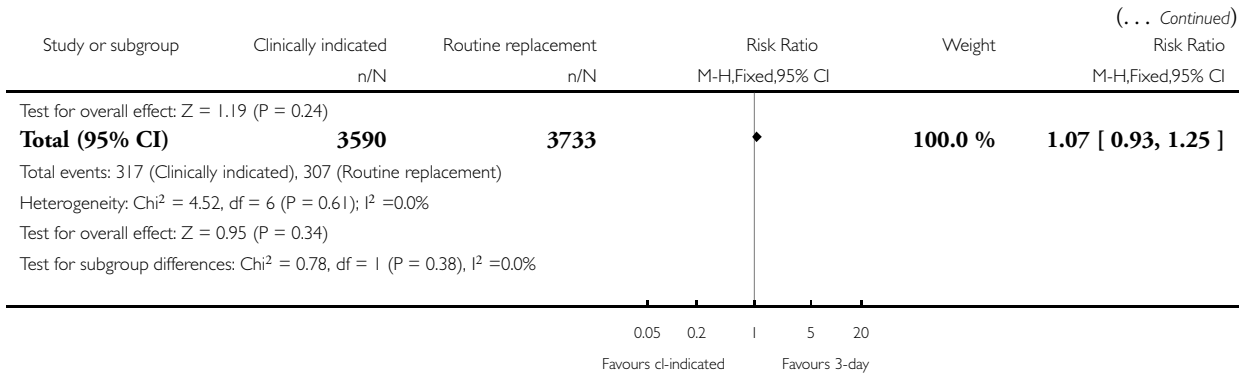
Review: Clinically-indicated replacement versus routine replacement of peripheral venous catheters

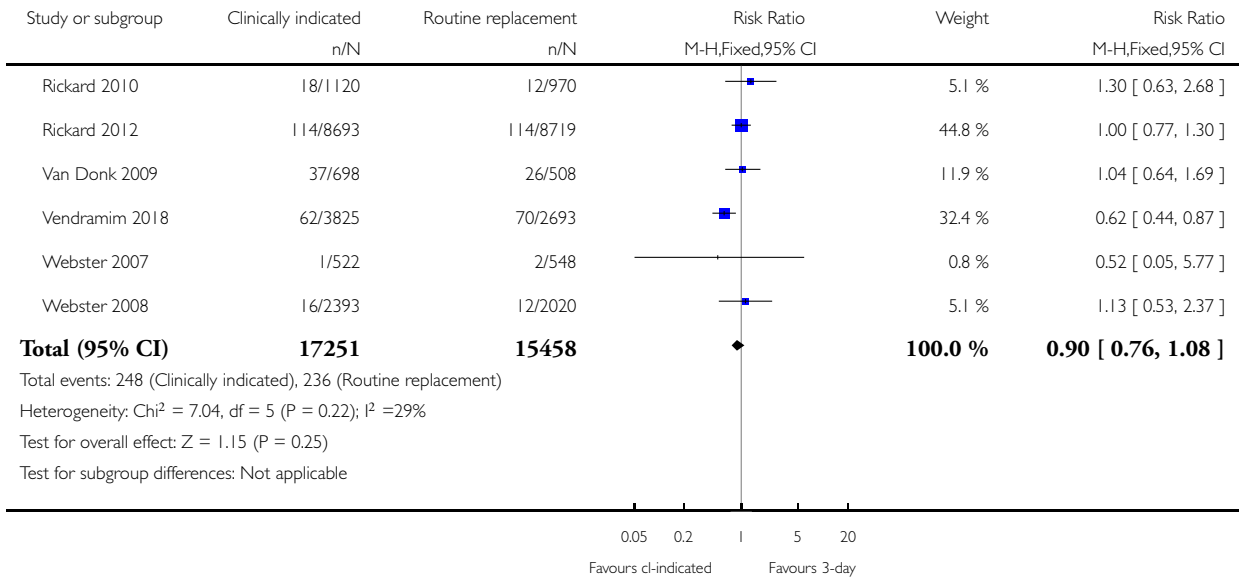Comparison: 1 Clinically-indicated versus routine change

Outcome: 6 Infiltration

Study or subgroup	Clinically indicated	Routine replacement	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H,Fixed,95% CI		M-H,Fixed,95% CI
Rickard 2010	61/185	53/177		7.4 %	1.10 [0.81, 1.49]
Rickard 2012	279/1593	235/1690		31.2 %	1.26 [1.07, 1.48]
Vendramim 2018	172/672	134/647		18.7 %	1.24 [1.01, 1.51]
Webster 2007	43/103	44/103		6.0 %	0.98 [0.71, 1.35]
Webster 2008	135/379	120/376		16.5 %	1.12 [0.91, 1.36]
Xu 2017	144/553	161/645		20.3 %	1.04 [0.86, 1.27]
Total (95% CI)	**3485**	**3638**		**100.0 %**	**1.16 [1.06, 1.26]**

Total events: 834 (Clinically indicated), 747 (Routine replacement)

Heterogeneity: Chi^2 = 3.92, df = 5 (P = 0.56); I^2 =0.0%

Test for overall effect: Z = 3.36 (P = 0.00077)

Test for subgroup differences: Not applicable

0.5   0.7   1   1.5   2

Favours cl-indicated   Favours 3-day

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

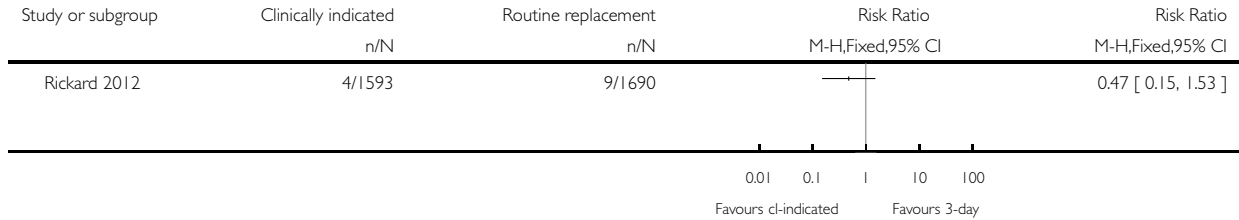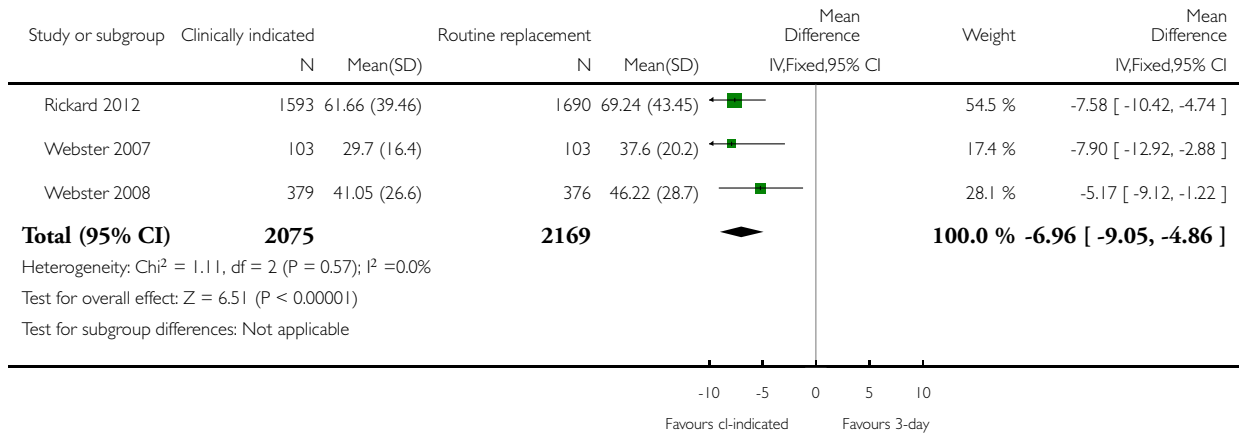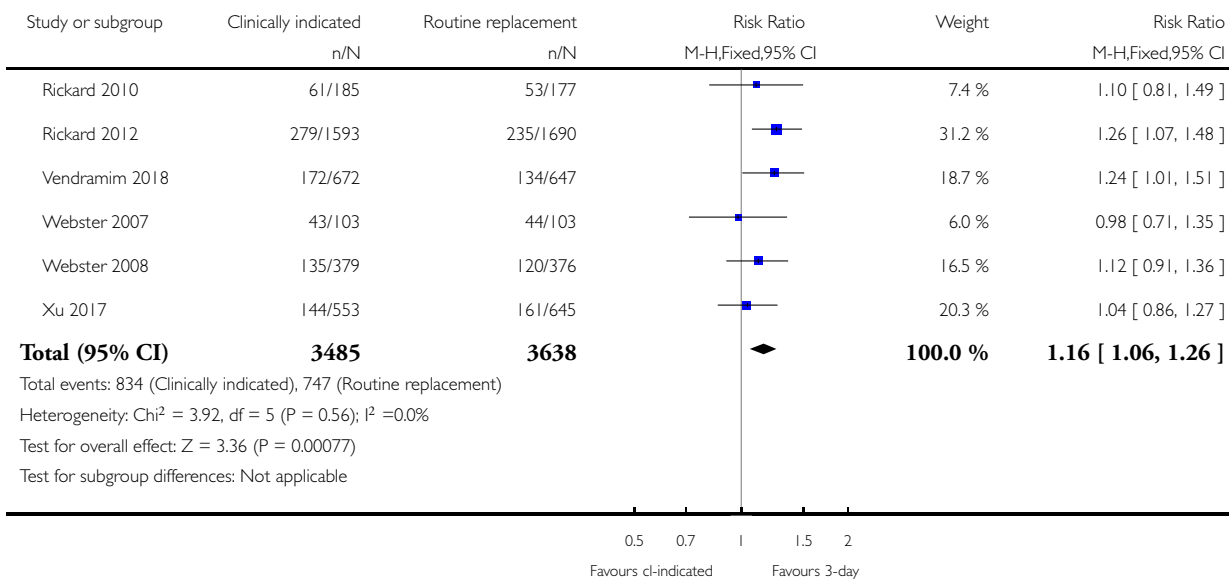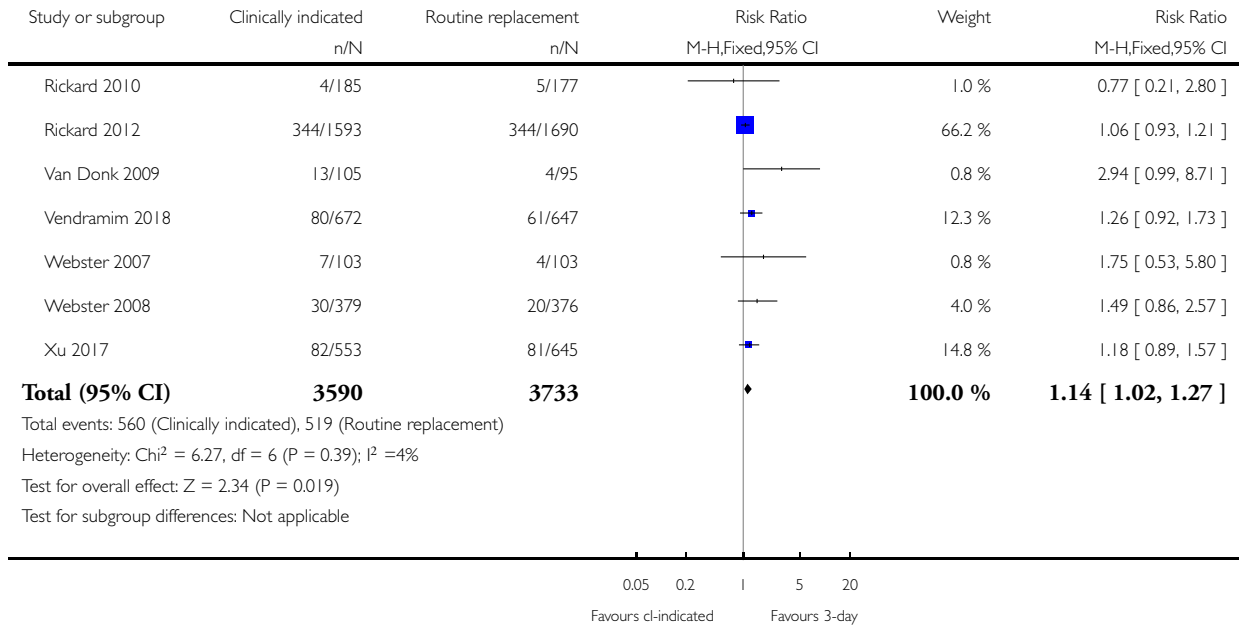Comparison: 1 Clinically-indicated versus routine change

Outcome: 7 Catheter blockage

Study or subgroup	Clinically indicated n/N	Routine replacement n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Rickard 2010	4/185	5/177		1.0 %	0.77 [0.21, 2.80]
Rickard 2012	344/1593	344/1690		66.2 %	1.06 [0.93, 1.21]
Van Donk 2009	13/105	4/95		0.8 %	2.94 [0.99, 8.71]
Vendramim 2018	80/672	61/647		12.3 %	1.26 [0.92, 1.73]
Webster 2007	7/103	4/103		0.8 %	1.75 [0.53, 5.80]
Webster 2008	30/379	20/376		4.0 %	1.49 [0.86, 2.57]
Xu 2017	82/553	81/645		14.8 %	1.18 [0.89, 1.57]
Total (95% CI)	**3590**	**3733**		**100.0 %**	**1.14 [1.02, 1.27]**

Total events: 560 (Clinically indicated), 519 (Routine replacement)

Heterogeneity: Chi² = 6.27, df = 6 (P = 0.39); I² =4%

Test for overall effect: Z = 2.34 (P = 0.019)

Test for subgroup differences: Not applicable

```
        0.05    0.2      1      5     20
    Favours cl-indicated      Favours 3-day
```
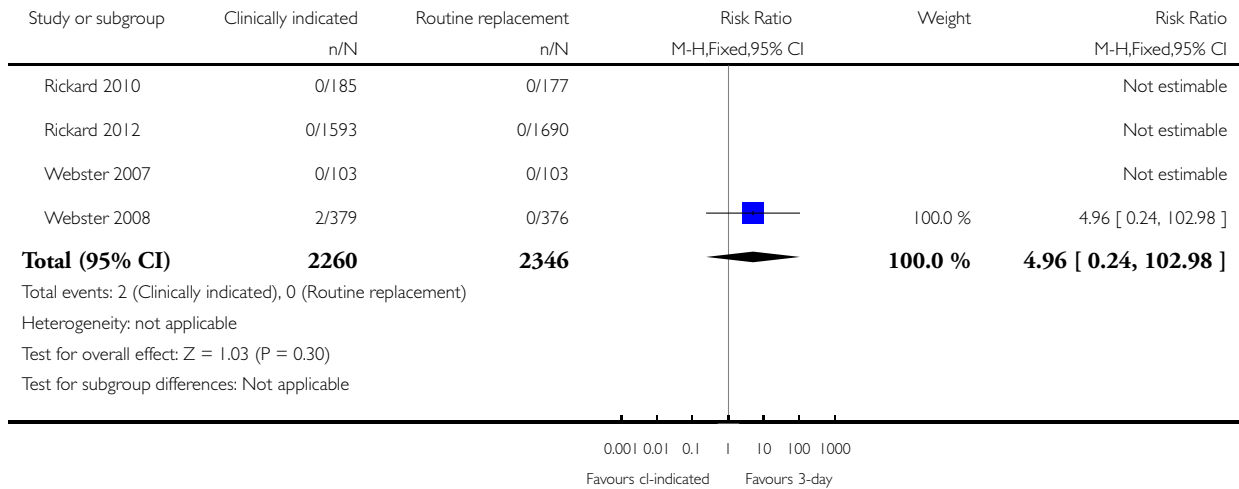
Analysis 1.8. Comparison 1 Clinically-indicated versus routine change, Outcome 8 Local infection.

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	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Rickard 2010	0/185	0/177			Not estimable
Rickard 2012	0/1593	0/1690			Not estimable
Webster 2007	0/103	0/103			Not estimable
Webster 2008	2/379	0/376		100.0 %	4.96 [0.24, 102.98]
Total (95% CI)	**2260**	**2346**		**100.0 %**	**4.96 [0.24, 102.98]**

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

Heterogeneity: not applicable

Test for overall effect: Z = 1.03 (P = 0.30)

Test for subgroup differences: Not applicable

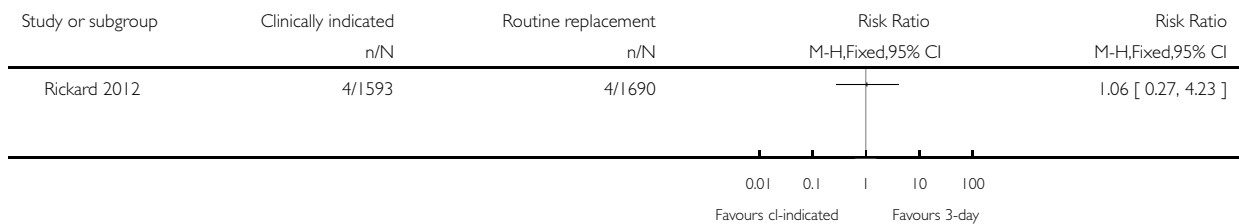0.001 0.01 0.1 1 10 100 1000

Favours cl-indicated   Favours 3-day

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

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

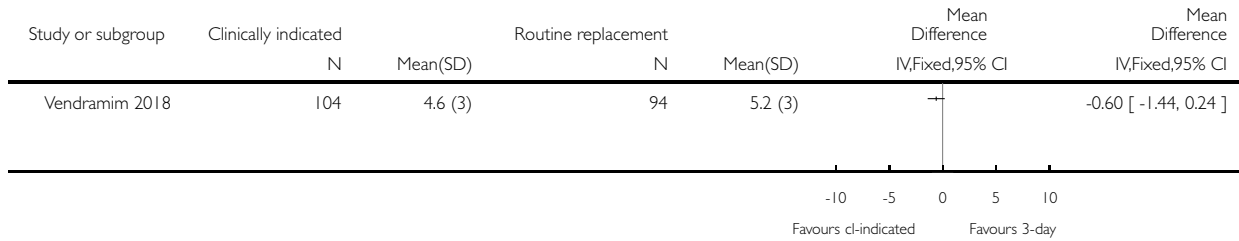Comparison: 1 Clinically-indicated versus routine change

Outcome: 9 Mortality

Study or subgroup	Clinically indicated n/N	Routine replacement n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Rickard 2012	4/1593	4/1690		1.06 [0.27, 4.23]

0.01 0.1 1 10 100

Favours cl-indicated   Favours 3-day

Analysis 1.10. Comparison I Clinically-indicated versus routine change, Outcome 10 Pain during infusion.

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

Comparison: 1 Clinically-indicated versus routine change

Outcome: 10 Pain during infusion

Study or subgroup	Clinically indicated		Routine replacement		Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
	N	Mean(SD)	N	Mean(SD)		
Vendramim 2018	104	4.6 (3)	94	5.2 (3)		-0.60 [-1.44, 0.24]

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        -10   -5    0    5    10
     Favours cl-indicated   Favours 3-day
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A P P E N D I C E S

Appendix 1. Search strategies

Cochrane Central Register of Controlled Trials (1 January 2015 to 18 April 2018)	#1 MESH DESCRIPTOR Infusions, Intravenous EXPLODE ALL TREES 9657 #2 MESH DESCRIPTOR Catheters, Indwelling EXPLODE ALL TREES 933 #3 MESH DESCRIPTOR Catheterization, Peripheral EXPLODE ALL TREES 804 #4 catheter*:TI,AB,KY 19185 #5 cannul*:TI,AB,KY 2736 #6 (iv near2 (therapy or treatment or device)):TI,AB,KY 817 #7 (intravenous near2 (therapy or treatment or device)):TI,AB,KY 2643 #8 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 32660 #9 MESH DESCRIPTOR Device Removal EXPLODE ALL TREES 340 #10 change:TI,AB,KY 100383 #11 routine:TI,AB,KY 22763 #12 (resit* or re-sit*):TI,AB,KY 28 #13 replace* :TI,AB,KY 23906 #14 remov* 18920 #15 #9 OR #10 OR #11 OR #12 OR #13 OR #14 157711 #16 #8 AND #15 6531 #17 01/01/2015 TO 17/04/2018:CD 301940 #18 #16 AND #17 1946	1946
US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov; (1 January 2015 to 18 April 2018))	catheter* OR cannul* OR Intravenous Infusions	change OR routine OR replace* OR remov*	66
World Health Organization International Clinical Trials Registry Platform (1 January 2015 to 18 April 2018)	change OR routine OR replace* OR remov* AND catheter* OR cannul* OR Intravenous Infusions	103
Medline (Ovid MEDLINE® Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE® 1 January 2017 to 18 April 2018)	1 exp Infusions, Intravenous/ 52357 2 exp Catheters, Indwelling/ 17598 3 exp Catheterization, Peripheral/ 10253 4 catheter*.ti,ab. 183558 5 cannul*.ti,ab. 40302 6 (iv adj2 (therapy or treatment or device)).ti,ab. 5132 7 (intravenous adj2 (therapy or treatment or device)).ti,ab. 16429 8 1 or 2 or 3 or 4 or 5 or 6 or 7 293380 9 exp Device Removal/ 11178	725

	10 change.ti,ab. 920194 11 routine.ti,ab. 255410 12 (resit* or re-sit*).ti,ab. 365 13 replace*.ti,ab. 351071 14 remov*.ti,ab. 559748 15 or/9-14 2002880 16 8 and 15 48953 17 randomized controlled trial.pt. 458816 18 controlled clinical trial.pt. 92332 19 randomized.ab. 409164 20 placebo.ab. 188261 21 drug therapy.fs. 2009753 22 randomly.ab. 288857 23 trial.ab. 425230 24 groups.ab. 1785641 25 or/17-24 4184693 26 exp animals/ not humans.sh. 4446961 27 25 not 26 3616731 28 16 and 27 12988 29 (2017* or 2018*).ed. 1226025 30 28 and 29 725	
Embase 1974 to present via Ovid (1 January 2017 to 18 April 2018)	1 exp intravenous drug administration/ 369547 2 exp indwelling catheter/ 13600 3 exp catheterization/ 165359 4 catheter*.ti,ab. 271161 5 cannul*.ti,ab. 54348 6 (iv adj2 (therapy or treatment or device)).ti,ab. 9056 7 (intravenous adj2 (therapy or treatment or device)).ti,ab. 22346 8 or/1-7 771672 9 exp device removal/ 23201 10 change.ti,ab. 1179753 11 routine.ti,ab. 367917 12 (resit* or re-sit*).ti,ab. 778 13 replace*.ti,ab. 447612 14 remov*.ti,ab. 704736 15 or/9-14 2585379 16 8 and 15 101630 17 randomized controlled trial/ 498849 18 controlled clinical trial/ 460351 19 random$.ti,ab. 1293791 20 randomization/ 77793 21 intermethod comparison/ 233320 22 placebo.ti,ab. 270839 23 (compare or compared or comparison).ti. 465805	2866

(Continued)

	24 ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab. 1727440 25 (open adj label).ti,ab. 63597 26 ((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab. 207274 27 double blind procedure/ 148944 28 parallel group$1.ti,ab. 21584 29 (crossover or cross over).ti,ab. 92096 30 ((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant$1)).ti,ab. 279492 31 (assigned or allocated).ti,ab. 328034 32 (controlled adj7 (study or design or trial)).ti,ab. 291440 33 (volunteer or volunteers).ti,ab. 222779 34 trial.ti. 247887 35 or/17-34 3991617 36 16 and 35 23176 37 (2017* or 2018*).em. 3311287 38 36 and 37 2866	
CINAHL EBSCO (Cumulative Index to Nursing and Allied Health Literature 1 January 2017 to 18 April 2018)	S32 S30 AND S31 163 S31 EM 2018 OR EM 2017 316,890 S30 S16 AND S29 2,084 S29 S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 337,787 S28 (MH "Random Assignment") 37,759 S27 (MH "Single-Blind Studies") or (MH "Double-Blind Studies") or (MH "Triple-Blind Studies") 32,600 S26 (MH "Crossover Design") 11,106 S25 (MH "Factorial Design") 914 S24 (MH "Placebos") 8,344 S23 (MH "Clinical Trials") 93,083 S22 TX "multi-centre study" OR "multi-center study" OR "multicentre study" OR "multicenter study" OR "multi-site study" 4,386 S21 TX crossover OR "cross-over" 14,384 S20 AB placebo* 27,965 S19 TX random* 216,193 S18 TX trial* 247,155 S17 TX "latin square" 141 S16 S8 AND S15 9,028	163

(Continued)

	S15 S9 OR S10 OR S11 OR S12 OR S13 OR S14 380,613 S14 TX remov* 35,451 S13 TX replace* 49,936 S12 TX (resit* or re-sit*) 71 S11 TX routine 39,406 S10 TX change 279,795 S9 (MH "Device Removal+") 2,141 S8 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 52,305 S7 TX (intravenous n2 (therapy or treatment or device)) 7,224 S6 TX (iv n2 (therapy or treatment or device)) 1,512 S5 TX cannul* 3,489 S4 TX catheter* 38,647 S3 (MH "Catheterization, Peripheral+") 2,413 S2 (MH "Catheters+") 8,493 S1 (MH "Infusions, Intravenous") 5,632	
AMED Ovid (Allied and Complementary Medicine 1 January 2017 to 18 April 2018)	1 exp catheterization/ 179 2 catheter*.ti,ab. 413 3 cannul*.ti,ab. 138 4 (iv adj2 (therapy or treatment or device)).ti,ab. 45 5 (intravenous adj2 (therapy or treatment or device)).ti,ab. 89 6 1 or 2 or 3 or 4 or 5 732 7 "Device Removal".ti,ab. 1 8 change.ti,ab. 10950 9 routine.ti,ab. 1844 10 (resit* or re-sit*).ti,ab. 5 11 replace*.ti,ab. 2253 12 remov*.ti,ab. 2128 13 or/7-12 16623 14 6 and 13 106 15 exp CLINICAL TRIALS/ 3720 16 RANDOM ALLOCATION/ 314 17 DOUBLE BLIND METHOD/ 650 18 Clinical trial.pt. 1210 19 (clinic* adj trial*).tw. 5347 20 ((singl* or doubl* or trebl* or tripl*) adj (blind* or mask*)).tw. 2804 21 PLACEBOS/ 583 22 placebo*.tw. 3084 23 random*.tw. 17338 24 PROSPECTIVE STUDIES/ 1065 25 or/15-24 22298	1

	26 14 and 25 23 27 ("2017" or "2018").yr. 699 28 26 and 27 1	

WHAT'S NEW

Date	Event	Description
23 August 2018	New citation required but conclusions have not changed	Searches re-run. Two new studies included. No new studies excluded. One study awaiting classification. Text updated. No change to conclusions
23 August 2018	New search has been performed	Searches re-run. Two new studies included. No new studies excluded. One study awaiting classification

HISTORY

Protocol first published: Issue 2, 2009

Review first published: Issue 3, 2010

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

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

CR: critically reviewed the protocol before final submission, selected trials for inclusion, assessed methodological quality of trials, extracted data, assisted with interpreting results and drafting of the final review.

NM: selected trials for inclusion, assessed methodological quality of trials, extracted data, and commented on the review update.

DECLARATIONS OF INTEREST

JW: none known

SO: none known

CR: CR's employer has received unrestricted research grants in aid from manufacturers of peripheral intravenous catheters and products, on her behalf for academic research projects. CR's employer has also received competitively awarded research grants through professional bodies where the funds came from commercial suppliers. These sponsors (3M, Adhezion, Angiodynamics, BD-Bard, Baxter, Medtronic, Centurion Medical, Entrotech Life Sciences, Cook, Smiths Medical) had no involvement in the study design, execution, analysis or publication of these projects, had no control over the projects, and they were unrelated to the topic of this review. CR is an academic researcher and her employer has received funding on her behalf for her to provide consultancies (expert advice, advisory panel participation, and educational lectures about her research at professional symposia and other events) from ResQDevices, Smiths Medical and BD-Bard.

NM: NM's employer has received unrestricted grants in aid from manufacturers of peripheral intravenous catheters and products, on her behalf for academic research projects. These sponsors (3M, Adhezion, BD, Centurion Medical Products, Cook Medical, Entrotech, Teleflex) had no involvement in the study design, execution, analysis or publication of these projects and they were unrelated to the topic of this review. NM 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 from BD and Hospira.

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.
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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

2018 update

- We added funding source; ethics approval and consent; and prospective registration on a clinical trials register; to our data extraction tool

- We also added the following outcome to the 'Summary of Findings' table:

  ○ all-cause blood stream infection

Previous updates

We changed the primary outcome to catheter-related bloodstream infection; and added all-cause bloodstream infection as a separate primary outcome. This was to more closely differentiate between the two outcomes. The methodological quality assessment of the included studies was updated to the Cochrane Collaboration tool for assessing risk of bias (Higgins 2017).

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; Thrombophlebitis [epidemiology; etiology]; Time Factors

MeSH check words

Humans