Skin preparation with alcohol versus alcohol followed by any antiseptic for preventing bacteraemia or contamination of blood for transfusion (Review)

Webster J, Bell-Syer SEM, Foxlee R

THE COCHRANE COLLABORATION®

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2015, Issue 2

http://www.thecochranelibrary.com

WILEY

TABLE OF CONTENTS

[Intervention Review]

Skin preparation with alcohol versus alcohol followed by any antiseptic for preventing bacteraemia or contamination of blood for transfusion

Joan Webster[1,2,3], Sally EM Bell-Syer[4], Ruth Foxlee[5]

[1]Centre for Clinical Nursing, Royal Brisbane and Women's Hospital, Brisbane, Australia. [2]NHMRC Centre of Research Excellence in Nursing, Centre for Health Practice Innovation, Griffith Health Institute, Griffith University, Brisbane, Australia. [3]School of Nursing and Midwifery, University of Queensland, Brisbane, Australia. [4]Department of Health Sciences, University of York, York, UK. [5]Cochrane Editorial Unit, Cochrane, London, UK

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

Editorial group: Cochrane Wounds Group.
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 2, 2015.
Review content assessed as up-to-date: 18 December 2014.

Citation: Webster J, Bell-Syer SEM, Foxlee R. Skin preparation with alcohol versus alcohol followed by any antiseptic for preventing bacteraemia or contamination of blood for transfusion. *Cochrane Database of Systematic Reviews* 2015, Issue 2. Art. No.: CD007948. DOI: 10.1002/14651858.CD007948.pub3.

ABSTRACT

Background

Blood for transfusion may become contaminated at any point between collection and transfusion and may result in bacteraemia (the presence of bacteria in the blood), severe illness or even death for the blood recipient. Donor arm skin is one potential source of blood contamination, so it is usual to cleanse the skin with an antiseptic before blood donation. One-step and two-step alcohol based antiseptic regimens are both commonly advocated but there is uncertainty as to which is most effective.

Objectives

To assess the effects of cleansing the skin of blood donors with alcohol in a one-step compared with alcohol in a two-step procedure to prevent contamination of collected blood or bacteraemia in the recipient.

Search methods

In December 2014, for this third update, we searched the Cochrane Wounds Group Specialised Register; The Cochrane Central Register of Controlled Trials (CENTRAL), *The Cochrane Library*; Ovid MEDLINE; Ovid MEDLINE (In-Process & Other Non-Indexed Citations); Ovid EMBASE; and EBSCO CINAHL.

Selection criteria

All randomised trials (RCTs) comparing alcohol based donor skin cleansing in a one-step versus a two-step process that includes alcohol and any other antiseptic for pre-venepuncture skin cleansing were considered. Quasi randomised trials were to have been considered in the absence of RCTs.

Data collection and analysis

Two review authors independently assessed studies for inclusion.

Main results

No studies (RCTs or quasi RCTs) met the inclusion criteria.

Authors' conclusions

We did not identify any eligible studies for inclusion in this review. It is therefore unclear whether a two-step, alcohol followed by antiseptic skin cleansing process prior to blood donation confers any reduction in the risk of blood contamination or bacteraemia in blood recipients, or conversely whether a one-step process increases risk above that associated with a two-step process.

PLAIN LANGUAGE SUMMARY

Alcohol, with or without antiseptic, for preparing the skin before blood collection to prevent bacteraemia or contamination of blood for transfusion.

When blood is collected from blood donors for transfusion it may become contaminated during collection, storage or transfusion. Blood contamination can cause bacteraemia (the presence of bacteria in the blood), severe illness or even death in the blood recipient. When blood is being taken from donors, the skin on the arm of the donor is one potential source of contamination, so it is usual to cleanse the arm with an antiseptic first, and both one-step and two-step alcohol based regimens are commonly used, however there is uncertainty about which regimen is the most effective for reducing the microbial load (the number of microscopic bacterial organisms) on the donor arm. We looked for studies that compared the use of alcohol alone versus the use of alcohol followed by another antiseptic to clean the arm before the needle is inserted to draw blood, but we did not find any relevant studies. It is currently unclear whether donor skin cleansing with a one-step alcohol based regimen reduces the risk of blood contamination compared with a two-step alcohol based regimen during blood donation.

BACKGROUND

Complications associated with the infusion of blood and blood-related products have reduced in recent years, due to considerable advances in detecting transfusion-related viral pathogens, such as human immunodeficiency virus (HIV) and hepatitis C and B virus (HCV and HBV). In contrast, bacteraemia, resulting from bacterial contamination of blood products continues to be an ongoing problem (Klausen 2014; Kulkarni 2014). Exogenous contamination of donor blood may occur at any point during collection, storage and transfusion (McDonald 2001). One of the sources of contamination is thought to be the donor's skin, as a result of inadequate skin cleansing (de Korte 2006; McDonald 2006).

Description of the condition

Bacteraemia, or the presence of bacteria in the blood, is a potentially fatal condition. It is associated with high rates of morbidity (Bassetti 2012; Wolkewitz 2011). Microorganisms may enter the blood stream through almost any organ (for example the lungs following pneumonia), through a surgical site, or via an implanted device such as an intravenous catheter. Prognosis is related to the virulence of the infective organism, severity of the sepsis at diagnosis, age and the underlying health of the patient (Herchline 1997; Mejer 2012). Although the aetiology of bacteraemia is often difficult to identify, transfusion-transmitted infection is a rare cause. The incidence of bacterial transmission through donated blood is estimated at between 1 per 100,000 and 1 per 1,000,000 units for packed red blood cells, and between 1 per 900 and 1 per 100,000 units for platelets (Walther-Wenke 2008). Fatalities are associated with 1 in 8,000,000 red cell units and 1 in 50,000 to 500,000 white cell units (Wagner 2004). The reason for higher rates in platelet transfusion is thought to be because frozen platelets are thawed and stored at room temperature before infusion and if they are not used immediately there is an opportunity for any organisms that may be present to multiply before the product is transfused. Further reduction of infection rates depends on ensuring that blood for transfusion is free of contaminants. One way of achieving this is through careful preparation and cleansing of the donor's skin at the collection site.

Description of the intervention

There is no standard method for cleansing the site on the blood donor's skin from which the blood will be taken (generally the cubital fossa, or the inner aspect of the elbow). However, alcohol, followed by an application of povidone iodine has been traditionally used (Shahar 1990; Kiyoyama 2009). Consequently, the interventions of interest for this review are skin cleansing with alcohol (usually 70% isopropyl alcohol) for skin preparation in a one-step process, compared with a two-step process involving alcohol followed by povidone iodine or other antiseptic solution. Antiseptics are antimicrobial substances that are applied to living tissue or skin to reduce the possibility of infection, sepsis or putrefaction. They should generally be distinguished from antibiotics that destroy bacteria within the body, and from disinfectants, which destroy microorganisms found on non-living objects. Alcohol is widely used prior to venepuncture and is available from a number of manufacturers as easy-to-use disinfection wipes.

How the intervention might work

Alcohol kills most bacteria and fungi by acting on lipid and protein components of the cell. It is less effective against viruses (Adams 2007). Isopropyl alcohol has some advantages over other products because it requires a shorter contact time to achieve antisepsis. For example some two-step procedures take up to two minutes to perform, which is considered too long for some blood bank services (McDonald 2006). Antiseptics are toxic to living tissues as well as bacterial cells, some antiseptics are true germicides, capable of destroying microbes (bacteriocidal), whilst others are bacteriostatic and only prevent or inhibit their growth (Morgan 1993).

Why it is important to do this review

Although a range of antiseptics has been used to cleanse the skin of the donor arm, a two-step process, including alcohol and iodine is widely used (Kiyoyama 2009; Shahar 1990). The effectiveness of this regimen, and other forms of cleansing has been evaluated in a number of studies by measuring the microbial load on the donor arm (Cid 2003; Follea 1997; Goldman 1997; McDonald 2001; Wong 2004) and any contamination of platelet concentrates (de Korte 2006; Lee 2002; Benjamin 2011) however it remains unclear whether isopropyl alcohol alone is as effective as alcohol plus povidone iodine (or any other antiseptic) in preventing the clinical consequences of contaminated blood. This review question was brought to us by the World Health Organisation (WHO) and a scoping search did not identify any existing systematic review which had previously addressed this question.

OBJECTIVES

To assess the effects of cleansing the donor arm with alcohol in a one-step regimen compared with a two-step regimen including alcohol followed by any other antiseptic to prevent donor blood contamination or recipient bacteraemia.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs) comparing a one-step alcohol regimen with any two-step regimen that includes alcohol followed by another antiseptic for pre-venepuncture skin cleansing were considered. Cluster randomised trials and crossover trials were also eligible for inclusion. Quasi randomised trials were to have been considered in the absence of RCTs.

Types of participants

Studies enrolling people of any age and in any setting, having venepuncture and blood collection were eligible, irrespective of whether the venepuncture was for the purpose of blood donation. Studies should also include follow up from the recipients of the donated blood in order to measure outcomes occurring in the recipient.

Types of interventions

Studies which compared one-step donor skin cleansing with alcohol (any concentration or application method) with a two-step method which involved alcohol (any strength or application method) followed by any other antiseptic (any concentration or application method) were eligible.

Types of outcome measures

At least one of the primary or secondary outcomes was to have been reported for the study to be considered for inclusion in the review.

Primary outcomes

- Bacteraemia in the blood recipient (the presence of bacteria in the blood stream) as measured by blood culture.
- Blood product contamination (blood products include whole blood, platelets, red blood cells or any other product derived from the blood collection) at any time between collection and transfusion as detected most commonly by blood culture.

Proxy outcome measures, such as skin contamination or skin colonisation, were not considered for several reasons. Namely, any antiseptic will reduce levels of microflora on the skin and swabbing skin for bacteria is really a 'sampling procedure' which is subject to inconsistencies in sampling. In addition, a positive skin culture does not automatically mean that the blood collected for transfusion will be positive for bacteria (in the same way that a positive skin culture before surgery does not mean the person will develop a surgical site infection).

Secondary outcomes

- Death of the blood recipient, attributed to the transfusion.
- Any adverse effects in the blood recipient associated with the transfusion. This may include sepsis (a grouping of signs such as fever, chills, or hypotension), septic shock (severe disturbances of temperature, respiration, heart rate or white blood cell count) or multiple organ dysfunction syndrome (altered organ function in a severely ill patient that requires medical intervention to prevent death).

Search methods for identification of studies

The search methods used in the second update of this review can be found in Appendix 1.

Electronic searches

In December 2014, for this third update, we searched the following databases:

- Cochrane Wounds Group Specialised Register (searched 8 December 2014);
- The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2014, Issue 11);
- Ovid MEDLINE (2012 to January Week 2 2015);Ovid MEDLINE (In-Process & Other Non-Indexed Citations January 9, 2015);
- Ovid EMBASE (2012 to 2015 Week 2);
- EBSCO CINAHL (2012 to 9 January 2015).

The Cochrane Central Register of Controlled Trials (CENTRAL) was searched using the following strategy:
#1 MeSH descriptor: [Blood Specimen Collection] explode all trees 554
#2 MeSH descriptor: [Blood Transfusion] explode all trees 3297
#3 MeSH descriptor: [Blood Donors] explode all trees 294
#4 (blood next collection*) or (blood next donor*) or (blood next donation*):ti,ab,kw 1021
#5 (collection near/1 blood) or (donation near/1 blood):ti,ab,kw 506
#6 ven*puncture next site*:ti,ab,kw 22
#7 (#1 or #2 or #3 or #4 or #5 or #6) 4590
#8 MeSH descriptor: [Antisepsis] explode all trees101
#9 MeSH descriptor: [Anti-Infective Agents, Local] explode all trees1691
#10 MeSH descriptor: [Iodine Compounds] explode all trees 544
#11 MeSH descriptor: [Povidone-Iodine] explode all trees 409
#12 MeSH descriptor: [Alcohols] explode all trees 29960
#13 MeSH descriptor: [Disinfectants] explode all trees 598
#14 MeSH descriptor: [Disinfection] explode all trees 284
#15 skin next preparation:ti,ab,kw 144
#16 disinfect*:ti,ab,kw 1230
#17 ("alcohol" or "alcohols" or iodine or povidone-iodine or chlorhexidine):ti,ab,kw 15882
#18 #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 44904
#19 #7 and #18 in Trials 112
The search strategies for Ovid MEDLINE, Ovid EMBASE and EBSCO CINAHL can be found in Appendix 2, Appendix 3 and Appendix 4 respectively. The Ovid MEDLINE search was combined with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision) (Lefebvre 2011). The Ovid EMBASE and EBSCO CINAHL searches were combined with the trial filters developed by the Scottish Intercollegiate Guidelines Network (SIGN 2009). There was no restriction on the basis of date or language of publication.

Searching other resources

Reference lists of articles retrieved in full were searched.

Data collection and analysis

Selection of studies

Titles and abstracts identified through the search process were independently reviewed by two review authors. Full reports of all potentially relevant studies were retrieved for further assessment of eligibility based on the inclusion criteria. Differences of opinion were settled by consensus or referral to a third review author. There was no blinding to study authorship when we did these assessments.

Data extraction and management

We had planned to extract the following data, where available (to be extracted by one review author and checked by a second review author):

- details of the trial/study (first author, year of publication, journal, publication status, period);
- setting and country of study;
- source of funding;

- inclusion and exclusion criteria;
- baseline characteristics of participants (age, sex);
- aspects of morbidity of the blood recipients, e.g. predictors of susceptibility to bacteraemia;
- number of participants in each arm of the trial;
- description of intervention (type, duration);
- description of control intervention (type, duration);
- details and duration of follow up;
- primary and secondary outcomes (by group);
- design / methodological quality data as per risk of bias criteria;
- unit of randomisation (where relevant);
- unit of analysis;
- results and primary statistical analysis.

Assessment of risk of bias in included studies

Two review authors were to independently assess study risk of bias using the Cochrane Collaboration tool (Higgins 2011b).This tool addresses six specific domains, namely sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and other issues (e.g. co-interventions)(see Appendix 5 for details of criteria on which the judgements were to have been based). Blinding and completeness of outcome data would have been assessed for each outcome separately and we had planned to complete a risk of bias table for each eligible study.
We planned to contact investigators of included studies to resolve any ambiguities. We also planned to include data from duplicate publications only once, but to retrieve all publications pertaining to a single study to enable full data extraction and risk of bias quality assessment.
For any eligible study, we planned to present assessment of risk of bias using a 'risk of bias summary figure', which presents the judgments in a cross-tabulation of study by entry. This display of internal validity indicates the weight the reader may give the results of each study.

Measures of treatment effect

For individual trials, effect measures for categorical outcomes (e.g. rates of bacteraemia) would have included relative risk (RR) with its 95% confidence interval (CI). For continuous outcomes, we planned to use the mean difference (MD) or, if the scale of measurement differed across trials, standardized mean difference (SMD), each with its 95% CI. For any meta-analyses (see below), for categorical outcomes the typical estimates of RR with their 95% CI would have been calculated; and for continuous outcomes the weighted mean difference (WMD) or a summary estimate for SMD, each with its 95% CI, would have been calculated.
We planned to analyse data using The Cochrane Collaboration's Review Manager 5 software.

Dealing with missing data

If outcome data had remained missing despite our attempts to obtain complete outcome data from authors, we would have performed an available-case analysis, based on the numbers of patients for whom outcome data were known. If standard deviations were missing, we would have imputed them from other studies or, where possible, computed them from standard errors using the formula SD = SE x $\sqrt{N}$, where these were available (Higgins 2011c).

Assessment of heterogeneity

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

Assessment of reporting biases

Reporting bias would have been assessed using guidelines in the Cochrane Handbook for Systematic Reviews of Interventions (Sterne 2011).

Data synthesis

Where appropriate, results of comparable trials would have been pooled and the pooled estimate together with its 95% CI would have been reported. We planned to conduct a narrative review of eligible studies if 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 analysis: concealment of allocation (adequate versus not reported).

Sensitivity analysis

We planned to undertake a sensitivity analysis to explore the effect of excluding studies where concealment of allocation was unclear

RESULTS

Description of studies

We did not find any randomised or quasi-randomised controlled trials that met the inclusion criteria.

Results of the search

Our initial search and first update identified 547 citations of which 22 were considered potentially relevant. Full copies of these papers were obtained and reviewed independently by two review authors, however, none met the inclusion criteria. The search for the first, second and third updates identified in total 372 citations none of which were relevant, 4 further citations were identified through internet searching but did not meet the inclusion criteria and were added to the Characteristics of excluded studies.

Included studies

No studies were included.

Excluded studies

The Table: Characteristics of excluded studies contains reasons for excluding 23 potentially eligible studies. In summary, two citations were for unsystematic literature reviews (Blajchman 2004; Wendel 2002) eight trials did not compare the eligible interventions (Calfee 2002; Choudhuri 1990; Little 1999; Mimoz 1999; Schifman 1993; Sutton 1999; Suwanpimolkul 2008; Trautner 2002). Nine studies were not randomised or quasi randomised controlled trials (de Korte 2006; Goldman 1997; Kiyoyama 2009; Lee 2002; McDonald 2006; Pleasant 1994; Shah 2014; Shahar 1990; Wong 2004). One study examined techniques for quantifying bacterial reduction (Follea 1997) and three were neither randomised controlled trials nor did they address any of the reviews' primary or secondary outcomes (Benjamin 2011; McDonald 2010; Ramirez-Arcos 2010).

Risk of bias in included studies

No studies were included.

Effects of interventions

We did not identify any eligible randomised or quasi randomised controlled trials, nor were we able to identify any ongoing trials.

DISCUSSION

We have been unable to identify any trials addressing the effectiveness of alcohol alone compared with alcohol followed by any other antiseptic to prevent bacteraemia from transfused blood or blood products. This may be because infusion related bacteraemia is a relatively rare event and very large trials would be needed to investigate the effect of donor-arm cleansing. Sepsis rates for platelet transfusions are around 1:50,000 and for red cell transfusions around 1:500,000 (Sandler 2003). Therefore mounting a trial large enough to detect differences in clinical outcomes, based on products used for arm cleansing, would be prohibitively expensive and lengthy.

Because of this, surrogate measures, such as contamination of stored blood have been used to evaluate antisepsis efficacy. However, again, we found no trials that compared alcohol alone with alcohol followed by any other antiseptic for cleansing the donor skin. A number of studies used the surrogate outcome of post-cleansing skin microbial load at the venepuncture site however we excluded such studies *a priori* on the grounds that this is a surrogate outcome of unproven validity; it is not known how skin contamination relates to blood recipient outcomes. Moreover none of these trials compared a one-step with a two-step cleansing process (de Korte 2006; Follea 1997; Goldman 1997).

Whilst we did identify a number of studies that compared the effects of the eligible interventions they were otherwise ineligible for important methodological reasons and did not meet our pre-specified study design eligibility criteria. The first compared blood culture contamination following pre-venepuncture cleansing with 70% alcohol for one minute followed by povidone iodine solution for an additional minute with brief swabbing of the skin three to five times with 70% alcohol. Patients who were suspected of having bacteraemia had two blood samples taken; once using the two-step method and once with the standard method. Unfortunately it appeared from the report that the order in which the methods were used was not randomised and samples may have been taken from the same or a closely adjacent site with an unreported time lapse between sampling. Of the 181 cultures tested in each group, eight (4.4%) were positive in the two-step group compared with six (3.3%) in the one-step preparation group (no statistically significant difference) (Shahar 1990). The second study potentially suffers from important selection bias in that the treatment groups were in different settings as well as receiving different modes of skin cleansing and compared blood culture contamination rates between patients in whom blood had been drawn in the emergency department and who received a one-step 70% alcohol cleansing with inpatients who received a two-step 70% alcohol followed by povidone iodine procedure. Although there was a statistically significant difference in positive culture rates in favour of the one step process (189 (6.6%) positive cultures in the one-step group versus 248 (8.9%) in the two step, alcohol plus iodine group (p = 0.0015) (Kiyoyama 2009) this study was not eligible for inclusion in the review due to the inherent risk of selection bias (inpatients and emergency department patients may well be at different levels of risk of positive blood culture). Thus whilst the authors presented additional data to suggest that baseline positive blood culture rates

were similar between inpatients and emergency department patients the risk of selection bias remains and this study was excluded (Kiyoyama 2009). The third, non-randomised study compared a two-step povidone iodine method with a one-step 2% chlorhexidine/70% isopropyl alcohol method for skin preparation before blood donation. A total of 32 centres used the two-step process during 2007 and 2008 whilst three trial centres used the one-step process during 2009. A sample of 8mL of blood, drawn from the site following disinfection was used to test for bacterial contamination. Similar rates of true positives were seen across the three time periods (Benjamin 2011). The most recent study compared a three step process of decontamination (antisepsis with spirit, followed by 10% alcoholic povidone iodine, then a final application of spirit), compared with 2% (w/v) alcoholic chlorhexidine gluconate). The interventions were used sequentially with a wash-out period between the two interventions. There was no contamination of blood products in either study phase (Shah 2014).

In addition, we found a recent systematic review that compared head to head comparisons of various antiseptics (such as povidone-iodine, alcoholic iodine, alcoholic chlorhexidine) for the prevention of blood culture contamination but the review did not include any one-step versus two-step processes for the collection of blood for storage (Caldeira 2011).

In conclusion there is currently no RCT evidence of a difference in either blood contamination or bacteraemia when donor skin is cleansed pre-venepuncture with a one-step alcohol based process or a two-step alcohol plus antiseptic process. This lack of evidence for a difference however results from a complete absence of research and therefore a real difference cannot be discounted. Until better evidence emerges, decisions about which mode of pre-blood donation skin cleansing to use are likely to be driven by convenience and cost. It is also important to note that arm cleansing is only one of the points at which blood contamination may occur. Careful collection and storage of blood and blood products, and systematic surveillance to detect bacterial contamination can all contribute to the safety of patients requiring blood transfusions. Eliminating all bacteria from stored blood may not be possible. So, following relevant clinical guidelines (for example UK BTS Guidelines 2005) for collection and for detecting bacterial contamination in stored blood, both at the time of collection and at the time of issue, may be the most effective way of reducing infusion related bacteraemia (Yomtovian 2006).

Summary of main results

We did not identify any eligible studies for inclusion in this review. It is therefore unclear whether a two-step, alcohol followed by antiseptic skin cleansing process prior to blood donation confers any reduction in the risk of blood contamination or bacteraemia in blood recipients (or conversely whether a one-step process increases risk above that associated with a two-step process).

Potential biases in the review process

Biases in the review process were minimised as far as possible by adhering to the guidance provided by the Cochrane Handbook (Higgins 2011a). We believe that publication bias is unlikely in this case; whilst no trials met the inclusion criteria , this is probably due to the difficulty and expense associated with mounting a trial large enough to answer the question.

AUTHORS' CONCLUSIONS

Implications for practice

We did not find any eligible randomised or quasi randomised controlled trials. Until further research emerges, decisions about which mode of pre-blood donation skin cleansing to use are likely to be driven by convenience and cost. It is also important to note that arm cleansing is only one of the points at which blood contamination may occur.

Implications for research

Cleansing the donor skin before taking blood for transfusion is important, but conducting a trial to compare the effects of using specific antiseptics on bacteraemia rates would be logistically difficult given the relatively rare event rate. It may be possible to estimate the effects of disinfecting with alcohol alone versus alcohol plus other antiseptics on blood contamination rates but this would still require very large sample sizes to detect clinically important differences. Alternatively, high quality observational studies may provide additional information to guide practice. A future comprehensive evidence synthesis that summarised the evidence for all competing alternative approaches to pre-blood donation skin cleansing would be worthwhile.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the peer referees: Martin Bland, Julie Bruce, Mike Clarke, Jo Dumville, Carmel Hughes, Susan O'Meara, Ian Roberts and David Tovey. Nicky Cullum provided editorial input throughout the review process and checked the search results.

REFERENCES

References to studies excluded from this review

Benjamin 2011 *{published data only}*
Benjamin RJ, Dy B, Warren R, Lischka M, Eder AF. Skin disinfection with a single-step 2% chlorhexidine swab is more effective than a two-step povidone-iodine method in preventing bacterial contamination of apheresis platelets. *Transfusion* 2011;**51**(3):531–8.

Blajchman 2004 *{published data only}*
Blajchman MA, Goldman M, Baeza F. Improving the bacteriological safety of platelet transfusions. *Transfusion Medicine Reviews* 2004;**18**(1):11–24.

Calfee 2002 *{published data only}*
Calfee DP, Farr BM. Comparison of four antiseptic preparations for skin in the prevention of contamination of percutaneously drawn blood cultures: a randomized trial. *Journal of Clinical Microbiology* 2002;**40**(5):1660–5.

Choudhuri 1990 *{published data only}*
Choudhuri M, McQueen R, Inoue S, Gordon RC. Efficiency of skin sterilization for a venipuncture with the use of commercially available alcohol or iodine pads. *American Journal of Infection Control* 1990;**18**(2):82–5.

de Korte 2006 *{published data only}*
de Korte D, Curvers J, de Kort WL, Hoekstra T, van der Poel CL, Beckers EA, et al. Effects of skin disinfection method, deviation bag, and bacterial screening on clinical safety of platelet transfusions in the Netherlands. *Transfusion* 2006; **46**(3):476–85.

Follea 1997 *{published data only}*
Folléa G, Saint-Laurent P, Bigey F, Gayet S, Bientz M, Cazenave JP. Quantitative bacteriological evaluation of a method for skin disinfection in blood donors. *Transfusion Clinique et Biologique* 1997;**4**(6):523–31.

Goldman 1997 *{published data only}*
Goldman M, Roy G, Fréchette N, Décary F, Massicotte L, Delage G. Evaluation of donor skin disinfection methods. *Transfusion* 1997;**37**(3):309–12.

Kiyoyama 2009 *{published data only}*
Kiyoyama T, Tokuda Y, Shiiki S, Hachiman T, Shimasaki T, Endo K. Isopropyl alcohol compared with isopropyl alcohol plus povidone-iodine as skin preparation for prevention of blood culture contamination. *Journal of Clinical Microbiology* 2009;**47**(1):54–8.

Lee 2002 *{published data only}*
Lee CK, Ho PL, Chan NK, Mak A, Hong J, Lin CK. Impact of donor arm skin disinfection on the bacterial contamination rate of platelet concentrates. *Vox Sanguinis* 2002;**83**(3):204–8.

Little 1999 *{published data only}*
Little JR, Murray PR, Traynor PS, Spitznagel E. A randomized trial of povidone-iodine compared with iodine tincture for venipuncture site disinfection: effects on rates of blood culture contamination. *American Journal of Medicine* 1999;**107**(2):119–25.

McDonald 2006 *{published data only}*
McDonald CP. Bacterial risk reduction by improved donor arm disinfection, diversion and bacterial screening. *Transfusion Medicine* 2006;**16**(6):381–96.

McDonald 2010 *{published data only}*
McDonald C, McGuane S, Thomas J, Hartley S, Robbins S, Roy A, et al. A novel rapid and effective donor arm disinfection method. *Transfusion* 2010;**50**(1):53–8.

Mimoz 1999 *{published data only}*
Mimoz O, Karim A, Mercat A, Cosseron M, Falissard B, Parker F, et al. Chlorhexidine compared with povidone-iodine as skin preparation before blood culture. A randomized, controlled trial. *Annals of Internal Medicine* 1999;**131**(11):834–7.

Pleasant 1994 *{published data only}*
Pleasant H, Marini J, Stehling L. Evaluation of three skin preps for use prior to phlebotomy. *Tranfusion* 1994;**34** (Supp):14S.

Ramirez-Arcos 2010 *{published data only}*
Ramirez-Arcos S, Goldman M. Skin disinfection methods: prospective evaluation and post implementation results. *Transfusion* 2010;**50**(1):59–64.

Schifman 1993 *{published data only}*
Schifman RB, Pindur A. The effect of skin disinfection materials on reducing blood culture contamination. *American Journal of Clinical Pathology* 1993;**99**(5):536–8.

Shah 2014 *{published data only}*
Shah S, Mehta NA, Jadhav SG. Prospective evaluation of 2% (w/v) alcoholic chlorhexidine gluconate as an antiseptic agent for blood donor arm preparation. *Asian Journal of Transfusion Science* 2014;**8**(2):92–5.

Shahar 1990 *{published data only}*
Shahar E, Wohl-Gottesman BS, Shenkman L. Contamination of blood cultures during venepuncture: fact or myth?. *Postgraduate Medical Journal* 1990;**66**(782): 1053–8.

Sutton 1999 *{published data only}*
Sutton CD, White SA, Edwards R, Lewis MH. A prospective controlled trial of the efficacy of isopropyl alcohol wipes before venesection in surgical patients. *Annals of the Royal Collegeof Surgeons of England* 1999;**81**(3):183–6.

Suwanpimolkul 2008 *{published data only}*
Suwanpimolkul G, Pongkumpai M, Suankratay C. A randomized trial of 2% chlorhexidine tincture compared with 10% aqueous povidone-iodine for venipuncture site disinfection: Effects on blood culture contamination rates. *Journal of Infection* 2008;**56**(5):354–9.

Trautner 2002 *{published data only}*
Trautner BW, Clarridge JE, Darouiche RO. Skin antisepsis kits containing alcohol and chlorhexidine gluconate or

tincture of iodine are associated with low rates of blood culture contamination. *Infection Control and Hospital Epidemiology* 2002;**23**(7):397–401.

Wendel 2002 ***{published data only}***
Wendel S. Chemoprophylaxis of transfusion-transmitted agents in labile blood components. *Revista da Sociedade Brasileira de Medicina Tropical* 2002;**35**(4):275–81.

Wong 2004 ***{published data only}***
Wong P-Y, Colville VL, White V, Walker HM, Morris RA. Validation and assessment of a blood-donor arm disinfectant containing chlorhexidine and alcohol. *Transfusion* 2004;**44**(8):1238–42.

Additional references

Adams 2007
Adams D, Elliot TS. Skin antiseptics used prior to intravascular catheter insertion. *British Journal of Nursing* 2007;**16**(5):278–80.

Bassetti 2012
Bassetti M, Trecarichi EM, Mesini A, Spanu T, Giacobbe DR, Rossi M, et al. Risk factors and mortality of healthcare-associated and community-acquired Staphylococcus aureus bacteraemia. *Clinical Microbiology and Infection* 2012;**18**(9):862–9.

Caldeira 2011
Caldeira D, David C, Sampaio C. Skin antiseptics in venous puncture-site disinfection for prevention of blood culture contamination: systematic review with meta-analysis. *Journal of Hospital Infection* 2011;**77**(3):223–32.

Cid 2003
Cid J, Ortín X, Ardanuy C, Contreras E, Elies E, Martín-Vega C. Bacterial persistence on blood donors' arms after phlebotomy site preparation: analysis of risk factors. *Haematologica* 2003;**88**(7):839–40.

Deeks 2008
Deeks, JJ, Higgins JPT, Altman DG on behalf of the Cochrane Statistical Methods Group and the Cochrane Bias Methods Group (Editors). Chapter 9: Analysing data and undertaking meta-analyses. In: Higgins JPT, Green S (editors), Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.0 (updated February 2008).The Cochrane Collaboration, 2008. Available from www.cochrane-handbook.org. Wiley–Blackwell.

Herchline 1997
Herchline T, Gros S. Improving clinical outcome in bacteremia. *Journal of Evaluation in Clinical Practice* 1997;**4**(3):191–5.

Higgins 2011a
Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Higgins 2011b
Higgins JPT, Altman DG on behalf of the Cochrane Statistical Methods Group and the Cochrane Bias Methods Group (Editors). Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org. Wiley–Blackwell.

Higgins 2011c
Higgins JPT, Deeks JJ, Altman DG on behalf of the Cochrane Statistical Methods Group and the Cochrane Bias Methods Group (Editors). Chapter 16: Special topics in statistics. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org. Wiley–Blackwell.

Klausen 2014
Klausen SS, Hervig T, Seghatchian J, Reikvam H. Bacterial contamination of blood components: Norwegian strategies in identifying donors with higher risk of inducing septic transfusion reactions in recipients. *Transfusion and Apheresis Science* 2014;**51**(2):97–102.

Kulkarni 2014
Kulkarni N. A prospective study to determine the frequency of bacterial contamination of platelets. *The Indian Journal of Hematology and blood transfusion* 2014;**30**(4):309–20.

Lefebvre 2011
Lefebvre C, Manheimer E, Glanville J, on behalf of the Cochrane Information Retrieval Methods Group. Chapter 6: Searching for studies. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

McDonald 2001
McDonald CP, Lowe P, Roy A, Robbins S, Hartley S, Harrison JF, et al. Evaluation of donor arm disinfection techniques. *Vox Sanguinis* 2001;**80**(3):135–41.

Mejer 2012
Mejer N, Westh H, Schønheyder HC, Jensen AG, Larsen AR, Skov R, et al. Stable incidence and continued improvement in short term mortality of Staphylococcus aureus bacteraemia between 1995 and 2008. *BMC Infectious diseases* 2012;**12**(1):260.

Morgan 1993
Morgan D. Is there still a role for antiseptics?. *Journal of Tissue Viability* 1993;**3**(3):80–4.

Sandler 2003
Sandler SG, Yu H, Rassai N. Risks of blood transfusion and their prevention. *Clinical Advances in Hematology and Oncology* 2003;**1**(5):307–13.

SIGN 2009
Scottish Intercollegiate Guidelines Network (SIGN). Search filters. http://www.sign.ac.uk/methodology/filters.html#random (accessed 20 February 2009).

Sterne 2011

Sterne JAC, Egger M, Moher D on behalf of the Cochrane Bias Methods Group (Editors). Chapter 10: Addressing reporting biases. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org. Wiley–Blackwell.

UK BTS Guidelines 2005

Virge J (Editor). Collection of a blood donation. *Guidelines for the Blood Transfusion Services in the United Kingdom*. 7th Edition. London: TSO (The Stationery Office), 2005: 33–9.

Wagner 2004

Wagner SJ. Transfusion-transmitted bacterial infection: risks, sources and interventions. *Vox Sanguinis* 2004;**86**(3): 157–63.

Walther-Wenke 2008

Walther-Wenke G. Incidence of bacterial transmission and transfusion reactions by blood components. *Clinical Chemistry and Laboratory Medicine* 2008;**46**(7):919–25.

Wolkewitz 2011

Wolkewitz M, Frank U, Philips G, Schumacher M, Davey P, BURDEN Study Group. Mortality associated with in-hospital bacteraemia caused by Staphylococcus aureus: a multistate analysis with follow-up beyond hospital discharge. *Journal of Antimicrobial Chemotherapy* 2011;**66** (2):381–6.

Yomtovian 2006

Yomtovian RA, Palavecino EL, Dysktra AH, Downes KA, Morrissey AM, Bajaksouzian S, et al. Evolution of surveillance methods for detection of bacterial contamination of platelets in a university hospital, 1991 through 2004. *Transfusion* 2006;**46**(5):719–30.

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Study	Reason for exclusion
Benjamin 2011	Not a randomised or quasi-randomised controlled trial.
Blajchman 2004	Narrative, non-systematic literature review.
Calfee 2002	None of the four study arms involved a two-step skin preparation process
Choudhuri 1990	Comparison of two one-step processes; alcohol swab compared with iodine swab
de Korte 2006	Single arm study evaluating a double-swab isopropyl alcohol disinfection process
Follea 1997	Examined techniques for quantifying bacterial reduction by comparing a three-step process with no skin disinfection
Goldman 1997	Abstract only available and it was unclear how patients where allocated to groups. Though this was not likely to have been randomised or quasi-randomised because one group was treated in a particular way on the basis that they were allergic to iodine. Also there was no one-step, alcohol-only skin preparation group
Kiyoyama 2009	Not a randomised or quasi-randomised controlled trial. Two independent groups were considered; one group from an inpatient ward was treated with isopropyl alcohol + povidone-iodine and the other from an emergency department was treated with isopropyl alcohol alone
Lee 2002	Not a randomised or quasi-randomised controlled trial. Comparison of two two-step processes in consecutive time periods. Cetrimide/ chlorhexidine solution + isopropyl alcohol compared with povidone-iodine + isopropyl alcohol
Little 1999	Povidone-iodine was compared with iodine tincture, i.e. not a comparison of a one-step with a two-step skin preparation
McDonald 2006	An uncontrolled before and after evaluation of a two-step process involving isopropyl alcohol + tincture of iodine
McDonald 2010	Not a randomised or quasi-randomised controlled trial.
Mimoz 1999	Povidone-iodine compared with chlorhexidine, i.e. not a comparison of a one-step with a two-step skin preparation
Pleasant 1994	Only available in abstract form; no information to suggest this was a randomised controlled trial; attempts to contact the authors were unsuccessful
Ramirez-Arcos 2010	Not a randomised or quasi-randomised controlled trial.

(*Continued*)

Schifman 1993	Comparison of two, two-step processes, namely, isopropyl alcohol pads + povidone-iodine swabs compared with isopropyl alcohol/acetone scrub + povidone-iodine dispenser
Shah 2014	Prospective study where a three-step process was used for 3-months and, following a wash out process, a one-step process with 2% (w/v) alcoholic chlorhexidine gluconate was implemented for 3-months
Shahar 1990	Not a randomised or quasi-randomised controlled trial; the venepuncture site was cleansed with a two-step process after which a culture was taken, at a later time point the venepuncture site was cleansed with a one-step process after which a culture was taken. The two samples were collected from the same person but it is not clear from the report if the two venepuncture sites were different, if there was a possibility of cross contamination between sites and what time period separated the sampling process
Sutton 1999	Isopropyl alcohol (IPA) compared with no IPA skin preparation, i.e. not a comparison of a one-step with a two-step skin preparation
Suwanpimolkul 2008	Chlorhexidine in alcohol compared with povidone-iodine, i.e. not a comparison of a one-step with a two-step skin preparation
Trautner 2002	Chlorhexidine gluconate compared with iodine tincture, i.e. not a comparison of a one-step with a two-step skin preparation
Wendel 2002	Narrative, non-systematic literature review.
Wong 2004	An uncontrolled before and after study of a one-step process involving chlorhexidine gluconate

DATA AND ANALYSES

This review has no analyses.

APPENDICES

Appendix 1. Search methods for the second update - 2012

Electronic searches

For this second update we searched the following databases:

- Cochrane Wounds Group Specialised Register (searched 20 November 2012);
- The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2012, Issue 11);
- Ovid MEDLINE (2011 to November Week 2 2012);Ovid MEDLINE (In-Process & Other Non-Indexed Citations November 20, 2012);
- Ovid EMBASE (2011 to 2012 Week 46);
- EBSCO CINAHL (2008 to 15 November 2012).

The Cochrane Central Register of Controlled Trials (CENTRAL) was searched using the following strategy:
#1 MeSH descriptor Blood Specimen Collection explode all trees
#2 MeSH descriptor Blood Transfusion explode all trees
#3 MeSH descriptor Blood Donors explode all trees
#4 (blood NEXT collection*) or (blood NEXT donor*) or (blood NEXT donation*):ti,ab,kw
#5 (collection NEAR/1 blood) or (donation NEAR/1 blood):ti,ab,kw
#6 ven*puncture NEXT site*:ti,ab,kw
#7 (#1 OR #2 OR #3 OR #4 OR #5 OR #6)
#8 MeSH descriptor Antisepsis explode all trees
#9 MeSH descriptor Anti-Infective Agents, Local explode all trees
#10 MeSH descriptor Iodine Compounds explode all trees
#11 MeSH descriptor Povidone-Iodine explode all trees
#12 MeSH descriptor Alcohols explode all trees
#13 MeSH descriptor Disinfectants explode all trees
#14 MeSH descriptor Disinfection explode all trees
#15 skin NEXT preparation:ti,ab,kw
#16 disinfect*:ti,ab,kw
#17 (“alcohol” or “alcohols” or iodine or povidone-iodine or chlorhexidine):ti,ab,kw
#18 (#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17)
#19 (#7 AND #18)
The search strategies for Ovid MEDLINE, Ovid EMBASE and EBSCO CINAHL can be found in Appendix 2, Appendix 3 and Appendix 4 respectively. The Ovid MEDLINE search was combined with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision) (Lefebvre 2011). The Ovid EMBASE and EBSCO CINAHL searches were combined with the trial filters developed by the Scottish Intercollegiate Guidelines Network (SIGN 2009). There was no restriction on the basis of date or language of publication.

Searching other resources

Reference lists of articles retrieved in full were searched.

Appendix 2. Ovid MEDLINE search strategy

1 exp Blood Specimen Collection/
2 exp Blood Transfusion/
3 exp Blood Donors/
4 (blood collection$ or blood donor$ or blood donation$).ti,ab.
5 ((collect$ adj1 blood) or (donat$ adj1 blood)).ti,ab.
6 ven?puncture site$.ti,ab.
7 or/1-6
8 exp Antisepsis/
9 exp Anti-Infective Agents, Local/
10 exp Iodine Compounds/
11 exp Povidone-Iodine/
12 exp Alcohols/
13 exp Disinfectants/
14 exp Disinfection/
15 skin preparation.ti,ab.
16 disinfect$.ti,ab.
17 (alcohol$1 or iodine or povidone-iodine or chlorhexidine).ti,ab.
18 or/8-17
19 7 and 18

Appendix 3. Ovid EMBASE search strategy

1 exp Blood Sampling/
2 exp Blood Transfusion/
3 exp Blood Donor/
4 (blood collection$ or blood donor$ or blood donation$).ti,ab.
5 ((collect$ adj1 blood) or (donat$ adj1 blood)).ti,ab.
6 exp Vein Puncture/
7 ven?puncture site$.ti,ab.
8 or/1-7
9 exp Antisepsis/
10 exp Topical Antiinfective Agent/
11 exp Iodine/
12 exp Povidone Iodine/
13 exp Chlorhexidine/
14 exp Alcohol/
15 exp Disinfectant Agent/
16 exp Disinfection/
17 skin preparation.ti,ab.
18 disinfect$.ti,ab.
19 (alcohol$1 or iodine or povidone-iodine or chlorhexidine).ti,ab.
20 or/9-19
21 8 and 20

Appendix 4. EBSCO CINAHL search strategy

S19 S9 and S18
S18 S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17
S17 TI (alcohol or alcohols or iodine or povidone-iodine or chlorhexidine) or AB (alcohol or alcohols or iodine or povidone-iodine or chlorhexidine)
S16 TI disinfect* or AB disinfect*
S15 TI skin preparation or AB skin preparation
S14 (MH "Disinfectants")
S13 (MH "Alcohols+")
S12 (MH "Povidone-Iodine")
S11 (MH "Iodine")
S10 (MH "Antiinfective Agents, Local+")
S9 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8
S8 TI venepuncture site* or AB venepuncture site*
S7 (MH "Venipuncture+")
S6 TI blood donation* or AB blood donation*
S5 TI blood donor* or AB blood donor*
S4 TI blood collection* or AB blood collection*
S3 (MH "Blood Donors")
S2 (MH "Blood Transfusion+")
S1 (MH "Blood Specimen Collection+")

Appendix 5. *Criteria for a judgment of 'yes' for the sources of bias*

1. Was the allocation sequence randomly generated?

Low risk of bias

The investigators describe a random component in the sequence generation process such as: referring to a random number table; using a computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots.

High risk of bias

The investigators describe a non-random component in the sequence generation process. Usually, the description would involve some systematic, non-random approach, for example: sequence generated by odd or even date of birth; sequence generated by some rule based on date (or day) of admission; sequence generated by some rule based on hospital or clinic record number.

Unclear

Insufficient information about the sequence generation process to permit judgement of low or high risk of bias.

2. Was the treatment allocation adequately concealed?

Low risk of bias

Participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: central allocation (including telephone, web-based and pharmacy-controlled randomisation); sequentially-numbered drug containers of identical appearance; sequentially-numbered, opaque, sealed envelopes.

High risk of bias

Participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on: using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or non opaque or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure.

Unclear

Insufficient information to permit judgement of low or high risk of bias. This is usually the case if the method of concealment is not described or not described in sufficient detail to allow a definite judgement, for example if the use of assignment envelopes is described, but it remains unclear whether envelopes were sequentially numbered, opaque and sealed.

3. Blinding - was knowledge of the allocated interventions adequately prevented during the study?

Low risk of bias

Any one of the following.

- No blinding, but the review authors judge that the outcome and the outcome measurement are not likely to be influenced by lack of blinding.
- Blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken.
- Either participants or some key study personnel were not blinded, but outcome assessment was blinded and the non-blinding of others unlikely to introduce bias.

High risk of bias

Any one of the following.

- No blinding or incomplete blinding, and the outcome or outcome measurement is likely to be influenced by lack of blinding.
- Blinding of key study participants and personnel attempted, but likely that the blinding could have been broken.
- Either participants or some key study personnel were not blinded, and the non-blinding of others likely to introduce bias.

Unclear

Any one of the following.

- Insufficient information to permit judgement of low or high risk of bias.
- The study did not address this outcome.

4. Were incomplete outcome data adequately addressed?

Low risk of bias

Any one of the following.

- No missing outcome data.
- Reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias).
- Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups.
- For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate.
- For continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size.
- Missing data have been imputed using appropriate methods.

High risk of bias

Any one of the following.

- Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups.
- For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate.
- For continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size.
- 'As-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation.
- Potentially inappropriate application of simple imputation.

Unclear

Any one of the following.

- Insufficient reporting of attrition/exclusions to permit judgement of low or high risk of bias (e.g. number randomised not stated, no reasons for missing data provided).
- The study did not address this outcome.

5. Are reports of the study free of suggestion of selective outcome reporting?

Low risk of bias

Any of the following.

- The study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way.
- The study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon)

High risk of bias

Any one of the following.

- Not all of the study's pre-specified primary outcomes have been reported.
- One or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not pre-specified.
- One or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect).
- One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis.
- The study report fails to include results for a key outcome that would be expected to have been reported for such a study.

Unclear

Insufficient information to permit judgement of low or high risk of bias. It is likely that the majority of studies will fall into this category.

6. Other sources of potential bias

Low risk of bias

The study appears to be free of other sources of bias.

High risk of bias

There is at least one important risk of bias. For example, the study:

- had a potential source of bias related to the specific study design used; or
- had extreme baseline imbalance; or
- has been claimed to have been fraudulent; or
- had some other problem.

Unclear

There may be a risk of bias, but there is either:

- insufficient information to assess whether an important risk of bias exists; or
- insufficient rationale or evidence that an identified problem will introduce bias.

Appendix 6. Protocol for the review ready for submission March 2009

The protocol for this review was completed and ready for submission in March 2009, the review being completed and ready for submission in April 2009. As the protocol has not been previously published in the Cochrane Library it is appended below in full.

Skin preparation with alcohol versus alcohol followed by any antiseptic for preventing bacteraemia or contamination of blood for transfusion.

Protocol information

Authors

Joan Webster[1], Sally EM Bell-Syer[2], Ruth Foxlee[2]

[1]Centre for Clinical Nursing, Royal Brisbane and Women's Hospital, Herston, Australia

[2]Department of Health Sciences, University of York, York, UK

Background

Complications associated with the infusion of blood and blood-related products have reduced in recent years, due to considerable advances in detecting transfusion-related viral pathogens, such as human immunodeficiency virus (HIV) and hepatitis C and B virus (HCV and HBV). In contrast, bacteraemia, resulting from bacterial contamination of blood products continues to be an ongoing problem (Sandler 2003; Wagner 2004). Exogenous contamination may occur at any point during collection and storage (McDonald 2001). One of these sources is thought to be the donors arm, as a result of inadequate skin disinfection (de Korte 2006; McDonald 2006).

Description of the condition

Bacteraemia, or the presence of bacteria in the blood, is a potentially fatal condition and associated with high rates of morbidity (Hakim 2007; Sligl 2006). Microorganisms may enter the blood stream through almost any organ (for example the lungs following pneumonia); through a surgical site, or via an implanted device such as an intravenous catheter. Prognosis is related to the virulence of the infective organism, severity of the sepsis at diagnosis and the underlying health of the patient (Herchline 1997). Although the aetiology of bacteraemia is often difficult to identify, transfusion-transmitted infection is a rare cause. The incidence of bacterial transmission through donated blood is estimated at between 1 per 100,000 and 1 per 1,000,000 units for packed red blood cells and between 1 per 900 and 1 per 100,000 units for platelets (Walther-Wenke 2008). Fatalities are associated with 1 in 8,000,000 red cell units and 1 in 50,000 to 500,000 white cell units (Wagner 2004). Further reduction of these rates depends on ensuring that blood for transfusion is free of contaminants. One way of achieving this is through careful preparation and disinfection of the arm of the blood donor.

Description of the intervention

There is no standard method for cleansing the site on the blood donor's skin from which the blood will be taken (generally the cubital fossa, or the inner aspect of the elbow). However, alcohol, followed by an application of povidone iodine has been traditionally used (Shahar 1990; Kiyoyama 2009). Consequently, the interventions of interest for this review are skin cleansing with alcohol (usually 70% isopropyl alcohol) for skin preparation in a one-step process, compared with a two-step process involving alcohol followed by povidone iodine or other antiseptic solution. Antiseptics are antimicrobial substances that are applied to living tissue or skin to reduce the possibility of infection, sepsis or putrefaction. They should generally be distinguished from antibiotics that destroy bacteria within the body, and from disinfectants, which destroy microorganisms found on non-living objects. Alcohol is widely used for venepuncture and is available, from a number of manufacturers as easy-to-use disinfection wipes. Isopropyl alcohol is a flammable, colourless liquid; also know as 2-propanol (Safety (MSDS) data for 2-propanol accessed 3 March 2009).

How the intervention might work

Alcohol kills most bacteria and fungi by acting on lipid and protein components of the cell. It is less effective against viruses (Adams 2007). Isopropyl alcohol has some advantages over other products because it requires a shorter contact time for disinfection. For example some two-stage disinfection procedures take up to two minutes to perform, which is considered too long for some blood bank services (McDonald 2006). Antiseptics are toxic to living tissues as well as bacterial cells, some antiseptics are true germicides, capable of destroying microbes (bacteriocidal), whilst others are bacteriostatic and only prevent or inhibit their growth (Morgan 1993).

Why it is important to do this review

Although a range of antiseptics have been used to disinfect the donor arm, a two-step process, including alcohol and iodine is widely used. The effectiveness of this process, and other forms of disinfection have been evaluated in a number of studies by measuring the microbial load on the donor arm (Cid 2003; Follea 1997; Goldman 1997; McDonald 2001; Wong 2004) and any contamination of platelet concentrates de Korte 2006; Lee 2002). Despite this, it remains unclear if isopropyl alcohol alone is as effective as alcohol plus povidone iodine in preventing blood product contamination or bacteraemia. This review question was brought to us by the World Health Organisation (WHO) and a scoping search did not identify any existing systematic review which had previously addressed this question.

Objectives

To assess the effects of cleansing the donor arm with alcohol in a one-step regimen compared with a two-step regimen including alcohol followed by any other antiseptic to prevent donor blood contamination or recipient bacteraemia.

Methods

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs) comparing a one-step alcohol regimen with any two-step regimen that includes alcohol followed by another antiseptic for pre-venepuncture skin cleansing will be considered. Cluster randomised trials and crossover trials will also be eligible for inclusion. Quasi randomised trials will be considered in the absence of RCTs.

Types of participants

Studies enrolling people of any age and in any setting, having venepuncture and blood collection will be eligible, irrespective of whether the venepuncture was for the purpose of blood donation. Studies should also include follow up from the recipients of the donated blood in order to measure outcomes occurring in the recipient.

Types of interventions

Studies which compare a one-step donor skin cleansing with alcohol (any concentration or application method) with a two-step method which involves alcohol (any strength or application method) followed by any other antiseptic (any concentration or application method) will be eligible.

Types of outcome measures

At least one of the primary outcomes must be reported for inclusion of the review.

Primary outcomes

- Bacteraemia in the blood recipient (the presence of bacteria in the blood stream) as measured by blood culture.
- Blood product contamination (blood products include whole blood, platelets, red blood cells or any other product derived from the blood collection) at any time between collection and transfusion as detected most commonly by blood culture.

Proxy outcome measures, such as skin contamination or skin colonisation, will not be considered.

Secondary outcomes

- Death of the blood recipient, attributed to the transfusion.
- Any adverse effects in the blood recipient associated with the transfusion. This may include sepsis (a grouping of signs such as fever, chills, or hypotension), septic shock (severe disturbances of temperature, respiration, heart rate or white blood cell count) or multiple organ dysfunction syndrome (altered organ function in a severely ill patient that requires medical intervention to prevent death).

Search methods for identification of studies

Electronic searches

The following databases will be searched:
Cochrane Wounds Group Specialised Register;
The Cochrane Central Register of Controlled Trials (CENTRAL) latest issue;
Ovid MEDLINE - 1950 to Current;
Ovid EMBASE - 1980 to Current;
EBSCO CINAHL - 1982 to Current.
The Cochrane Central Register of Controlled Trials (CENTRAL) will also be searched (latest issue) using the following strategy:
#1 MeSH descriptor Blood Specimen Collection explode all trees
#2 MeSH descriptor Blood Transfusion, Autologous explode all trees
#3 MeSH descriptor Blood Donors explode all trees
#4 (blood NEXT collection*) or (blood NEXT donor*) or (blood NEXT donation*):ti,ab,kw

#5 ven*puncture:ti,ab,kw
#6 (#1 OR #2 OR #3 OR #4 OR #5)
#7 MeSH descriptor Antisepsis explode all trees
#8 MeSH descriptor Anti-Infective Agents, Local explode all trees
#9 MeSH descriptor Iodine Compounds explode all trees
#10 MeSH descriptor Povidone-Iodine explode all trees
#11 MeSH descriptor Alcohols explode all trees
#12 MeSH descriptor Disinfectants explode all trees
#13 MeSH descriptor Disinfection explode all trees
#14 skin NEXT preparation:ti,ab,kw
#15 skin NEXT disinfection:ti,ab,kw
#16 ("alcohol" or "alcohols" or iodine or povidone-iodine or chlorhexidine):ti,ab,kw
#17 (#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16)
#18 (#6 AND #17)
This strategy will be adapted were appropriate for the other databases. The Ovid MEDLINE search will be combined with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision) (Lefebvre 2011). The Ovid EMBASE and EBSCO CINAHL searches will be combined with the trial filters developed by the Scottish Intercollegiate Guidelines Network (SIGN 2009). There was no restriction on the basis of date or language of publication.

Searching other resources

Reference lists of potentially useful articles will also be searched.

Data collection and analysis

Selection of studies

Titles and abstracts identified through the search process will be independently reviewed by two review authors. Full reports of all potentially relevant trials will be retrieved for further assessment of eligibility based on the inclusion criteria. Differences of opinion will be settled by consensus or referral to a third review author. There will be no blinding of authorship.

Data extraction and management

Two review authors will independently assess the quality of eligible trials, using the quality assessment criteria outlined below. Disagreements between review authors will be resolved by consensus or referral to a third review author. We will contact investigators of included trials to resolve any ambiguities. Whilst data from duplicate publications will be included only once, all publications pertaining to a single study will be retrieved and used to enable full data extraction and quality assessment.
We will extract the following data, where possible:

- details of the trial/study (first author, year of publication, journal, publication status, period);
- setting and country of study;
- source of funding;
- inclusion and exclusion criteria;
- baseline characteristics of participants (age, sex);
- aspects of morbidity of the blood recipients, e.g. predictors of susceptibility to bacteraemia;
- number of participants in each arm of the trial;
- description of intervention (type, duration);
- description of control intervention (type, duration);
- details and duration of follow up;
- primary and secondary outcomes (by group);
- design / methodological quality data as per risk of bias criteria;
- unit of randomisation (where relevant);
- unit of analysis;

- results and primary statistical analysis.

Assessment of risk of bias in included studies

Two authors will independently assess each included study using the Cochrane Collaboration tool for assessing risk of bias Higgins 2011a. This tool addresses six specific domains, namely sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and other issues (e.g. co-interventions)(see Appendix 5 for details of criteria on which the judgement will be based). Blinding and completeness of outcome data will be assessed for each outcome separately. We will complete a risk of bias table for each eligible study. We will discuss any disagreement amongst all authors to achieve a consensus.
We will present assessment of risk of bias using a 'risk of bias summary figure', which presents all of the judgments in a cross-tabulation of study by entry. This display of internal validity indicates the weight the reader may give the results of each study.

Measures of treatment effect

For individual trials, effect measures for categorical outcomes will include relative risk (RR) with its 95% confidence interval (CI). For statistically significant effects, number needed to treat (NNT), or number needed to harm (NNH), will be calculated. For continuous outcomes, the effect measure will be mean difference (MD) or, if the scale of measurement differs across trials, standardized mean difference (SMD), each with its 95% CI. For any meta-analyses (see below), for categorical outcomes the typical estimates of RR with their 95% CI will be calculated; and for continuous outcomes the weighted mean difference (WMD) or a summary estimate for SMD, each with its 95% CI, will be calculated.
Data will be analysed using The Cochrane Collaboration's Review Manager 5 software.

Dealing with missing data

If some outcome data remain missing despite our attempts to obtain complete outcome data from authors, we will perform an available-case analysis, based on the numbers of patients for whom outcome data are known. If standard deviations are missing, we will impute them from other studies or, where possible, compute them from standard errors using the formula SD = SE x ?N , where these are available (Higgins 2011a).

Assessment of heterogeneity

Heterogeneity will be assessed visually and by using the chi-squared statistic with significance being set at $p < 0.10$. In addition, the degree of heterogeneity will be investigated by calculating the I^2 statistic Higgins 2011a. If evidence of significant heterogeneity is identified (>50%), we will explore potential causes and a random-effects approach to the analysis will be used if a meta analysis is appropriate.

Assessment of reporting biases

Reporting bias will be assessed using guidelines in Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011a).

Data synthesis

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

Subgroup analysis and investigation of heterogeneity

We plan to analyse potential sources of heterogeneity using the following subgroup analysis - concealment of allocation (adequate versus not reported).

Sensitivity analysis

We will perform a sensitivity analysis to explore the effect of concealment of allocation (adequate versus not reported).

Acknowledgements

The authors would like to acknowledge the peer referees: Mike Clarke, Jo Dumville, Carmel Hughes and Ian Roberts. Thanks also to Martin Bland for statistical advice. Nicky Cullum provided editorial input and advice throughout the development of the protocol.

Contributions of authors

Joan Webster: designed the protocol, wrote the protocol draft, responded to the peer referee feedback and approved the final protocol prior to submission.
Sally Bell-Syer: coordinated the protocol, edited the protocol draft, responded to the peer referee feedback and approved the final protocol prior to submission.
Ruth Foxlee: designed the search strategy, edited the search methods section and responded to the peer referee feedback and approved the final protocol prior to submission.

Declarations of interest

none known

Other references

Additional references

Adams 2007

Adams D, Elliot TS. Skin antiseptics used prior to intravascular catheter insertion. British Journal of Nursing 2007;16(5):278-80.

Cid 2003

Cid J, Ortín X, Ardanuy C, Contreras E, Elies E, Martín-Vega C. Bacterial persistence on blood donors' arms after phlebotomy site preparation: analysis of risk factors. Haematologica 2003;88(7):839-40.

Hakim 2007

Hakim H, Mylotte JM, Faden H. Morbidity and mortality of Staphylococcal bacteremia in children. Americal Journal of Infection Control 2007;35(2):102-5.

Herchline 1997

Herchline T, Gros S. Improving clinical outcome in bacteremia. Journal of Evaluation in Clinical Practice 1997;4(3):191-5.

Higgins 2008

Higgins JPT and Altman DG on behalf of the Cochrane Statistical Methods Group and the Cochrane Bias Methods Group (Editors). In: Higgins JPT, Green S (editors), Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.0 (updated February 2008).The Cochrane Collaboration, 2008. Available from www.cochrane-handbook.org. Wiley-Blackwell, 2008.

Lefebvre 2008

Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.0 (updated February 2008). The Cochrane Collaboration, 2008.Available from www.cochrane-handbook.org.

McDonald 2001

McDonald CP, Lowe P, Roy A, Robbins S, Hartley S, Harrison JF, et al. Evaluation of donor arm disinfection techniques. Vox Sanguinis 2001;80(3):135-41.

Mimoz 1999

Mimoz O, Karim A, Mercat A, Cosseron M, Falissard B, Parker F, Richard C, Samii K, Nordmann P. Chlorhexidine compared with povidone-iodine as skin preparation before blood culture. A randomized, controlled trial. Annals of Internal Medicine 1999;131:834-7.

Sandler 2003

Sandler SG, Yu H, Rassai N. Risks of blood transfusion and their prevention. Clinical Advances in Hematology and Oncology 2003; 1(5):307-13.

Shahar 1990

Shahar E, Wohl-Gottesman BS, Shenkman L. Contamination of blood cultures during venepuncture: fact or myth? Postgraduade Medical Journal 1990;66(782):1053-8.

SIGN 2008

Scottish Intercollegiate Guidelines Network (SIGN). Search filters. http://www.sign.ac.uk/methodology/filters.html#random (accessed 2 June 2008).

Sligl 2006

Sligl W, Taylor G, Brindley PG. Five years of nosocomial Gram-negative bacteremia in a general intensive care unit: epidemiology, antimicrobial susceptibility patterns, and outcomes. International Journal of Infectious Diseases 2006;10(4):320-5.

Trautner 2002

Trautner BW, Clarridge JE, Darouiche RO. Skin antisepsis kits containing alcohol and chlorhexidine gluconate or tincture of iodine are associated with low rates of blood culture contamination. Infection Control and Hospital Epidemiology 2002;23(7):397-401.

Wagner 2004

Wagner SJ. Transfusion-transmitted bacterial infection: risks, sources and interventions. Vox Sanguinis 2004;86(3):157-63.

Walther-Wenke 2008

Walther-Wenke G. Incidence of bacterial transmission and transfusion reactions by blood components. Clinical Chemistry and Laboratory Medicine 2008;46(7):919-25.

Wong 2004

Wong PY, Colville VL, White V, Walker HM, Morris RA, Microbial Contamination and Infection Control Subcommittee, Australian Red Cross Blood Service. Validation and assessment of a blood-donor arm disinfectant containing chlorhexidine and alcohol. Transfusion 2004;44(8):1238-42.

Yomtovian 2006

Yomtovian RA, Palavecino EL, Dysktra AH, Downes KA, Morrissey AM, Bajaksouzian S, et al. Evolution of surveillance methods for detection of bacterial contamination of platelets in a university hospital, 1991 through 2004. Transfusion 2006;46:719-30.

Other published versions of this review

Classification pending references

Data and analyses

Figures

Sources of support

Internal sources

- Department of Health Sciences, University of York, UK

External sources

- No sources of support provided

Feedback

Appendices

1 *Criteria for a judgment of 'yes' for the sources of bias*

1. Was the allocation sequence randomly generated?

Yes, low risk of bias

A random (unpredictable) assignment sequence.

Examples of adequate methods of sequence generation are computer-generated random sequence, coin toss (for studies with two groups), rolling a dice (for studies with two or more groups), drawing of balls of different colours, dealing previously shuffled cards.

No, high risk of bias

- Quasi-randomised approach: Examples of inadequate methods are: alternation, birth date, social insurance/security number, date in which they are invited to participate in the study, and hospital registration number

- Non-random approaches: Allocation by judgement of the clinician; by preference of the participant; based on the results of a laboratory test or a series of tests; by availability of the intervention.

Unclear

Insufficient information about the sequence generation process to permit judgement

2. Was the treatment allocation adequately concealed?

Yes, low risk of bias

Assignment must be generated independently by a person not responsible for determining the eligibility of the participants. This person has no information about the persons included in the trial and has no influence on the assignment sequence or on the decision about whether the person is eligible to enter the trial. Examples of adequate methods of allocation concealment are: Central allocation, including telephone, web-based, and pharmacy controlled,randomization; sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes.

No, high risk of bias

Examples of inadequate methods of allocation concealment are: alternate medical record numbers, unsealed envelopes; date of birth; case record number; alternation or rotation; an open list of random numbers any information in the study that indicated that investigators or participants could influence the intervention group.

Unclear

Randomisation stated but no information on method of allocation used is available.

3. Blinding was knowledge of the allocated interventions adequately prevented during the study?

Was the participant blinded to the intervention?

Yes, low risk of bias

The treatment and control groups are indistinguishable for the participants or if the participant was described as blinded and the method of blinding was described.

No, high risk of bias

- Blinding of study participants attempted, but likely that the blinding could have been broken; participants were not blinded, and the nonblinding of others likely to introduce bias.

Unclear

Was the care provider blinded to the intervention?

Yes, low risk of bias

The treatment and control groups are indistinguishable for the care/treatment providers or if the care provider was described as blinded and the method of blinding was described.

No, high risk of bias

Blinding of care/treatment providers attempted, but likely that the blinding could have been broken; care/treatment providers were not blinded, and the nonblinding of others likely to introduce bias.

Unclear

Was the outcome assessor blinded to the intervention?

Yes, low risk of bias

Adequacy of blinding should be assessed for the primary outcomes. The outcome assessor was described as blinded and the method of blinding was described.

No, high risk of bias

No blinding or incomplete blinding, and the outcome or outcome measurement is likely to be influenced by lack of blinding

Unclear

4. Were incomplete outcome data adequately addressed?

Was the drop-out rate described and acceptable?

The number of participants who were included in the study but did not complete the observation period or were not included in the analysis must be described and reasons given.

Yes, low risk of bias

If the percentage of withdrawals and drop-outs does not exceed 20% for short-term follow-up and 30% for long-term follow-up and does not lead to substantial bias. (N.B. these percentages are arbitrary, not supported by literature);

No missing outcome data;

Reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias);

Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups;

Missing data have been imputed using appropriate methods.

No, high risk of bias

Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups;

Unclear

Were all randomised participants analysed in the group to which they were allocated? (ITT analysis)

Yes, low risk of bias
Specifically reported by authors that ITT was undertaken and this was confirmed on study assessment, or not stated but evident from study assessment that all randomised participants are reported/analysed in the group they were allocated to for the most important time point of outcome measurement (minus missing values) irrespective of non-compliance and co-interventions.
No, high risk of bias
Lack of ITT confirmed on study assessment (patients who were randomised were not included in the analysis because they did not receive the study intervention, they withdrew from the study or were not included because of protocol violation) regardless of whether ITT reported or not
'As-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation; potentially inappropriate application of simple imputation.
Unclear
Described as ITT analysis, but unable to confirm on study assessment, or not reported and unable to confirm by study assessment.
5. Are reports of the study free of suggestion of selective outcome reporting?
Yes, low risk of bias
If all the results from all pre-specified outcomes have been adequately reported in the published report of the trial. This information is either obtained by comparing the protocol and the final trial report, or in the absence of the protocol, assessing that the published report includes enough information to make this judgment. Alternatively a judgement could be made if the trial report lists the outcomes of interest in the methods of the trial and then reports all these outcomes in the results section of the trial report.
No, high risk of bias
Not all of the study's pre-specified primary outcomes have been reported;
One or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not prespecified;
One or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect);
One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis;
The study report fails to include results for a key outcome that would be expected to have been reported for such a study.
Unclear
6. Other sources of potential bias:
Were co-interventions avoided or similar?
There were no co-interventions or there were co-interventions but they were similar between the treatment and control groups.
Was the compliance acceptable in all groups?
The review author determines if the compliance with the interventions is acceptable, based on the reported intensity, duration, number and frequency of sessions for both the treatment intervention and control intervention(s). For example, ultrasound treatment is usually administered over several sessions; therefore it is necessary to assess how many sessions each participant attended or if participants completed the course of an oral drug therapy. For single-session interventions (for example: surgery), this item is irrelevant.

WHAT'S NEW

Last assessed as up-to-date: 18 December 2014.

Date	Event	Description
18 December 2014	New citation required but conclusions have not changed	Third update, no change to conclusions
18 December 2014	New search has been performed	New search, no new studies identified

HISTORY

Review first published: Issue 3, 2009

Date	Event	Description
4 December 2014	New citation required but conclusions have not changed	Second update, no change to conclusions
18 December 2012	New search has been performed	New search, no new studies identified.
30 August 2011	Amended	republish, update affiliations, risk of bias terminology
2 February 2011	New search has been performed	New search, no new studies identified for inclusion, 3 studies added to the Table of Excluded studies (Benjamin 2011; McDonald 2010; Ramirez-Arcos 2010). The review conclusions remain unchanged.

CONTRIBUTIONS OF AUTHORS

Joan Webster: designed the review, checked the search results and all papers retrieved in full, wrote the review draft, responded to the peer referee feedback, made an intellectual contribution to the review and approved the final review prior to submission, updated the review. Guarantor of the review.

Sally Bell-Syer: coordinated the review, edited the review draft, responded to the peer referee feedback, made an intellectual contribution to the review and approved the final review and review updates prior to submission.

Ruth Foxlee: designed the search strategy, conducted the literature searches, retrieved papers, checked all papers retrieved in full. Edited the search methods section and responded to the peer referee feedback and approved the final review and updated review prior to submission.

DECLARATIONS OF INTEREST

Joan Webster: none.

Sally Bell-Syer: none.

Ruth Foxlee: none.

SOURCES OF SUPPORT

Internal sources

- Department of Health Sciences, University of York, UK.
- School of Nursing and Midwifery, Queensland University of Technology, Queensland, Australia.
- School of Nursing and Midwifery, Griffith University, Brisbane, Australia.

External sources

- The National Institute for Health Research (NIHR) is the sole funder of Cochrane Wounds, UK.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Nil

NOTES

This rapid response review was undertaken at the request of the World Health Organisation (WHO). This organisation framed the review question but they did not provide funding or influence its publication.

The protocol for this review was completed and ready for submission in March 2009, the review being completed and ready for submission in April 2009. As the protocol has not been previously published in the Cochrane Library it is appended to this review in the interests of transparency (Appendix 6).

INDEX TERMS

Medical Subject Headings (MeSH)

*Blood Donors; Anti-Infective Agents, Local [*administration & dosage]; Bacteremia [*prevention & control]; Blood Transfusion; Disinfection [*methods]; Ethanol [*administration & dosage]; Skin [*microbiology]

MeSH check words

Humans