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Chlorhexidine wash prior to clean surgical procedures

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VÄSTRA GÖTALANDSREGIONEN
SAHLGRENSKA UNIVERSITETSSJUKHUSET

Chlorhexidine wash prior to clean surgical procedures [Preoperativ klorhexidintvätt]

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Table of contents

1. Abstract

Background
Surgical wound infection (SSI) following clean surgery occurs in from 1-3% after major joint implant surgery up to 20% after, e.g., vascular surgery. Implant infection is a devastating complication with significant morbidity and mortality. Between 50 and 95 % of SSIs occur after discharge from the hospital. Risk reducing strategies target environmental as well as patient related factors. Chlorhexidine gluconate (CHX) has a broad spectrum activity and is known to reduce the risk for colonization of micro-organisms as well as nosocomial infections in high risk settings. The routine to recommend patients two or three double showers with CHX soap before clean surgery is well established but recently questioned.

Objective
To assess whether preoperative chlorhexidine whole body wash is better than no chlorhexidine wash prior to "clean surgery" through intact skin regarding mortality, implant infection, septicaemia, surgical site infection, reintervention and length of hospital stay.

Methods
A systematic literature search was conducted in PubMed, Embase, the Cochrane Library, Cinahl and a number of HTA-databases. At least two persons independently screened titles, abstracts and full-text articles for inclusion and extracted data. The certainty of evidence was defined according to GRADE.

Main results
The literature search identified seven randomised controlled trials (RCT), three cohort studies and three systematic reviews (SR) but the SRs included not only clean surgery patients as defined in the current HTA. Chlorhexidine was compared with placebo, soap, no wash, local wash or no instructions. The intervention varied between the studies from one double to three double preoperative washes.

Mortality and septicaemia were not reported by group in any study.

Implant infection
Chlorhexidine versus "no instruction" was studied in two cohort studies. In one study (n=4,042) on arthroplasties, no difference was seen between the study groups (implant infection rate 1.1% versus 0.9% in the CHX versus the "no instruction" group). In the second study (n=2,458) there was a lower implant infection rate in the CHX versus "no instruction" group (0.5% versus 1.7%, p=0.043 and 0.6% versus 2.2%, p=0,021) for hip and knee surgery patients respectively.
Conclusion: It is uncertain whether the implant infection rate is different after preoperative CHX wash compared with no instructions. Very low certainty of evidence (GRADE ⊕○○○).

Surgical site infection (five different comparisons)
- Chlorhexidine versus placebo was studied in four RCTs with n.s. intergroup differences. Meta-analysis showed an effect estimate of RR 0.85 (95% CI: 0.68 to 1.07, p=0.18)
Conclusion: Preoperative CHX wash as compared with preoperative placebo wash may result in little or no difference in surgical site infection rate in mixed clean surgery patient populations. Low certainty of evidence (GRADE ⊕⊕○○).

- Chlorhexidine versus soap was studied in three RCTs and one cohort study with n.s. intergroup differences. The effect estimate was RR 1.04 (CI95%: 0.58 to 1.86, p=0.91).
Conclusion: It is uncertain whether the surgical site infection rate is different after preoperative CHX wash compared with preoperative soap wash.
Very low certainty of evidence (GRADE ⊕◯◯◯).

- Chlorhexidine versus no wash was studied in two RCTs: one showed a difference in SSI rates, 1.7% and 4.6% (p< 0.01) in the CHX versus the no wash group respectively. The other RCT showed no difference (37.5% vs. 28.1% in the CHX versus no wash group, n.s.).
The effect estimate (meta-analysis) was RR 0.70 (CI95%: 0.19 to 2.58, p=0.59).
Conclusion: It is uncertain whether the surgical site infection rate is different after preoperative CHX wash compared with no preoperative wash. Very low certainty of evidence (GRADE ⊕◯◯◯).

- Chlorhexidine versus local wash was studied in one RCT with 1.7% versus 4.2% (p<0.05) SSI rates in the CHX and control group respectively.
Conclusion: It is uncertain whether the surgical site infection rate is different after preoperative CHX wash compared with preoperative local wash.
Very low certainty of evidence (GRADE ⊕◯◯◯).

- Chlorhexidine versus no instruction was studied in one RCT and two cohort studies. One cohort study is described under implant infection. The RCT and the second cohort study showed n.s. intergroup differences: 2% for CHX and 0% and 2% in the control group, respectively.
Conclusion: It is uncertain whether the surgical site infection rate is different after preoperative CHX wash compared with no instructions. Very low certainty of evidence (GRADE ⊕◯◯◯).

Reintervention and number of days in hospital were not reported

Complications were rare and mild (mainly mild skin irritation)

Concluding remarks
The question at issue was studied in seven RCTs and three cohort studies. Drawbacks of the included studies were that the time of follow-up was often short and only two cohort studies investigated implant infections, a more critical outcome than SSI in general. All included studies had some or major limitations regarding blinding, definition of outcomes, length of follow up and heterogeneity of patient populations. The current systematic review shows that preoperative CHX compared with placebo showering/bathing may be associated with little or no difference in SSI in patients undergoing "clean" surgery. For all other comparisons the certainty of evidence was very low. The confidence interval of the pooled effect estimate includes a negative effect and there is a need for further large studies.

2. Svensk sammanfattning – Swedish summary

Bakgrund
Sårinfektion (SSI) efter ren kirurgi förekommer i från 1-3% efter ortopedisk proteskirurgi upp till 20% efter tex kärlkirurgi. Implantatinfektion är en mycket allvarlig komplikation med avsevärd morbiditet och mortalitet. Mellan 50 och 95% av SSI diagnosticeras efter utskrivning från sjukhuset. Preoperativa riskreducerande strategier inkluderar optimering av den kirurgiska miljön samt av patienterna. Klorhexidin glukonat (CHX) har antibakteriell effekt med brett spektrum och har rapporterats reducera risken för koloniseringen av mikroorganismer och vårdrelaterad infektion i samband med operationer med hög infektionsrisk. Det är praxis att rekommendera patienter två eller tre dubbelduschar med CHX tvål innan ren kirurgi, men denna rutin har nyligen ifrågasatts.

Syfte
Att utvärdera huruvida preoperativ helkroppsdusch med klorhexidin är bättre än ingen klorhexidindusch vid "ren kirurgi" genom intakt hud, avseende mortalitet, implantatinfektion, blodförgiftning, sårinfektion, behov av reintervention och vårdtid.

Metod
Systematisk litteratursökning utfördes i PubMed, Embase, och the Cochrane Library, Cinahl samt ett antal HTA-databaser. Minst två av författarna granskade oberoende av varandra artiklarna på titel- och abstrakt nivå, samt fulltextartiklar, avseende inklusion och gjorde data extraktion. Det vetenskapliga underlaget bedömdes enligt GRADE.

Resultat
Litteratursökningen identifierade sju RCT, tre kohortstudier och tre systematiska översikter (SR). Samtliga SR hade inkluderat även icke ren kirurgi, till skillnad från föreliggande HTA där endast ren kirurgi inkluderades. Klorhexidindusch jämfördes mot placebo, tvål, ingen preoperativ tvätt, lokal preoperativ tvätt, eller inga preoperativa tvättinstruktioner. Interventionen varierade mellan studierna från en dubbel till tre dubbla preoperativa klorhexidinduschar.

Mortalitet och blodförgiftning rapporterades inte per grupp i någon av de inkluderade studierna

Implantatinfektion
Implantatinfektion rapporterades i två kohortstudier. I en studie (n=4 042) avseende ledprotesoperationer, sågs ingen skillnad mellan grupperna (1,1% respektive 0,9% implantatinfektioner i CHX gruppen jämfört med "ingen instruktion"-gruppen). I den andra studien (n=2 458) sågs färre implantatinfektioner i CHX gruppen jämfört med "ingen instruktion"-gruppen (0,5% respektive 1,7%, p=0,043 vid höftproteskirurgi, samt 0,6% respektive 2,2%, p=0,021) vid knäproteskirurgi.
Slutsats: Det är osäkert huruvida förekomsten av implantatinfektioner skiljer sig åt efter preoperativ CHX dusch jämfört med ingen preoperativ tvättinstruktion.
Otillräckligt vetenskapligt underlag (GRADE ⊕○○○).

Sårinfektion (SSI)
- Klorhexidin jämfört med placebo studerades i fyra RCT med icke signifikanta skillnader mellan grupperna i samtliga. Effektuppskattning i en metaanalys var RR 0,85 (95%CI: 0,68 till 1,07, p=0,18)
Slutsats: Preoperativ CHX-dusch jämfört med placebotvätt kan resultera i liten eller ingen skillnad i sårinfektioner vid ren kirurgi. Begränsat vetenskapligt underlag (GRADE ⊕⊕○○).
- Klorhexidin jämfört med tvål studerades i tre RCT och en kohortstudie utan signifikanta skillnader mellan grupperna. Effektuppskattningen (metaanalys) var RR 1,04 (CI 95%: 0,58 till 1,86, p=0,91).
Slutsats: Det är osäkert huruvida förekomsten av sårinfektioner skiljer sig åt efter preoperativ CHX-dusch jämfört med preoperativ tvätt med tvål. Otillräckligt vetenskapligt underlag (GRADE ⊕○○○).

- Klorhexidin jämfört med ingen preoperativ tvätt studerades i två RCT varav en visade färre sårinfektioner, 1,7% respektive 4,6% (p< 0,01), i CHX gruppen jämfört ingen tvätt gruppen. I den andra RCTn sågs ingen signifikant skillnad (37,5% i CHX jämfört 28,1% i ”ingen tvätt” gruppen, n.s.).
Effektuppskattningen (metaanalys) var RR 0,70 (CI 95%: 0,19 till 2,58, p=0,59).
Slutsats: Det är osäkert huruvida förekomst av sårinfektioner skiljer sig åt efter preoperativ CHX-dusch jämfört ingen preoperativ tvätt. Otillräckligt vetenskapligt underlag (GRADE ⊕◯◯◯).

- Klorhexidin jämfört med lokal tvätt studerades i en RCT med 1,7% sårinfektioner i CHX gruppen jämfört 4,2% (p<0,05) i gruppen med lokal tvätt.
Slutsats: Det är osäkert huruvida förekomst av sårinfektioner skiljer sig åt efter preoperativ CHX-dusch jämfört lokal preoperativ tvätt. Otillräckligt vetenskapligt underlag (GRADE ⊕◯◯◯).

- Klorhexidin jämfört med ingen preoperativ tvätt instruktion studerades i en RCT och två kohortstudier. En av kohortstudierna beskrivs ovan under rubriken implantat infektion. Ingen av studierna fann några signifikanta skillnader mellan grupperna avseende sårinfektioner: 2% i CHX gruppen jämfört 0% respektive 2% i kontrollgrupperna.
Slutsats: Det är osäkert huruvida förekomsten av sårinfektioner skiljer sig åt efter preoperative CHX-dusch jämfört ingen preoperativ tvätt instruktion. Otillräckligt vetenskapligt underlag (GRADE ⊕◯◯◯).

Behov av reintervention och vårdtid rapporterades inte i någon av studierna.

Komplikationer var sällsynt förekommande och bestod främst av lätt hudirritation.

Sammanfattande slutsats
Den fokuserade frågan studerades i sju RCT och tre kohortstudier. De inkluderade studierna hade ofta för korta uppföljningstider och endast två kohortstudier hade studerat implantatinfektioner, ett mer kritiskt utfall än sårinfektioner i allmänhet. Samtliga inkluderade RCT och kohortstudier hade brister avseende blindning, definitionen av studerade utfall, korta uppföljningstider samt heterogenitet avseende patientunderlaget. Sammanfattningsvis visar denna systematiska översikt att preoperativ dusch med klorhexidin kan resultera i liten eller ingen skillnad i sårinfektioner jämfört med preoperativ placebotvätt vid olika typer av ren kirurgi. För alla andra jämförelser var det vetenskapliga underlaget otillräckligt. Konfidensintervallen i metaanalyserna inkluderar negativa effekter och det finns ett behov av större studier.

The above summaries were written by HTA-centrum and approved by the Regional board for quality assurance of activity-based HTA. The Regional Health Technology Assessment Centre (HTA-centrum) Region Västra Götaland, Sweden has the task to make statements on HTA reports carried out in VGR. The English summary is a concise summary of similar outline as the summaries in the Cochrane systematic reviews. The Swedish summary addresses the question at issue, results and quality of evidence regarding efficacy and risks, and economical and ethical aspects of the particular health technology that has been assessed in the report, and is ended with a final statement/concluding remark from HTA-centrum.

Christina Bergh, Professor, MD
Head of HTA-centrum of Region Västra Götaland, Sweden, 2015-10-21

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3. Summary of Findings (SoF-table)

Chlorhexidine wash prior to clean surgical procedures

Outcome	Study design Number of studies	Effect estimate	Certainty of evidence GRADE[1]
		Absolute effect	
Mortality	RCT 2	0.6-3.1% in total Not reported per group	Not appraised
		Absolute effect	
Chlorhexidine wash versus no instruction (C5)			
Implant infection	Cohort 2	Hip: 0.5% vs 1.7% (p=0.043) Knee: 0.6% vs 2.2% (p=0.021) Arthroplasties: 1.1% vs 0.9% (n.s.)	⊕◯◯◯ Very low [1]
		Relative effect (95%CI)	
Chlorhexidine wash versus placebo (C1)			
Surgical site infection	RCT 4	RR: 0.85 (95%CI: 0.68 to 1.07) p=0.18	⊕⊕◯◯ Low [2]
Chlorhexidine wash versus soap (C2)			
Surgical site infection	RCT 3	RR: 1.04 (95%CI: 0.58 to 1.86) p=0.91	⊕◯◯◯ Very low [3]
Chlorhexidine wash versus no wash (C3)			
Surgical site infection	RCT 2	RR: 0.70 (CI95%: 0.19 to 2.58) p=0.59	⊕◯◯◯ Very low [4]
		Absolute effect	
Chlorhexidine wash versus local wash (C4)			
Surgical site infection	RCT 1	1.7% vs 4.2% (p<0.05)	⊕◯◯◯ Very low [5]
Chlorhexidine wash versus no instruction (C5)			
Surgical site infection	RCT 1 Cohort 2	2% vs 0% (n.s.) 2% vs 2% (n.s.) Hip: 0.5% vs 1.7% (p=0.043) Knee: 0.6% vs 2.2% (p=0.021)	⊕◯◯◯ Very low [6]

1: Study limitations (blinding, reporting of drop-outs, selection bias), Inconsistency (unclear reporting of confounders: baseline differences, socio economy, length of surgery), Precision (few events).
2: Study limitations (blinding, definitions of outcomes), Inconsistency, Indirectness, Imprecision across the studies (including unfavorable effects).
3: Study limitations (blinding, reporting of drop-outs, Inconsistency, Imprecision across the studies (including unfavorable effects).
4: Study limitations (randomization, blinding, selection bias, definition of outcomes), Indirectness.
5: Study limitations (blinding, selection bias), Indirectness.
6: Study limitations (blinding, reporting of drop-outs, selection bias), Inconsistency, Some indirectness, Imprecision (few events).

Certainty of evidence:

High	⊕⊕⊕⊕	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	⊕⊕⊕◯	We aremoderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	⊕⊕◯◯	Confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low	⊕◯◯◯	We have very little confidence in the effect estimate: The true effect is likely to be substantiallydifferent from the estimate of effect.

4. Abbreviations

CHX	Chlorhexidine gluconate
RCT	Randomised controlled trial
SSI	Surgical site infection

5. Background

Surgical site infections following clean surgery

Surgical site infection (SSI) is a preventable complication associated with increased postoperative length of hospital stay, costs, hospital re-admission rates, and the use of antimicrobial agents (Vogel *et al*., 2009). The adverse effects related to SSI vary depending on the category of surgery and type of SSI. Superficial incisional SSI is more common than deep organ/space SSI, and the cost and risks associated with SSI increase with the depth and extent of infection (Urban, 2006). De Lissovoy *et al*., (2009) examined cardiovascular, gynaecologic and orthopaedic surgery (with the exception of major joint surgery) with the aim to analyse the effect of SSI on length of hospital stay associated with SSI and cost. The greatest increase in length of hospital stay was observed for cardiovascular surgery, including 723,490 surgical procedures with an SSI rate at 1%, with a mean extension of 13.7 days. On average, any SSI extended the length of stay by 9.7 days and produced increased costs of USD 20,842 per hospital admission.

The Harvard Medical Practice Study II (Leape *et al*., 1991) found that surgical wound infections was the second-largest category of adverse events, after urinary tract infection, in hospitalised patients, and that hospital acquired Staphylococcal infections constituted a substantial risk for patients receiving surgical care.
The reported rates for SSI following clean surgery vary greatly from 1-3% after major joint implant procedures (Kurtz *et al*., 2012) to 2-9% following closed fracture surgery (Acklin *et al.*, 2011) and 1- 20% after vascular and cardiac surgery (Bandyk, 2008). Moreover, between 50-95 % of the SSIs occur after discharge from the hospital (Berg *et al*., 2001; Brown *et al*., 1987; Darle *et al*., 1997; Sands *et al*., 1996) and the true SSI rates are therefore most likely higher than often reported.

The most common causal infectious agents following clean and implant surgery are coagulase-negative staphylococci and *S. aureus*, followed by enterococci and, more rarely, streptococci and *Propionibacterium acnes* (Frei *et al*., 2011).

The route of transmission can be endogenous as well as exogenous. Whyte *et al*. (1982) concluded that the most consistent and important route of contamination in orthopaedic implant surgery is airborne. However, in patients with exceptionally high skin carriage of bacteria, gross wound contamination can occur. More recently, *S. aureus* carriage has been associated with postoperative and device related infections, with a reported 2 to 9-fold increased risk for infection (Perl, 2003).

Deep infection after implant surgery is a devastating complication associated with significant morbidity and mortality (Cayci *et al*., 2008; Salehi Omran *et al*., 2007), prolonged hospitalization, multiple re-operations, and long-term patient suffering (Swenne *et al*., 2007; Andersson *et al*., 2010). The need to find ways of minimizing the risk factors for infections is strong. Evidence based strategies include optimizing the surgical environment by the use of effective ventilation systems (Lidwell *et al*., 1983; Hansen *et al*., 2005), and surgical scrubs with low permeability (Tammelin *et al*., 2013). In addition, enhanced surgical techniques minimizing blood loss, thereby avoiding the need for (allogeneic) blood transfusions and eliminating postoperative hematoma, reduce the risks for SSI. Optimizing the patients by addressing risk factors associated with SSI (such as smoking, malnutrition, diabetes, infections and conditions that compromise the immunological defence systems) in combination with the timely distribution of antibiotic prophylaxis and to maintain perioperative normothermia can significantly improve postoperative outcomes (AlBuhairn *et al*., 2008; Lindstrom *et al*., 2008).

Chlorhexidine wash prior to surgery

The practice of skin preparation before surgery has been in use since Joseph Lister in 1867 scientifically tested, and reported, antiseptic methods for the reduction of wound infections (Lister, 1867).

Chlorhexidine gluconate (CHX) is widely used since the mid 1950's, and routinely for preoperative washes in Sweden since the 1980's. The antimicrobial effect on transient and resident skin microbes such as *S. aureus* is well documented. Chlorhexidine is safe for oral and topical use (Milstone *et al*., 2008). Severe adverse reactions are very rare, although there are reports on minor skin irritations (Milstone *et al*., 2008). Chlorhexidine gluconate has a broad spectrum activity that affects both gram positive and gram negative bacteria, yeast, facultative anaerobes and aerobes and some (lipid – enveloped) viruses like Human Immunodeficiency Virus (McDonnell and Russell, 1999). The effect is instant and cumulative with repeated applications. Moreover, CHX inhibits bacterial growth on the skin for several hours (Edmiston *et al*., 2007). The effect is dose dependent. In low concentrations the membrane integrity is affected, while high concentrations may lead to cell death (McDonnell and Russell, 1999).

Several studies have shown that bathing with soap containing CHX reduces the risk for colonization and cross transmission of microorganisms as well as nosocomial infections in high risk settings (Armellino *et al*., 2014; Petlin *et al*., 2014; Popp *et al*., 2014).

Does CHX lead to a reduction in SSIs? Some studies have demonstrated a positive effect while others have not (Colling *et al*., 2015; Webster and Osborne, 2015). Even so, the currently used clinical routine in Sweden to recommend patients two or three double showers with a CHX based soap before orthopaedic implant surgery is well established.

The normal pathway through the health care system

The information given to patients regarding how and when to take a double shower varies between hospitals and regions, there is no standardized procedure for this. The following instruction is only an approximate description of recommendations.

Patients undergoing elective surgery are often admitted to the hospital on the operation day. Only patients with special needs regarding, e.g., help with their activities of daily living are admitted the day before surgery. With regard to clean surgery the patient is often recommended two double showers before the admission to the hospital.

The first double shower is taken the day before surgery. The patient is recommended to put on clean clothes and sleep on clean sheets. The next double shower is taken the morning before surgery.

A double shower starts by thorough washing of the whole body with a soap containing CHX. The instructions include recommendations to give special attention to the area around the nose, the navel and the armpits followed by the groins and genital area. The soap should be rinsed off and the procedure repeated before drying the skin with a clean towel.

Number of patients per year who undergo preoperative chlorhexidine wash

The total number of patients undergoing preoperative CHX wash is unknown since there are no systematic records kept for the treatment. As an example we have looked at the total number of patients undergoing knee and hip joint operations where a prosthetic implant is used as well as open abdominal aortic aneurysm operations, since these patient groups are recommended CXH wash. The number of patients was 4,718, during 2014 in Region Västra Götaland, which probably is a small proportion of the all patients undergoing "clean surgery".

Present recommendations from medical societies or health authorities

A national group of experts representing Swedish Orthopaedic Association, Swedish Association of Infectious Disease Specialists, Orthopaedic Nurses Association in Sweden, National Association for Surgical Nursing, Swedish Association of Professional Physiotherapists and Swedish Association for Infection Control, has written best practice guidelines for the prevention of orthopaedic implant related infections within the PRISS project - a national, interdisciplinary collaboration for safer prosthetic knee and hip operations. The recommendations are “at least two full-body showers with soap containing CHX should be taken preoperatively” (http://lof.se/wp-content/uploads/2015/05/Selektion-och-optimering-av-patienter-infoer-ledprotesoperation.pdf)

6. Preoperative chlorhexidine wash

Chlorhexidine is an antiseptic agent. It has been shown to decrease skin bacterial count. Preoperative CHX double wash is a procedure where the patient washes the whole body, including the hair, 2-3 times (depending on type of surgery) starting the day before surgery. The procedure is well established in Region Västra Götaland where every patient who will undergo elective surgery is recommended CHX double wash. It is used within all surgical fields with a particular attention in orthopaedic surgery.

7. Objective

The focused question
Prior to "clean surgery" through intact skin, is chlorhexidine whole body wash better than no chlorhexidine wash regarding mortality, implant infection, septicaemia, surgical site infection, reintervention and length of hospital stay?

PICO: P= Patients, I= Intervention, C= Comparison, O=Outcome

P	Patients undergoing so called "clean surgery" where the operation is performed through intact skin
I	Preoperative whole body wash with chlorhexidine
C	No chlorhexidine wash: C1: Placebo C2: Soap C3: No wash C4: Local wash C5: No instruction
O	<u>Critical for decision making</u> Mortality Implant infection Septicaemia Surgical site infection <u>Important but not critical for decision making</u> Reintervention Number of days in hospital <u>Not important for decision making</u> (None)

8. Methods

The activity based HTA-process

Systematic literature search (Appendix 1)
During May 2015 two authors (TS, KF) performed systematic searches in PubMed, Embase, the Cochrane Library, Cinahl and a number of HTA-databases. Reference lists of relevant articles were also scrutinised for additional references. Search strategies, eligibility criteria and a graphic presentation of the selection process are presented in Appendix 1. These authors conducted the literature searches, selected studies, and independently of one another assessed the obtained abstracts and made a first selection of full-text articles for inclusion or exclusion. Any disagreements were resolved in consensus. The remaining articles were sent to all the participants of the project group. All authors read the articles independently of one another and it was finally decided in a consensus meeting which articles should be included in the assessment.

Critical appraisal and certainty of evidence
The primary publications were critically appraised using checklists modified from SBU (Swedish Council on Health Technology Assessment). The included studies are presented in Appendix 2, and the excluded articles in Appendix 3.

Ongoing research
A search in the Clinical Trials database (clinicaltrials.gov, September 16, 2015) identified 148 ongoing trials. Six of these were relevant for the question at issue (see Section 14 – Future perspectives).

9. Results

Literature search (Appendix 1)

The literature search identified 817 articles after removal of duplicates. After reading the abstracts 753 articles were excluded. Another 38 articles were excluded by two authors after reading the articles in full text. The remaining 26 articles were sent to all participants of the project group, and ten articles (seven RCTs and three cohort studies) were finally included in the assessment (Appendix 2). In addition, three systematic reviews (SR) and two health economy studies were commented upon.

Results

All included studies reported the outcome SSI, two of which also reported the outcome implant infection.

The three SRs, Chleblicki *et al*. (2013), Kamel *et al*. (2012), and Webster and Osborne (2015) included studies with patient populations from all kinds of surgical procedures, and not only clean surgery as defined in the current HTA. Chleblicki *et al*. (2013) concluded that there is no appreciable benefit of preoperative whole-body CHX bathing for prevention of SSI, and Kamel *et al*., (2012) concluded that the results regarding SSI were inconclusive. Webster and Osborne (2015) reported no significant difference in SSI rates between preoperative CHX wash compared with placebo (GRADE ⊕⊕⊕⊕), soap or no wash for patients undergoing clean as well as not clean surgery, thus allowing comparison of all kinds of surgical patients. Our current PICO was limited to patients undergoing "clean" surgery.

All included RCTs and cohort studies in the present SR had some or major limitations regarding blinding, definition of outcomes, length of follow up and heterogeneity of patient populations. Chlorhexidine was compared with placebo, soap, no wash, local wash or no instructions. The intervention varied between the studies from one double to three double preoperative washes, showers/baths. The concentration of CHX also varied between the studies.

Mortality

Only total mortality in both intervention and control groups combined was reported in two RCTs (Byrne, 1992; Earnshaw, 1989). One RCT reported 23 deaths in total (0.6%, n=3,733) (Byrne, 1992), and the other RCT reported two deaths (3.1%) among 64 high-risk vascular patients (Earnshaw, 1989).

Implant infection – chlorhexidine versus no instruction (C5) (Appendix 4:1)

Implant infection (by group) was reported in two cohort studies. Both had major study limitations. In one cohort study (n=4,042) on arthroplasties no significant difference was seen in the infection rate between the study groups with 1.1% implant infection rate in the preoperative CHX group versus 0.9% in the “no instruction” group (Colling *et al*., 2015). In the other cohort study (n=2,458) there was a significantly lower implant infection rate in the CHX group with 0.5% (p=0.043) infections among hip surgery patients and 0.6% (p=0.021) among knee surgery patients, compared with 1.7%, and 2.2% in the “no instruction” groups, respectively (Kapadia *et al*., 2013c).

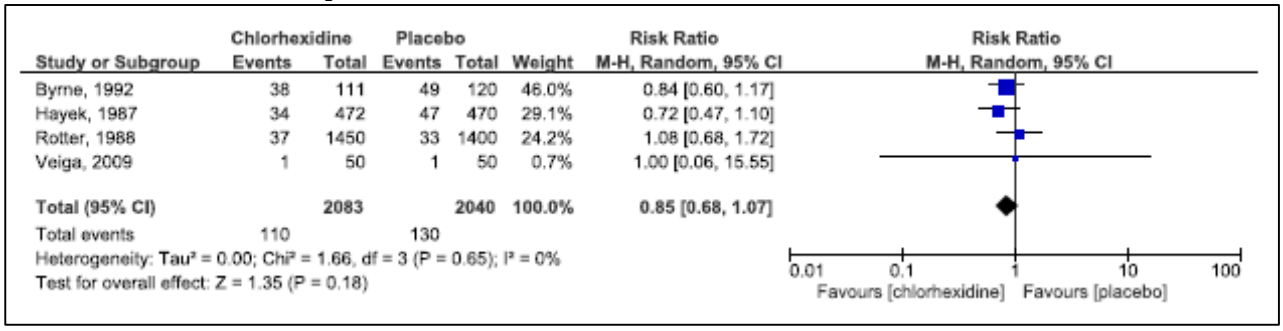
Conclusion: It is uncertain whether the implant infection rate is different after preoperative CHX wash compared with no instructions. Very low certainty of evidence (GRADE ⊕◯◯◯)

Septicemia

The per group incidence of septicemia was not reported in any of the studies.

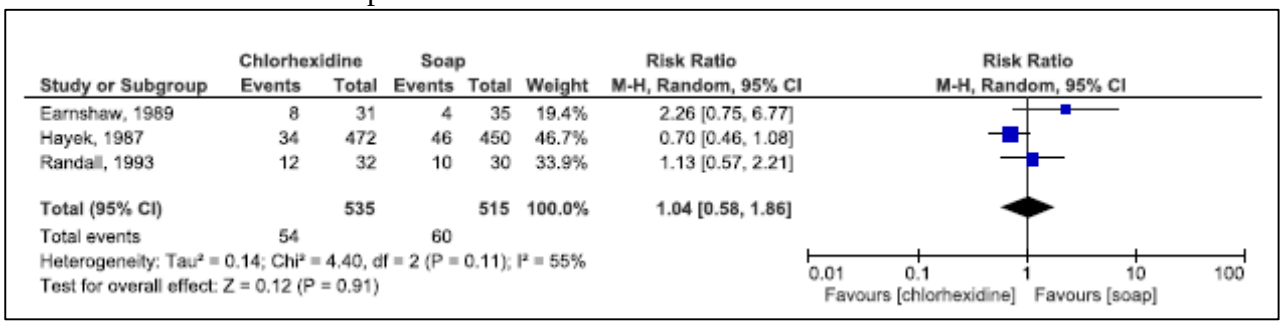
Surgical site infection (SSI) - chlorhexidine versus placebo (C1) (Appendix 4:2)
Four RCTs compared preoperative CHX versus placebo wash with regard to SSI (Byrne *et al*., 1992; Hayek *et al*., 1987, Rotter *et al*., 1988; Veiga *et al*., 2009). None of the studies found any significant differences between the study groups. The SSI rates varied between two and 34% in the CHX groups, and between two and 41% in the placebo groups.
Based on a meta-analysis of the included RCTs the effect estimate was RR 0.85 (95%CI: 0.68 to 1.07, p=0.18) (Figure 1.)
Conclusion: Preoperative CHX compared with placebo wash may result in little or no difference in short term surgical site infections rate in mixed clean surgery patient populations.
Low certainty of evidence (GRADE ⊕⊕◯◯).

Figure 1. Meta-analysis of the outcome surgical site infection from RCTs comparing preoperative chlorhexidine wash with placebo wash



Surgical site infection (SSI) - chlorhexidine versus soap (C2) (Appendix 4:2)
Three RCTs (Earnshaw *et al*., 1989; Hayek *et al*., 1987; Randall *et al*., 1993) and one cohort study (Ayliffe *et al*., 1983) compared preoperative CHX wash versus soap with regard to SSI. There were no significant differences between the study groups. The SSI rates ranged between four and 38% in the CHX groups and between four and 11% in the soap groups.
A meta-analysis of the three RCTs did not reveal any difference between the studied interventions, with an overall RR of 1.04 (CI95%: 0.58 to 1.86, p=0.91) (Figure 2).
Conclusion: It is uncertain whether the surgical site infection rate is different after preoperative CHX wash compared with preoperative soap wash.
Very low certainty of evidence (GRADE ⊕◯◯◯).

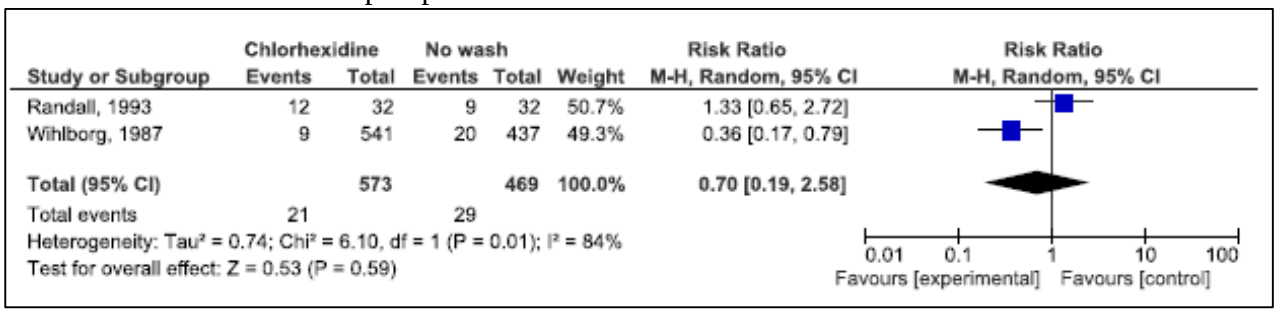
Figure 2. Meta-analysis of the outcome surgical site infection from RCTs comparing preoperative chlorhexidine wash with soap



Surgical site infection (SSI) - chlorhexidine versus no wash (C3) (Appendix 4:2)
Two RCTs compared preoperative CHX wash with no wash with regard to SSI (Randall *et al*., 1993; Wihlborg, 1987). One RCT found a significant difference in favour of CHX, with 1.7% SSI in the CHX group compared with 4.6% (p<0.01) in the control group (Wihlborg, 1987). In the other RCT there was no significant difference between the study groups (37.5% vs. 28.1%, n.s.).

A meta-analysis of the two RCTs did not reveal any difference between the studied interventions, with an overall RR of 0.70 (CI95%: 0.19 to 2.58, p=0.59) (Figure 3).
Conclusion: It is uncertain whether the surgical site infection rate is different after preoperative CHX wash compared with no preoperative wash.
Very low certainty of evidence (GRADE ⊕◯◯◯).

Figure 3. Meta-analysis of the outcome surgical site infection from RCTs comparing preoperative chlorhexidine wash with no preoperative wash



Surgical site infection - chlorhexidine versus local wash (C4) (Appendix 4:2)
One RCT compared preoperative CHX wash with local wash with regard to SSI (Wihlborg, 1987). There was a significant difference in the surgical site infection rate with 1.7% infections in the CHX group and 4.2% ($p<0.05$) in the control group.
Conclusion: It is uncertain whether the surgical site infection rate is different after preoperative CHX wash compared with preoperative local wash.
Very low certainty of evidence (GRADE ⊕◯◯◯).

Surgical site infection - chlorhexidine versus no instruction (C5) (Appendix 4:2)
One RCT (Veiga *et al.*, 2009), and two cohort studies (Colling *et al.*, 2015; Kapadia *et al.*, 2013c) compared preoperative CHX wash with no instruction with regard to SSI. The cohort study with implant infections (n=2,458) found a significantly lower SSI rate in the CHX group, with 0.5% (p=0.043) infection rate among hip surgery patients and 0.6% (p=0.021) among knee surgery patients, compared with 1.7%, and 2.2% in the corresponding "no instruction" groups, respectively (Kapadia *et al.*, 2013c). The RCT (n=100) and the other cohort study (n=4,042) found no significant difference in SSI rates between the study groups, with 2% rates for CHX compared with 0% and 2% in the control groups, respectively (Colling *et al.*, 2015; Veiga *et al.*, 2009).
Conclusion: It is uncertain whether the surgical site infection rate is different after preoperative CHX wash compared with no instructions. Very low certainty of evidence (GRADE ⊕◯◯◯).

Reintervention
Reinterventions were not reported in any of the studies.

Number of days in hospital
Number of days in hospital was not reported in any of the studies.

Complications
Adverse events were reported in four RCTs. Only minor adverse events, such as skin irritation or reddening of the skin, were reported with frequencies of less than 1% in both CHX and control groups.

10.Ethical consequences

Ethical consequences

The widespread use of preoperative CHX wash may constitute an ethical dilemma since it is a treatment that has not been shown to be of proven benefit for the patient. The treatment could cause some unnecessary harm for the patient such as extra costs and effort, especially for the elderly and weak patients already struggling with their activities of daily living. Another ethical aspect is that CHX is paid for by the patient, at some hospitals/departments, and is not covered by the high-cost protection which creates an unequal care not available for everyone.
Short term adverse effects such as skin rash are unusual. We could not identify any studies on the risk of long term adverse effects. On the other hand if CHX is effective in reducing SSI the benefits for the patient might exceed the risks and costs, especially looking at serious complications such as vascular graft infections which are life threatening. These serious complications should be included as outcomes in future studies.

11.Organisation

Time frame for putative introduction of preoperative chlorhexidine wash

Preoperative CHX washes are in use since many years.

Present use of preoperative chlorhexidine wash in Region Västra Götaland

Preoperative CHX washes are widely used in Region Västra Götaland.

Consequences of preoperative chlorhexidine wash for personnel

There is a need of personnel informing patients.

Consequences for other clinics or supporting functions at the hospital or in the Region Västra Götaland

None.

12.Economy aspects

The costs of preoperative chlorhexidine wash

At most hospitals/departments the patient has to cover the cost of CHX which is around 300 SEK for two preoperative washes. When looking at knee and hip joint operations as well as abdominal aortic aneurysm operations in Region Västra Götaland in 2014 (a small proportion of patients in the "clean surgery" category) the cost for this patient group alone would be 1.4 million SEK.

Preoperative washes are included in routine patient care procedures at the hospital ward. Thus, if the patient is admitted to hospital prior to surgery, and needs help with the procedure, there are no additional personnel costs associated with the preoperative washes/showers.

Expected costs of preoperative chlorhexidine wash

See above.

Total change of cost

The patients´ own expenses for the preoperative CHX washes could be saved.

Possibility to adopt and use preoperative chlorhexidine washing within the present budget

Usually, the patient covers the cost of CHX.

Available analyses of health economy or cost advantages or disadvantages

The literature search identified two health economy articles (Kapadia *et al*., 2013b; Lynch *et al*., 1992). The more recent study from USA (Kapadia *et al*., 2013b), based the calculations on reports from National Healthcare Safety Network and previously published reports, reported a potential net saving with preoperative CHX washes per 1,000 knee arthroplasty patients of approximately USD 2.1 million. The earlier study, based on the years 1987-1989 in UK, reported a somewhat higher average hospital cost of both non-infected and infected patients in the CHX group, and concluded that preoperative whole-body disinfection with chlorhexidine was not cost-effective for reducing wound infection (Lynch *et al*., 1992).

13.Discussion

The current assessment of preoperative showering/bathing with CHX compared with placebo wash found that it may be associated with little or no difference in surgical site infections (SSI) in patients undergoing "clean" surgery. For all other comparisons the certainty of evidence was very low. The confidence interval of the pooled effect estimate includes a negative effect and there is a need for further large studies.

In the included studies, preoperative CHX wash was compared with placebo (C1), regular soap (C2), no wash (C3), local wash (C4), and no instruction (C5). Meta-analyses were done for the outcome surgical site infection (SSI) for three different comparisons: CHX vs placebo (C1), CHX vs soap (C2), and CHX vs no wash (C3). They showed no significant differences in SSI rates between CHX and the control groups (Figures 1-3).

A majority of the included studies had some or major problems with regard to directness, study limitations and/or precision. Regarding the outcome SSI, when CHX was compared with placebo, the certainty of evidence was low (GRADE ⊕⊕◯◯). We defined the certainty of evidence lower than that reported (GRADE ⊕⊕⊕⊕) in a recent Cochrane review (Webster and Osborne, 2015). However, the latter review had a different PICO allowing comparison of all kinds of surgical patients. Our current PICO was limited to patients undergoing "clean" surgery. When both clean and potentially contaminated operations were included in a study, only the "clean" surgery patients were included in our analyses. Furthermore, we also included cohort studies, while the Cochrane analysis was confined to RCTs. In addition, we considered the quality of several of the studies somewhat lower than the Cochrane reviewers (Webster and Osborne, 2015).

A drawback of nearly all included studies in our present SR was the short time of follow-up, usually varying between two to six weeks. The length of follow-up was not adequately reported in some studies. Only two cohort studies investigated infections after prosthetic implant surgery, which is a more critical outcome than SSI in general. The latter is usually defined as reddening of the operation scar and/or formation of pus. Infections after prosthetic surgery are often caused by low-virulence opportunistic bacteria, e.g. coagulase-negative staphylococci, and may appear many months after surgery. Whether preoperative CHX wash has a protective effect on such infections was not possible to evaluate. Only one study investigated such infections, comparing CHX with no instruction, and found a significant preventive effect of CHX washes, but the study had severe limitations, e.g. possible selection bias as the surgeon him/herself decided whether to advice the patients to use CHX or not (Wihlborg, 1987). Earnshaw *et al*. (1989) reported that three of the 64 study participants (high risk vascular patients) developed prosthetic graft infection (i.e. implant infection). Two of these patients died from cardiac failure, and one required amputation due to graft rejection.

The widespread belief in the use of preoperative CHX showering to reduce SSI rate is likely to originate from an extrapolation of results in studies that have shown that this procedure significantly reduces the number of skin bacteria. However, such a reduction in bacterial numbers is no guarantee for a lowered risk of SSI, because 1) The bacteria causing SSI may not derive from the patient, but from the hospital staff, air or other sources, 2) The bacteria causing SSI may derive from the patient. Although the bacteria are reduced at the time of surgery, they might rebound in the area and cause infection at a later time-point. 3) Although CHX kills pathogens, it also kills normal commensal bacteria that might provide protection against infection.

However, the observed limited documentation in the current systematic review of available studies cannot rule out a favourable treatment effect of CHX against SSI. Therefore, adequately powered well-conducted, randomised controlled double-blind studies are needed, particularly investigating the potential benefit of CHX wash in relation to the most critical outcomes, including prosthetic infections.

14.Future perspective

Scientific knowledge gaps

Regarding our focused question, there were no studies that had compared CHX with placebo (C1), regular soap (C2), no wash (C3), local wash (C4), and no instruction (C5) for the outcomes mortality, septicaemia, reintervention, or number of days in hospital. Only two cohort studies had addressed the critical outcome implant infection, but only for the comparison CHX vs no instruction (C5). For the most frequently studied outcome SSI, covering all here issued comparisons the follow up periods in general were too short to evaluate late SSI. The identified knowledge gaps could be addressed in adequately powered RCTs with longer follow up periods, or validated large scale register studies.

Ongoing research

A search in the Clinical trials database (clinicaltrials.gov) identified six RCTs potentially relevant for the current PICO:

NCT01090479: RCT comparing the CHX cloths with a control group which will be performing an ordinary shower prior to surgery. Primary Outcome Measure: clinically diagnosed infection. Status: completed. Published: Murray *et al*., (2011).

NCT02469311: RCT comparing 2% CHX-impregnated cloth skin wash the night before and the morning of surgical admission with bath with soap and water, in patients scheduled for total hip arthroplasty or total knee arthroplasty. Primary Outcome Measure: incidence of periprosthetic infection. Status: completed - last updated: June 12, 2015.

NCT02490631: RCT comparing 2% chlorhexidine skin preparation cloths for the prevention of SSI in spine patients with standard of care skin cleansing by nursing staff. Primary Outcome Measure: SSI. Status: recruiting.

NCT00130221: RCT comparing 2% CHX bath with soap and water bath. Primary Outcome Measure: Primary blood stream infections and culture negative sepsis. Status: completed. Published: not surgery patients, but medical intensive care unit patients (Bleasdale *et al*., 2007).

NCT01425697: RCT comparing 2% CHX cloths with standard of care preoperative preparation. Primary Outcome Measure: SSI. Status: completed. No study results posted.

NCT02385708: RCT comparing 2% CHX gluconate cloths with routine standard of care. Primary Outcome Measure: SSI. Status: recruiting.

Interest at the clinic/research group/organisation to start studies/trials within the research field at issue

There is an interest to initiate studies (e.g. Infection Control at Sahlgrenska University Hospital is planning to participate in a multicenter study on preoperative CHX wash prior to thoracic surgery).

15.Participants in the project

The question was nominated by

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Participants from the clinical departments

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Annette Erichsen Andersson, PhD, The Sahlgrenska Academy, Institute of Health and Care Sciences, University of Gothenburg, Gothenburg, Sweden
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Marie Studahl, MD, Department of Infectious Diseases, Sahlgrenska University Hospital/Östra, Gothenburg, Sweden

Conflicts of interest

None

Project time

HTA was accomplished during the period of 2015-05-13 – 2015-10-21.
Literature searches were made in May 2015

Appendix 1, Search strategy, study selection and references

Question(s) at issue:

Prior to "clean surgery" through intact skin, is chlorhexidine whole body wash better than no chlorhexidine wash regarding mortality, implant infection, septicaemia, surgical site infection, reintervention and length of hospital stay?

PICO: (*P=Patient I=Intervention C=Comparison O=Outcome*)

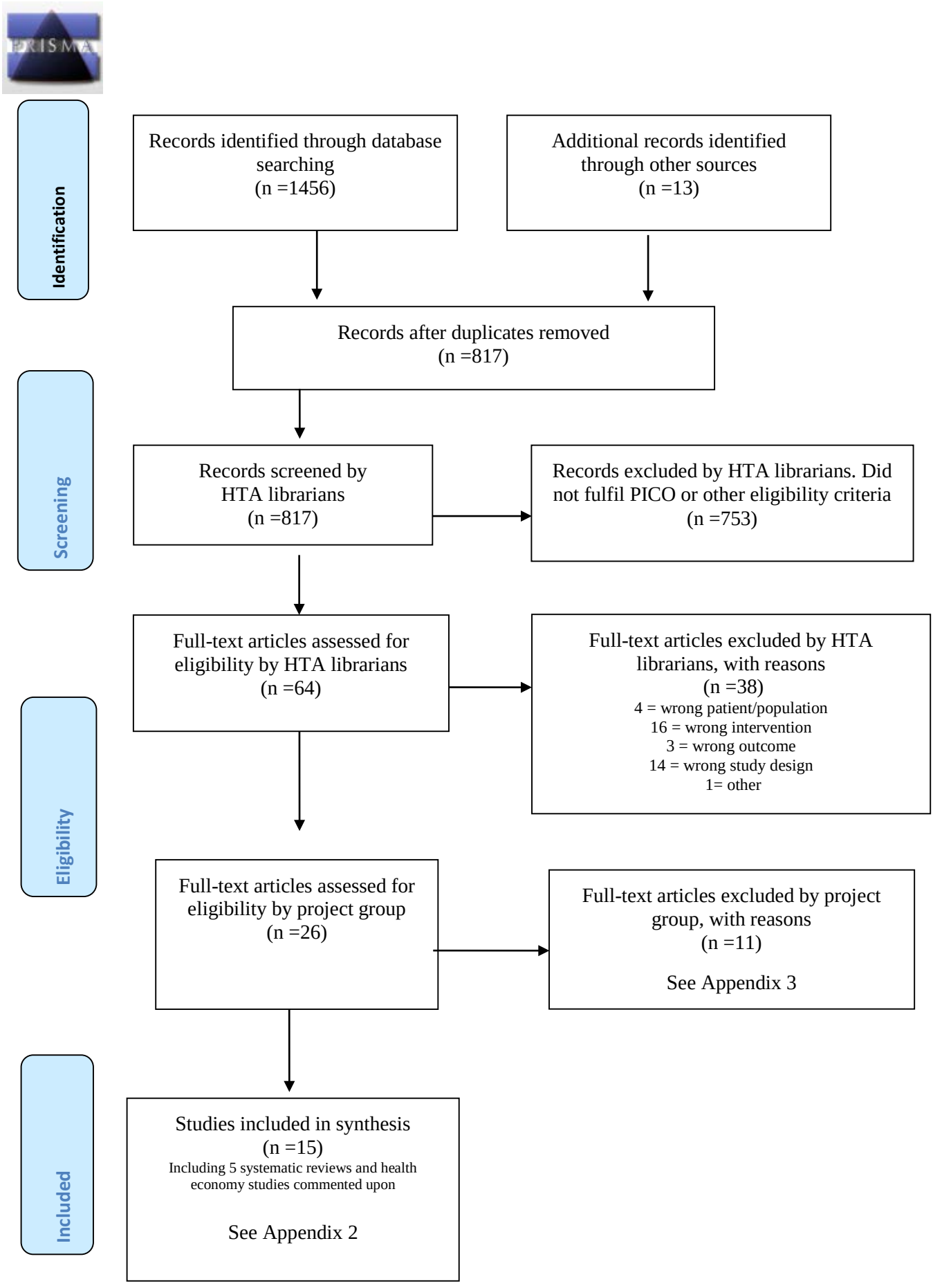
P	Patients undergoing so called "clean surgery" where the operation is performed through intact skin
I	Preoperative whole body wash with chlorhexidine
C	No chlorhexidine wash C1: placebo C2: soap C3: no wash C4: local wash C5:no instruction
O	<u>Critical for decision making</u> Mortality Implant infection Septicaemia Surgical site infection <u>Important but not critical for decision making</u> Reintervention Number of days in hospital <u>Not important for decision making</u> None

<u>Eligibility criteria</u>

Study design:
Systematic reviews
Randomized controlled trials
Non-randomized controlled studies with ≥ 1000 patients
Case series etc. if ≥ 1000 patients

Language:
English, Swedish, Norwegian, Danish

Selection process – flow diagram



Search strategies

Database: PubMed
Date: 2015-05-21
No of results: 481

Search	Query	Items found
#20	**Search #13 NOT #16 Filters: English; Danish; Norwegian; Swedish**	**481**
#17	Search #13 NOT #16	504
#16	Search #14 OR #15	5349225
#15	Search ((animals[mh]) NOT (animals[mh] AND humans[mh]))	4003060
#14	Search (Editorial[ptyp] OR Letter[ptyp] OR Comment[ptyp])	1399871
#13	Search #12 AND #10 AND #1	560
#12	Search #7 OR #11	1488526
#11	Search preadmission [tiab]	1089
#10	Search #9 OR #8	156441
#9	Search Baths[mesh]	4198
#8	Search Shower*[tiab] OR bath*[tiab] OR wash*[tiab] OR cleans*[tiab] OR cloth[tiab] OR cloths[tiab] OR scrub[tiab] OR soap[tiab]	154690
#7	Search #3 OR #4 OR #5 OR #6	1487644
#6	Search preoperative [tiab] OR pre-operative [tiab] OR perioperative [tiab] OR peri-operative [tiab]	240083
#5	Search preoperative care [mesh] OR perioperative care [mesh]	125862
#4	Search infection[tiab] OR infections[tiab] OR infected[tiab]	1170201
#3	Search "Surgical Wound Infection"[Mesh]	29060
#1	Search chlorhexidine	9011

Database: EMBASE 1980 to Present (OvidSP)
Date: 2015-05-21
No of results: 461

#	Searches	Results
1	exp chlorhexidine/ or exp chlorhexidine acetate/ or exp chlorhexidine gluconate/	14783
2	chlorhexidine.ti,ab,tn,rn.	14379
3	1 or 2	15822
4	exp surgical infection/	28081
5	(infection or infections or infected).ti,ab.	1359320
6	exp preoperative care/	34210
7	exp perioperative period/	30101
8	(preoperative or pre-operative or perioperative or peri-operative or preadmission).ti,ab.	309892
9	4 or 5 or 6 or 7 or 8	1682622
10	(Shower$ or bath$ or wash$ or cleans$ or cloth or cloths or scrub or soap).ti,ab.	176679

11	exp bath/	7619
12	10 or 11	178866
13	3 and 9 and 12	899
14	**limit 13 to (embase and (danish or english or norwegian or swedish) and (article or "conference review" or "review"))**	**461**

Database: The Cochrane Library
Date: 2015-05-21
No of results: 194
Cochrane reviews 10
Other reviews 4
Clinical trials 171
Technology assessments 5
Economic evaluations 4

ID	Search	Hits
#1	chlorhexidine:ti,ab,kw (Word variations have been searched)	2440
#2	infection or infections or infected:ti,ab,kw (Word variations have been searched)	58546
#3	preoperative or pre-operative or perioperative or peri-operative or preadmission:ti,ab,kw (Word variations have been searched)	23200
#4	#2 or #3	79416
#5	Shower* or bath* or wash* or cleans* or cloth or cloths or scub or soap:ti,ab,kw (Word variations have been searched)	16693
#6	#1 and #4 and #5	194

Database: Cinahl (Ebsco)
Date: 2015-05-21
No of results: 273

#	Query	Results
S14	**S3 AND S9 AND S12** *Limits: Danish, English, Norwegian, Swedish*	**273**
S13	S3 AND S9 AND S12	277
S12	S10 OR S11	20,783
S11	(MH "Bathing and Baths")	2,162
S10	TI (shower* OR bath* OR wash* OR cleans* OR cloth OR cloths OR scrub OR soap) OR AB (shower* OR bath* OR wash* OR cleans* OR cloth OR cloths OR scrub OR soap)	19,785
S9	S4 OR S5 OR S6 OR S7 OR S8	156,417
S8	TI (infection OR infections OR infected) OR AB (infection OR infections OR infected)	114,223
S7	TI (preoperative or pre-operative or perioperative or peri-operative or preadmission) OR AB (preoperative or pre-operative or perioperative or peri-operative or preadmission)	28,368
S6	(MH "Perioperative Care")	6,879
S5	(MH "Preoperative Care+")	15,554
S4	(MH "Surgical Wound Infection")	6,503
S3	S1 OR S2	2,638

S2	TI chlorhexidine OR AB chlorhexidine	1,680
S1	(MH "Chlorhexidine")	2,203

Database: CRD
Date: 2015-05-21
No of results: 47

Line	Search	Hits
1	(chlorhexidine) AND (preoperative or pre-operative or perioperative or peri-operative or preadmission OR infection OR infections OR infected) AND (shower* OR bath* OR wash* OR cleans* OR cloth OR cloths OR scrub OR soap)	47

Reference lists

A comprehensive review of reference lists brought 13 new records

Included articles

Ayliffe GA, Noy MF, Babb JR, Davies JG, Jackson J. A comparison of pre-operative bathing with chlorhexidine-detergent and non-medicated soap in the prevention of wound infection. J Hosp Infect. 1983;4(3):237-44.

Byrne DJ, Napier A, Cuschieri A. The value of whole body disinfection in the prevention of postoperative wound infection in clean and potentially contaminated surgery. A prospective, randomised, double-blind, placebo-controlled clinical trial. Surg Res Commun. 1992;12(1):43-52.

Colling K, Statz C, Glover J, Banton K, Beilman G. Pre-operative antiseptic shower and bath policy decreases the rate of S. aureus and methicillin-resistant S. aureus surgical site infections in patients undergoing joint arthroplasty. Surg Infect (Larchmt). 2015;16(2):124-32.

Earnshaw JJ, Berridge DC, Slack RC, Makin GS, Hopkinson BR. Do preoperative chlorhexidine baths reduce the risk of infection after vascular reconstruction? Eur J Vasc Surg. 1989;3(4):323-6.

Hayek LJ, Emerson JM, Gardner AM. A placebo-controlled trial of the effect of two preoperative baths or showers with chlorhexidine detergent on postoperative wound infection rates. J Hosp Infect. 1987;10(2):165-72.

Kapadia BH, Issa K, McElroy MJ, Pivec R, Daley JA, Mont MA. Advance pre-operative chlorhexidine preparation reduces periprosthetic infections following total joint arthroplasty. Semin Arthroplasty. 2013c;24(2):83-6.

Randall PE, Ganguli L, Marcuson RW. Wound infection following vasectomy. Br J Urol. 1983;55(5):564-7.

Rotter ML, Larsen SO, Cooke EM, Dankert J, Daschner F, Greco D, et al. A comparison of the effects of preoperative whole-body bathing with detergent alone and with detergent containing chlorhexidine gluconate on the frequency of wound infections after clean surgery. The European Working Party on Control of Hospital Infections. J Hosp Infect. 1988;11(4):310-20.

Veiga DF, Damasceno CA, Veiga-Filho J, Figueiras RG, Vieira RB, Garcia ES, et al. Randomized controlled trial of the effectiveness of chlorhexidine showers before elective plastic surgical procedures. Infect Control Hosp Epidemiol. 2009;30(1):77-9.

Wihlborg O. The effect of washing with chlorhexidine soap on wound infection rate in general surgery. A controlled clinical study. Ann Chir Gynaecol. 1987;76(5):263-5.

Systematic reviews and health economy studies, no appraisal done:

Chlebicki MP, Safdar N, O'Horo JC, Maki DG. Preoperative chlorhexidine shower or bath for prevention of surgical site infection: a meta-analysis. Am J Infect Control. 2013;41(2):167-73.

Kamel C, McGahan L, Polisena J, Mierzwinski-Urban M, Embil JM. Preoperative skin antiseptic preparations for preventing surgical site infections: A systematic review. Infect Control Hosp Epidemiol. 2012;33(6):608-17.

Kapadia BH, Johnson AJ, Issa K, Mont MA. Economic evaluation of chlorhexidine cloths on healthcare costs due to surgical site infections following total knee arthroplasty. J Arthroplasty. 2013b;28(7):1061-5.

Lynch W, Davey PG, Malek M, Byrne DJ, Napier A. Cost-effectiveness analysis of the use of chlorhexidine detergent in preoperative whole-body disinfection in wound infection prophylaxis. J Hosp Infect. 1992;21(3):179-91.

Webster J, Osborne S. Preoperative bathing or showering with skin antiseptics to prevent surgical site infection. Cochrane Database Syst Rev. 2015;2:Cd004985.

Excluded articles

Bailey RR, Stuckey DR, Norman BA, Duggan AP, Bacon KM, Connor DL, et al. Economic value of dispensing home-based preoperative chlorhexidine bathing cloths to prevent surgical site infection. Infect Control Hosp Epidemiol. 2011;32(5):465-71.

Byrne DJ, Lynch W, Napier A, Davey P, Malek M, Cuschieri A. Wound infection rates: the importance of definition and post-discharge wound surveillance. J Hosp Infect. 1994;26(1):37-43.

Chien CY, Lin CH, Hsu RB. Care bundle to prevent methicillin-resistant Staphylococcus aureus sternal wound infection after off-pump coronary artery bypass. Am J Infect Control. 2014;42(5):562-4.

Dizer B, Hatipoglu S, Kaymakcioglu N, Tufan T, Yava A, Iyigun E, et al. The effect of nurse-performed preoperative skin preparation on postoperative surgical site infections in abdominal surgery. J Clin Nurs. 2009;18(23):3325-32.

Garibaldi RA, Skolnick D, Lerer T, Poirot A, Graham J, Krisuinas E, et al. The impact of preoperative skin disinfection on preventing intraoperative wound contamination. Infect Control Hosp Epidemiol. 1988;9(3):109-13.

Hayek LJ, Emerson JM. Preoperative whole body disinfection--a controlled clinical study. J Hosp Infect. 1988;11 Suppl B:15-9.

Johnson AJ, Daley JA, Zywiel MG, Delanois RE, Mont MA. Preoperative chlorhexidine preparation and the incidence of surgical site infections after hip arthroplasty. J Arthroplasty. 2010;25(6 Suppl):98-102.

Johnson AJ, Kapadia BH, Daley JA, Molina CB, Mont MA. Chlorhexidine reduces infections in knee arthroplasty. J Knee Surg. 2013;26(3):213-8.

Kapadia BH, Johnson AJ, Daley JA, Issa K, Mont MA. Pre-admission cutaneous chlorhexidine preparation reduces surgical site infections in total hip arthroplasty. J Arthroplasty. 2013a;28(3):490-3.

Rao N, Schilling D, Rice J, Ridenour M, Mook W, Santa E. Prevention of postoperative mediastinitis: a clinical process improvement model. J Healthc Qual. 2004;26(1):22-7; quiz 8.

Savage MW, Pottinger JM, Chiang HY, Yohnke KR, Bowdler NC, Herwaldt LA. Surgical site infections and cellulitis after abdominal hysterectomy. Am J Obstet Gynecol. 2013;209(2):108.e1-.e10.

Other references

Acklin YP, Widmer AF, Renner RM, Frei R, Gross T. Unexpectedly increased rate of surgical site infections following implant surgery for hip fractures: problem solution with the bundle approach. Injury 2011;42:209-16.

AlBuhairn B, Hind D, Hutchinson A. Antibiotic prophylaxis for wound infections in total joint arthroplasty : A systematic review. J Bone Joint Surg Br 2008;90:915-9.

Andersson AE, Bergh I, Karlsson J, Nilsson K. Patients' experiences of acquiring a deep surgical site infection: An interview study. Am J Infect Control 2010;38:711-7.

Armellino D, Woltmann J, Parmentier D, Musa N, Eichorn A, Silverman R, et al. Modifying the risk: once-a-day bathing "at risk" patients in the intensive care unit with chlorhexidine gluconate. Am J Infect Control. 2014;42(5):571-3.

Bandyk DF. Vascular surgical site infection: risk factors and preventive measures. Semin Vasc Surg 2008;21:119-23.

Berg TC, Kjørstad KE, Akselsen PE, et al. National surveillance of surgical site infections after coronary artery bypass grafting in Norway: incidence and risk factors. Eur J Cardiothorac Surg 2011;40:1291-7.

Bleasdale SC, Trick WE, Gonzalez IM, Lyles RD, Hayden MK, Weinstein RA. Effectiveness of chlorhexidine bathing to reduce catheter-associated bloodstream infections in medical intensive care unit patients. Arch Intern Med. 2007 Oct 22;167(19):2073-9.

Brown RB, Bradley S, Opitz E, Cipriani D, Pieczarka R, Sands M. Surgical wound infections documented after hospital discharge. Am J Infect Control 1987;15:54-8.

Cayci C, Russo M, Cheema FH, et al. Risk analysis of deep sternal wound infections and their impact on long-term survival: a propensity analysis. Ann Plast Surg 2008;61:294-301.

Darle N, Falk A, Hall-Angeras M, Laknas E. [The importance of follow-up of wound infections. 100 percent registration at the Ostra hospital in Gothenburg]. Lakartidningen 1997;94:1915-8.

de Lissovoy G, Fraeman K, Hutchins V, Murphy D, Song D, Vaughn BB. Surgical site infection: incidence and impact on hospital utilization and treatment costs. Am J Infect Control 2009;37:387-97.

Edmiston CE, Jr., Seabrook GR, Johnson CP, Paulson DS, Beausoleil CM. Comparative of a new and innovative 2% chlorhexidine gluconate-impregnated cloth with 4% chlorhexidine gluconate as topical antiseptic for preparation of the skin prior to surgery. Am J Infect Control 2007;35:89-96.

Frei E, Hodgkiss-Harlow K, Rossi PJ, Edmiston CE, Jr., Bandyk DF. Microbial pathogenesis of bacterial biofilms: a causative factor of vascular surgical site infection. Vasc Endovascular Surg 2011;45:688-96.

Hansen D, Krabs C, Benner D, Brauksiepe A, Popp W. Laminar air flow provides high air quality in the operating field even during real operating conditions, but personal protection seems to be necessary in operations with tissue combustion. Int J Hyg Environ Health 2005;208:455-60.

Kurtz SM, Lau E, Watson H, Schmier JK, Parvizi J. Economic burden of periprosthetic joint infection in the United States. J Arthroplasty 2012;27:61-5 e1.

Leape LL, Brennan TA, Laird N, et al. The nature of adverse events in hospitalized patients. Results of the Harvard Medical Practice Study II. N Engl J Med 1991;324:377-84.

Lidwell OM, Lowbury EJL, Whyte W. Airborne contamination of wounds in joint replacement operations: the relationship to sepsis rates. J Hosp Infect 1983;4:111-31.

Lindstrom D, Sadr Azodi O, Wladis A, et al. Effects of a perioperative smoking cessation intervention on postoperative complications: a randomized trial. Ann Surg 2008;248:739-45.

Lister J. On the Antiseptic Principle in the Practice of Surgery. Br Med J 1867;2:246-8.

McDonnell G, Russell AD. Antiseptics and disinfectants: activity, action, and resistance. Clin Microbiol Rev 1999;12:147-79.

Milstone AM, Passaretti CL, Perl TM. Chlorhexidine: expanding the armamentarium for infection control and prevention. Clin Infect Dis 2008;46:274-81.

Murray MR, Saltzman MD, Gryzlo SM, Terry MA, Woodward CC, Nuber GW. Efficacy of preoperative home use of 2% chlorhexidine gluconate cloth before shoulder surgery. J Shoulder Elbow Surg. 2011 Sep;20(6):928-33.

Perl TM. Prevention of Staphylococcus aureus infections among surgical patients: beyond traditional perioperative prophylaxis. Surgery 2003;134:S10-7.

Petlin A, Schallom M, Prentice D, Sona C, Mantia P, McMullen K, et al. Chlorhexidine gluconate bathing to reduce methicillin-resistant Staphylococcus aureus acquisition. Crit Care Nurse. 2014;34(5):17-25; quiz 6.

Popp JA, Layon AJ, Nappo R, Richards WT, Mozingo DW. Hospital-acquired infections and thermally injured patients: chlorhexidine gluconate baths work. Am J Infect Control. 2014;42(2):129-32.

Salehi Omran A, Karimi A, Ahmadi SH, et al. Superficial and deep sternal wound infection after more than 9000 coronary artery bypass graft (CABG): incidence, risk factors and mortality. BMC Infect Dis 2007;7:112.

Sands K, Vineyard G, Platt R. Surgical site infections occurring after hospital discharge. J Infect Dis 1996;173:963-70.

Swenne CL, Skytt B, Lindholm C, Carlsson M. Patients' experiences of mediastinitis after coronary artery bypass graft procedure. Scand Cardiovasc J 2007;41:255-64.

Tammelin A, Ljungqvist B, Reinmuller B. Single-use surgical clothing system for reduction of airborne bacteria in the operating room. J Hosp Infect 2013;84:245-7.

Urban JA. Cost analysis of surgical site infections. Surg Infect (Larchmt) 2006;7 Suppl 1:S19-22.

Vogel TR, Dombrovskiy VY, Carson JL, Haser PB, Lowry SF, Graham AM. Infectious complications after elective vascular surgical procedures in the United States. J Vasc Surg 2010; 51:122-9; discussion 129-30.

Whyte W, Hodgson R, Tinkler J. The importance of airborne bacterial contamination of wounds. J Hosp Infect 1982;3:123-35.

Appendix 2 – Characteristics of included studies alphabetically according to study design

Author, Year, Country	Study Design	Study Duration	Study Groups; Intervention vs control	Patients total (n)	Mean Age (years)	Men (%)	Outcome variables
Byrne, 1992	RCT	32 months	Chlorhexidine vs Placebo	1,754 1,753	Not stated	47% 48%	Mortality SSI Adverse events
Earnshaw, 1989	RCT	Not specified	Chlorhexidine vs Soap	31 35	66 (group median)	84%	Mortality SSI
Hayek, 1987	RCT	24 months	Chlorhexidine vs Placebo vs Soap	689 700 626	57 56 55	35%	SSI
Randall, 1993	RCT	6 months	Chlorhexidine vs Soap vs No washing	32 30 32	Not specified	Not specified	SSI
Rotter, 1988	RCT	Not specified	Chlorhexidine vs Placebo	1,450 1,400	Not stated	52% 52%	SSI Adverse events
Veiga, 2009	RCT	16 months	Chlorhexidine vs Placebo vs No instruction	50 50 50	38 (group mean)	21% (alla)	SSI Adverse events
Wihlborg, 1987	RCT	6 years	Chlorhexidine vs Local wash vs No washing	541 552 437	> 60 years: 43% > 60 years: 45% > 60 years: 42%	Not specified	SSI Adverse events
Ayliffe, 1983	Cohort	15 months	Chlorhexidine vs Soap	2,703 2,833	Not specified	Not specified	SSI
Colling, 2015	Cohort	32 months	Chlorhexidine vs No instruction	2,349 1,693	62 (median) 66 (median)	39% 43%	Implant infection SSI
Kapadia, 2013c	Cohort	4 years	Chlorhexidine vs No instruction	557 1,901	Not specified	Not specified	Implant infection SSI

RCT = randomized controlled trial, SSI = Surgical site infection

Appendix 3. Excluded articles – HTA preoperative chlorhexidine wash

Study First author, publication year	Reason for exclusion
Bailey, 2011	Wrong O (only computer simulated outcomes)
Byrne, 1994	Duplicate publication (Byrne, 1992)
Chien,2014	Wrong I (mixed interventions)
Dizer, 2009	Wrong P (mixed abdominal surgery patients)
Hayek, 1988	Wrong O (no data on SSI for clean surgery)
Johnsson, 2010	Duplicate publication (Kapadia 2013c)
Johnson, 2013	Duplicate publication (Kapadia 2013c)
Garibaldi, 1988	Wrong outcome (no relevant SSI data)
Kapadia, 2013a	Duplicate publication (Kapadia, 2013c)
Rao, 2004	Wrong I (mixed interventions)
Savage, 2013	Wrong study design (case-control). No extractable data

Appendix 4:1. HTA preoperative chlorhexidine wash
Outcome variable: Implant infections
Abbreviations: Chx = Chlorhexidine, Pl = Placebo, S = Soap, NI = No instructions, NW = No wash, LW = Local wash

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	With drawals - dropouts	Results						Comments	* Directness	* Study limitations	* Precision
				Chlor-hexidine I	Placebo C1	Soap C2	No wash C3	Local wash C4	No Instruc-tion C5				
Colling, 2015	Cohort	I = 2,349 C5 = 1,693	Not specified	1.1%	NR	NR	NR	NR	0.9% n.s.*	Arthroplasties, retrospective, 1 year follow up, control in different hospital, 2 showers, SSI = CDC definition * Calculated from data, Fischer's exact test	?	-	?
Kapadia, 2013c	Cohort	I = 557 C5 = 1,901	Not specified	0.5%* 0.6%≠	NR	NR	NR	NR	1.7%* p=0.043 2.2%≠ p=0.021	2 showers, 1 year follow up * Hip surgery ≠ Knee surgery	+	-	+/?

CDC = Centers for Disease Control and Prevention, NR = Not reported, RCT = randomised controlled trial, SSI = Surgical site infection.

Appendix 4:2. HTA preoperative chlorhexidine wash
Outcome variable: SSI
Abbreviations: Chx = Chlorhexidine, Pl = Placebo, S = Soap, NI = No instructions, NW = No wash, LW = Local wash

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	With drawals - dropouts	Results						Comments	* Directness	* Study limitations	* Precision
				Chlor-hexidine I	Placebo C1	Soap C2	No wash C3	Local wash C4	No Instruc-tion C5				
Byrne, 1992	RCT	I = 111 C1= 120	NR	34.2%	40.8% n.s.	NR	NR	NR	NR	Mixed surgery (vascular surgery separated), 1 month follow up Pus, ASEPSIS score > 10 3 showers	?	?/+	+
Earnshaw, 1989	RCT	I = 31 C2 = 35	0	26%	NR	11% p=0.12	NR	NR	NR	Vascular reconstructive surgery SSI definition: pus discharge, cellulitis 1 month follow up 2 baths	-	-	-
Hayek, 1987	RCT	I = 472 C1 = 470 C2 = 450	?	7.2%	10.0% n.s.	10.2% n.s.	NR	NR	NR	Placebo had antimicrobial properties, 6 weeks follow up, 2 showers	-	-	-
Randall, 1993	RCT	I = 32 C2 = 30 C3 = 32	?	37.5%	NR	33.3% n.s.	28.1% n.s.	NR	NR	Vasectomy, 7 days follow up, 1 single shower, SSI = open wound, purulent or serous discharge	?	-	?
Rotter, 1988	RCT	I = 1,450 C1 = 1,400	140 (group drop out)	2.62%	2.36% n.s.	NR	NR	NR	NR	”Clean surgery”, 21 days follow up, , SSI = pus discharge 2 showers	+	+/?	?
Veiga, 2009	RCT	I = 50 C1 = 50 C5 = 50	0	2%	2% p=0.6	NR	NR	NR	0% n.s	Plastic surgery, 1 double shower, SSI = CDC classification, 30 days follow up	?	?	-

Appendix 4:2. HTA preoperative chlorhexidine wash
Outcome variable: SSI
Abbreviations: Chx = Chlorhexidine, Pl = Placebo, S = Soap, NI = No instructions, NW = No wash, LW = Local wash

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	With drawals - dropouts	Results						Comments	* Directness	* Study limitations	* Precision
				Chlor-hexidine I	Placebo C1	Soap C2	No wash C3	Local wash C4	No Instruc-tion C5				
Wihlborg, 1987	RCT	I = 541 C3 = 437 C4 = 552	3 (group drop out)	1.7%	NR	NR	4.6% p<0.01	4.2% p<0.05	NR	Biliary, breast, inguinal hernia, , SSI definition: pus. 1 double shower Follow-up during hospital stay.	?/+	?/-	?
Ayliffe, 1983	Cohort	I = 787 C2 = 750	Not specified	3.6%	NR	4.0% n.s.	NR	NR	NR	Mixed surgery, 1 shower, SSI = serous or purulent discharge, follow up not specified	+	-	-
Colling, 2015	Cohort	I = 2,349 C5 = 1,693	Not specified	1.96%	NR	NR	NR	NR	1.95% (n.s.)	Arthroplasties, retrospective, 1 year follow up, control in different hospital, 2 showers, SSI = CDC definition	?	-	?
Kapadia, 2013c	Cohort	I = 557 C5 = 1,901	Not specified	0.5%* 0.6%±	NR	NR	NR	NR	1.7%* p=0.043 2.2%± p=0.021	2 showers, 1 year follow up * Hip surgery ± Knee surgery Only periprosthetic infections reported	+	-	+/?

CDC = Centers for Disease Control and Prevention, NR = Not reported, RCT = randomised controlled trial, SSI = Surgical site infection.

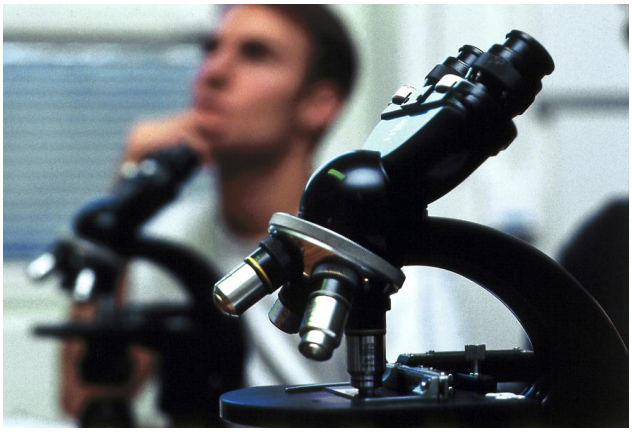
Project: HTA preoperative chlorhexidine wash
Appendix 4:3
Outcome variable: Adverse events

Author, year, country	Study design	Number of patients n=	With drawals - dropouts	Results						Comments
				Chlorhex-idine I	Placebo C1	Soap C2	No wash C3	Local wash C4	No Instruc-tion C5	
Byrne, 1992	RCT	I = 1,754 C1= 1,753	23 (group dropout)	0.51% (n=9)	0.57% (n=10)	NR	NR	NR	NR	Skin irritation
Rotter, 1988	RCT	I = 1,450 C1 = 1,400	140 (group drop out)	0.34% (n=5)	0.36% (n=5)	NR	NR	NR	NR	Itching or reddening of skin
Veiga, 2009	RCT	I = 50 C1 = 50 C5 = 50	0	0	0	NR	NR	NR	0	No adverse events seen
Wihlborg, 1987	RCT	I = 541 C4 = 552 C5 = 437	3 (group drop out)	<1%	NR	NR	Not specified	Not specified	NR	Skin irritation

NR = Not reported, RCT = Randomised controlled trial.

Region Västra Götaland, HTA-centrum

Health Technology Assessment
Regional activity-based HTA



HTA

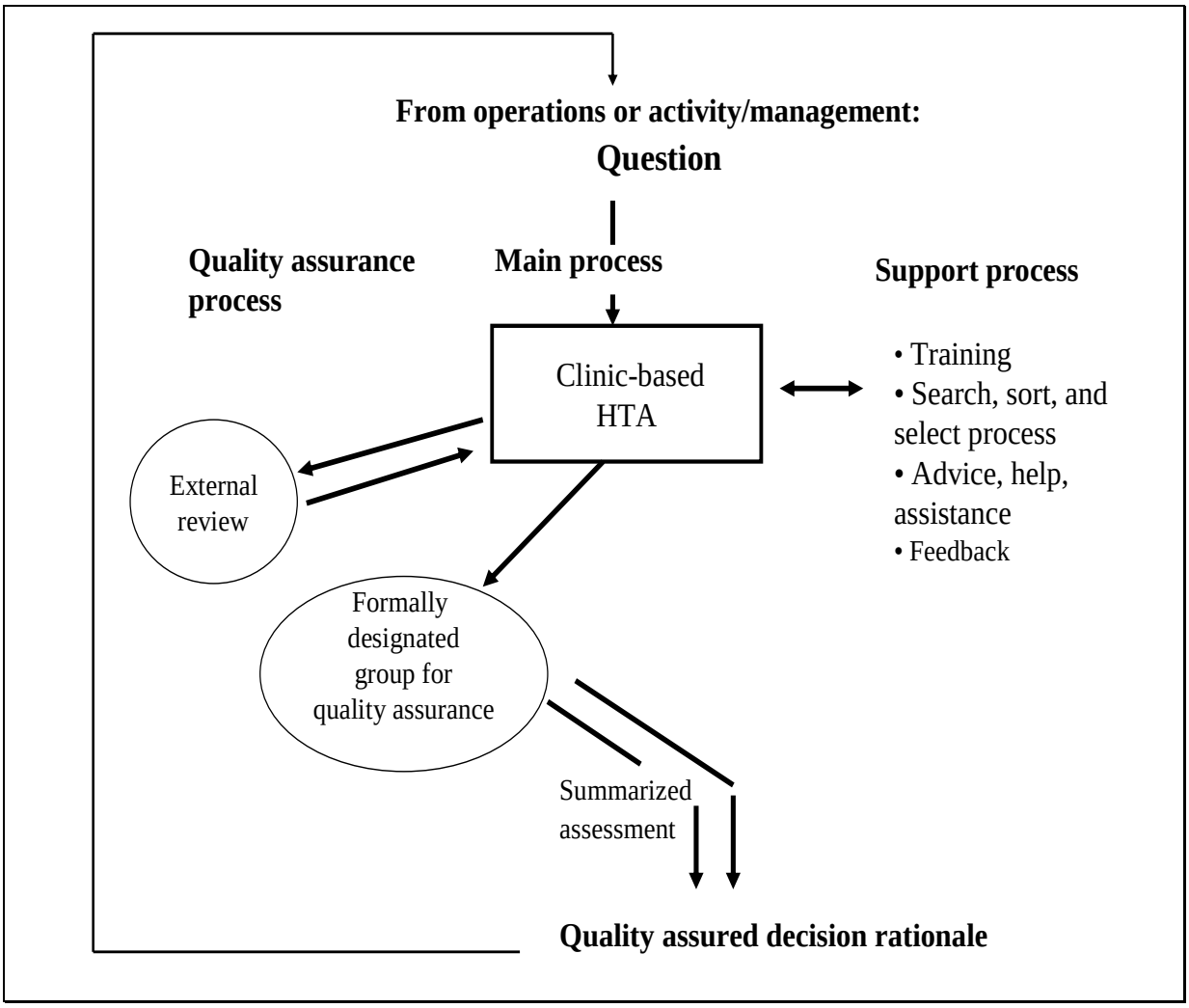
Health technology assessment (HTA) is the systematic evaluation of properties, effects, and/or impacts of health care technologies, i.e. interventions that may be used to promote health, to prevent, diagnose or treat disease or for rehabilitation or long-term care. It may address the direct, intended consequences of technologies as well as their indirect, unintended consequences. Its main purpose is to inform technology-related policymaking in health care.

To evaluate the quality of evidence the Centre of Health Technology Assessment in Region Västra Götaland is currently using the GRADE system, which has been developed by a widely representative group of international guideline developers. According to GRADE the level of evidence is graded in four categories:

High quality of evidence	= (GRADE⊕⊕⊕⊕)
Moderate quality of evidence	= (GRADE ⊕⊕⊕O)
Low quality of evidence	= (GRADE ⊕⊕OO)
Very low quality of evidence	= (GRADE ⊕OOO)

In GRADE there is also a system to rate the strength of recommendation of a technology as either “strong” or “weak”. This is presently not used by the Centre of Health Technology Assessment in Region Västra Götaland. However, the assessments still offer some guidance to decision makers in the health care system. If the level of evidence of a positive effect of a technology is of high or moderate quality it most probably qualifies to be used in routine medical care. If the level of evidence is of low quality the use of the technology may be motivated provided there is an acceptable balance between benefits and risks, cost-effectiveness and ethical considerations. Promising technologies, but a very low quality of evidence, motivate further research but should not be used in everyday routine clinical work.

Christina Bergh, Professor, MD.
Head of HTA-centrum


From operations or activity/management:
Question
Quality assurance process
Main process
Support process
Clinic-based HTA
• Training
• Search, sort, and select process
• Advice, help, assistance
• Feedback
External review
Formally designated group for quality assurance
Summarized assessment
Quality assured decision rationale

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