Preoperative bathing or showering with skin antiseptics to prevent surgical site infection (Review)

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ABSTRACT

Background
Surgical site infections (SSIs) are wound infections that occur after invasive (surgical) procedures. Preoperative bathing or showering with an antiseptic skin wash product is a well-accepted procedure for reducing skin bacteria (microflora). It is less clear whether reducing skin microflora leads to a lower incidence of surgical site infection.

Objectives
To review the evidence for preoperative bathing or showering with antiseptics for the prevention of hospital-acquired (nosocomial) surgical site infection.

Search strategy
We searched the Cochrane Wounds Group Specialised Register (December 2005), the Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 4, 2005), MEDLINE (January 1966 to December 2005) and reference lists of articles.

Selection criteria
Randomised controlled trials comparing any antiseptic preparation used for preoperative full-body bathing or showering with non-antiseptic preparations in patients undergoing surgery.

Data collection and analysis
Two authors independently assessed studies for selection, trial quality and extracted data. Study authors were contacted for additional information.

Main results
Six trials involving a total of 10,007 participants were included. Three of the included trials had three comparison groups. The antiseptic used in all trials was 4% chlorhexidine gluconate (Hibiscrub). Three trials involving 7691 participants compared chlorhexidine with a placebo. Bathing with chlorhexidine compared with a placebo did not result in a statistically significant reduction in SSIs; the relative risk of SSI (RR) was 0.91 (95% confidence interval (CI) 0.80 to 1.04). When only trials of high quality were included in this comparison, the RR of SSI was 0.95 (95%CI 0.82 to 1.10). Three trials of 1443 participants compared bar soap with chlorhexidine; when combined there was no difference in the risk of SSIs (RR 1.02, 95% CI 0.57 to 1.84). Two trials of 1092 patients compared bathing with chlorhexidine with no washing, one large study found a statistically significant difference in favour of bathing with chlorhexidine (RR 0.36, 95%CI 0.17 to 0.79). The second smaller study found no difference between patients who washed with chlorhexidine and those who did not wash preoperatively.

Authors' conclusions
This review provides no clear evidence of benefit for preoperative showering or bathing with chlorhexidine over other wash products, to reduce surgical site infection. Efforts to reduce the incidence of nosocomial surgical site infection should focus on interventions where effect has been demonstrated.
Surgical site infection is a serious complication of surgery and may be associated with increased length of hospital stay for the patient and higher hospital costs. The use of an antiseptic solution for pre-operative bathing or showering is widely practiced in the belief that it will help to prevent surgical site infection. However, the review found six trials that included over 10,000 patients that did not show clear evidence of benefit for the use of chlorhexidine solution over other wash products.

**BACKGROUND**

Surgical site infections (SSIs) are wound infections that occur after invasive procedures. SSI is the third most frequently hospital-acquired (nosocomial) infection (Smyth 2000) amongst hospital patients. The Centers for Disease Control and Prevention (CDC) have used the National Nosocomial Infections Surveillance system (NNIS) to monitor nosocomial infections in acute care hospitals in the United States since 1970. Between 1986 and 1996 the CDC studied approximately 600,000 operations. Surgical site infections developed after three per cent (15,523) of these operations. During the period of data collection, 551 patients (out of the 15,523 who developed an surgical site infection) died, and 77% of deaths were attributed to the infection (Mangram 1999). Apart from the morbidity and mortality associated with surgical site infections, there are significant cost implications. A recent study, using the NNIS system found that it cost over $3000 more to treat a patient with an SSI than a non-infected patient. These costs were attributable to a greater likelihood of admission to an intensive care unit, a longer than usual post-operative stay (five days) and an increased rate of hospital re-admission (Kirkland 1999). Potential litigation is also a concern (Rubinstein 1999). Consequently, prevention of surgical site infection has become a priority for health care facilities.

An SSI is defined as one occurring within 30 days after the operation and involves either a purulent discharge, with or without laboratory confirmation, an organism isolated from an aseptically obtained culture or signs and symptoms of infection, such as localised swelling, redness, tenderness (Mangram 1999). The CDC has developed a set of standardised criteria for defining SSI in an attempt to make surveillance and rate calculation more accurate and amenable to comparison (Mangram 1999). SSIs are classified as being: superficial incisional (involving only skin or subcutaneous tissues); deep incisional (involving deeper soft tissue and fascia); or organ/space (involving any other part of the anatomy that was opened or manipulated). To help predict the likelihood or SSI risk, surgical sites can be assessed preoperatively and classified into one of four categories with clear definitions: Class I (clean), Class II (clean-contaminated), Class III (contaminated) and Class IV (dirty/infected) (Mangram 1999). Clean wounds are defined as uninfected surgical wounds in which the respiratory, alimentary, genital or uninfected urinary tract are not present and in which no inflammation is encountered. Non-clean wounds are defined according to the anatomical area of operation, aetiology of wound, presence of existing clinical infection, and intra-operative contamination. Since clean wounds are less likely to become infected, SSIs following clean surgery are usually associated with either (1) patient risk factors: such as age, nutritional status, diabetes and obesity; (2) risk factors related to the procedure: including incomplete preoperative hand and forearm antisepsis by one of the surgical team, length of surgical procedure and surgical technique; or (3) risk factors associated with preoperative preparation of the patient: for example, antimicrobial prophylaxis, preoperative hair removal and preoperative antiseptic showering (Mangram 1999).

Skin is not sterile. Indeed, thousands of bacteria live on skin permanently and contribute to health by maintaining a steady colony that inhibits establishment of harmful yeast and fungal infections. These bacterial populations are referred to as the 'resident flora'. A number of bacteria are present on the skin for a short period due to transfer from other people or the environment, and these constitute the 'transient flora'. At present, whole body bathing or showering with skin antiseptic in order to prevent SSIs is a widespread practice before surgery. The aim of washing is to make the skin as clean as possible by removing transient flora and some resident flora. Chlorhexidine 4% in detergent (' Hibiscrub' or 'Hibiclens') or a triclosan preparation is usually used for this purpose, and there is evidence that the numbers of bacteria on the skin are reduced when it is applied (Byrne 1991; Kaiser 1988). Moreover, use of a skin antiseptic on consecutive days not only reduces microbial counts from baseline measurements, but also reduces the counts progressively over time (Paulson 1993). Although this body of evidence demonstrates the effectiveness of antiseptics as skin cleansing agents, the more important question is whether preoperative bathing or showering with an antiseptic reduces the incidence of SSI. In a 10-year prospective surveillance study, the SSI rate was lower amongst patients showering with hexachlorophene before surgery than in those who either did not shower or showered using a non-mediated soap (Cruse 1980). In addition, at least two studies have used a before and after design to test the effect of introducing preoperative showering with triclosan to control meticillin-resistant Staphylococcus aureus (MRSA) SSIs. In the first of these, showering before and after surgery was introduced to reduce the MRSA SSI rate. However, this intervention was only one of a battery of measures introduced, so it was not possible to de-
termine the independent effect of preoperative showering (Brady 1990). In the second, the incidence of MRSA SSI was reduced amongst orthopaedic patients after presurgical showering with triclosan was introduced, however, the patients were also treated with nasal mupirocin for five days before surgery (Wilcox 2003). While these observational studies provide some support for the practice of preoperative showering with an antiseptic, the evidence is not definitive.

Patterns of resistance have developed with some antiseptics (Thomas 2000), leading to calls to restrict their use to situations where effectiveness can be demonstrated. In addition, hypersensitivity to chlorhexidine is not uncommon. Consequently, the potential benefit of bathing/showering with antiseptics needs to be assessed alongside the potential for harm (Beaudounin 2004; Krauthem 2004). As it is unclear whether the use of antiseptics for preoperative bathing or showering leads to lower rates of SSIs, a systematic review is justified to guide practice in this area.

**OBJECTIVES**

To review the evidence for preoperative bathing or showering with antiseptics for the prevention of surgical site infection.

**CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW**

**Types of studies**

All published and unpublished randomised controlled trials that allocate surgical patients individually or by cluster, comparing any antiseptic preparation used for preoperative full body or showering, with non-antiseptic preparations. Quasi-randomised trials were not included (e.g. trials that allocate treatment by day of the week, medical record number, sequential admitting order).

**Types of participants**

Men, women and children undergoing any type of surgery in any setting.

**Types of intervention**

Any type of antiseptic solution (any strength, any regimen at any time before surgery) used for preoperative tub or bed bathing or showering compared with:

1. non-antiseptic soap;
2. non-antiseptic soap solution;
3. no shower or bath.

Antiseptic solutions were defined as liquid soap products containing an antimicrobial ingredient such as chlorhexidine, triclosan, hexachlorophene, povidone–iodine or benzalkonium chloride. Trials comparing different types of antiseptic with each other would also be compared if evidence for the benefit of showering was either equivocal, or if there was evidence of benefit with showering with antiseptic.

**Types of outcome measures**

Trials were considered if they reported the primary outcome:

**Primary outcome**

Surgical site infection. (Note: Despite development of standardised criteria for defining SSI, the diagnosis of SSIs continues to vary between studies. We therefore accepted the definition used by the original authors to determine the proportion of patients who develop any SSI before or after discharge).

**Secondary outcomes**

1. Mortality (any cause).
2. Allergic reactions (e.g. contact dermatitis, anaphylaxis).
3. Postoperative antibiotic use.
4. Length of hospital stay.
5. Re-admission to hospital.
7. Other serious infection or infectious complication, such as septicemia or septic shock.
8. Postoperative fever higher than 38°C on at least two occasions more than four hours apart, excluding the day of surgery.

Secondary outcomes were only extracted if the primary outcome was reported.

**SEARCH METHODS FOR IDENTIFICATION OF STUDIES**

See: Cochrane Wounds Group methods used in reviews.

We searched the Cochrane Wounds Group Specialised Register (December 2005).

The Cochrane Wounds Group Specialised Register is maintained by searching:

1. MEDLINE, CINAHL and EMBASE;
2. the Cochrane Central Register of Controlled Trials (CENTRAL);
3. hand searching of wound care journals and relevant conference proceedings.

There was no restriction by language or date of publication. Reference lists of all retrieved articles were searched for additional studies. Manufacturers of antiseptic products were contacted in order to obtain any unpublished data.

In addition, we searched MEDLINE (2002 to 2005) to allow for any lag-time in the Wounds Group Specialised Register.

The following strategy was used to search CENTRAL (Issue 4 2005):

1. DETERGENTS explode all trees (MeSH)
2. POVIDONE-IODINE explode all trees (MeSH)
3. CHLORHEXIDINE explode all trees (MeSH)
4. DISINFECTION explode all trees (MeSH)
5. ALCOHOL DETERGENTS explode all trees (MeSH)
6. detergent*
7. Betadine
8. chorhexidine
9. (povidone and iodine)
10. (alcohol or alcohols or soap)
11. ANTI-INFECTIVE AGENTS LOCAL single term (MeSH)
12. antiseptic*
13. iodophor*
14. (#1 or #2 or #3 or #4 or #5 or #6 or #7)
15. (#8 or #9 or #10 or #11 or #12 or #13)
16. (#14 or #15)
17. SURGICAL WOUND INFECTION explode all trees (MeSH)
18. PREOPERATIVE CARE explode all trees (MeSH)
19. PERIOPERATIVE CARE explode all trees (MeSH)
20. (preoperative near care)
21. (perioperative near care)
22. (wound* near infect*)
23. (surg* near infect*)
24. (surg* near wound*)
25. (#17 or #18 or #19 or #20 or #21 or #22 or #23 or #24)
26. shower*
27. bath*
28. wash*
29. clean*
30. (#26 or #27 or #28 or #29)
31. (#16 and #25 and #30)

METHODS OF THE REVIEW

Selection of studies
Both authors independently assessed the titles and abstracts of references identified by the search strategy. Full reports of all potentially relevant trials were then retrieved for assessment of eligibility based on the inclusion criteria. Reference lists of retrieved studies were screened to identify further studies, which were also retrieved. Differences of opinion were settled by consensus or referral to the editorial base of the Wounds Group.

Methodological quality assessment
The two authors assessed the quality of eligible trials independently. A pre-defined quality assessment form, based on the assessment criteria listed below, was used. Once again, disagreements between authors were resolved by consensus or referral to the editorial base of the Wounds Group. When possible, contact was made with investigators of included trials to resolve any ambiguities.

Trials that met the eligibility criteria were coded as follows for:

- Generation of random allocation sequence
  A = Adequate (if the method used was described and the resulting sequences were unpredictable);
  B = Unclear (if the method was not described);
  C = Inadequate (for sequences such as alternative allocation).

Allocation concealment
- A = Adequate (if participants and the investigators enrolling participants could not foresee assignment);
- B = Unclear (method not described);
- C = Inadequate (if investigators enrolling participants could foresee next assignment).

Blinding of intervention
- A = Double blind (neither the participant nor the person providing the intervention knew which treatment was given);
- B = Single blind (the participant or person providing the intervention knew which treatment was given);
- C = No blinding (all parties were aware of treatment);
- D = Unclear (method not described).

Blinding of outcome assessment
- A = Outcome assessment was blinded (person performing assessment did not know which treatment had been given);
- B = Cannot tell whether outcome assessment was blinded;
- C = Outcome assessment was not blinded (person performing assessment was aware of treatment given).

Intention to treat analysis (analysed according to allocated treatment group, irrespective of adherence to treatment)
- A = Yes, intention to treat analysis performed;
- B = Cannot tell;
- C = No, intention to treat analysis not performed.

Completeness of primary outcome reporting
- A = Adequate (more than 90% of all participants randomised were included in the analysis);
- B = Unclear (not clear how many participants were originally randomised);
- C = Inadequate (less than 90% of those randomised were included in the analysis).

High quality trials were defined as those receiving an A rating for the criterion of allocation concealment (central computerised randomisation service or sealed opaque envelopes) and for blinding of the intervention (from the person providing the intervention and from trial participants).

Data extraction
The following data were extracted from each study by both authors independently using a piloted data extraction sheet: type of study, study setting, number of participants, sex, mean age, predisposing risk factors, type of antiseptic solutions, use of prophylactic antibiotics, procedure and timing for full body wash, period of community follow-up, all primary and secondary outcome descriptions and outcome measures reported, including infection rates and authors’ conclusions.
Data synthesis
Analyses were performed using the RevMan 4.2 software. Relative risks and 95% confidence intervals (CI) were calculated for dichotomous outcomes, and mean differences and 95% CI calculated for continuous outcomes. Results of comparable trials were pooled using the fixed-effect model and 95% CI. Heterogeneity was investigated by calculating the I² statistic (Higgins 2002). If evidence of significant heterogeneity was identified (a value greater than 50%), potential sources of heterogeneity were explored and a random-effects approach to the analysis undertaken. A narrative review of eligible studies was conducted where statistical synthesis of data from more than one study was not possible or considered inappropriate.

One trial (Rotter 1988) used a multi-centre design but patients were allocated individually to the treatment or control arm. Two trials (Hayek 1987; Wihlborg 1987) allocated clusters of patients to each intervention. In this review results were not analysed using the number of clusters as the unit of analysis but analysed as if the allocation was by individual. This was necessary because the authors of the trial did not use the cluster as the unit of analysis. Analysing cluster trials in this way has the potential to over-estimate the effect of treatment (Mollison 2000).

We included all eligible trials in the initial analysis and carried out sensitivity analyses to evaluate the effect of trial quality. This was done by excluding those trials most susceptible to bias based on the following quality assessment criteria: those with inadequate allocation concealment; or unblinded outcome assessment; or where blinding of outcome assessment was uncertain.

Sub-group analyses:
The planned sub-group analyses (one preoperative bath or shower compared with more than one preoperative bath or shower; and clean surgery compared with clean contaminated surgery) were not conducted due to the format of the reported data.

DESCRIPTION OF STUDIES
For a detailed description of studies see table of 'Characteristics of included studies'.

Our search strategy identified 43 articles. Full-text assessment was conducted of 16 potentially eligible papers. Ten of these papers were excluded from further review because the studies were not randomised, or were randomised trials evaluating other interventions (e.g. preoperative scrub solutions), or other outcomes (e.g. intraoperative wound colonisation). The six remaining trials reported outcomes for 10,007 participants and were included in the review (Byrne 1992; Earnshaw 1989; Hayek 1987; Randall 1983; Rotter 1988; Wihlborg 1987). The results of these six trials were reported in nine publications (Byrne 1992; Byrne 1994; Earnshaw 1989; Hayek 1987; Hayek 1988; Lynch 1992; Randall 1983; Rotter 1988; Wihlborg 1987). Four authors of included trials (Byrne 1992; Earnshaw 1989; Randall 1983; Wihlborg 1987) and one non-included trial author (Garabaldi 1988) responded to queries about study methods and/or requests for additional unpublished information.

Participants
The age range of the participants in the six included studies was nine to 90 years old. The trials enrolled men, women and children booked for elective surgery.

Byrne 1992 included clean and potentially infected cases but all other studies were of clean surgery. Two studies included general surgical patients (Byrne 1992; Hayek 1987); one involved participants undergoing general, orthopaedic and vascular surgery (Rotter 1988); and one included biliary tract, inguinal hernia or breast surgery (Wihlborg 1987). The remaining studies involved only one type of surgery (Earnshaw 1989 (vascular reconstruction); Randall 1983 (vasectomy)). Participants in the vasectomy study (Randall 1983) were day patients.

Four of the centres in which the studies were conducted were in the United Kingdom (Byrne 1992; Earnshaw 1989; Hayek 1987; Randall 1983); one was in Sweden (Wihlborg 1987) and one (Rotter 1988) included a number of European centres (eight from Denmark, five from the United Kingdom, four from Sweden, two from Austria, and one from both Germany and Italy).

All of the studies included the presence of pus in their definition of infection. Earnshaw 1989 and Hayek 1987 also included patients with severe cellulitis (although there was only such patient) and Randall 1983 included patients with a discharge of serous fluid in his definition of infection.

Interventions
There were inconsistencies in both the interventions and the control procedures between studies. One trial compared a regimen that included three preoperative washes (Byrne 1992), three trials included a two-wash regimen (Earnshaw 1989; Hayek 1987; Rotter 1988), and participants in two trials had only one wash preoperatively (Randall 1983; Wihlborg 1987).

The breakdown of the studies according to timing of bathing were as follows:

- One wash on admission, a second on the night before surgery and a third on the morning of surgery (Byrne 1992).
- One wash immediately after admission, and a second on the day of surgery (Hayek 1987).
- One wash on the day before surgery, and a second on the day of surgery (Rotter 1988).
- Two washes preoperatively, timing not specified (Earnshaw 1989).
- One wash on the day before surgery only (Wihlborg 1987).
- One wash not more than one hour before surgery (Randall 1983).

Three of the studies had two arms (Byrne 1992; Earnshaw 1989; Rotter 1988), whilst three had three arms (Hayek 1987; Randall 1983; Wihlborg 1987). The breakdown of studies according to bathing products is as follows:

- 4% Chlorhexidine gluconate (Hibiscrub) detergent solution compared with a matching placebo (i.e. the same detergent without chlorhexidine) (Byrne 1992; Hayek 1987; Rotter 1988).
- 4% Chlorhexidine gluconate (Hibiscrub) compared with bar soap (Earnshaw 1989; Hayek 1987; Randall 1983).
- Chlorhexidine with no shower or bath (Randall 1983; Wihlborg 1987).
- Chlorhexidine full body bathing compared with localised washing, i.e. restricted to the part of the body to be subjected to surgery (chlorhexidine used in both arms of trial) (Wihlborg 1987).

Antibiotic prophylaxis was used routinely in only one study (Earnshaw 1989). In three other studies (Byrne 1992; Rotter 1988; Wihlborg 1987) there was no attempt to alter the treating surgeons’ usual routine for administering antibiotic prophylaxis but, in these studies, the reported rate of prophylactic antibiotic use was low (1% - 15%). Two studies (Hayek 1987; Randall 1983) did not mention whether antibiotics were used before surgery.

**Outcome measures**

**Primary outcome**

The primary outcome measure for this review, the effectiveness of preoperative washing or showering with an antiseptic in preventing SSI, was reported in all of the studies (Byrne 1992; Earnshaw 1989; Hayek 1987; Randall 1983; Rotter 1988; Wihlborg 1987).

**Secondary outcomes**

The secondary outcomes of the review were reported as follows:

1. Mortality (any cause) was reported in two studies (Byrne 1992; Earnshaw 1989).
2. Allergic reactions (e.g. contact dermatitis, anaphylaxis) were reported in one study (Byrne 1992).
3. Post operative antibiotic use was not reported in any of the studies.
4. Length of hospital stay was not reported in any of the studies.
5. Re-admission to hospital was not reported in any of the studies.
6. Cost was reported in one study (Byrne 1992).
7. Other serious infection or infectious complication, such as septicaemia or septic shock was not reported in any of the studies.
8. Postoperative fever exceeding 38°C on at least two occasions more than four hours apart, excluding the day of surgery, was not reported in any of the studies.

**METHODOLOGICAL QUALITY**

Two of the six included studies (Byrne 1992; Rotter 1988) were assessed as being of high methodological quality using the assessment criteria described above.

**Generation of random allocation sequence**

All studies mentioned a process of randomisation. The method of generating the random allocation sequence was adequate in some studies (Byrne 1992; Randall 1983; Rotter 1988; Wihlborg 1987) and unclear in others (Earnshaw 1989; Hayek 1987). In three of the studies, the random sequence was computer generated (Byrne 1992; Randall 1983; Rotter 1988). One study used block randomisation in groups of six using computer generated random numbers (Byrne 1992). A large multi-centre study used cluster randomisation whereby randomisation was carried out for each surgical unit in the study by means of computer generated numbers (Rotter 1988). Personal correspondence with authors of two of the studies confirmed that they used either computer generated random numbers (Randall 1983) or a randomisation list (Wihlborg 1987).

**Allocation concealment**

As with generation of the allocation sequence, concealment of allocation was adequate in some studies (Byrne 1992; Randall 1983; Rotter 1988; Wihlborg 1987) and unclear in others (Earnshaw 1989; Hayek 1987).

**Blinding of intervention**

Blinding of intervention in two studies was by a double blind method (Byrne 1992; Rotter 1988). In one study there was single blinding of the intervention in two arms of the study but no blinding in the third arm of the study (Hayek 1987). In the remaining studies, there was no blinding of intervention (Earnshaw 1989; Randall 1983; Wihlborg 1987).

**Blinding of outcome assessment**

In four of the studies, there was no blinding of outcome assessment (Byrne 1992; Earnshaw 1989; Hayek 1987; Rotter 1988). In one of the studies there was no blinding of the outcome assessment (Wihlborg 1987). In one study it is unclear whether blinding of outcome assessment occurred (Randall 1983).

**Sample size calculations**

None of the trials reported how the sample size was calculated.

**Intention to treat analysis**

In one study analysis by intention to treat was not done (Byrne 1992). For all of the other studies it could not be determined whether analysis by intention to treat occurred (Earnshaw 1989; Hayek 1987; Randall 1983; Rotter 1988; Wihlborg 1987).

**Completeness of reporting**

All of the studies reported the status of all people entered into the trials. One study reported only one of 94 patients lost to follow up (Randall 1983). Byrne 1992 reported a 99.4% completeness of
follow up. All other studies reported that all patients were followed up (Earnshaw 1989; Hayek 1987; Rotter 1988; Wihlborg 1987). In one study, 140 patients out of the 2953 enrolled were withdrawn from the study for several reasons: failure to have two preoperative showers, not meeting inclusion criteria, transferring out of unit, or no identification number on patient protocol (Rotter 1988). Despite this, the study reports on all remaining patients (n = 2813), resulting in 95.2% completeness of reporting.

Two authors (Byrne 1992; Hayek 1987) recorded SSIs during hospitalisation and then followed patients for 6 weeks after hospital discharge, Rotter 1988 followed patients for 3 weeks, Randall 1983 for 7 days, Wihlborg monitored SSIs that occurred in hospital and among those returning for an outpatient visit and Earnshaw reviewed patients twice weekly until hospital discharge.

Of the six included studies, two (Byrne 1992; Rotter 1988) were assessed as having high methodological quality using the assessment criteria described above.

**RESULTS**

This review includes outcomes data from six trials with a total of 10,007 participants. Six comparisons were undertaken: chlorhexidine 4% versus placebo (Analysis: 01), (Byrne 1992; Hayek 1987; Rotter 1988) chlorhexidine 4% versus bar soap (Analysis: 02), (Earnshaw 1989; Hayek 1987; Randall 1983) chlorhexidine versus no bath or shower (Analysis: 03) (Randall 1983; Wihlborg 1987) whole body wash with chlorhexidine versus washing only that part of the body to be submitted to surgery (Analysis: 04) (Wihlborg 1987) more than one wash versus one wash (Analysis: 05) (Byrne 1992; Hayek 1987; Randall 1983; Rotter 1988), and one post hoc comparison, individual allocation versus cluster allocation (Analysis: 06) (Byrne 1992; Earnshaw 1989; Hayek 1987; Randall 1983; Rotter 1988; Wihlborg 1987). A random-effect meta-analysis was used when significant heterogeneity was present (i.e. where the I² value was greater than 50%).

**Chlorhexidine compared with placebo (Analysis 01)**

This comparison includes three trials (Byrne 1992; Hayek 1987; Rotter 1988) of 7691 participants and includes four outcomes (SSI, allergic reactions, mortality and cost).

**Surgical site infection (Analysis 01:01)**

Participants in each trial had more than one wash. Hayek 1987 and Rotter 1988 included patients having elective surgery whereas Byrne 1992 included patients undergoing “clean or potentially infected surgery”. It should be noted that in the Hayek 1987 trial the placebo was found to contain antimicrobial properties and was changed during the study. None of the individual trials found that washing with chlorhexidine had a statistically significant effect on SSI. All of the trials were included in the meta-analysis. When compared with placebo, bathing with chlorhexidine did not result in a statistically significant reduction in the SSI rate (chlorhexidine 9.2%, placebo 10.1%); the relative risk (RR) was 0.91 (95% confidence interval (CI) 0.80 to 1.04).

**Surgical site infection - high quality trials (Analysis 01:02)**

For this outcome we conducted a separate analysis of trials rated as high quality by the criteria described in the ‘Methods of the Review’ section (Byrne 1992; Rotter 1988) and obtained a similar result, the RR was 0.95 (95% CI 0.82 to 1.10). The event rate was 9.3% for the chlorhexidine group and for 9.7% for the placebo group.

**Allergic reaction (Analysis 01:03)**

One study (Byrne 1992) included allergic reaction as an outcome. There were 19 events reported, nine (0.5%) in the chlorhexidine group and 10 (0.6%) in the placebo group; no evidence of a statistically significant difference in allergy rate, the RR was 0.89 (95% CI 0.36 to 2.19).

**Mortality (any cause)**

One trial in this comparison reported mortality data (Byrne 1992). A total of 23 patients died in the study period but these were not reported in groups.

**Cost**

There was an estimate of cost in one study (Byrne 1992). The average total cost (based on drug costs, hotel costs, dressing costs and outpatients' costs) of patients washing with chlorhexidine was UK £936 compared with UK £897 when patients washed with a placebo. Standard deviations were not reported but, according to the authors, the difference was not statistically significant.

**Chlorhexidine compared with bar soap (Analysis 02)**

Three trials compared washing with chlorhexidine with washing with bar soap (Earnshaw 1989; Hayek 1987; Randall 1983). These included 1443 participants and reported on two outcomes (SSI and mortality). Due to small numbers in two of the trials (Earnshaw 1989; Randall 1983) and methodological inconsistencies in the Hayek 1987 trial estimates of effect are imprecise and need to be interpreted with caution. Heterogeneity was high for this comparison (P = 0.08, I² = 60%), so we used a random-effects model for the meta-analysis. There are two possible explanations for heterogeneity. First, different types of surgery were conducted in each trial; Earnshaw 1989 included patients undergoing vascular reconstruction, Hayek 1987 included patients booked for routine elective surgery and Randall 1983 included only vasectomy patients. Alternatively, a different definition of SSI was used by Randall 1983, who included patients with a wound which discharged pus or serous fluid, whereas Earnshaw 1989 and Hayek 1987 defined SSI as the discharge of pus.

**Surgical site infection (Analysis 02: 01)**

Two of the trials that compared washing with chlorhexidine with washing with soap (Earnshaw 1989; Randall 1983) found no difference between the treatments in postoperative SSI rate. However, the largest trial (Hayek 1987), reported significantly fewer SSIs when patients washed preoperatively with chlorhexidine com-
pared with patients who washed with soap; the RR was 0.70 (95% CI 0.51 to 0.96). When results of the three trials were combined there was no statistically significant difference; the RR was 1.02 (95% CI 0.57 to 1.84), an event rate of 10.9% for chlorhexidine and 13.6% for bar soap.

**Mortality (any cause)**

Two patients died in the Earnshaw 1989 trial but these were not reported by group.

**Chlorhexidine compared with no wash (Analysis 03)**

Two trials compared washing with chlorhexidine with not washing (Randall 1983; Wihlborg 1987). These included 1042 patients and reported on SSI only. There was significant statistical heterogeneity between the two trials (P value < 0.01), and clinical heterogeneity (outpatient surgery versus inpatient surgery; different types of included patients). Randall 1983 enrolled patients undergoing vasectomy, whereas Wihlborg 1987 included patients undergoing elective surgery of the biliary tract, inguinal hernia or breast cancer. In addition, Randall 1983 defined SSI as a wound which discharged pus or serous fluid, whereas Wihlborg 1987 defined SSI as the discharge of pus. Because of these differences, we did not pool the results of the two studies.

**Surgical site infection**

Randall 1983 found no difference in the postoperative SSI rate between patients who washed with chlorhexidine compared with patients who did not wash preoperatively (12 of the 32 (37.5%) patients in the chlorhexidine group developed an infection compared with 9 of 32 (28.1%) in the no wash group. In the other larger trial, Wihlborg 1987 found that chlorhexidine wash when compared with no wash resulted in a statistically significant reduction in the number of patients with a SSI; (9 of the 541 (1.7%) patients in the chlorhexidine group developed an infection compared with 20 of 437 (4.6%) in the no wash group (RR 0.36; 95% CI 0.17 to 0.79). Although patients in the no-wash groups were given no instructions to shower or bathe pre-operatively, it is unclear whether any did so.

**Chlorhexidine total body compared with partial wash (Analysis 04)**

One trial compared washing the whole body with chlorhexidine with a partial localised wash with chlorhexidine soap (Wihlborg 1987). This trial included 1093 participants and assessed one outcome; SSI.

**Surgical site infection (Analysis 04: 01)**

Data from one trial making this comparison (Wihlborg 1987) showed a statistically significant reduction in SSIs when whole body washing (1.7%) was compared with partial localised washing (4.1%); the RR was 0.40 (95% CI 0.19 to 0.85).

**Discussion**

Widespread use of preoperative antiseptic washing agents to pre-vent SSI continues. This review summarises trial data from over 10,000 patients, that compared washing with chlorhexidine with either a placebo solution, or a bar soap, or no preoperative washing at all. There was no clear evidence that washing with chlorhexidine reduced the incidence of SSI. The results of the review are strengthened by the heterogeneous nature of the participants; the trials included men, women and children undergoing a range of surgeries that were either clean or potentially infected, and undertaken in both inpatient and outpatient settings. These studies were published over a nine-year period between 1983 and 1992. There have been no recent studies published in this area. The product used in the trials (chlorhexidine 0.4%) remains unchanged and the quality of the two largest trials (that included over 6,000 participants) was high, concealing the randomisation process and blinding the interventions. Both of these trials also included community follow up.

One of the limitations of the review was the quality of some of the studies. Community follow-up was attempted in only three studies, none of the authors provided justification for their sample sizes and in both studies where a cluster design was used, analysis was conducted as if participants had been allocated individually. However, results from the high quality trials and from trials where participants were allocated individually, resulted in no statistically significant reduction in SSIs when chlorhexidine was used for pre-operative washing.

Only one of the trials provided data for other important outcomes. Byrne 1992 assessed complications or undesirable effects attributable to the use of an antiseptic. In this trial patients assigned to chlorhexidine use were no more likely to suffer an adverse reaction than those assigned to the placebo group. There were no comparisons with bar soap for this outcome. Byrne 1992 also assessed the cost of washing with chlorhexidine compared with placebo and found a non-significant cost reduction in the placebo group. Costs included length of hospital stay, so, even though the SSI rate was 1.1% higher in the placebo group, using a placebo still resulted in an overall cost benefit.

**Authors’ Conclusions**

**Implications for practice**

This review provides no clear evidence of a benefit associated with pre-operative showering or bathing with chlorhexidine compared with other wash products in reducing SSI rates. Efforts to reduce the incidence of nosocomial SSI should focus on interventions where effect has been demonstrated.

**Implications for research**

Any future trials designed to assess the effectiveness of chlorhexidine as a pre-operative body wash to prevent surgical site infection should:
Follow the CONSORT statement when designing and reporting the trial

Conduct a priori sample size calculations based on results of this review

Document pre-operative and intra-operative antibiotic use

Include a follow-period of at least 4 weeks

Include clinically relevant secondary endpoints (mortality, adverse effects, cost effectiveness, length of hospital stay)

FEEDBACK

Molnlycke feedback

Summary
A detailed letter was received from Mölnlycke Health Care along with comments from a statistical consultant. Responses to the feedback are detailed below.

Author’s reply
Response of J Webster and S Osborne to Comments received from Mölnlycke Healthcare

Firstly we would like to thank Mölnlycke Healthcare and Mr P N Lee for submitting comments and for helping to improve the contents of the Cochrane Library.

We have carefully considered the Comments made and respond to each individually below; we also consulted with Gill Worthy, recently appointed Statistical Editor of the Cochrane Wounds Group in compiling our response.

In summary whilst on reflection we feel that several of the points raised have merit and we have amended the review accordingly (by amending the conclusion to “no clear evidence of benefit”, by removing the subgroup analyses, and by not synthesising the data from the “no wash” comparison) we do not agree with many of the points raised, including several of those raised in the letter from Möllynlycke.


“the conclusion [of the review] is inaccurate”
We agree that the conclusion that there is “evidence of no benefit for preoperative showering or bathing with chlorhexidine…” is badly worded and in the next update of the Library this has been changed to read “no clear evidence of benefit for preoperative showering or bathing with chlorhexidine over other wash products”.

“In our view, the erroneous conclusion was reached by reliance on data of poor quality and diversity, and statistical analysis errors and omissions. For example the study states that antibiotic prophylaxis routinely was used in Earnshaw study (n=66), but the antibiotic prophylaxis was not administered using a standardized protocol” The quality of the many of the studies reviewed was poor and this was clearly acknowledged in the review (e.g. Discussion, paragraph 2) and is typical of research quality in many areas of medical and health care. Unfortunately reviewers can only deal with the data that exists and this is frequently different from the data one would wish to have. Nevertheless it is highly worthwhile to review even poor quality data as it allows identification of unanswered research questions.

As you have not referenced specifics, we are not sure what you mean by statistical analysis errors and omissions. This statement does not reflect the critique of the review made by your statistician, Mr Lee who did not highlight major statistical analysis errors and omissions. We do not understand the point being made about the Earnshaw study nor how you think this affected the results and conclusions. All participants in the Earnshaw study received antibiotic prophylaxis irrespective of which arm they were allocated to and therefore no bias is introduced as both arms received the same co-interventions. They did in fact receive standardized prophylaxis, viz. 3 perioperative doses of intravenous amoxicillin/clavulanic acid (or erythromycin in the case of sensitivity to the former). Since many patients do receive antibiotic prophylaxis in real life, inclusion of this study, if anything, increases external validity.

“in the Byrne (n=3733) , Rotter (n=2813), and Wihlborg (n=1530) studies the prophylaxis rate was only 1-15%. Hayek (n=1989) and Randall (n=94) studies did not mention antibiotic usage. One cannot pool these study patients when it is known that antibiotic prophylaxis can have an effect on surgical site infections (SSI)”.

The decision of which studies are pooled together is a matter of judgment, not fact. Byrne, Hayek and Rotter were pooled together and the amount of statistical heterogeneity was low at only 4.6%. There was more heterogeneity evident when Earnshaw, Hayek and Randall were pooled (60%) and therefore a more conservative random effects model was applied which takes account of between study as well as within study variance. Pooling studies which may have different antibiotic usage rates is not “wrong” nor does it introduce bias, since both arms within trials were treated the same; the only impact may be to reduce precision.

 “…the omission of the SSI rate for the different types of surgeries at each institution makes it impossible to understand the significance of the data. A lower SSI rate requires a greater number of subjects to discern the differences between antiseptic and placebo. The placebo effect needs better explanation, because review of the clinical outcomes of SSI for the placebo controlled studies shows that the SSI rate for placebo ranges from 2.4 to 33.3%. The great variation in the SSI rate for placebo calls into question the sensitivity of the method in the hands of the authors and the ability of the method to detect differences between antiseptic and placebo”. 
Again, if we understand the point being made here correctly, it is the same one as in the previous paragraph, and our response is the same; whilst there may be variation in the baseline infection rates, pooling these studies does not introduce bias and does not therefore threaten internal validity. The rates quoted are not placebo rates since the 33.3% figure relates to the “shower with normal soap” arm of the Randall study. Furthermore we have reported a relative measure of outcome rather than absolute differences (which are more greatly affected by variations in baseline event rates).

“…many of the studies are underpowered to detect differences between antiseptic and placebo… Few of the studies provided information about calculation of sample size. For this reason it appears that they pooled data from multiple references to try and provide a sufficient sample size to draw inferences of effect”.

This paragraph succinctly explains the whole rationale of meta-analysis.

Response of J Webster and S Osborne to Comments received from Mr PN Lee (Independent Statistician) forwarded by Mölnlycke Healthcare

Much of Mr Lee’s 15 page document is merely a description of the review so we will confine our response to his substantive criticisms:

“It should be noted that in the Hayek 1987 study the placebo used was found, 5 months into the 2 year study, to have some antimicrobial activity and was subsequently changed… in the Cochrane review, both the discussion on chlorhexidine vs bar soap and the detail of the characteristics of the Hayek study wrongly state that the soap, and not the placebo, originally used… was changed”.

(p3)

Thank you for spotting this error. We have amended this and drawn attention to it, although it does not materially change anything and we cannot amend the analysis as we do not know how many participants were affected.

“…it certainly seems that many of the studies will be considerably underpowered to detect any plausible true level of risk reduction”.

(p5)

We agree and the small sample sizes and frequent lack of sample size calculations were discussed in the review.

“There is uncertainty as to how valid either estimate is, given the heterogeneity. The dubious nature of the random effects estimate…together with its wide CI, provides little evidence against chlorhexidine actually reducing risk of SSI” (p6)

We agree, there is a great deal of uncertainty around the individual study estimates and hence the pooled estimates however we are not claiming that chlorhexidine increases the risk of SSI. We believe that amending the review conclusions to “no clear evidence of benefit” from “evidence of no benefit” will deal with this issue.

“For the two studies where the comparison is with no wash both (pooled) estimates… show a non significant reduction in risk of SSI… the data are difficult to interpret, because there are two widely differing estimates… both with very wide CIs”. (p7)

We agree that there is great heterogeneity here and it is probably not sensible to pool these studies; we have amended the review and removed the pooling. This does not materially affect the overall conclusions however.

“It would seem not unreasonable to carry out an additional analysis using data for each study comparing the chlorhexidine whole body group with the combined results for each study with no chlorhexidine…” (p7)

We don’t see the rationale for this additional analysis; it was not pre-planned in the protocol (unlike all the analyses presented) and it would not alter the conclusions.

“I find the conclusions of the authors of the Cochrane review … to be surprising and misleading… even if they did mean “evidence of no benefit” it does not seem justified bearing in mind that i) two of the six studies showed a statistically significant advantage to chlorhexidine

ii) all the meta analyses (with the minor exception of the dubious random effects analysis for soap) provided estimates less than 1.00 i.e., an advantage to chlorhexidine, and

iii) the meta analyses based on the largest numbers of SSIs showed a near significant advantage to chlorhexidine… My own conclusion is that the data suggest a possible advantage to chlorhexidine but that more studies are needed.” (p8)

We agree that the conclusions are erroneously worded and have been amended to “no clear evidence of benefit for preoperative showering or bathing with chlorhexidine…”. We note that:

i) the two studies that showed a statistically significant advantage associated with chlorhexidine were not of high quality (by pre-specified quality criteria).

ii) none of the meta analyses showed a statistically significant advantage in favour of chlorhexidine.

iii) Mr Lee’s own analysis (which is post hoc unlike the pre-planned analyses presented in the Cochrane review) is the most favourable to chlorhexidine but still not significant.

Other issues:

“It is stated on page 5 that for four of the included trials (Byrne 1992, Earnshaw 1989, Randall 1983, Wihlborg 1987) the authors ‘responded to queries about study methods and/or requests for additional unpublished information.’ It is interesting to note that in various places in the review there is reference to information from some of these studies as unknown or unclear. Were the original authors not asked about this, or did they no longer remember or have records of the relevant details?’

The authors were unable to recall or obtain these details.

“The assessment of quality is in fact inconsistently described. In the section ‘Methodological quality assessment’ on p4 it is stated that trials were coded on six criteria… it is then stated that trials were defined as ‘high quality’ based on receiving an A rating.
for criteria 2 and 3, making one wonder why criteria 1, 4, 5 and 6 were coded at all... However, in the ‘Data synthesis’ section on p5 it was stated that the effect of trial quality was carried out based on excluding those trials most susceptible to bias based on three criteria; two (2 and 4) essentially as defined above and another not mentioned before… the fact that the authors have been inconsistent in their definitions is not crucial to the selection of which studies are considered to be of high quality.”

The other criteria were coded to facilitate full discussion of all aspects of quality. We have amended the inconsistency in the explanation of how trial quality was used in sensitivity analysis and agree that this does not affect the results or conclusions.

"On page 15, comparison 05 'More than one wash versus one wash' is stated to have an effect size of 0.92 (95% CI 0.80-1.04). This is totally misleading and the relative risk has nothing whatsoever to do with how risk of SSI depends on the number of washes! Similar problems relate to the comparison of individual versus cluster randomization.”

We agree and have removed these subgroup analyses, however this does not materially affect the overall results or conclusions.

Contributors

Joan Webster and Sonja Osborne, authors of the review.
Gill Worthy, Statistical Editor Cochrane Wounds Group.
Nicky Cullum, Coordinating Editor Cochrane Wounds Group.

References to studies included in this review

Byrne 1992 [published data only]


Earnshaw 1989 [published data only]

Hayek 1987 [published data only]


Randall 1983 [published and unpublished data]

Rotter 1988 [published data only]
References to studies excluded from this review

Ayliffe 1983

Bergman 1979

Brandberg 1980

Garabaldi 1988

Leigh 1983

Newsom 1988

Wells 1983

Additional references

Beaudouin 2004

Brady 1990

Byrne 1991

Cruse 1980

Higgins 2002

Kaiser 1988

Kirkland 1999

Krautheim 2004

Mangram 1999

Mollison 2000

Paulson 1993

Rubinstein 1999

Smyth 2000

Thomas 2000

Wilcox 2003

References to other published versions of this review

Webster 2006
Webster J, Osborne S. Preoperative bathing or showering with skin antiseptics to prevent surgical site infection. *Cochrane Database*
### Characteristics of included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Byrne 1992</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methods</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>RCT</td>
</tr>
<tr>
<td></td>
<td>Generation of random number sequence: adequate</td>
</tr>
<tr>
<td></td>
<td>Blinding of intervention: double</td>
</tr>
<tr>
<td></td>
<td>Blinding of outcome: yes</td>
</tr>
<tr>
<td></td>
<td>Completeness of reporting: yes</td>
</tr>
<tr>
<td></td>
<td>Power calculation: yes</td>
</tr>
<tr>
<td></td>
<td>Follow up period: 6 weeks after discharge</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>3733 patients undergoing elective or potentially contaminated surgery</td>
</tr>
<tr>
<td></td>
<td>Exclusion: patients undergoing day surgery, emergency surgery, re-operation or contaminated surgery and those unable to comply with the washing procedure, or with a known allergy to chlorhexidine or having more than the standard prophylactic antibiotic regimen</td>
</tr>
<tr>
<td></td>
<td>Baseline comparability: age, sex, type of surgery, ASEPSIS score</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>All patients showered 3 times (on admission, the night before surgery and the morning of surgery) using 50 mls of either</td>
</tr>
<tr>
<td></td>
<td>(1) 4% chlorhexidine or</td>
</tr>
<tr>
<td></td>
<td>(2) a placebo.</td>
</tr>
<tr>
<td></td>
<td>Written instructions were provided to all participants.</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Primary outcome:</td>
</tr>
<tr>
<td></td>
<td>Wound infection was defined as discharge of pus from a wound for inpatients or outpatients; or an ASEPSIS score greater than 10.</td>
</tr>
<tr>
<td></td>
<td>(1) 256/1754 (14.6%)</td>
</tr>
<tr>
<td></td>
<td>(2) 272/1735 (15.7%)</td>
</tr>
<tr>
<td></td>
<td>Secondary outcomes:</td>
</tr>
<tr>
<td></td>
<td>Death</td>
</tr>
<tr>
<td></td>
<td>Allergic reactions</td>
</tr>
<tr>
<td></td>
<td>Cost</td>
</tr>
<tr>
<td><strong>Notes</strong></td>
<td>Data were extracted from 3 papers reporting results from the one study (see Lynch 1992 &amp; Byrne 1994).</td>
</tr>
<tr>
<td></td>
<td>There were minor discrepancies in numbers reported between the 3 studies. The version reported is the definitive study (personal correspondence with author). The abstract stated there were 1753 patients in the placebo group but this should have been 1735</td>
</tr>
<tr>
<td><strong>Allocation concealment</strong></td>
<td>A – Adequate</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Earnshaw 1989</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methods</strong></td>
<td>RCT</td>
</tr>
<tr>
<td></td>
<td>Generation of random allocation sequence: unclear</td>
</tr>
<tr>
<td></td>
<td>Blinding of intervention: none</td>
</tr>
</tbody>
</table>
Characteristics of included studies (Continued)

Blinding of outcome: yes
Completeness of reporting: yes
Power calculation: no
Follow up period: Until hospital discharge

Participants
66 patients undergoing vascular reconstruction surgery
Exclusion: none reported
Baseline comparability: Stated that groups were similar, no data

Interventions
All patients had 2 baths.
(1) painted entire body with undiluted 4% chlorhexidine followed by rinsing in the bath. Precise instructions given
(2) Non-medicated soap used. No specific instructions provided.

Outcomes
Primary outcome:
Wound infection was defined as discharge of pus from a wound; one patient with severe cellulitis was also included.
(1) 8/31 26%
(2) 4/35 11.4%
Secondary outcome:
Death

Notes
Different washing information provided to participants in each group.

Allocation concealment
B – Unclear

Study
Hayek 1987

Methods
Cluster RCT
Generation of random allocation sequence: unclear
Blinding of intervention: none
Blinding of outcome: yes
Completeness of reporting: yes
Power calculation: no
Follow up period: until hospital discharge

Participants
2015 patients undergoing routine surgery
Exclusion: those receiving antibiotics or with an existing infection
Baseline comparability: age, sex, preoperative skin preparation, wound classification, proportion who washed their hair

Interventions
All patients had either a shower or bath on the day before and morning of their operation.
(1) Chlorhexidine 4%. Instruction card for washing provided
(2) Placebo. Instruction card for washing provided (Five months into the study, the placebo was found to have antimicrobial properties and was changed).
(3) Bar soap. No washing instructions provided.

Outcomes
Primary outcome:
Wound infection was defined as discharge of pus from a wound or erythema or swelling considered greater than expected.
(1) 62/689 (9.0%)
(2) 83/700 (11.7%)
(3) 80/626 (12.8%)

Notes
Data were extracted from 2 papers reporting results from the one study (Hayek 1988)

Allocation concealment
B – Unclear

Study
Randall 1983

Methods
RCT
Characteristics of included studies (Continued)

Generation of random allocation sequence: adequate
Blinding of intervention: none
Blinding of outcome: cannot tell
Completeness of reporting: yes
Power calculation: no
Follow up period: 1 week after discharge

Participants
94 patients undergoing vasectomy
Exclusion: none stated
Baseline comparability: none stated

Interventions
1) One preoperative shower with Chlorhexidine 4%
2) One shower with normal soap
3) No shower

Outcomes
Primary outcome:
Wound infection was defined as discharging either purulent or serous fluid.
1) 12/32 (37.5%)
2) 10/30 (33.3%)
3) 9/32 (28.1%)

Notes
Allocation concealment A – Adequate

Study  Rotter 1988

Methods
Cluster RCT
Generation of random number sequence: adequate
Blinding of intervention: double
Blinding of outcome: yes
Completeness of reporting: yes
Power calculation: no
Follow up period: 3 weeks after discharge

Participants
2953 patients undergoing elective clean surgery
Exclusion: patients with fever > or = to 37.5 on the day of or day before surgery, infection remote from operation site, antibiotics given within 7 days prior to surgery for infection, incarcerated inguinal hernia, radical mastectomy
Baseline comparability: age, sex, type of surgery, antibiotic prophylaxis, hair washed, hair removal method, wound drainage

Interventions
All patients had two showers. One on the day before and one on the day of surgery
1) Using 50 ml of Chlorhexidine 4% for each shower
2) Placebo
Special application instructions were provided to all participants.

Outcomes
Primary outcome:
Wound infection was defined as inflammation of the surgical wound with discharge of pus, spontaneous and/or after surgical intervention that occurs during hospitalisation or during routine follow-up
1) 37/1413 (2.6%)
2) 33/1400 (2.4%)

Notes
Allocation concealment B – Unclear

Study  Wihlborg 1987

Methods
RCT
Generation of random number sequence: adequate
Blinding of intervention: none
Blinding of outcome: no
Completeness of reporting: yes
Power calculation: no
Follow up period: until hospital discharge

Participants
1530 patients undergoing elective surgery of the biliary tract, inguinal hernia and breast cancer
Exclusion: none stated
Baseline comparability: age, duration of surgery > 2 hours, steroids, diabetes, malignancy (other than breast cancer), type of surgery

Interventions
1) Patients washed their entire body with chlorhexidine on the day before surgery using two consecutive application followed by rinsing under the shower
2) Washed only that part of the body to be submitted to surgery with chlorhexidine soap.
3) No chlorhexidine wash

Outcomes
Primary outcome:
Wound infection was defined as a definite collection of pus emptying itself spontaneously or after incision
1) 9/541 (1.7%)
2) 23/552 (4.2%)
3) 20/437 (4.6)

Notes
This study was conducted over a 7 year period between 1978 through 1984.
It was unclear from the text whether patients allocated to the 'no chlorhexidine wash' group had any preoperative shower. Three patients died and were not included in the analysis.
Strength of wash solution not stated.

Allocation concealment A – Adequate

Characteristics of excluded studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ayliffe 1983</td>
<td>Not a randomised controlled trial</td>
</tr>
<tr>
<td>Bergman 1979</td>
<td>No data on wound infection.</td>
</tr>
<tr>
<td></td>
<td>Not a randomised controlled trial</td>
</tr>
<tr>
<td>Brandberg 1980</td>
<td>Not a randomised controlled trial</td>
</tr>
<tr>
<td></td>
<td>Local wash versus full body wash with chlorhexidine</td>
</tr>
<tr>
<td>Garabaldi 1988</td>
<td>No none antiseptic group</td>
</tr>
<tr>
<td></td>
<td>Did not report infection rates by group</td>
</tr>
<tr>
<td>Leigh 1983</td>
<td>Not a randomised controlled trial</td>
</tr>
<tr>
<td>Newsom 1988</td>
<td>Not a randomised controlled trial. Patients were allocated by month.</td>
</tr>
<tr>
<td>Wells 1983</td>
<td>Not a randomised controlled trial</td>
</tr>
<tr>
<td></td>
<td>Did not report infection rates by group</td>
</tr>
</tbody>
</table>
### ANALYSES

**Comparison 01. Chlorhexidine 4% versus placebo**

<table>
<thead>
<tr>
<th>Outcome title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Surgical site infection</td>
<td>3</td>
<td>7691</td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>0.91 [0.80, 1.04]</td>
</tr>
<tr>
<td>02 Surgical site infection (high quality studies)</td>
<td>2</td>
<td>6302</td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>0.95 [0.82, 1.10]</td>
</tr>
<tr>
<td>03 Allergic reaction</td>
<td>1</td>
<td>3489</td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>0.89 [0.36, 2.19]</td>
</tr>
</tbody>
</table>

**Comparison 02. Chlorhexidine 4% versus bar soap**

<table>
<thead>
<tr>
<th>Outcome title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Surgical site infection</td>
<td>3</td>
<td>1443</td>
<td>Relative Risk (Random) 95% CI</td>
<td>1.02 [0.57, 1.84]</td>
</tr>
</tbody>
</table>

**Comparison 03. Chlorhexidine 4% versus no wash**

<table>
<thead>
<tr>
<th>Outcome title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Surgical site infection</td>
<td></td>
<td></td>
<td>Relative Risk (Random) 95% CI</td>
<td>Totals not selected</td>
</tr>
</tbody>
</table>

**Comparison 04. Chlorhexidine full wash versus partial wash**

<table>
<thead>
<tr>
<th>Outcome title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Surgical site infection</td>
<td>1</td>
<td>1093</td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>0.40 [0.19, 0.85]</td>
</tr>
</tbody>
</table>

### INDEX TERMS

**Medical Subject Headings (MeSH)**

- Anti-Infective Agents, Local [*administration & dosage*]; Baths [*methods*]; Chlorhexidine [*administration & dosage; *analogs & derivatives*]; Disinfection [*methods*]; Preoperative Care [*methods*]; Randomized Controlled Trials; Soaps [*administration & dosage*]; Surgical Wound Infection [*prevention & control*]

**MeSH check words**

Female; Humans; Male

### COVER SHEET

**Title**

Preoperative bathing or showering with skin antiseptics to prevent surgical site infection

**Authors**

Webster J, Osborne S

**Contribution of author(s)**

JW conceived, designed, coordinated the review and conducted the initial literature search. The protocol was jointly written by JW and SO. JW and SO separately reviewed the abstracts and selected papers for review. JW and SO separately reviewed and scored the trials. Both authors contributed to the final version of the review.

**Issue protocol first published**

2004/4

**Review first published**

2006/2

**Date of most recent amendment**

16 February 2007
Date of most recent SUBSTANTIVE amendment: 06 February 2007

What's New: Information not supplied by author

Date new studies sought but none found: Information not supplied by author

Date new studies found but not yet included/excluded: Information not supplied by author

Date new studies found and included/excluded: 09 December 2005

Date authors' conclusions section amended: 06 February 2007

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Cochrane Library number: CD004985

Editorial group: Cochrane Wounds Group

Editorial group code: HM-WOUNDS
### Analysis 01.01. Comparison 01 Chlorhexidine 4% versus placebo, Outcome 01 Surgical site infection

**Review:** Preoperative bathing or showering with skin antiseptics to prevent surgical site infection

**Comparison:** 01 Chlorhexidine 4% versus placebo

**Outcome:** 01 Surgical site infection

<table>
<thead>
<tr>
<th>Study</th>
<th>Chlorhexidine n/N</th>
<th>Placebo n/N</th>
<th>Relative Risk (Fixed) 95% CI</th>
<th>Weight (%)</th>
<th>Relative Risk (Fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Byrne 1992</td>
<td>256/1754</td>
<td>272/1735</td>
<td>0.93 [0.80, 1.09]</td>
<td>70.3</td>
<td></td>
</tr>
<tr>
<td>Hayek 1987</td>
<td>62/689</td>
<td>83/700</td>
<td>0.76 [0.56, 1.04]</td>
<td>21.2</td>
<td></td>
</tr>
<tr>
<td>Rotter 1988</td>
<td>37/1413</td>
<td>33/1400</td>
<td>1.11 [0.70, 1.77]</td>
<td>8.5</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>3856</td>
<td>3835</td>
<td>0.91 [0.80, 1.04]</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 355 (Chlorhexidine), 388 (Placebo)

Test for heterogeneity chi-square=2.10 df=2 p=0.35 I² =4.6%

Test for overall effect z=1.38 p=0.2

### Analysis 01.02. Comparison 01 Chlorhexidine 4% versus placebo, Outcome 02 Surgical site infection (high quality studies)

**Review:** Preoperative bathing or showering with skin antiseptics to prevent surgical site infection

**Comparison:** 01 Chlorhexidine 4% versus placebo

**Outcome:** 02 Surgical site infection (high quality studies)

<table>
<thead>
<tr>
<th>Study</th>
<th>Chlorhexidine 4% n/N</th>
<th>Placebo n/N</th>
<th>Relative Risk (Fixed) 95% CI</th>
<th>Weight (%)</th>
<th>Relative Risk (Fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Byrne 1992</td>
<td>256/1754</td>
<td>272/1735</td>
<td>0.93 [0.80, 1.09]</td>
<td>89.2</td>
<td></td>
</tr>
<tr>
<td>Rotter 1988</td>
<td>37/1413</td>
<td>33/1400</td>
<td>1.11 [0.70, 1.77]</td>
<td>10.8</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>3167</td>
<td>3135</td>
<td>0.95 [0.82, 1.10]</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 293 (Chlorhexidine 4%), 305 (Placebo)

Test for heterogeneity chi-square=0.50 df=1 p=0.48 I² =0.0%

Test for overall effect z=0.67 p=0.5
### Analysis 01.03. Comparison 01 Chlorhexidine 4% versus placebo, Outcome 03 Allergic reaction

**Review:** Preoperative bathing or showering with skin antiseptics to prevent surgical site infection  
**Comparison:** 01 Chlorhexidine 4% versus placebo  
**Outcome:** 03 Allergic reaction

<table>
<thead>
<tr>
<th>Study</th>
<th>Chlorhexidine 4% n/N</th>
<th>placebo n/N</th>
<th>Relative Risk (Fixed) 95% CI</th>
<th>Weight (%)</th>
<th>Relative Risk (Fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Byrne 1992</td>
<td>9/1754</td>
<td>10/1735</td>
<td>100.0 0.89 [ 0.36, 2.19 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1754</td>
<td>1735</td>
<td>100.0 0.89 [ 0.36, 2.19 ]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 9 (Chlorhexidine 4%), 10 (placebo)  
Test for heterogeneity: not applicable  
Test for overall effect z=0.25  p=0.8

### Analysis 02.01. Comparison 02 Chlorhexidine 4% versus bar soap, Outcome 01 Surgical site infection

**Review:** Preoperative bathing or showering with skin antiseptics to prevent surgical site infection  
**Comparison:** 02 Chlorhexidine 4% versus bar soap  
**Outcome:** 01 Surgical site infection

<table>
<thead>
<tr>
<th>Study</th>
<th>Chlorhexidine 4% n/N</th>
<th>Bar soap n/N 95% CI</th>
<th>Relative Risk (Random) 95% CI</th>
<th>Weight (%)</th>
<th>Relative Risk (Random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Earnshaw 1989</td>
<td>8/31</td>
<td>4/35</td>
<td>19.0 2.26 [ 0.75, 6.77 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hayek 1987</td>
<td>62/689</td>
<td>80/626</td>
<td>48.6 0.70 [ 0.51, 0.96 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Randall 1983</td>
<td>12/32</td>
<td>10/30</td>
<td>32.4 1.13 [ 0.57, 2.21 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>752</td>
<td>691</td>
<td>100.0 1.02 [ 0.57, 1.84 ]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 82 (Chlorhexidine 4%), 94 (Bar soap)  
Test for heterogeneity chi-square=5.02 df=2  p=0.08 I² =60.2%  
Test for overall effect z=0.07  p=0.9
### Analysis 03.01. Comparison 03 Chlorhexidine 4% versus no wash, Outcome 01 Surgical site infection

Review: Preoperative bathing or showering with skin antiseptics to prevent surgical site infection

Comparison: 03 Chlorhexidine 4% versus no wash

Outcome: 01 Surgical site infection

<table>
<thead>
<tr>
<th>Study</th>
<th>Chlorhexidine 4%</th>
<th>No wash</th>
<th>Relative Risk (Random)</th>
<th>Relative Risk (Random)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>95% CI</td>
</tr>
<tr>
<td>Randall 1983</td>
<td>12/32</td>
<td>9/32</td>
<td>1.33 [0.65, 2.72]</td>
<td></td>
</tr>
<tr>
<td>Wihlborg 1987</td>
<td>9/541</td>
<td>20/437</td>
<td>0.36 [0.17, 0.79]</td>
<td></td>
</tr>
</tbody>
</table>

### Analysis 04.01. Comparison 04 Chlorhexidine full wash versus partial wash, Outcome 01 Surgical site infection

Review: Preoperative bathing or showering with skin antiseptics to prevent surgical site infection

Comparison: 04 Chlorhexidine full wash versus partial wash

Outcome: 01 Surgical site infection

<table>
<thead>
<tr>
<th>Study</th>
<th>CHX full wash</th>
<th>CHX partial wash</th>
<th>Relative Risk (Fixed)</th>
<th>Weight (%)</th>
<th>Relative Risk (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td></td>
<td>95% CI</td>
</tr>
<tr>
<td>Wihlborg 1987</td>
<td>9/541</td>
<td>23/552</td>
<td>0.40 [0.19, 0.85]</td>
<td>100.0</td>
<td>0.40 [0.19, 0.85]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>541</td>
<td>552</td>
<td>100.0</td>
<td></td>
<td>0.40 [0.19, 0.85]</td>
</tr>
</tbody>
</table>

Total events: 9 (CHX full wash), 23 (CHX partial wash)
Test for heterogeneity: not applicable
Test for overall effect $z=2.36$ $p=0.02$