TITLE: Preoperative Skin Antiseptic Preparations and Application Techniques for Preventing Surgical Site Infections: A Systematic Review of the Clinical Evidence and Guidelines

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EXECUTIVE SUMMARY

CONTEXT AND POLICY ISSUES

Surgical site infections (SSIs) occur in patients who undergo clean extra-abdominal surgeries, such as thoracic and orthopaedic surgery, and in patients who undergo intra-abdominal procedures. SSIs are associated with increased morbidity and mortality in some patients after surgery, and with prolonged hospital stay and increased costs. Topical antiseptics may be applied to the patient as a preoperative skin preparation to reduce the risk of SSIs. The three main types of antiseptics are iodine or iodophor, alcohol, and chlorhexidine gluconate. Iodine and chlorhexidine disinfectants are sometimes mixed with alcohol or aqueous base, which may influence their clinical effectiveness. The techniques used to apply antiseptics may also influence their effectiveness in reducing SSIs.

The current Canadian practices of antiseptic skin preparation vary. The objective of this systematic review is to evaluate the clinical effectiveness of preoperative skin antiseptic preparations and application techniques for preventing SSIs, and assess evidence-based guidelines on their use to help standardize practice.

RESEARCH QUESTIONS

1. What is the comparative clinical effectiveness of preoperative skin antiseptic preparations for preventing surgical site infections?
2. What is the comparative clinical effectiveness of preoperative skin antiseptic application techniques for preventing surgical site infections?
3. What preoperative skin antiseptic preparations and application techniques are recommended in clinical practice guidelines as best practice for preventing surgical site infections?

METHODS

A peer-reviewed literature search was conducted using the following bibliographic databases: PubMed, MEDLINE, Embase, The Cochrane Library, CINAHL, and the University of York Centre for Reviews and Dissemination databases. Grey literature (literature that is not commercially published) was identified by searching relevant sections of the Grey Matters checklist (http://www.cadth.ca/en/resources/grey-matters). Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials (RCTs), non-randomized controlled clinical trials, and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2001, and February 9, 2011. Regular alerts were established to update the search until June 2, 2011.

Two reviewers independently screened citations and selected articles based on the inclusion criteria. The reviewers independently extracted the clinical effectiveness and clinical practice guidelines data and critically appraised selected studies.

SUMMARY OF FINDINGS

Twelve RCTs, nine observational studies, and one evidence-based guideline were included in the review. The results indicated that pre-surgical antiseptic showering is effective for reducing skin flora and SSI rates. The cost-effectiveness of providing patients with antiseptic agents for pre-surgical showering, compared with usual hygiene regimens, is to be determined.

Two RCTs indicated that povidone-iodine (PI) antisepsis was no better than soap and water or saline irrigation for preventing SSIs. Because of the studies' limitations, the effectiveness of PI scrub or scrub and paint compared with soap and water is inconclusive, and more research is needed to determine whether antiseptics are more effective in reducing SSIs than usual hygiene. No similar research was identified using chlorhexidine gluconate (CHG) in place of PI.

Eight clinical trials of varying design compared different antiseptic solutions for SSI reduction. Given the heterogeneity of the studies and the results, conclusions about which antiseptic, if any, is more effective at reducing SSIs cannot be drawn.

Based on limited evidence, the use of iodophor-impregnated incise drapes is effective in reducing wound infections in surgical patients when draping is required, although more research is needed, particularly comparisons of iodophor-impregnated drapes with non-antimicrobial counterparts.

Three RCTs and one retrospective cohort study compared different techniques for applying preoperative skin antiseptics to prevent SSIs. The RCTs found no difference in SSI reduction between paint and scrub compared with paint alone for antiseptic application, and the retrospective study reported a reduction in composite wound infections when scrub with 13% PI solution was used, followed by paint with 10% PI solution, compared with paint with 10% PI solution only.

One evidence-based guideline published in the United Kingdom in 2008 presented recommendations for the prevention and treatment of SSIs. Formal consensus was used in the consideration of all clinical practice and research recommendations. For the most part, the recommendations were consistent with the evidence in this systematic review. One difference was noted in the recommendations on pre-surgical showering because they were based on studies published in 1992 or earlier.

CONCLUSIONS AND IMPLICATIONS FOR DECISION- OR POLICY-MAKING

The evidence suggests that preoperative antiseptic showers are effective for preventing SSIs. The method of antiseptic application is inconsequential, and it is unclear which antiseptic solution is most effective. Disinfectant products are often mixed with alcohol or aqueous base, which makes it difficult to form overall conclusions about an active ingredient. Large, well-conducted RCTs with consistent protocols comparing agents in the same bases are needed, to provide unequivocal evidence regarding the effectiveness of one antiseptic preparation over another for the prevention of SSIs.

ACRONYMS AND ABBREVIATIONS

AE	adverse events
BCC	bacterial colony counts
CDC	Centers for Disease Control and Prevention
CHG	chlorhexidine gluconate
CI	confidence interval
EL	evidence level
IPA	isopropyl alcohol
NICE	National Institute of Clinical Excellence
NNIS	National Nosocomial Infections Surveillance
OR	odds ratio
PI	povidone-iodine
PLC	placebo
RCT	randomized controlled trial
RR	relative risk
SAE	serious adverse event
SSI	surgical site infection

CONTEXT AND POLICY ISSUES

Surgical site infections (SSIs) occur in approximately 2% to 5% of patients who undergo clean extra-abdominal surgeries, such as thoracic and orthopaedic surgery, and in up to 20% of patients who undergo intra-abdominal surgery interventions.[1] SSIs can be responsible for increased morbidity and mortality in some patients after surgery. In addition, they are associated with prolonged hospital stay and greater costs of hospitalization.[1] The Institute for Healthcare Improvement reports that SSIs increase the length of hospital stay by an average of 7.5 days, at an estimated cost of $130 million to $845 million per year in the United States.[2]

The Centers for Disease Control and Prevention (CDC) classify SSIs as being incisional or organ/space.[3] Incisional SSIs are divided into superficial incisional SSIs, involving only skin and subcutaneous tissue, and deep incisional SSIs, involving deeper soft tissues.[3] Organ/space SSIs involve any part of the anatomy other than incised body wall layers that were opened or manipulated during an operation.[3] Common clinical symptoms include tenderness, inflammation, fever, purulent drainage, and presentation of abscess.[3,4]

The development of an SSI depends on the microbial contamination of the surgical site. In most cases, the contamination source is endogenous skin flora, although exogenous contamination may be introduced by surgical staff or through the instruments, or by environmental organisms in a dirty wound.[3,5] The risk of developing an SSI can be increased by the level of contamination, which is described using the classification of surgical wounds (Appendix 1).[5] Because microbial contamination is a requirement for the development of an SSI, prevention techniques are used to minimize the presence and spread of microorganisms at the operative site.

Surgical site infection prevention includes antibiotic prophylaxis, antiseptic prophylaxis, hair removal, perioperative glucose control, and maintenance of perioperative normothermia.[6] Topical antiseptics may be applied to the patient as a preoperative skin preparation to reduce the risk of SSIs. The three main types of antiseptics are iodine or iodophor, alcohol, and aqueous or alcoholic chlorhexidine gluconate.[7] Sometimes, the disinfectants are mixed with alcohol or aqueous base, which may have implications for effectiveness. The antiseptic application techniques also influence the effectiveness of preoperative skin preparation.[7] The considerations include size of area of application, mechanism of application (for example, application in concentric circles), type of instrument used, and timing and duration of application of solution.[3]

CDC guidelines recommend that patients shower or bathe with an antiseptic the night before surgery and that the skin be prepared with “an appropriate antiseptic agent.”[3] A 2008 survey of Alberta doctors revealed that 63% of respondents were not in compliance with CDC guidelines (42% response rate).[8] Current Canadian practices vary. Safer Healthcare Now! faculty recommend cleansing the skin before surgery using no-rinse disposable chlorhexidine gluconate (CHG)-impregnated washcloths.[6] They recommend alcohol-based CHG.[6] Surgical teams should allow at least three minutes for CHG-alcohol solutions to dry before making an incision, or use povidone-iodine (PI) instead. To maximize efficacy, CHG-alcohol skin preparations should not be washed off for at least six hours after surgery.[6]

This systematic review will be used to help standardize practice and inform the development of clinical practice guidelines on preoperative skin antiseptic preparations and application techniques for preventing surgical site infections.

RESEARCH QUESTIONS

1. What is the comparative clinical effectiveness of preoperative skin antiseptic preparations for preventing surgical site infections?
2. What is the comparative clinical effectiveness of preoperative skin antiseptic application techniques for preventing surgical site infections?
3. What preoperative skin antiseptic preparations and application techniques are recommended in clinical practice guidelines as best practice for preventing surgical site infections?

KEY MESSAGE

Available evidence suggests that preoperative antiseptic showers are effective at preventing SSIs. The method of antiseptic application is inconsequential, but the antiseptic of choice is inconclusive.

METHODS

Literature Search Strategy

An information specialist performed the literature search using a peer-reviewed search strategy.

Published literature was identified by searching the following bibliographic databases: MEDLINE with in-process records and daily updates via Ovid; Embase; EBM Reviews — Cochrane Central Register of Controlled Trials 4th Quarter 2010 via Ovid; EBM Reviews — Cochrane Database of Systematic Reviews via Ovid; EBM Reviews — Database of Abstracts of Reviews of Effects 1st Quarter 2011 via Ovid; EBM Reviews — Health Technology Assessment 1st Quarter 2011 via Ovid; CINAHL via EBSCO; and PubMed. The search strategy consisted of controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were preoperative and skin preparation.

Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials (RCTs), non-randomized controlled clinical trials, and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2001, and February 9, 2011. Regular alerts were established to update the search until June 2, 2011. See Appendix 2 for the detailed search strategies.

Grey literature (literature that is not commercially published) was identified by searching relevant sections of the Grey Matters checklist (http://www.cadth.ca/en/resources/grey-matters). Google and other Internet search engines were used to search for additional materials. These searches were supplemented by reviewing the bibliographies of key papers and through contacts with appropriate experts and industry. See Appendix 2 for more information on the grey literature search strategy.

Selection Criteria and Methods

Two reviewers (CK and LM) independently screened citations and selected RCTs, non-randomized studies, and clinical practice guidelines on preoperative skin antiseptic preparations and application techniques for preventing surgical site infections. The decision to order a full-

text article was based on the title and abstract, where available. In cases where there was insufficient information, the article was ordered. Two reviewers (CK and LM) selected articles for inclusion in the review based on full-text publications. A study or guideline was included for review based on the selection criteria that were established before the research was started (Table 1 and Appendix 3). Any disagreement between reviewers was discussed until consensus was reached. The references of HTAs, systematic reviews, and meta-analyses were searched for any trials that could have been missed in the literature search.

Table 1: Selection Criteria

Population	Adult and pediatric patients preparing for thoracic, cardiac, plastic, orthopaedic, neurological, abdominal, or pelvic surgery.
Intervention	Question 1. All three types of preoperative skin antiseptics in various preparations (solution, powder, drape, shower, bathing): • iodophors (PI aqueous or alcohol) • alcohol • CHG (aqueous or alcohol). Question 2. Preoperative skin antiseptic application: Size of area prepared, application of antiseptics in circles using friction, dedicated sterile tool, time allotted for drying of antiseptic, single or multiple applications. Question 3. All of the above.
Comparator	Other antiseptic agents, including combination agents, or PLC.
Outcomes	Primary: SSI (for example, pus, swelling, pain, redness, or heat) Secondary: reoperation, bacterial colony counts, antibacterial treatments Adverse events and mortality Guideline recommendations
Study design	RCTs, non-randomized studies, evidence-based clinical practice guidelines.

CHG = chlorhexidine gluconate; PI = povidone-iodine; PLC = placebo; RCT = randomized control trial; SSI = surgical site infection.

Exclusion Criteria

Studies were excluded if they did not meet the selection criteria; had an incomplete methods section; presented preliminary results in abstract form; were duplicate publications, narrative reviews, or editorials; or were published before 2001.

Data Extraction Strategy

Two reviewers (CK and LM) piloted data extraction forms before the research began. In addition, they independently extracted the clinical effectiveness and clinical practice guidelines data for each article using data extraction forms to tabulate relevant characteristics and outcomes from the included studies. A calibration exercise using one RCT and one non-randomized study was undertaken to ensure consistency between reviewers. A template of the form that was used for data extraction appears in Appendix 4.

Critical Appraisal of Individual Studies

Two reviewers (CK and LM) independently evaluated the quality of RCTs and non-randomized studies using a Downs and Black instrument[9] that was modified to include the source of funding for studies. The methodological quality of clinical effectiveness evidence was assessed based on randomization, adequate concealment of randomization, degree of blinding, use of intention-to-treat analysis, and description of dropouts and withdrawals, where appropriate. A numeric score was not calculated for each study. Instead, the strengths and weaknesses were described. The Appraisal of Guidelines for Research and Evaluation (AGREE) instrument[10] was used to appraise clinical practice guidelines. The domains assessed were scope and purpose, stakeholder involvement, rigour of development, clarity and presentation, applicability, and editorial independence. These domains are described in Appendix 5. Any disagreements were resolved through discussion until consensus was reached. A calibration exercise to ensure consistency between reviewers was performed using one RCT and one non-randomized study. The template forms used for study quality assessment appear in Appendix 6.

Data Analysis Methods

Because of clinical heterogeneity across the selected studies, a formal meta-analysis was not conducted. The studies are described using a narrative approach in response to each research question.

RESULTS

Quantity of Research Available

The electronic literature search and updates yielded 1,240 citations. After screening titles and abstracts, 1,176 citations were excluded, and 64 potentially relevant articles were retrieved for full-text review. An additional 10 potentially relevant reports were identified through grey literature and handsearching. Of the 74 potentially relevant reports, 52 reports did not meet the inclusion criteria. This review included 22 publications. The study selection process is presented in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart (Appendix 7).[11] The included and excluded studies are listed in Appendices 8 and 9, respectively.

Of the 22 publications included in this review, 18 report on the comparative clinical effectiveness of preoperative skin antiseptic preparations, four report on application techniques, and one evidence-based guideline reports on best practice for preventing surgical site infections (one study examined comparative clinical effectiveness and application techniques). Overall, 12 RCTs, eight cohort studies, one case-control study, and one guideline were reviewed. The study characteristics, critical appraisal, and data analysis and synthesis of the selected studies are presented separately for each research question.

1. Clinical effectiveness of preoperative skin antiseptic preparations for preventing surgical site infections

Eighteen studies on the comparative clinical effectiveness of preoperative skin antiseptic preparations were categorized under the headings of pre-surgical showers, antiseptic preparation compared with hygiene, comparison of antiseptics, and draping. The study characteristics, critical appraisal, and results appear in Appendices 11, 12, and 13, respectively.

Pre-surgical Showers

Study characteristics

The clinical effectiveness of pre-surgical showers was reported in two RCTs and four cohort studies published between 2007 and 2010.[12-16] Four studies were conducted in hospitals in Brazil,[12,13] Turkey,[14] and the United States,[15,17] and one was conducted in a clinic in the United States.[16] The sample sizes ranged from 82[14] to 1,054[15] patients.

Patient characteristics

Two studies involved plastic surgery,[12,13] while the others involved abdominal,[14] orthopaedic knee[17] or hip arthroplasty,[15] or pelvic artificial urinary sphincter implant surgery.[16] The mean ages cited in four studies were 38 years,[12,13] 58 years,[15] and 63 years.[17] The remaining two studies reported age using different measures (median of 74 years in one study,[16] and 50% of patients greater than 51 years of age in another[14]). All urinary sphincter patients were male,[16] 50% of those undergoing orthopaedic hip and abdominal surgery were male,[14,15] one-third of orthopaedic knee patients were male,[17] and 80% of plastic surgery patients were female.[12,13]

Interventions and comparators

In one RCT, patients who underwent surgery after showering with 10% liquid PI detergent were compared with those who did not receive specific instructions about bathing before surgery.[12] All other studies considered a CHG preparation compared with placebo,[13] control,[13,14] non-compliance,[15] or usual hygiene.[16] In one study, patients who showered with 4% CHG were compared with those who showered with placebo containing no active ingredient, or with controls who were given no showering instructions.[13] In two cohort studies, patients using 2% CHG-impregnated cloths the night before and the morning of surgery were compared with patients who did not complete skin preparation.[15,17] In another cohort study, patients who showered with CHG soap upon admission and the night before surgery were compared with those who performed usual hygiene.[14] In a single surgeon cohort study, twice daily, five-day topical 4% CHG scrub was compared with usual hygiene.[16]

Outcomes

Skin colonization was reported in both RCTs[12,13] and in one cohort study,[16] and SSIs were reported in both RCTs[13,14] and in three cohort studies.[14,15,17] Bacterial colony counts were reported pre- and post-shower in one RCT,[12] post-operatively in another RCT,[13] and after disinfection and post-surgery in a cohort study,[16] and bacterial types were described in another cohort study.[14] One RCT and one cohort study reported SSI for up to 30 days, based on CDC criteria;[13,14] one cohort study reported deep SSIs, based on CDC criteria, occurring within a year of surgery;[17] one RCT reported SSI by observation;[12] and one cohort study reported SSI based on the National Nosocomial Infections Surveillance (NNIS).[15]

Critical appraisal

One RCT provided detailed patient information, described adverse reactions, and reported on patients lost to follow-up.[13] Five studies did not report adverse events and patients lost to follow-up.[12,14-17] Four of these studies[12,14,16,17] also did not disclose the source of funding. All trials reported study objectives, patient characteristics, main outcome measures, and estimates of variability in outcome measures.[12-17] Distributions of principal confounders in each group of patients were also described in all studies.[12-16] All studies were compromised in terms of

external validity because they did not identify how patients were selected from the source population[12] or the participation rate.[12-16] One study was conducted in a military medical academy and may not represent the treatment that similar patients might receive.[14] All studies were clear about unplanned data analysis, all reported the same time between intervention and outcome among groups, and five provided statistical analyses.[12-16] One study[17] did not perform any statistical analysis and did not describe whether results were statistically significant. Internal validity was compromised by a lack of blinding of patients[12,14-17] and assessors.[14-17] Compliance was an issue in two studies[15,17] in which patients were using CHG cloths and the non-compliant group served as controls. All studies reported the selection of patients in different intervention groups from a common population over the same period,[12,13,15,16] except the time period cohort study.[14] Both RCTs reported the randomization of patients into intervention groups,[12,13] and one used an appropriate method of randomization and concealed allocation.[13] Three studies did not adjust for confounding,[12,13,15] and five did not account for losses to follow-up.[12,14-17]

Data analyses and synthesis

Colonization

Skin colonization was reported in two RCTs[12,13] and one cohort study.[16] The RCTs reported that pre-surgical showering with PI[12] or CHG[13] is effective in reducing skin colonization. One PI shower patient (1.8%) and 12 patients who received no showering instruction (21%) had *Staphylococcus aureus*-positive post-shower skin cultures (P = 0.0019, 95% CI not reported).[12] One CHG patient, two placebo patients, and four control patients had *S. aureus*-positive abdominal skin cultures after showering ($\chi^2 = 2.10$, P = 0.35).[13] Twice daily, five-day topical 4% CHG antimicrobial scrubbing reduced preoperative perineal colonization four-fold compared with usual hygiene for patients in a cohort undergoing artificial urinary sphincter placement [odds ratio (OR) 0.24, 95% confidence interval (CI) 0.08 to 0.65].[16]

Infection

SSIs were reported in two RCTs[12,13] and three cohort studies.[14-16] Two RCTs suggest there is no difference in postoperative infection rates between patients who undergo pre-surgical showering with PI[12] or CHG[13] compared with patients who receive no showering instructions,[12] patients who receive PLC, or control.[13] No SSIs were observed in PI or control patients.[12] Superficial SSIs were observed in one (2%) CHG patient, one (2%) PLC patient, and zero (0%) control patients ($\chi^2 = 1.01$, P = 0.6).[13] Two cohort studies report no infections in patients who washed with CHG-impregnated cloths (0%) compared with patients who were not compliant with skin preparation (1.6%, P = 0.231 for hip arthroplasty; 3.0%, no P-value reported for knee surgery).[15,17] In one study, SSIs were reported in three (7%) and 10 (25.6%) CHG and control patients, respectively, after abdominal surgery (OR 4.76, 95% CI 1.2 to 18.8, P = 0.026).[14] No SSIs were noted in CHG scrub recipients. One SSI was reported in a patient who performed usual hygiene before undergoing artificial urinary sphincter placement.[16]

Adverse events

All patients in one RCT completed 30-day follow-up, and none experienced an adverse reaction.[13] No other studies reported adverse events.

Antiseptic Preparation Compared with Hygiene

Study characteristics

The clinical effectiveness of antiseptic preparation compared with hygiene for reducing SSIs was reported in two RCTs published in 2001 and 2005.[18,19] One study was conducted in a hospital in Nigeria[18] and the other in a hospital in Iran.[19] The sample sizes were 200[18] and 1,810,[19] respectively.

Patient characteristics

One study involved clean elective hernia repair[18] and the other involved clean plastic surgery.[19] The mean age of patients was 33 years.[19,20] Of the hernia patients, 91% were male,[18] and 64% of plastic surgery patients were female.[19]

Interventions and comparators

One RCT studied PI scrub and paint compared with soap scrub and paint with methylated spirit,[18] and the other compared PI scrub and paint with saline irrigation.[19] All patients in the study that compared PI with saline underwent a pre-surgical shower with soap and water two hours before surgery.[19]

Outcomes

Skin colonization was reported in both RCTs.[18,19] Patients undergoing hernia repair were followed up by one of the investigators five to 10 days post-operatively, and again four to eight weeks later.[18] Those who underwent plastic surgery procedures were followed for up to one month.[19] A diagnosis of SSI was based on swelling, redness, discharge, and wound dehiscence in one study,[19] and redness of the wound or purulent discharge in the other RCT.[18]

Critical appraisal

Both RCTs described the objective of the study, characteristics of included patients, main outcome measures, confounders, and findings.[18,19] The RCT comparing PI with soap and methylated spirit did not report the strength or source of PI.[19] In both studies, the time between intervention and outcome assessment was the same between groups, statistical tests were described, and compliance with interventions was high.[18,19] Neither study reported adverse events, characteristics of patients lost to follow-up, or source of funding.[18,19] The external validity is weak because study participants may not be representative of the recruited population.[18,19] The internal validity is compromised because one study used an inappropriate method of randomization.[19] Neither study tried to blind patients or assessors, or conceal allocation.[18,19] It is unclear whether confounding factors and losses to follow-up were accounted for, or whether these studies had an appropriate sample size for detecting a clinically meaningful difference between groups.[18,19]

Data analyses and synthesis

Colonization

Neither RCT reported bacteria colony counts.

Infection

Both RCTs reported that SSI rates were the same in patients who received PI antiseptic skin preparation and in those who were prepared using soap and methylated spirit or saline.[18,19] SSIs were reported in six (5.9%) PI patients and five (5.1%) soap and methylated spirit patients after hernia repair (P = 1.000).[18] The RCT involving patients undergoing plastic surgery procedures reported that no patients developed SSIs.[19]

Adverse events

Neither study reported adverse events.

Comparison of Antiseptics

Study characteristics

The clinical effectiveness of one antiseptic preparation compared with another for reducing bacterial colonization and SSIs was reported in five RCTs, two cohort studies, and one case-control study published between 2002 and 2011.[20-27] The studies were conducted in hospitals in Thailand,[21] Kuwait,[22] Brazil,[23] Israel,[25] and the United States.[20,24,26,27] The sample sizes ranged from 133[27] to 1,621.[26]

Patient characteristics

Studies involved urological,[22] plastic,[23] cardiac,[20] pelvic,[25] general,[26] orthopaedic,[27] and mixed[21,24] surgeries with clean,[23] clean-contaminated,[24] and mixed wound types.[21,26] Four studies[20,25,27,28] did not state the wound classification, although it may be implicit in the surgery performed. The mean age of patients who were included in the studies ranged from 50[21] to 61 years.[20] Most mixed-surgery, urology, and cardiac patients were male,[20-22,24] and most pelvic, orthopaedic, and general surgery patients were female.[25-27]

Interventions and comparators

Among two-armed studies, interventions included 2% CHG with 70% isopropyl alcohol (IPA) scrub,[24] PI scrub, and paint,[21,25] scrubbing three times with CHG-cetrimide,[22] and 0.5% CHG paint.[23] Comparators included 10% aqueous PI scrub, then paint;[24] 4% CHG with 70% isopropyl (IPA) scrub, then paint;[21] scrubbing twice with CHG-cetrimide scrub, then with PI scrub;[22] and 2% CHG scrub, then 70% alcohol paint.[25] One RCT[20] compared four interventions: PI paint, PI scrub and paint, one-step iodophor and alcohol film, and one-step iodophor and alcohol water-insoluble film with iodine-impregnated incise drape. A cohort study included iodine and DuraPrep (iodine povacrylex in IPA), iodine only, CHG, and other antiseptics.[27] Another cohort study compared iodine povacrylex in isopropyl alcohol with 2% CHG and 70% IPA scrub or PI scrub and paint.[26]

Outcomes

Skin colonization was reported in three RCTs.[21-23] SSIs were reported in seven of eight studies.[20,21,23-27] A diagnosis of SSI was based on CDC criteria in plastic,[23] pelvic,[25] orthopaedic,[27] general,[26] and mixed-surgery patients.[24]

Critical appraisal

All studies reported study objectives and main outcome measures.[20,21,23-27,29] All but one study described confounders.[23] Most studies did not report the characteristics of patients lost to follow-up[20-24,26] or adverse events.[20,22,23,25-27] The staff and facilities where patients were treated in these RCTs were representative of treatment that most patients in the source population would receive, but external validity is compromised because participation rates were not reported.[20-24] The external validity of the cohort studies was sound.[25-27] The studies had good internal validity because the time between intervention and outcome was the same for intervention and control groups, statistical methods were described, compliance with interventions was high, and main outcomes were accurate and reliable.[20-25,27] There is potential for selection bias in that it is unclear whether confounding factors[20,23] and losses to follow-up were accounted for in the analyses.[20-23] Selection bias may occur in cohort studies, because patients are not randomized and allocation is not concealed.[25-27] Five of eight studies did not provide power calculations.[21-23,25,27]

Data analyses and synthesis

Colonization

Three RCTs reported that bacterial colonization was reduced in patients who underwent antiseptic preoperative cleansing with CHG[21,23] or CHG with PI.[22] A statistically significant reduction in bacterial colonization was noted in patients prepared with 4% CHG in 70% isopropyl alcohol compared with patients prepared with PI (14.4% compared with 31.2%, RR 2.69, 95% CI 2.15 to 3.55).[21] In Kehinde et al.'s RCT, patients who were scrubbed with CHG-cetrimide had a higher proportion of positive cultures post-surgery compared with those receiving PI (11.4% compared with 2.6%, $P < 0.001$).[22] A higher number of patients developed bacteremia or septicemia among those prepared for surgery with CHG-cetrimide only, compared with those who were also scrubbed with PI (eight [7.1%] compared with three [2.6%], $P < 0.01$).[22] In another RCT, post-operative *Staphylococcus* species colony counts were 2.7 ± 26.9 and 7.9 ± 45.5 for CHG compared with PI, respectively (PI > CHG, $z = 2.72$, $P = 0.006$).[23] Post-operative *S. aureus* colony counts were 7.8 ± 46.1 and 17.6 ± 64.7 for CHG compared with PI, respectively (PI > CHG, $z = 2.45$, $P = 0.014$).[23]

Infection

Three RCTs and a cohort study reported reduced SSI rates in CHG-prepared patients compared with PI-prepared patients, but in one case this difference was not statistically significant.[21,23-25] In a study of surgical-site antisepsis, the relative risk of SSI in patients receiving CHG-alcohol compared with those receiving PI was 0.59 (95% CI 0.41 to 0.85).[24] In Paocharoen et al.'s study, the group receiving preoperative CHG skin antisepsis had a statistically significant reduction in the risk of SSI compared with the group receiving PI [relative risk (RR) 1.61, 95% CI 1.40 to 1.81].[21] Two cohort studies suggest that PI is more effective than CHG for reducing SSIs.[26,27] In particular, Swenson et al. reported that patients who were prepared for surgery with CHG had statistically significant higher rates of infection ($P = 0.01$) due to a higher rate of superficial incisional infection (3.2% compared with 5.4% compared with 3.3% for PI, CHG, and iodine povacrylex, respectively, $P = 0.019$).[26] In another study, Boston et al. reported that, based on findings from a multivariable logistic regression analysis of risk factors for case and control patients undergoing spinal surgery at a hospital, the use of PI alone was protective against SSIs (OR 0.16, 95% CI 0.06 to 0.45, $P < 0.001$).[27] In Segal et al.'s study, a statistically significant difference in SSI rates was not observed between patients receiving PI

paint, PI scrub and paint, film only, or film and drape preparations (χ^2 = 5.889, P = 0.117). In a secondary analysis, the two aqueous iodine groups (PI paint, and PI scrub and paint) and the two insoluble iodine groups (one-step film, and film with incise drape) were combined, showing reduced SSI in the insoluble iodine group (χ^2 = 5.3, P = 0.02). A statistically significant correlation was found between skin preparation and rate of infection (Pearson product moment correlation, r = 0.160, P = 0.05).

Adverse events

Darouiche et al. reported four deaths (1.0%) not due to infection in the CHG group, and three (0.7%) in the PI group related to sepsis due to organ/space infection. Three patients (0.7%) in each group had pruritis, erythema, or both around the wound. No fire or chemical skin burns occurred in the operating room.[24] Skin irritation was reported in two PI patients (0.8%) in Paocharoen et al.'s[21] study. Adverse events were not reported in three RCTs and three cohort studies.[20,22,23,25-27]

Incise Drapes

Two RCTs[20,30] and one retrospective observational study[31] focused on the use of iodophor-impregnated incise drapes in preventing surgical wound infection.

Study characteristics

Patient population

One RCT[20] and one retrospective cohort study[31] took place in hospitals. One RCT[30] was performed in a clinic. Two studies[20,30] were based in the United States, and one[31] was conducted in Japan.

Surgery

One RCT[30] involved patients undergoing primary or revision total hip or knee arthroplasty, one[20] included patients undergoing coronary artery bypass graft surgery, and the cohort study[31] examined patients who underwent liver resection for hepatocellular carcinoma. All surgeries in the cohort study[31] were classified as clean-contaminated, and the other two studies[20,30] did not report surgical wound classification.

Interventions and comparators

One study[30] investigated the use of iodophor-impregnated surgical incise drapes (Ioban 2 drapes) in combination with DuraPrep (iodine povacrylex) or a PI-impregnated skin preparation tray.

Two studies compared surgeries with and without the use of iodophor-impregnated drapes. In one study,[20] each surgical site was prepared with a one-step iodophor and alcohol (0.7% available iodine in 74% IPA) water-insoluble film alone or in combination with an iodophor-impregnated drape. In the second study,[31] patients were prepared with iodophor solutions before the application of iodophor-impregnated drapes (Ioban 2), but the application method and strength of the iodophor skin-preparation solutions were not described.

Outcomes

All studies reported infection based on defined clinical criteria, although one[31] study excluded wound infections associated with intra-abdominal infections, because they may have been the cause of the wound infection. One study[30] reported on bacterial cultures based on two wound-edge swabs taken immediately before wound closure. All studies met the CDC-recommended[3] 30-day follow-up period, with one study[20] following up for six weeks.

Critical appraisal

Two studies[20,30] were RCTs. One study[20] described the method of randomization. Both RCTs reported blinding of outcome assessors and performed power calculations to determine the number of patients required to detect clinically important differences in SSI rates. One study[30] included only first- and second-case patients of the day. These patients and their treatment may not be representative of the general population or the treatment they would receive. This study did not report the outcomes of all randomized patients, and patients who were lost to follow-up were not described. One retrospective cohort analysis[31] lacked randomization and blinding. In this study, data were drawn from a large sample of patients who were representative of the general population, but the exclusion of intra-abdominal infections was not considered in the analysis and may have affected the reported results.

Data analyses and synthesis

Wound contamination

One study[30] reported on surgical wound culture growth and found no difference in the number of patients with positive cultures among those prepared with DuraPrep and Ioban 2 drapes (28%) and those prepared with PI solution and Ioban 2 drapes (36.4%, 95% CI −22.4% to 5.6%).

Infection

When comparing the number of SSIs among patients who were prepared with DuraPrep with those prepared with PI solution in combination with iodophor-impregnated drapes, one study[30] found no statistically significant difference (no SSIs were reported in either group). Similarly, one study[20] found no statistically significant difference in the number of SSIs among patients prepared with a one-step iodophor and alcohol water-insoluble film with or without iodophor-impregnated drapes (2% without drape compared with 5.9% with drape, 95% CI not reported). In contrast, one study[31] found statistically significant lower rates of wound infection with the use of Ioban 2 drapes compared with surgeries without drape use (12.1% without drape compared with 3.1% with drape, P = 0.0096; multiple regression analysis regression coefficient −0.075 for drapes, 95% CI −0.139 to 0.011).

Adverse events

One study[30] reported adverse events in nine patients (11%) prepared with DuraPrep and eight (9.1%) receiving PI. A total of 11 serious adverse events (SAEs) were recorded across both groups, and none were judged by the investigators to be treatment related. One study[31] reported no evidence of allergic reaction among patients and did not report on other adverse events. The third study did not report on adverse events.

Table 2: Clinical Effectiveness of Preoperative Skin Preparations

Intervention	Evidence	Results
Pre-surgical showering	2 RCTs, 4 cohort studies	Pre-surgical antiseptic showering is effective for reducing skin flora and SSI rates
Antiseptic versus hygiene	2 RCTs	PI antisepsis is no better than soap and water or saline irrigation for preventing SSIs
Choice of antiseptic	5 RCTs, 2 cohort, 1 case-control	Antiseptic choice is unclear because of mixed results on comparative effectiveness
Incise drapes	2 RCTs, 1 cohort	Iodophor-impregnated drapes appear effective for reduction of SSI rates

RCT = randomized controlled trial; SSI = surgical site infection

2. Clinical effectiveness of preoperative skin antiseptic application techniques for preventing surgical site infections

Three RCTs[20,32,33] and a retrospective cohort study[34] published between 2002 and 2011 compared different techniques for applying preoperative skin antiseptics to prevent surgical site infections. The study characteristics, critical appraisal, and results appear in Appendices 11, 12, and 13, respectively.

Study characteristics

Patient population

All four studies were performed in hospitals. Three studies were conducted in the United States[20,33,34] and one[32] took place in Jordan.

Surgery

One study[20] involved patients undergoing coronary artery bypass graft surgery, two[33,34] involved abdominal surgery, and one[32] included all patients undergoing elective and emergency operations (excluding anorectal surgery). More than one classification[32,33] of surgical wounds was included in the patient population, or classification was not reported.[20,34]

Interventions and comparators

Three studies compared a PI scrub followed by a PI paint protocol with PI paint alone. In one study,[33] patients underwent a five-minute scrub using sponges saturated with PI (0.75% available iodine), followed by painting of the operative site with aqueous PI (1.0% available iodine). Patients who were randomized to the paint-only arm were subject to the painting step only. The second study[20] compared a five-minute PI scrub followed by paint with painting alone, but did not report on the application method or solution strength. In the third study, patients underwent a three-minute scrub using the sponge side of a surgical scrub brush saturated with 13% PI solution, followed by painting with 10% PI solution.[34] Patients undergoing Caesarean section before protocol revision received painting with 10% PI only.[34]

One study[32] compared a 10-minute scrub with 0.75% CHG and 1.5% cetrimide, followed by an application of 1% iodine in 70% alcohol, with painting with the CHG-cetrimide solution, followed by iodine paint.

Outcomes

All studies reported infections based on defined clinical criteria. Three studies[20,33,34] met the CDC-recommended[3] 30-day follow-up time for measuring SSI (one study[20] followed patients for six weeks). One[32] did not report the length of follow-up.

Critical appraisal

Two[20,33] of the three studies that were randomized trials reported the method of randomization. One study[20] reported the blinding of outcome assessors, but blinding was not reported in the other two.[32,33] None of the studies reported on patient withdrawals or losses to follow-up, which may compromise internal validity due to attrition bias. In two studies,[20,33] power calculations were performed before the research began, to determine the number of patients required to detect clinically important differences in SSI rates. The retrospective cohort study included a large sample of patients who were representative of the general population, but there was no randomization or blinding in this study.[34]

Data analyses and synthesis

Infection

All four studies reported on SSI rates. One study[32] comparing CHG scrubbing with painting observed similar numbers of infection in each group. Three studies compared a PI scrub and paint protocol with painting alone. One[20] did not find a statistically significant difference in the number of patients with an SSI between the interventions (12.5% of paint-only patients compared with 13.5% of scrub and paint patients). The second study[33] differentiated between wound and intra-abdominal infection, finding no statistically significant difference in either outcome (3% of paint-only patients, compared with 2% of scrub and paint patients, experienced intra-abdominal infection; 10% of each group had a wound infection). In each case, $P > 0.05$, but the 95% CI was not reported. The retrospective cohort study reported that scrub and paint was associated with a 38% reduction in major puerperal infection (incident rate ratio 0.62, 95% CI 0.42 to 0.93, $P = 0.2$) and a 31% reduction in composite wound infection (incident rate ratio 0.69, 95% CI 0.50 to 0.96, $P = 0.03$) compared with paint alone.[34]

Adverse events

None of the included studies reported on patient adverse events.

Table 3: Clinical Effectiveness of Antiseptic Application Techniques

Intervention	Evidence	Results
Paint versus scrub for antiseptic application	3 RCTs, 1 cohort	Based on RCT data, no difference in SSI reduction due to application technique. One cohort study found scrub and paint protocol reduces composite wound infection.

RCT = randomized controlled trial; SSI = surgical site infection.

3. Clinical practice guidelines for preventing surgical site infections

Clinical practice guideline characteristics

In 2008, the National Collaborating Centre for Women's and Children's Health[5] published clinical guidelines for the prevention and treatment of surgical site infection. The guidelines were developed according to the National Institute for Clinical Evidence (NICE) process.[35] Guidelines

were formulated based on a systematic literature review, and stakeholder organizations were invited to submit additional evidence for consideration.

Literature searches were not date specific and were conducted between September 2007 and April 2008. Evidence published after this date was not included in the guidelines. Only studies published in English were considered for inclusion, and there was no systematic attempt to search grey literature or perform handsearching. Evidence supporting each recommendation was graded. A summary of the evidence grading system appears in Appendix 10. Formal consensus methods were used to consider all clinical care recommendations and research recommendations. The strength of each recommendation was not reported.

Critical appraisal of clinical practice guidelines

One guideline[5] had a defined scope and purpose that represented the views of its intended users. Guidelines were developed based on a systematic literature review. Recommendations for antiseptic skin preparation were based on evidence from RCTs, although it was unclear whether additional tools were developed for implementation. Potential organizational barriers to guideline implementation were not discussed. Conflict of interest statements were not provided for all guideline development members, and editorial independence from the funding body was not stated, which creates a moderate risk of bias. AGREE[10] domain appraisal is summarized in Table 4. The domains are described in Appendix 5. Overall, the guideline is of high quality and suitable for use in practice, although it was produced by a UK organization and the recommendations may not be generalizable to a Canadian health care context.

Table 4: Critical Appraisal of NICE Clinical Practice Guideline[5]

Domain	Appraisal
Scope and purpose	Objectives and clinical questions are defined, but specific patient populations to whom the recommendations apply are unclear.
Stakeholder involvement	Target users of the guideline are defined, guideline development group includes members of relevant professional groups, and patient input has been sought. Recommendations have not been pilot tested among target users.
Rigour of development	Evidence was gathered using systematic literature review, and selection criteria and methods for recommendation formulation were described. Explicit links have been drawn between evidence and recommendations, guideline was externally peer reviewed, and updating procedures are provided.
Clarity and presentation	Recommendations are identifiable, specific, and unambiguous. It was unclear whether additional tools were developed for effective guideline implementation.
Applicability	Potential cost implications for, but not organizational barriers to, recommendation application have been considered.
Editorial independence	Conflict of interest statements provided for some, but not all, guideline development members. No statement about editorial independence from the funding body.

NICE = National Institute for Clinical Evidence.

Data analyses and synthesis on best practice

The guideline[5] identified one systematic review of six RCTs examining the evidence for preoperative bathing or showering with antiseptics for the prevention of SSIs. The meta-analysis of two RCTs showed a reduction in SSIs after CHG showering compared with no shower, and the meta-analysis of five RCTs showed no difference in showering with CHG compared with detergent or bar soap. No evidence was available on the recommended number of preoperative

showers. Based on this evidence (Evidence Level [EL] 1+), the guideline recommends advising patients to shower or bathe using soap the day before or the day of surgery.

The guideline identified one systematic review (six trials) and four RCTs examining the effects of preoperative skin antiseptics for SSI prevention. The analysis of RCTs (EL 1+) showed insufficient evidence to recommend a particular antiseptic formulation (CHG compared with PI compared with alcohol). The meta-analysis of two RCTs (EL 1+) showed no difference in SSI rate between scrub and paint of aqueous PI compared with paint alone. Preparation of the skin at the surgical site immediately before incision using an aqueous or alcohol-based antiseptic preparation of PI or CHG was recommended based on available evidence.

The included guideline presented evidence from one systematic review of five trials and an RCT that suggested that the use of non-iodophor-impregnated incise drapes increases the risk of SSI (EL 1+). Available evidence indicated there is no difference in risk of SSI between iodophor-impregnated drapes and no incise drape (EL 1+). The guideline recommends against the routine use of non-iodophor-impregnated incise drapes. If an incise drape is required, iodophor-impregnated drapes are recommended, unless the patient has an iodine allergy.

Table 5: NICE Clinical Practice Guidelines[5]

Recommendation	Evidence Level
"Advise patients to shower or have a bath (or help patients shower, bath, or bed bath) using soap, either the day before, or on the day of, surgery" (page 25)	1+
"Prepare the skin at the surgical site immediately before incision using an antiseptic (aqueous or alcohol base) preparation: povidone-iodine or chlorhexidine are most suitable" (page 60)	1+
"Do not use non-iodophor-impregnated incise drapes routinely for surgery as they may increase the risk of surgical site infection" (page 53)	1+
"If an incise drape is required, use an iodophor-impregnated drape unless the patient has an iodine allergy" (page 53)	1+

NICE = National Institute for Clinical Evidence.

DISCUSSION

Summary of Evidence

This review on preoperative skin antiseptic preparations and application techniques summarizes clinical trial data and recommendations from 21 clinical studies and one evidence-based clinical practice guideline.[5,12-27,30-34] Eighteen studies on the comparative clinical effectiveness of preoperative skin antiseptic preparations provided information about pre-surgical showers,[12-17] and antiseptic preparation compared with hygiene,[18,19] antiseptics,[20-27] and draping.[20,30,31] Three RCTs and one cohort study compared different techniques for applying preoperative skin antiseptics.[20,32-34]

Two previous systematic reviews[36,37] examined the effectiveness of pre-surgical showering on the reduction of skin flora and SSIs. The findings in these reviews were mixed. One[36] found no evidence of the benefit of pre-surgical bathing with CHG, and the other[37] found CHG bathing to be effective at reducing skin flora. These reviews were based on literature published before 2001. This review, which is based on more recent clinical trials, supports the idea that pre-surgical showering with CHG is effective for reducing skin flora and SSIs. In one included study, PI was used as a pre-surgical showering solution, and two studies compared PI surgical site

preparation with soap and water or saline wound irrigation. None of these studies found a reduction in SSIs with PI use. Current UK clinical practice guidelines[5] found that CHG showering or bathing reduces SSIs, but is no more effective than soap and water.

Current Canadian practice is guided by the Safer Healthcare Now! "Preventing Surgical Site Infection" bundles,[6] which recommend the use of CHG in alcohol for infection prevention. In this review, no conclusions could be drawn about which surgical site antiseptic is more effective for reducing SSIs. A meta-analysis was not possible because of the heterogeneity of antiseptic preparations and surgery types among the studies. These mixed results are in contrast to two systematic reviews[38,39] that suggest CHG is more effective than PI for skin disinfection before surgery. These previous reviews consider some studies that were excluded from this review based on a lack of post-operative assessment, or inappropriate population or procedures of interest (Bibbo,[40] Ostrander,[41] Culligan,[42] and Saltzman[29]). However, the findings of this systematic review agree with those of a previous review[43] that indicates there is insufficient evidence to support one antiseptic over another, and those of a clinical practice guideline[5] that recommends the use of CHG or PI for preoperative skin preparation. The Safer Healthcare Now! guidelines[6] were not included in this review, because they were not based on a systematic literature search.

Three studies[20,30,31] described the use of iodophor-impregnated incise drapes. They agree with current evidence-based clinical practice guidelines,[5] published in the UK, in finding that the use of iodophor-impregnated incise drapes reduces the rate of SSI. The guideline also recommends against the use of non-antimicrobial drapes, but no studies making that comparison were identified for inclusion in this review.

Preoperative skin antiseptics were applied in a variety of ways (for example, scrubbing, painting, or combination) across all studies included in this review. Four studies[20,32-34] directly compared the effectiveness of different application methods. Evidence from three RCTs indicates that the application method is not a crucial factor in reducing SSI rates in surgical patients, and this finding is consistent with clinical practice guidelines[5] that found no difference between PI scrub and paint and paint alone. One large retrospective cohort study suggests scrub and paint reduced composite wound infection after Caesarean section by 31% compared with paint alone.[34]

One clinical practice guideline[5] based on a systematic literature review provided recommendations for the prevention and treatment of surgical site infection in the UK. These guidelines were partly based on some of the studies that were included in this review and are consistent with our findings, with the exception of the recommendations rergarding pre-surgical showering. This difference is likely due to the fact that there was no overlap in studies, because the guideline recommendations were based on a meta-analysis of trials that were published in 1992 or earlier.

Limitations

Overall, the studies were of varying quality. Evidence was drawn from a mix of RCTs and non-randomized trials, although the method of randomization was generally poorly reported. Efforts were made to blind outcome assessors, but patients and surgeons often were not blinded, thus compromising internal validity. Studies included a spectrum of surgical procedures and wound classifications, so the ability to form generalizations for all patients undergoing surgery is limited. Interventions and comparators were not always well described, and antisepsis methods varied from study to study. This limits the ability to draw conclusions about specific solution strengths

and protocols, but does provide a picture of the effectiveness of each antiseptic. However, disinfectant products are sometimes mixed with an alcohol or an aqueous base. Because alcohol has antiseptic properties, this makes it difficult to perform direct comparisons and draw overall conclusions about a particular disinfectant.

This review examines the evidence on the clinical effectiveness of pre-surgical antiseptic skin preparation solutions and application techniques. The adverse events related to antiseptic choice were considered in this review, but not every included study reported this outcome. This review, therefore, does not address the safety related to each skin preparation method, nor does it consider cost-effectiveness, which may be of interest when establishing clinical protocols. Safety issues will be addressed in a supplementary report. Because no Canadian trials were identified for inclusion in this review, generalizability to a Canadian health care context may be limited.

CONCLUSIONS AND IMPLICATIONS FOR DECISION- OR POLICY-MAKING

Pre-surgical Showers

In this review, results show that pre-surgical antiseptic showering is effective for reducing skin flora and SSI rates. However, because CHG was primarily used as the antiseptic agent with varying showering regimens and compliance rates in the included trials, more research is needed to determine the optimal preparation (solution, strength, cloth), number, and timing of applications. The cost-effectiveness of providing patients with antiseptic agents for pre-surgical showering, compared with usual hygiene regimens, is to be determined.

Antiseptic Preparation versus Hygiene

Two RCTs[18,19] indicated that PI antisepsis was no better than soap and water or saline irrigation for preventing SSIs. Patients and outcome assessors were not blinded in either study, and neither study reported whether it was adequately powered to detect clinically relevant differences. Because of these limitations, estimates of the effectiveness of PI scrub or scrub and paint compared with soap and water are inconclusive, and more research is needed to address this question. No similar research was identified using CHG in place of PI.

Comparison of Antiseptics

Eight clinical trials of varying design compared different antiseptic solutions for SSI reduction.[20-27] The direct comparison of each study is difficult because of heterogeneity in antiseptic preparation, application technique, patient population, and study design. Data from three trials,[21,24,25] including one well-designed RCT,[24] indicated CHG as a preferred antiseptic agent over PI. Two trials,[26,27] including a large cohort study,[26] showed PI to be more effective than CHG at reducing surgical site infections, and one[22] found that the addition of PI in combination with CHG resulted in longer and more effective skin disinfection, compared with CHG alone. One study[23] found no statistically significant difference in SSI rates between CHG and PI, but recommended CHG based on lower post-surgical bacterial counts. One study[20] compared aqueous iodine with insoluble iodine, finding that insoluble iodine film more effectively reduces SSI. One clinical practice guideline[5] recommends the use of CHG or PI for preoperative skin preparation. Given the heterogeneity of the studies and the results, conclusions cannot be drawn about which antiseptic, if any, is more effective at reducing SSIs.

Incise Drapes

The use of surgical drapes was examined in two RCTs[20,30] and one cohort study.[31] One RCT[30] found that the use of DuraPrep in combination with iodophor-impregnated surgical drapes was more effective than PI paint. One RCT[20] found no difference in SSI rates with or without iodophor-impregnated drapes. The cohort study found the use of iodine-impregnated incise drapes to be protective against SSIs. The guideline[5] recommends the use of iodophor-impregnated drapes where incise drapes are required. Based on limited evidence, iodophor incise drapes are effective in reducing wound infections in surgical patients when draping is required, although more research is needed, particularly comparing iodophor-impregnated drapes with non-antimicrobial counterparts.

Skin Antiseptic Application Techniques

Three RCTs[20,32,33] and a retrospective cohort study[34] compared application techniques (paint, scrub, or combination) for antiseptic agents. Two compared PI scrub and paint with paint only,[20,33] and one compared CHG scrub and iodine paint with CHG paint and iodine paint. None of the RCTs found a difference in SSI reduction with different application techniques. RCT evidence suggests that the method by which an antiseptic agent is applied is not a crucial factor in reducing the rates of wound infection in surgical patients. In contrast, one large retrospective cohort study suggests that scrub and paint with PI solution reduced composite wound infections by 31%, compared with paint alone.[34]

Overall, the evidence suggests that preoperative antiseptic showers are effective at preventing SSIs. In the operating theatre, no fires were reported in the studies that were reviewed, the method of applying antiseptic is inconsequential in preventing SSIs, and it is unclear which antiseptic is most clinically effective. Disinfectant products are often mixed with alcohol or aqueous base, which makes it difficult to form overall conclusions about an active ingredient. Large, well-conducted RCTs with consistent protocols are needed, to provide evidence on the effectiveness of one antiseptic preparation over another for the prevention of SSI. Issues of safety, such as operating room fires, were addressed in a supplementary report.

PREPARED BY

Christopher Kamel, BSc, MSc, Clinical Research Officer, Canadian Agency for Drugs and Technologies in Health (CADTH), Ottawa ON

Lynda McGahan, MSc, Clinical Research Officer, CADTH, Ottawa ON

Monika Mierzwinski-Urban, BA, MLIS, Information Specialist, CADTH, Ottawa ON

Dr. John Embil, MD, FRCPC, Consultant, Infectious Diseases, Health Sciences Centre, Winnipeg MB

Reviewers:

Patsy Rawding, RN, BScN, CIC
Provincial Infection Control Consultant
Nova Scotia Department of Health and Wellness
Halifax NS

Vi Burton, BScN, MN, CiC
Infection Control Nurse
Community and Hospital Infection Control Association (CHICA) — Canada
Nipawin SK

Suzanne Rhodenizer Rose, RN, BScN CIC
Infection Control Consultant
Nova Scotia Department of Health and Wellness
Halifax NS

Mark Miller, MD, FRCPC
Chair, Infection Prevention and Control
Jewish General Hospital
Montreal PQ

Rapid Response Service
Tel: 1-866-898-8439

www.cadth.ca

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APPENDICES

Appendix 1: Classification of surgical wounds

"Clean — an incision in which no inflammation is encountered in a surgical procedure, without a break in sterile technique, and during which the respiratory, alimentary and genitourinary tracts are not entered.

Clean-contaminated — an incision through which the respiratory, alimentary or genitourinary tract is entered under controlled conditions but with no contamination encountered.

Contaminated — an incision undertaken during an operation in which there is a major break in sterile technique or gross spillage from the gastrointestinal tract, or an incision in which acute, non-purulent inflammation is encountered. Open traumatic wounds that are more than 12–24 hours old also fall into this category.

Dirty or infected — an incision undertaken during an operation in which the viscera are perforated or when acute inflammation with pus is encountered during the operation (for example, emergency surgery for faecal peritonitis), and for traumatic wounds where treatment is delayed, and there is faecal contamination or devitalised tissue present" (p. xx*).[5]

*Page number from glossary in roman numerals

Appendix 2: Literature Search Strategy

OVERVIEW	
Interface:	OvidSP
Databases:	Embase 1980 to 2011 Week 05 Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present EBM Reviews — Cochrane Central Register of Controlled Trials 4th Quarter 2010 EBM Reviews — Cochrane Database of Systematic Reviews 2005 to January 2011 EBM Reviews — Database of Abstracts of Reviews of Effects 1st Quarter 2011 EBM Reviews — Health Technology Assessment 1st Quarter 2011 **Note:** Subject headings have been customized for each database. Duplicates between databases were removed in Ovid.
Date of Search:	February 9, 2011
Alerts:	Weekly search updates began February 9, 2011, and ran until June 2, 2011.
Study Types:	health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized controlled clinical trials, and guidelines
Limits:	Publication years January 1, 2001–February 9, 2011 Humans English

SYNTAX GUIDE	
/	At the end of a phrase, searches the phrase as a subject heading
MeSH	Medical Subject Heading
Exp	Explode a subject heading
*	Before a word, indicates that the marked subject heading is a primary topic; or, after a word, a truncation symbol (wildcard) to retrieve plurals or varying endings
?	Truncation symbol for one or no characters only
ADJ	Requires words are adjacent to each other (in any order)
ADJ#	Adjacency within # number of words (in any order)
.ti	Title
.ab	Abstract
.pt	Publication type
.mp	Mapping alias (searches title, abstract, heading words, table of contents, and key phrase identifiers)

CLINICAL MULTI-DATABASE STRATEGY		
#	**Searches**	**Results**
1	**Concept: Preoperative** exp Preoperative Care/ or Preoperative Period/ or Perioperative Care/ or Perioperative Period/	126988
2	(pre operative or preoperative or preop or pre op or perioperative or peri operative or periop or peri op or presurg*).ti,ab.	393719
3	((pre or prior or before or peri or prep or prepare or preparing or preparation* or hospitals in home or hospitals in the home) adj3 (operative or operation* or procedur* or surger*)).ti,ab.	187255
4	or/1-3	568697
5	**Concept: Skin preparation (concept & techniques)** exp Sterilization/ or instrument sterilization/ or exp Anti-Infective Agents, Local/ or exp topical antiinfective agent/ or exp Antisepsis/ or Surgical Wound Infection/pc or surgical infection/pc or exp disinfectants/ or exp detergents/ or detergent/ or soaps/ or soap/ or baths/ or bath/ or infection control/	691126
6	(preparation* or prepare or prepared or solution or wipes or shower* or scrub* or paint* or bath or bathe or bathing or antiseptic* or anti septic* or antibacterial* or anti bacterial* or antimicrobial* or anti microbial* or soap* or lavage* or gel or gels or steriliz* or sterilis* or disinfect* or antisepsis or biocides or pads or swabs or detergent* or washcloth* or wash or cleans* or bactericide or bactericidal or microbicide or microbicidal).ti,ab.	2526711
7	Chlorhexidine/ or exp alcohols/ or alcohol derivative/ or exp Iodophors/ or triclosan/ or Hexachlorophene/ or Benzalkonium Compounds/ or benzalkonium/ or povidone iodine/	793338
8	(tubulicid or novalsan or chlorhexidine or providone iodine or CHG or "PVP I" or PVPI or betadine or Soluprep or Polyvinylpyrrolidone Iodine or Providine or Disadine or Isodine or Pharmadine or Alphadine or alcohol* or iodophors or iodine or triclocarban or triclosan or irgasan or hexachlorophene or hexachlorophene or benzalkonium or asepsol or Osvan or LiquiDrape or cetrimide or savlon).ti,ab.	505409
9	or/5-8	3948406
10	exp Skin/ or skin care/ or (skin or dermal or derma or dermis or epidermis or epidermal or cutaneous or cutis or topical or surgical site).ti,ab.	1221550
11	4 and 9 and 10	5269
12	iodine povacrylex/ or (duraprep or dura prep or techni care or ChloraPrep or scrub care or scrubcare or Chlorascrub or Hibiclens or Chlorhex or avagard or bactoshield or betasept or dynahex or dyna hex or hibistat or povacrylex).ti,ab.	185
	Results for: Preoperative AND skin preparation	
13	11 or 12	5413
14	**Concept : SR/MA/HTA filter** meta-analysis.pt.	26760
15	meta-analysis/ or systematic review/ or meta-analysis as topic/ or exp technology assessment, biomedical/	127857
16	((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab.	75961

CLINICAL MULTI-DATABASE STRATEGY		
#	**Searches**	**Results**
17	((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).ti,ab.	8515
18	((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).ti,ab.	15137
19	(data synthes* or data extraction* or data abstraction*).ti,ab.	21460
20	(handsearch* or hand search*).ti,ab.	8732
21	(mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab.	21152
22	(met analy* or metanaly* or health technology assessment* or HTA or HTAs).ti,ab.	4542
23	(meta regression* or metaregression* or mega regression*).ti,ab.	2640
24	(meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp,hw.	196646
25	(medline or Cochrane or pubmed or medlars).ti,ab,hw.	124609
26	(cochrane or health technology assessment or evidence report).jw.	25964
27	(meta-analysis or systematic review).md.	0
28	or/14-27	324479
	Concept: Guidelines (CPG) filter	
29	exp clinical pathway/	7815
30	exp clinical protocol/	165601
31	exp consensus/	13868
32	exp consensus development conference/	13721
33	exp consensus development conferences as topic/	8213
34	critical pathways/	7815
35	exp guideline/	20233
36	guidelines as topic/	201454
37	exp practice guideline/	252557
38	practice guidelines as topic/	235902
39	health planning guidelines/	68291
40	exp treatment guidelines/	0
41	(guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt.	26285
42	(position statement* or policy statement* or practice parameter* or best practice*).ti,ab.	21918
43	(standards or guideline or guidelines).ti.	117787
44	((practice or treatment*) adj guideline*).ab.	24873
45	(CPG or CPGs).ti.	6915
46	consensus*.ti.	23981
47	consensus*.ab. /freq=2	23278
48	((critical or clinical or practice) adj2 (path or paths or pathway or pathways or protocol*)).ti,ab.	19481
49	recommendat*.ti.	41139

CLINICAL MULTI-DATABASE STRATEGY

#	Searches	Results
50	(care adj2 (standard or path or paths or pathway or pathways or map or maps or plan or plans)).ti,ab.	44965
51	(algorithm* adj2 (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)).ti,ab.	5822
52	(algorithm* adj2 (pharmacotherap* or chemotherap* or chemotreatment* or therap* or treatment* or intervention*)).ti,ab.	7533
53	or/29-52	736355
	Results for: Preoperative skin prep. AND (SR OR CPG filters)	
54	13 and (28 or 53)	517
	Concept: Clinical trials filter	
55	(Randomized Controlled Trial or Controlled Clinical Trial).pt.	731730
56	(Clinical Trial or Clinical Trial, Phase II or Clinical Trial, Phase III or Clinical Trial, Phase IV).pt.	742350
57	Multicenter Study.pt.	168132
58	Randomized Controlled Trial/	584907
59	Randomized Controlled Trials as Topic/	363624
60	Controlled Clinical Trial/	250074
61	Controlled Clinical Trials as Topic/	173693
62	Clinical Trial/ or Phase 2 Clinical Trial/ or Phase 3 Clinical Trial/ or Phase 4 Clinical Trial/	1290515
63	Clinical Trials as Topic/ or Clinical Trials, Phase II as Topic/ or Clinical Trials, Phase III as Topic/ or Clinical Trials, Phase IV as Topic/	1026798
64	Multicenter Study/ or Multicenter Study as Topic/	207132
65	Randomization/	143090
66	Random Allocation/	143090
67	Double-Blind Method/	298364
68	Double Blind Procedure/	101268
69	Double-Blind Studies/	256740
70	Single-Blind Method/	37456
71	Single Blind Procedure/	13816
72	Single-Blind Studies/	37456
73	Placebos/	222905
74	Placebo/	174425
75	Control Groups/	20665
76	Control Group/	20665
77	Cross-Over Studies/ or Crossover Procedure/	77429
78	(random* or sham or placebo*).ti,ab,hw.	1994392
79	((singl* or doubl*) adj (blind* or dumm* or mask*)).ti,ab,hw.	462029
80	((tripl* or trebl*) adj (blind* or dumm* or mask*)).ti,ab,hw.	785
81	(control* adj3 (study or studies or trial*)).ti,ab,hw.	4418254
82	(clinical adj3 (study or studies or trial*)).ti,ab,hw.	3208739
83	(Nonrandom* or non random* or non-random* or quasi-random* or	48431

CLINICAL MULTI-DATABASE STRATEGY

#	Searches	Results
	quasirandom*).ti,ab,hw.	
84	(phase adj3 (study or studies or trial*)).ti,ab,hw.	175948
85	((crossover or cross-over) adj3 (study or studies or trial*)).ti,ab,hw.	106946
86	((multicent* or multi-cent*) adj3 (study or studies or trial*)).ti,ab,hw.	295852
87	allocated.ti,ab,hw.	81135
88	((open label or open-label) adj5 (study or studies or trial*)).ti,ab,hw.	38224
89	trial.ti.	284423
90	or/55-89	7174346
91	exp animals/	16845408
92	exp animal experimentation/	1422602
93	exp models animal/	907230
94	exp animal experiment/	1422601
95	nonhuman/	3577082
96	exp vertebrate/	30155467
97	animal.po.	0
98	or/91-97	31897744
99	exp humans/	23923454
100	exp human experiment/	286007
101	human.po.	0
102	or/99-101	23924836
103	98 not 102	7973837
104	90 not 103	5622057
	Concept: Observational studies filter	
105	epidemiologic methods.sh.	26350
106	epidemiologic studies.sh.	4859
107	cohort studies/	210854
108	cohort analysis/	210854
109	longitudinal studies/	107772
110	longitudinal study/	107772
111	prospective studies/	501870
112	prospective study/	501862
113	follow-up studies/	942051
114	follow up/	501503
115	followup studies/	440561
116	retrospective studies/	589708
117	retrospective study/	589708
118	case-control studies/	163271
119	exp case control study/	542205
120	cross-sectional study/	167753
121	observational study/	18030

CLINICAL MULTI-DATABASE STRATEGY

#	Searches	Results
122	quasi experimental methods/	0
123	quasi experimental study/	729
124	(observational adj3 (study or studies or design or analysis or analyses)).ti,ab.	82615
125	(cohort adj7 (study or studies or design or analysis or analyses)).ti,ab.	166454
126	(prospective adj7 (study or studies or design or analysis or analyses or cohort)).ti,ab.	471753
127	((follow up or followup) adj7 (study or studies or design or analysis or analyses)).ti,ab.	157016
128	((longitudinal or longterm or (long adj term)) adj7 (study or studies or design or analysis or analyses or data or cohort)).ti,ab.	258525
129	(retrospective adj7 (study or studies or design or analysis or analyses or cohort or data or review)).ti,ab.	382442
130	((case adj control) or (case adj comparison) or (case adj controlled)).ti,ab.	120767
131	(case-referent adj3 (study or studies or design or analysis or analyses)).ti,ab.	1078
132	(population adj3 (study or studies or analysis or analyses)).ti,ab.	163036
133	(descriptive adj3 (study or studies or design or analysis or analyses)).ti,ab.	56117
134	((multidimensional or (multi adj dimensional)) adj3 (study or studies or design or analysis or analyses)).ti,ab.	3663
135	(cross adj sectional adj7 (study or studies or design or research or analysis or analyses or survey or findings)).ti,ab.	173235
136	((natural adj experiment) or (natural adj experiments)).ti,ab.	1408
137	(quasi adj (experiment or experiments or experimental)).ti,ab.	8508
138	((non experiment or nonexperiment or non experimental or nonexperimental) adj3 (study or studies or design or analysis or analyses)).ti,ab.	1167
139	(prevalence adj3 (study or studies or analysis or analyses)).ti,ab.	35496
140	case series.ti,ab.	47666
141	comparative study/	2092999
142	(comparative adj3 (study or studies or design or analysis or analyses)).ti,ab.	233513
143	or/105-142	4998009
144	exp animals/	16845408
145	exp animal experimentation/	1422602
146	exp models animal/	907230
147	exp animal experiment/	1422601
148	nonhuman/	3577082
149	exp vertebrate/	30155467
150	animal.po.	0
151	or/144-150	31897744
152	exp humans/	23923454
153	exp human experiment/	286007

CLINICAL MULTI-DATABASE STRATEGY		
#	**Searches**	**Results**
154	human.po.	0
155	or/152-154	23924836
156	151 not 155	7973837
157	143 not 156	4389222
158	**Results for: Preoperative skin prep. AND (clinical OR observ. studies filters)** 13 and (104 or 157)	3024
159	**Results for: Preoperative skin prep. AND search filters** 54 or 158	3247
160	remove duplicates from 159	1954
161	limit 160 to yr=2001-2011 [Limit not valid in DARE; records were retained]	1251
162	**Results for: Preoperative skin prep AND search filters AND search limits** limit 161 to english [Limit not valid in CCTR,DARE; records were retained]	1107

OTHER DATABASES	
PubMed	Same MeSH, keywords, limits, and study types used as per Medline search, with appropriate syntax used.
CINAHL (EBSCO interface)	Same keywords, and date limits used as per Medline search, excluding study types and human restrictions. Syntax adjusted for EBSCO.

GREY LITERATURE	
Dates for Search:	February 9, 2011;
Keywords:	Preoperative, presurgery, preop, antisepsis, antibacterial, bath, scrub, shower, disinfectant, washcloth, chlorhexidine, alcohol, iodine, betadine, povacrylex, duraprep
Limits:	Publication years: 2001–2011

The following sections of the CADTH grey literature checklist, “Grey matters: a practical tool for evidence-based searching” (http://www.cadth.ca/en/resources/grey-matters), were searched:

- Health Technology Assessment Agencies
- Clinical Practice Guidelines
- Databases (free)
- Internet Search
- Open Access Journals

Appendix 3: Study Inclusion and Exclusion Form

Preoperative Skin Antiseptic Preparations for Preventing Surgical Site Infections

CLINICAL REVIEW and ASSESSMENT OF GUIDELINES

Abstract #

Study type:

Title:
First author and year:

Reviewer: ***L. McGahan***_____ ***C. Kamel*** _____

INCLUSION CRITERIA:

1. Population: yes_____ no_____ can't tell_____

Adults, children, or mixed population
Preparing for thoracic, cardiac, plastic, orthopaedic, neurological, abdominal, or pelvic surgery

2. Intervention: yes_____ no_____ can't tell_____

Q1. A comparison of 2 or more of the following three types of antiseptics in various preparations (for example, solution, powder, drape, shower or bathing agents):
- a. One or more preoperative skin antiseptics, iodophors (providone iodine aqueous or alcohol), alcohol, or chlorhexidine gluconate (aqueous or alcoholic) versus placebo
- b. One type of antiseptic preparation compared to another

Q2. A comparison of 2 or more of the following:
- c. One or more preoperative skin antiseptic application techniques versus control
- d. One type of antiseptic application technique versus another

Q3. Any of the above

3. Study Design: yes_____ no_____ can't tell_____

a. HTA, systematic review, meta-analysis, RCT, non-RCT, clinical practice guideline

4. Outcome Measures (any of): yes_____ no_____ can't tell_____

a. Primary:
   - Surgical site infection defined as pus, swelling, pain, redness, or heat.
b. Secondary
   - Reoperation
   - Bacterial colony counts
   - Antibacterial treatments
c. Adverse events
   - resulting in death, or other adverse event
d. Guideline recommendations

EXCLUSION CRITERIA: For example, duplicate reports or preliminary reports of data presented in full.

- "yes" (1-4 inclusive): include study and order full paper_____
- at least one "can't tell" and others "yes" for 1-4: order full paper for further review_____
- "no" (any 1-4): exclude study _____

Appendix 4: Data Extraction Forms

Date:	**REVIEWER INITIALS:** **ID #:**
Article identification: *(author, year)* Full citation: Geographic location: Setting: *(e.g. hospital-based, clinic-based, other)* Declared conflict of interest: Source(s) of funding:	
STUDY CHARACTERISTICS	
Purpose/objective(s) of study *(include among whom)*:	
Design: *(RCT, clinical trial, cohort, cross-over, case-control, observational, guideline, other)* Duration of study: Method of randomization: Blinding: *(patients, surgeon, assessor)* Sample size: Sampling procedure: *(consecutive, selective, random, unreported, other)* Participation rate: *(total eligible for inclusion, total randomized, withdrawals/dropouts and reasons, total completing trial)* Exclusion criteria:	

Baseline Patient CHARACTERISTICS		
Inclusion Criteria	Intervention Group	Comparator Group
Mean age: *(years)* Gender: *(male/female) (%)* Surgery: *(thoracic, cardiac, plastic, orthopaedic, neurological, abdominal, pelvic)* Surgical site classification: *(clean, clean-contaminated, contaminated, dirty or infected)* Other risk factors: *(underlying conditions, immunosuppressants, other)* *Notes (inclusion/exclusion criteria, calculations, if any)*		

INTERVENTION DESCRIPTION	Intervention	Comparator	Total
Description of the intervention: Type of preoperative skin antiseptic and preparation: *(povidone iodine aqueous or alcohol, alcohol, chlorhexidine gluconate aqueous or alcohol)* Preoperative skin antiseptic application technique: *(application technique, showering or bathing, size of area, dedicated tool, time for drying or multiple application)* Details:			
Manufacturer and modifications (if any):			
Notes (calculations, if any)			

CLINICAL DATA EXTRACTION	Intervention	Comparator
Primary outcome: Surgical site infection		
Secondary outcomes: Bacterial colony counts Reoperation Antibacterial treatment		
Notes (calculations, if any)		

ADVERSE EVENTS	Intervention	Comparator
Total number of serious adverse events SAE):		
Deaths		
Toxicity or allergy		
Total number patients with major SAE:		
Number of participants withdrawn due to AE:		
Description of adverse events:		
Notes (calculations, if any)		

CLINICAL PRACTICE GUIDELINE
Article identification: *(author, year, Ref ID)*

Country:
Objective:
Method:
Grading System:
Population:
Recommendations:
Applicability:
Notes:

Appendix 5: AGREE Domain Descriptions

"Scope and Purpose is concerned with the overall aim of the guideline, specific clinical questions and the target patient population.

Stakeholder involvement focuses on the extent to which the guideline represents the views of its intended users.

Rigour of development relates to the process used to gather and synthesise the evidence, the methods to formulate the recommendations and to update them.

Clarity and presentation deals with the language and format of the guideline.

Applicability pertains to the likely organisational, behavioural and cost implications of applying the guideline.

Editorial independence is concerned with the independence of the recommendations and acknowledgement of possible conflict of interest from the guideline development group" (page 4).[10]

Appendix 6: Quality Assessment Forms

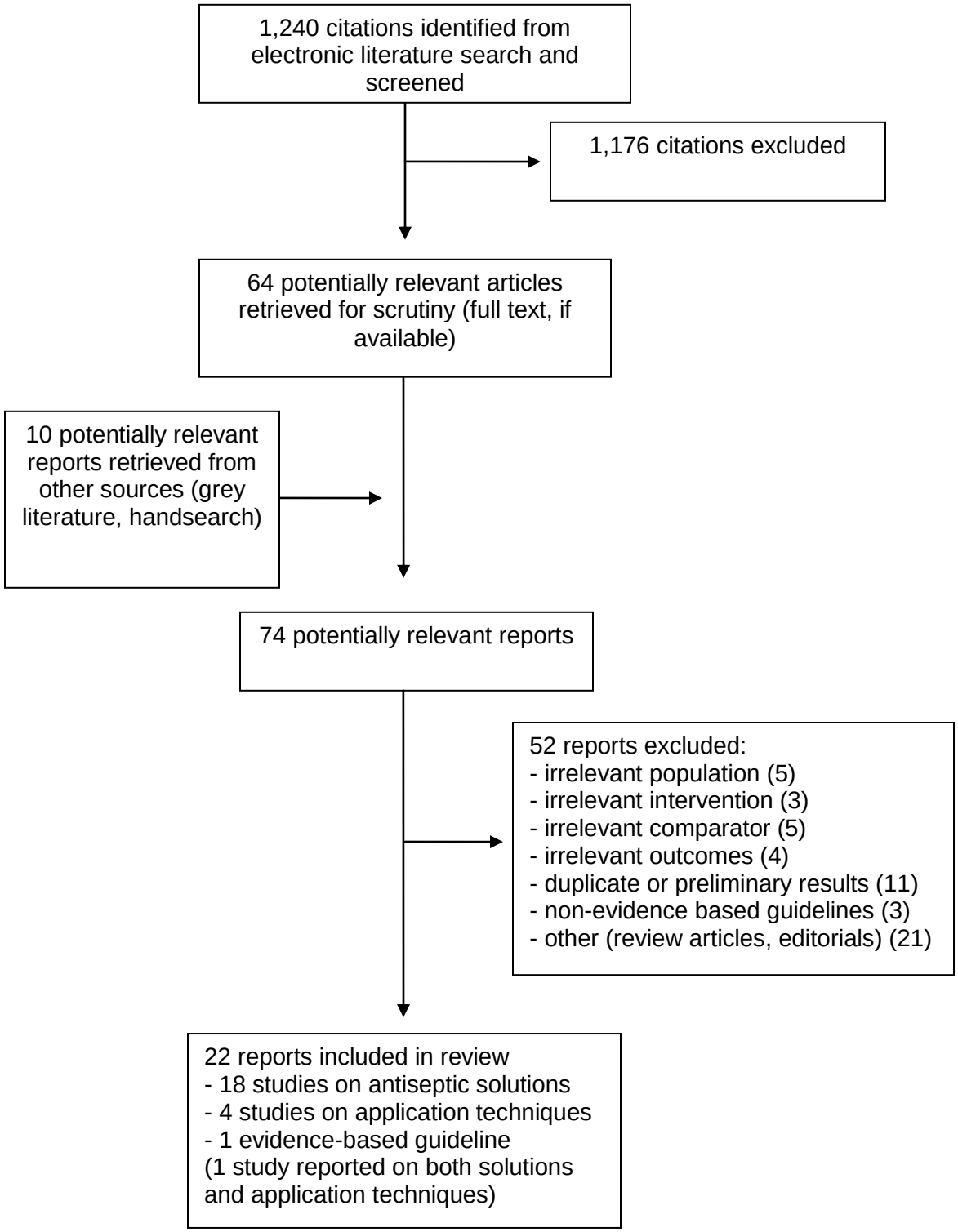
ASSESSMENT OF STUDY QUALITY MODIFIED DOWNS AND BLACK CHECKLIST FOR RANDOMIZED AND NON-RANDOMIZED STUDIES[9]		
REPORTING	Yes/No/Partially	**Score**
1. Is the objective of the study clear?	Yes=1, No=0	
2. Are the main outcomes clearly described in the Introduction or Methods?	Yes=1, No=0	
3. Are characteristics of the patients included in the study clearly described?	Yes=1, No=0	
4. Are the interventions clearly described?	Yes=1, No=0	
5. Are the distributions of principal confounders in each group of subjects clearly described?	Yes=2, Partially=1, No=0	
6. Are the main findings of the study clearly described?	Yes=1, No=0	
7. Does the study estimate random variability in data for main outcomes?	Yes=1, No=0	
8. Have all the important adverse events consequential to the intervention been reported?	Yes=1, No=0	
9. Have characteristics of patients lost to follow-up been described?	Yes=1, No=0	
10. Have actual probability values been reported for the main outcomes except probability <0.001?	Yes=1, No=0	
11. Is the source of funding clearly stated?	Yes=1, No=0	
EXTERNAL VALIDITY	Yes/No/Unclear	**Score**
12. Were subjects asked to participate in the study representative of the entire population recruited?	Yes=1, No=0, Unclear=0	
13. Were those subjects who were prepared to participate representative of recruited population?	Yes=1, No=0, Unclear=0	
14. Were staff, places, and facilities where patients were treated representative of treatment most received?	Yes=1, No=0, Unclear=0	
INTERNAL VALIDITY	Yes/No/Unclear	**Score**
15. Was an attempt made to blind study subjects to the intervention?	Yes=1, No=0, Unclear=0	
16. Was an attempt made to blind those measuring the main outcomes?	Yes=1, No=0, Unclear=0	
17. If any of the results of the study were based on data dredging was this made clear?	Yes=1, No=0, Unclear=0	
18. Was time period between intervention and outcome the same for intervention and control groups or adjusted for?	Yes=1, No=0, Unclear=0	
19. Were statistical tests used to assess main outcomes appropriate?	Yes=1, No=0, Unclear=0	
20. Was compliance with the interventions reliable?	Yes=1, No=0, Unclear=0	
21. Were main outcome measures used accurate? (valid and reliable)	Yes=1, No=0, Unclear=0	
INTERNAL VALIDITY-CONFOUNDING (SELECTION BIAS)	Yes/No/Unclear	**Score**
22. Were patients in different intervention groups recruited from the same population?	Yes=1, No=0, Unclear=0	
23. Were study subjects in different intervention groups recruited over the same period of time?	Yes=1, No=0, Unclear=0	
24. Were study subjects randomized to intervention groups?	Yes=1, No=0, Unclear=0	

25. Was the randomized intervention assignment concealed from patients and staff until recruitment was complete?	Yes=1, No=0, Unclear=0	
26. Was there adequate adjustment for confounding in the analyses from which main findings were drawn?	Yes=1, No=0, Unclear=0	
27. Were losses of patients to follow-up taken into account?	Yes=1, No=0, Unclear=0	
Power	Size of smallest intervention group Score 0-5	**Score**
28. Was the study sufficiently powered to detect clinically important effects where probability value for a difference due to chance is <5%?		

ASSESSMENT OF GUIDELINES QUALITY APPRAISAL OF GUIDELINES FOR RESEARCH AND EVALUATION (AGREE[10])		
SCOPE AND PURPOSE	4=Strong agree; 3=agree; 2=disagree; 1=strongly disagree	**Score**
1. The overall objective of the guideline is specifically described.		
2. The clinical question(s) covered by the guideline is (are) specifically described.		
3. The patients to whom the guideline is meant to apply are specifically described.		
STAKEHOLDER INVOLVEMENT	4=Strong agree; 3=agree; 2=disagree; 1=strongly disagree	**Score**
4. The guideline development group includes individuals from all the relevant professional groups.		
5. The patients' views and preferences have been sought.		
6. The target users of the guideline are clearly defined.		
7. The guideline has been piloted among target users.		
RIGOUR OF DEVELOPMENT	4=Strong agree; 3=agree; 2=disagree; 1=strongly disagree	**Score**
8. Systematic methods were used to search for evidence.		
9. The criteria for selecting the evidence are clearly described		
10. The methods used for formulating the recommendations are clearly described.		
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.		
12. There is an explicit link between the recommendations and the supporting evidence.		
13. The guideline has been externally reviewed by experts prior to its publication.		
14. A procedure for updating the guideline is provided.		
CLARITY AND PRESENTATION	4=Strong agree; 3=agree; 2=disagree; 1=strongly disagree	**Score**
15. The recommendations are specific and unambiguous.		
16. The different options for management of the condition are clearly presented.		
17. Key recommendations are easily identifiable.		
18. The guideline is supported with tools for application.		
APPLICABILITY	4=Strong agree; 3=agree; 2=disagree; 1=strongly disagree	**Score**
19. The potential organizational barriers in applying the recommendations have been discussed.		
20. The potential cost implications of applying the recommendations have been considered.		

21. The guideline presents key review criteria for monitoring and/audit purposes.		
EDITORIAL INDEPENDENCE	4=Strong agree; 3=agree; 2=disagree; 1=strongly disagree	**Score**
22. The guideline is editorially independent from the funding source.		
23. Conflicts of interest of guideline development members have been reported.		
OVERALL ASSESSMENT	4=Strong agree; 3=agree; 2=disagree; 1=strongly disagree	**Score**
24. Would you recommend these guidelines for use in practice?		

Appendix 7: Selection of Included Studies



Appendix 8: List of Included Studies

Randomized Controlled Trials

Al-Majaly R. The efficacy of method of scrubbing of operative site on post-operative wound infection. Middle East J Age Ageing 2006;4(1):15-18.
Darouiche RO, Wall MJ, Jr., Itani KM, Otterson MF, Webb AL, Carrick MM, et al. Chlorhexidine-Alcohol versus Povidone-Iodine for Surgical-Site Antisepsis. N Engl J Med. 2010 Jan 7;362(1):18-26.

Ellenhorn JD, Smith DD, Schwarz RE, Kawachi MH, Wilson TG, McGonigle KF, et al. Paint-only is equivalent to scrub-and-paint in preoperative preparation of abdominal surgery sites. J Am Coll Surg. 2005 Nov;201(5):737-41.

Jacobson C, Osmon DR, Hanssen A, Trousdale RT, Pagnano MW, Pyrek J, et al. Prevention of wound contamination using DuraPrep solution plus Ioban 2 drapes. Clin Orthop Relat Res. 2005 Oct;439:32-7.

Kalantar-Hormozi AJ, Davami B. No need for preoperative antiseptics in elective outpatient plastic surgical operations: a prospective study. Plast Reconstr Surg. 2005 Aug;116(2):529-31.

Kehinde EO, Jamal W, Ali Y, Khodakhast F, Sahsah M, Rotimi VO. Comparative efficacy of two methods of skin preparation of the perineal and genital skin of male urological patients. Kuwait Med J. 2009;41(2):103-7.

Meier DE, Nkor SK, Aasa D, OlaOlorun DA, Tarpley JL. Prospective randomized comparison of two preoperative skin preparation techniques in a developing world country. World J Surg. 2001 Apr;25(4):441-3.

Paocharoen V, Mingmalairak C, Apisarnthanarak A. Comparison of surgical wound infection after preoperative skin preparation with 4% chlohexidine and povidone iodine: A prospective randomized trial. J Med Assoc Thai. 2009;92(7):898-902.

Segal CG, Anderson JJ. Preoperative skin preparation of cardiac patients. AORN J. 2002 Nov;76(5):821-8.

Veiga DF, Damasceno CA, Veiga-Filho J, Figueiras RG, Vieira RB, Florenzano FH, et al. Povidone iodine versus chlorhexidine in skin antisepsis before elective plastic surgery procedures: a randomized controlled trial. Plast Reconstr Surg. 2008 Nov;122(5):170e-1e.

Veiga DF, Damasceno CA, Veiga FJ, Silva RV, Jr., Cordeiro DL, Vieira AM, et al. Influence of povidone-iodine preoperative showers on skin colonization in elective plastic surgery procedures. Plast Reconstr Surg. 2008 Jan;121(1):115-8.

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 Jan;30(1):77-9.

Clinical Trials

Prospective cohort

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 Dec;18(23):3325-32.

Magera JS, Jr., Inman BA, Elliott DS. Does preoperative topical antimicrobial scrub reduce positive surgical site culture rates in men undergoing artificial urinary sphincter placement? J Urol. 2007 Oct;178(4 Pt 1):1328-32.

Swenson BR, Hedrick TL, Metzger R, Bonatti H, Pruett TL, Sawyer RG. Effects of preoperative skin preparation on postoperative wound infection rates: a prospective study of 3 skin preparation protocols. Infect Control Hosp Epidemiol. 2009 Oct;30(10):964-71.

Retrospective cohort

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 Sep;25(6 Suppl):98-102.

Levin I, Amer-Alshiek J, Avni A, Lessing J, Satel A, Almog B. Chlorhexidine and alcohol versus providone-iodine for antisepsis in gynecological surgery. J Wom Health. 2011;20(3):1-4.

Weed S, Bastek JA, Sammel MD, Beshara M, Hoffman S, Srinivas SK. Comparing postcesarean infectious complication rates using two different skin preparations. Obstet Gynecol. 2011 May;117(5):1123-9.

Yoshimura Y, Kubo S, Hirohashi K, Ogawa M, Morimoto K, Shirata K, et al. Plastic iodophor drape during liver surgery operative use of the iodophor-impregnated adhesive drape to prevent wound infection during high risk surgery. World J Surg. 2003;27(6):685-8.

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Case-control

Boston KM, Baraniuk S, O'Heron S, Murray KO. Risk factors for spinal surgical site infection, Houston, Texas. Infect Control Hosp Epidemiol. 2009 Sep;30(9):884-9.

Clinical Practice Guidelines

National Institute for Health and Clinical Excellence (NICE). Surgical site infection: clinical guideline [Internet]. London: NICE; 2008. Available from: http://www.nice.org.uk/nicemedia/pdf/CG74NICEGuideline.pdf

Appendix 9: List of Excluded Studies and Rationale for Exclusion

Comparator Unclear

Eiselt D. Presurgical skin preparation with a novel 2% chlorhexidine gluconate cloth reduces rates of surgical site infection in orthopaedic surgical patients. Orthop Nurs. 2009 May;28(3):141-5.

Confounding

Finkelstein R, Rabino G, Mashiach T, Bar-El Y, Adler Z, Kerztman V, et al. Reducing surgical site infection rates in cardiac surgery: Results of 10-year infection control programme [abstract]. Clin Microbiol Infect. 2009;15:S555. (Presented at 19th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) Helsinki Finland;20090516;- 20090519).

Maher MM. Preventing mediastinitis: Success with the SCIP bundle and evidence based best practices [abstract]. Am J Infect Control. 2009;37(5): E184-E185. (Presented at 36th Annual Educational Conference and International Meeting, APIC Fort Lauderdale, FL United States;20090607;- 20090611).

Riley MMS, Pegues D, Suda D, Director U, Tabsh K, Devaskar U. Reduction of low transverse cesarean section-associated surgical site infections [abstract]. Am J Infect Control. 2010;38(5):E73-E74. (Presented at APIC 37th Annual Educational Conference and International Meeting New Orleans, LA United States;20100711;- 20100715).

Van Kerkhove M, Parsonnet J, Weingart M, Tompkins LS. Investigation of mediastinitis due to coagulase-negative staphylococci after cardiothoracic surgery. Infect Control Hosp Epidemiol. 2006 Mar;27(3):305-7.

Duplicate or Preliminary Results

Edwards PS, Lipp A, Holmes A. Preoperative skin antiseptics for preventing surgical wound infections after clean surgery. Cochrane Database Syst Rev. 2004;(3).

Noorani A, Rabey N, Walsh SR, Davies RJ. Systematic review and meta-analysis of preoperative antisepsis with chlorhexidine versus povidone-iodine in clean-contaminated surgery. Br J Surg. 2010 Nov;97(11):1614-20.

Open forum. Cochrane review: preoperative skin antisepsis. Br J Perioper Nurs. 2005 May;15(5):191.

Paocharoen V, Mingmalairak C, Apisarnthanarak A. Comparison of surgical wound infection after preoperative skin preparation with 4% chlorhexidine [correction of chlohexidine] and povidone iodine: a prospective randomized trial. J Med Assoc Thai. 2009 Jul;92(7):898-902.

Stewart A, Eyers PS, Earnshaw JJ. Prevention of infection in arterial reconstruction. Cochrane Database Syst Rev (Online). 2006;(3).

Stewart AH, Eyers PS, Earnshaw JJ. Prevention of infection in peripheral arterial reconstruction: a systematic review and meta-analysis. J Vasc Surg. 2007 Jul;46(1):148-55.

Webster J, Osborne S. Meta-analysis of preoperative antiseptic bathing in the prevention of surgical site infection. Br J Surg. 2006;93(11):1335-41.

Webster J, Osborne S. Preoperative bathing or showering with skin antiseptics to prevent surgical site infection. Cochrane Database Syst Rev. 2007;(2).

Webster J, Osborne S. Preoperative bathing or showering with skin antiseptics to prevent surgical site infection. Cochrane Database Syst Rev. 2010 Dec 6;(1).

Method Not Reported

Surgical skin antisepsis in operating theatres [Internet]. Brisbane, Queensland: Queensland Health; Centre for Healthcare Related Infection Surveillance and Prevention [cited 2011 May 30] 2009. Available from: http://www.health.qld.gov.au/chrisp/resources/rec_prac_skinprep.pdf

Recommended practices for skin preparation of patients. AORN J. 2002;75(1):184-7.

Recommended standards of practice for skin prep of the surgical patient [Internet]. Littleton (CO): Association of Surgical Technologists [cited 2011 May 30] 2008. Available from: http://www.ast.org/pdf/Standards_of_Practice/RSOP_Skin_Prep.pdf

Narrative Review or Editorial

Crosby CT, Tsj E, Lamber PA, Adams D. Preoperative skin preparation: a historical perspective. Br J Hosp Med. 2009 Oct: 70(10):579-82.

Edmiston CE, Jr., Okoli O, Graham MB, Sinski S, Seabrook GR. Evidence for using chlorhexidine gluconate preoperative cleansing to reduce the risk of surgical site infection. AORN J. 2010 Nov;92(5):509-18.

Galvin P. Cultivating quality: reducing surgical site infections in children undergoing cardiac surgery. Am J Nurs. 2009 Dec;109(12):49-55.

Hibbard JS. Analyses comparing the antimicrobial activity and safety of current antiseptic agents: a review. J Infus Nurs. 2005 May;28(3):194-207.

La CL, Mangano A, Albertin A. Erratum: Povidone-iodine versus chlorhexidine in skin antisepsis before elective plastic surgery procedures: a randomized controlled trial. Is statistical correctness always pursued? Plast Reconstr Surg. 2009;124(3):1013-4.

Leaper D, Burman-Roy S, Palanca A, Cullen K, Worster D, Gautam-Aitken E, et al. Prevention and treatment of surgical site infection: summary of NICE guidance. BMJ. 2008;337:a1924.

Lee JT. Preoperative Skin Preparation. J Am Coll Surg. 2006;202(5):853.

Lipp A. An evaluation of preoperative skin antiseptics. Br J Perioper Nurs. 2005 Jan;15(1):12-4.

Mangano A, Albertin A, La CL. Povidone-iodine versus chlorhexidine in skin antisepsis before elective plastic surgery procedures: a randomized controlled trial. is statistical correctness always pursued? Plast Reconstr Surg. 2009 Jul;124(1):340-2.

Murray BW, Huerta S, Dineen S, Anthony T. Surgical site infection in colorectal surgery: a review of the nonpharmacologic tools of prevention. J Am Coll Surg. 2010 Dec;211(6):812-22.

Spear M. Evidence-based prevention strategies for surgical site infections. Plast Surg Nurs. 2009 Jul;29(3):175-8.

Wenzel RP. Minimizing surgical-site infections. N Engl J Med. 2010;362(1):75-7.

Woods A. Key points in the CDC's surgical site infection guideline. Adv Skin Wound Care. 2005 May;18(4):215-20.

No Post-operative Assessment

Bibbo C, Patel DV, Gehrmann RM, Lin SS. Chlorhexidine provides superior skin decontamination in foot and ankle surgery: a prospective randomized study. Clin Orthop 2005:438: 204-208.

Moen MD, Noone MB, Kirson I. Povidone-iodine spray technique versus traditional scrub-paint technique for preoperative abdominal wall preparation. Am J Obstet Gynecol. 2002 Dec;187(6):1434-6.

Ostrander RV, Botte MJ, Brage ME. Efficacy of surgical preparation solutions in foot and ankle surgery. J Bone Joint Surg Am. 2005;87(5):980-985.

Saltzman MD, Nuber GW, Gryzlo SM, Marecek GS, Koh JL. Efficacy of surgical preparation solutions in shoulder surgery. J Bone Joint Surg Am. 2009 Aug;91(8):1949-53.

Not Selected Intervention

Hedin H, Larsson S. Technique and considerations when using external fixation as a standard treatment of femoral fractures in children. Injury. 2004 Dec;35(12):1255-63.

Schuster JM, Rechtine G, Norvell DC, Dettori JR. The influence of perioperative risk factors and therapeutic interventions on infection rates after spine surgery: a systematic review. Spine. 2010 Apr 20;35(9 Suppl):S125-S137.

Seibert D. Measured impact of two strategies to lower surgical site infection rates [abstract]. Am J Infect Control. 2009;37(5):E48-E49. (Presented at 36th Annual Educational Conference and International Meeting, APIC Fort Lauderdale, FL United States;20090607;- 20090611).

Not Selected Population

Culligan P, Kubik K, Murphy M, Blackwell L, Snyder J. A randomized trial that compared providone iodine and chlorhexidine as antiseptics for vaginal hysterectomy. Am J Obstet Gynecol. 2005;192:422-5.
Hibbard JS, Mulberry GK, Brady AR. A clinical study comparing the skin antisepsis and safety of ChloraPrep, 70% isopropyl alcohol, and 2% aqueous chlorhexidine. J Infus Nurs. 2002 Jul;25(4):244-9.

Ro K. Methicillin-resistant Staphylococcus aureus colonization: a review of the literature on prevention and eradication. Adv Emerg Nurs J. 2008 Oct;30(4):344-56.

Seal LA, Paul-Cheadle D. A Systems approach to preoperative surgical patient skin preparation. Am J Infect Control. 2004 Apr;32(2):57-62.

Segers P, Speekenbrink RG, Ubbink DT, van Ogtrop ML, de Mol BA. Prevention of nosocomial infection in cardiac surgery by decontamination of the nasopharynx and oropharynx with chlorhexidine gluconate: a randomized controlled trial. JAMA. 2006 Nov 22;296(20):2460-6.

Preliminary Results as Abstracts

Sammel M, Weed S, Bastek J, Beshara M, Hoffman S, Srinivas SK. New preoperative skin preparation protocol decreases post-cesarean infectious complications [abstract]. Am J Obstet Gynecol. 2011;204(1 Suppl):S241. (Presented at 2011 31st Annual Meeting of the Society for Maternal-Fetal Medicine: The Pregnancy Meeting San Francisco, CA United States;20110207;-20110212).

Out of Date Range

Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. Infect Control Hosp Epidemiol. 1999 Apr;20(4):250-78.

Protocol

Hadiati DR, Hakimi M, Nurdiati DS. Skin preparation for preventing infection following caesarean section. Cochrane Database Syst Rev. 2008;(4).

Systematic Review

HAYES. Preoperative whole-body bathing with chlorhexidine gluconate for prevention of surgical site infection. Lansdale (PA): HAYES, Inc. 2009.

Edwards P, Lipp A, Holmes A. Preoperative skin antiseptics for preventing surgical wound infections after clean surgery. Cochrane Database Syst Rev. 2009 May 12;(1).

Jakobsson J, Perlkvist A, Wann-Hansson C. Searching for evidence regarding using preoperative disinfection showers to prevent surgical site infections: a systematic review. Worldviews Evid Based Nurs. 2010 Sep 28.

Lee I, Agarwal RK, Lee BY, Fishman NO, Umscheid CA. Systematic review and cost analysis comparing use of chlorhexidine with use of iodine for preoperative skin antisepsis to prevent surgical site infection. Infect Control Hosp Epidemiol. 2010 Dec;31(12):1219-29.

Noorani A, Rabey N, Walsh S, Davies RJ. Pre-operative antisepsis with chlorhexidine versus povidone-iodine in cleancontaminated surgery: systematic review and meta-analysis of surgical site infection in randomised controlled clinical trials [abstract]. Colorectal Dis. 2010;12:36. (Presented at 5th Annual Meeting of the European Society of Coloproctology Sorrento Italy;20100922;- 20100925).

Stewart A, Eyers PS, Earnshaw JJ. Prevention of infection in arterial reconstruction. Cochrane Database Syst Rev. 2010 Oct 3;(11).

Webster J, Osborne S. Preoperative bathing or showering with skin antiseptics to prevent surgical site infection. Cochrane Database Syst Rev. 2010 Dec 6;(1).

Appendix 10: Levels of Evidence (EL) for Clinical Practice Guidelines[5]

Level	Source of Evidence
1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1−	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2++	High-quality systematic reviews of case-control or cohort studies; high-quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal
2+	Well-conducted case-control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal
2−	Case-control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal
3	Non-analytical studies (e.g., case reports, case series)
4	Expert opinion, formal consensus

Appendix 11: Study Characteristics

Author Year Country	Study Design, Setting (Sample Size)	Wound and Surgery Type	Interventions (Number of Patients)	Comparator (Number of Patients)	Patient Age (Years) Gender (Male, Female)	Outcomes Reported
Pre-surgical Showering						
Veiga[13] 2009 Brazil	RCT Hospital (150)	Clean Plastic Thorax	4% CHG liquid detergent shower (50)	PLC liquid detergent, no active ingredient (50); control given no showering instruction (50)	Mean: 38.3 ± 13.9 M: 32 (21%) F: 118 (79%)	BCC: post-operative SSI: CDC criteria up to 30 days
Veiga[12] 2008 Brazil	RCT Hospital (114)	Clean Plastic Abdominal or thorax	10% PI liquid detergent shower (57)	No showering instruction (57)	Mean: 38.3 (18 to 65) M: 26 (23%) F: 88 (77%)	BCC: pre- and post-shower SSI: by observation
Johnson[15] 2010 USA	Cohort Hospital (1,054)	Mixed Orthopaedic Hip arthroplasty	2% CHG-impregnated cloth for use night before and morning of surgery (157)	Non-compliance (no CHG) based on placing adhesive stickers from package on data sheet (897)	Mean: 58 M: 50% compliant M: 53% non-compliant	SSI: NNIS criteria, deep, perioprosthetic only
Zywiel[17] 2010 USA	Cohort Hospital (912)	Mixed Orthopaedic Knee arthroplasty	2% CHG-impregnated cloth for use night before and morning of surgery (136)	Non-compliance (no CHG) based on placing adhesive stickers from package on instruction sheet (711); partial compliance (65)	Mean: 63 M: 34% compliant M: 31% non-compliant	SSI: CDC criteria, deep incisional or joint space infection only
Dizer[14] 2009 Turkey	Cohort (time period)	NR Abdominal surgery	CHG soap showering upon admission and night before surgery (43):	Normal hygiene (39); enrolled Nov 2004 to Jan 2005	20 (51.3%) CHG and 22 (51.2%) control patients	SSI: CDC criteria

Author Year Country	Study Design, Setting (Sample Size)	Wound and Surgery Type	Interventions (Number of Patients)	Comparator (Number of Patients)	Patient Age (Years) Gender (Male, Female)	Outcomes Reported
	Hospital (82)		enrolled Feb 2004 to May 2005		were >51 years M: 58% CHG M: 74% control	BCC: NR Bacterial types described
Magera Jr.[16] 2007 USA	Cohort (single surgeon) Clinic (100)	NR Pelvic Artificial urinary sphincter implant	Twice daily, 5-day, topical 4% CHG scrub; first 50 men enrolled May 2003 to Nov 2005	Normal hygiene; last 50 men enrolled May 2003 to Nov 2005	Median: 74.1 CHG; 73.2 control M: 100%	BCC: abdominal and perineal, after skin disinfection, before incision, post-surgery. SSI
Antiseptic Preparation versus Hygiene						
Meier[18] 2001 Nigeria	RCT Hospital (200)	Clean Abdominal Hernia surgery	5-minute PI scrub, towel, and paint with PI (102)	5-minute soap scrub, towel and paint with methylated spirit (98)	Mean: 33 years M: 182 (91%) F: 18 (9%)	SSI, 10 days, and 4 to 8 weeks post-operatively based on redness and purulent discharge
Kalantar-Hormozi[19] 2005 Iran	RCT Hospital (1,810)	Clean Plastic	PI scrub and paint (905)	Saline irrigation (905)	Mean: 33 years PI, 34 years saline M: 648 (36%) F: 1162 (64%)	SSI, up to 1 month based on redness, swelling, discharge, wound

Author Year Country	Study Design, Setting (Sample Size)	Wound and Surgery Type	Interventions (Number of Patients)	Comparator (Number of Patients)	Patient Age (Years) Gender (Male, Female)	Outcomes Reported
						dehiscence
Comparison of Antiseptics						
Darouiche[24] 2010 USA	RCT Hospital (849)	Clean-contaminated Mixed surgery	2% CHG + 70% IPA scrub (409)	10% aqueous PI scrub then paint (440)	Mean: 53 years M: 487 (57%) F: 362 (43%)	SSI up to 30 days post-op; CDC criteria
Paochaoroen[21] 2009 Thailand	RCT Hospital (500)	Mixed Mixed surgery	PI scrub then paint (250)	4% CHG and 70% IPA scrub then paint (250)	Mean: 50.5 PI, 56.2 CHG M: 297 (59%) F: 213 (43%)	BCC SSI up to 30 days post-surgery
Kehinde[22] 2009 Kuwait	RCT Hospital (231)	NR Urological	3x CHG-cetrimide scrub (114)	2x CHG-cetrimide scrub + PI scrub (117)	Mean: 54 CHG, 55 CHG+PI M: 231 (100%)	BCC
Veiga[23] 2008 Brazil	RCT Hospital (250)	Clean Plastic	0.5% CHG paint (125)	10% PI paint (125)	Adults >18 years M: NR F: NR	BCC SSI up to 30 days, CDC criteria
Segal[20] 2002 USA	RCT Hospital (209)	NR Cardiac	PI paint (56); PI scrub then paint (52)	One-step iodophor and alcohol film (50); film plus iodine incise drape (51)	Mean: 60.9 years M: >75%	SSI, CDC criteria
Levin[25] 2011 Israel	Cohort Hospital (256)	Clean-contaminated Pelvic	10% PI scrub then 3x 10% PI/65% alcohol paint (145)	2% CHG scrub then 3x 70% alcohol paint (111)	Mean: 51 PI, 53 CHG	SSI, CDC criteria

Author Year Country	Study Design, Setting (Sample Size)	Wound and Surgery Type	Interventions (Number of Patients)	Comparator (Number of Patients)	Patient Age (Years) Gender (Male, Female)	Outcomes Reported
					F: 100%	
Swenson[26] 2009 USA	Cohort Hospital (1621)	Mixed General surgery	7.5% PI soap followed by 1x 70% IPA scrub, 3x 10% PI paint (1,514)	2% CHG and 70% IPA scrub (827); iodine povacrylex (794)	Mean: 53 years M: 738 (46%) F: 1243 (77%)	SSI, CDC-NNIS criteria
Boston[27] 2009 USA	Case-control Hospital (133)	NR Orthopaedic	Iodine and DuraPrep (case 39, control 79); Iodine only (case 5, control 84); CHG (case 1, control 2); Other (case 3, control 7)	NA	Median 44.5 M: 38% F: 62%	SSI, CDC criteria
Incise Drapes						
Jacobson[30] 2005 USA	RCT Clinic (176)	NR Orthopaedic	DuraPrep plus Ioban 2 drapes (86)	PI plus Ioban 2 drapes (90)	Mean: 67.5 DuraPrep, 67 PI M: 93 (52%) F: 86 (48%)	Wound culture growth SSI, CDC criteria
Segal[20] 2002 USA	See above					
Yoshimura[31] 2003 Japan	Cohort Hospital (296)	Clean-contaminated Abdominal	Iodophor only (174)	Iodophor plus Ioban 2 drape (122)	Mean 61.1 drape, 63.1 no drape M: 244 (82%) F: 52 (18%)	SSI, CDC criteria
Application Method						
Al-Majaly[32] 2006	RCT Hospital	Mixed Mixed	10 min 0.75% CHG and 1.5% cetrimide scrub	0.75% CHG and 1.5% cetrimide paint then 1%	Age: NR	SSI

Author Year Country	Study Design, Setting (Sample Size)	Wound and Surgery Type	Interventions (Number of Patients)	Comparator (Number of Patients)	Patient Age (Years) Gender (Male, Female)	Outcomes Reported
Jordan	(68)	surgery	then 1% iodine in 70% spirit paint (34)	iodine in 70% spirit paint (34)	M: NR F: NR	
Ellenhorn[33] 2005 USA	RCT Hospital (234)	Mixed Abdominal	5-min 0.75% PI scrub then 1.0% PI paint (115)	1.0% PI paint only (119)	Mean: 60.5 scrub + paint, 57.7 paint M: NR F: NR	Wound infection Intra-abdominal infection
Segal[20] 2002 USA	See above					
Weed[34] 2011 USA	Cohort Hospital (2,143)	NR Caesarean	3-min 13% PI scrub + 10% PI paint (1,004)	10% PI paint only (1,139)	Mean: 28.13 scrub + paint, 28.09 paint F: 2,143 (100%)	Major puerperal infection, Infectious wound complications (International Classification of Diseases coding)

BCC = bacterial colony counts; CDC = Centers for Disease Control and Prevention; CHG = chlorhexidine gluconate; F = female; IPA = isopropyl alcohol; M = male; NA = not applicable; NNIS = National Nosocomial Infections Surveillance; NR = not reported; PI = povidone-iodine; PLC = placebo; RCT = randomized controlled trial; SSI = surgical site infection.

Appendix 12: Critical Appraisal of Individual Studies

Author Year Country	Study Design, Setting	Study Strengths	Study Limitations
Pre-surgical Showering			
Veiga[13] 2009 Brazil	RCT Hospital	The study was well reported, patients were randomized, and outcome assessors were blinded to the interventions.	It is unclear whether patients who participated in the study are representative of the population from which they were recruited, whether adjustment was made for confounding in the analyses, and whether the study was sufficiently powered.
Veiga[12] 2008 Brazil	RCT Hospital	Study objective, patient characteristics, main outcomes, and estimates of variability were clearly stated. The microbiologist was blinded, the length of follow-up was constant, and appropriate statistical tests were used.	Usual hygiene practice, adverse events, characteristics of patients lost to follow-up, and funding were not reported. External validity is lacking, as the study did not report the proportion of the source population from which the patients were derived, nor the proportion of those asked who agreed to participate. Participants were not blinded, compliance with intervention was not reliable, and bacterial counts are a surrogate for SSI. There is a possibility of selection bias in that it is unclear whether intervention assignment was concealed from patients and staff until recruitment was complete, and whether confounding and losses in patients to follow-up were accounted for in analyses. No power calculations were reported.
Johnson[15] 2010 USA	Cohort Hospital	The study was well reported, and patients were representative of the population from which they were drawn.	Patients lost to follow-up, adverse events, and participant rate were not reported. Internal validity may be compromised, as no attempt was made to blind patients or assessors, and compliance with using the cloths may be unreliable. This study suffers from selection bias as patients were not randomized, allocation was not concealed from patients or assessors, and it is unclear

Author Year Country	Study Design, Setting	Study Strengths	Study Limitations
			whether the study was adequately powered, or whether adjustments were made for confounding and patients lost to follow-up.
Zywiel[17] 2010 USA	Cohort Hospital	The study reports detailed population data and potential confounders are considered in the analysis. Patients were representative of the population from which they were drawn. Study reflects clinical practice.	Adverse events and patients lost to analysis were not reported. Due to study design, no blinding of patients or assessors took place. Self-reported compliance with the intervention may not be reliable. No power calculation was performed to determine the sample size necessary to detect clinically relevant outcomes. Statistical analysis was not provided.
Dizer[14] 2009 Turkey	Cohort (time period) Hospital	Overall, this study was well reported and participants were representative of the recruited population.	No information was provided regarding funding, characteristics of patients lost to follow-up, or adverse events. The study lacked external validity, as the proportion who were asked and agreed to participate was not stated. The study was conducted at a military medical college and patients and interventions may not be representative of patients in other hospital settings. The study is prone to selection bias, as patients were not randomized, assignment was not concealed from patients or assessors, and it is unclear whether patients lost to follow-up were accounted for in analyses, or whether the study was sufficiently powered.
Magera Jr.[16] 2007 USA	Cohort (single surgeon) Clinic	This study was well reported. Patients were recruited from the same population over the same period.	The study did not report the source of funding, characteristics of patients lost to follow-up, or adverse events. The proportion of patients who were asked and participated in the study was not reported. Internal validity may be compromised, as patients were not randomized and no attempt was made to blind patients or assessors. It is unclear whether the study was

Author Year Country	Study Design, Setting	Study Strengths	Study Limitations
			adequately powered, and whether patients lost to follow-up and confounders were accounted for in the analyses.
Antiseptic Preparation versus Hygiene			
Meier[18] 2001 Nigeria	RCT Hospital	This study clearly described the objective of the study, characteristics of included patients, and main outcome measures. Distribution of confounders and main study findings were clearly described. The time between intervention and outcome assessment was the same between groups. Statistical tests were appropriate and compliance with interventions was reliable. Patients were randomized to interventions.	This study failed to describe the strength or source of interventions, provide estimates of variability in main outcome data, and report adverse events, source of funding or characteristics of patients lost to follow-up. External validity is weak, as the study did not specify how patients were selected or the proportion of those asked who agreed to participate in the study. Internal validity is compromised, as there was no mention of attempts to blind patients or assessors or whether allocation was concealed from patients and staff. It is unclear whether the study was of sufficient power to detect a clinically important effect. It is unclear whether confounding and losses of patients to follow-up were accounted for in the analyses.
Kalantar-Hormozi[19] 2005 Iran	RCT Hospital	This study clearly described the objective of the study, characteristics of included patients, interventions, main outcome measures, confounders, and study findings. The time between intervention and outcome assessment was the same between groups. Statistical tests were appropriate and compliance with interventions was reliable.	The study failed to report adverse events, characteristics of patients lost to follow-up, and sources of funding. The proportion of patients asked who agreed to participate in the study was not reported. Internal validity is compromised, as an inappropriate method of randomization was used, there was no mention of any attempts to blind patients or assessors, and assignments may not have been concealed until recruitment was complete. It is unclear whether confounding and losses of patients to follow-up were taken into account in analysis or whether the study was adequately powered.
Comparison of Antiseptics			

Author Year Country	Study Design, Setting	Study Strengths	Study Limitations
Darouiche[24] 2010 USA	RCT Hospital	This study was adequately powered and very well reported. Patients were randomized using an appropriate method, and investigators diagnosing SSIs were blinded to intervention. The study used an intention-to-treat approach to analysis.	The study findings may not be generalizable, as the method of sampling and the proportion of patients asked who agreed to participate in the study were not stated.
Paochaoroen[21] 2009 Thailand	RCT Hospital	The authors clearly reported study objectives, main outcomes, and characteristics of patients included in the study. Statistical analyses were appropriate, compliance with interventions was reliable, and outcome measures used were accurate and reliable. Patients were randomized to interventions.	This study failed to report the percentage of iodine in scrub and paint solution, an accurate number of patients in the PI group, the characteristics of patients lost to follow-up, and source of funding. The study holds weak external validity, as the proportion of those asked who agreed to participate was not provided, and the study may not be representative of the intervention most patients receive. Internal validity is compromised in that no attempts were made to blind patients or assessors to the intervention, or to conceal assignment from patients and staff until recruitment was complete. It is unclear whether losses of patients to follow-up were accounted for or whether the study was sufficiently powered.
Kehinde[22] 2009 Kuwait	RCT Hospital	Patient characteristics and interventions were well described, and potential confounders were adequately accounted for in the analysis.	The method of randomization was not reported, and no attempt to blind patients or outcome assessors was described. It is unclear whether the study was sufficiently powered to detect clinically relevant differences.
Veiga[23] 2008 Brazil	RCT Hospital	The authors clearly reported the study objective, main outcomes, interventions, and main findings. Participants were randomized to interventions, and compliance with interventions was reliable.	This study failed to report characteristics of study participants and those lost to follow-up, confounders, and adverse events. The study holds weak external validity, as the sampling procedure and the proportion of patients asked who agreed to participate is not reported. Internal validity is compromised, as there is no mention of any

Author Year Country	Study Design, Setting	Study Strengths	Study Limitations
			attempts to blind patients or assessors or to conceal assignments until recruitment had finished. It is unclear whether confounding and losses of patients to follow-up were accounted for in analyses or whether the study was appropriately powered.
Segal[20] 2002 USA	RCT Hospital	The authors performed a power calculation a priori and had adequate randomization and allocation concealment. Outcomes were independently assessed.	Interventions used were poorly described. Surgeons were not blinded. Adverse events and loss of patients to follow-up were not reported. The source of funding was not stated.
Levin[25] 2011 Israel	Cohort Hospital	Patient characteristics and interventions were well reported, and patients were representative of the general population.	The study lacked randomization or blinding. Patients were recruited over different time periods, compromising internal validity. No source of funding was reported.
Swenson[26] 2009 USA	Cohort Hospital	A power calculation was performed a priori. The analysis was performed in an intent-to-treat manner. Patient characteristics and interventions were well described.	Not all groups reached the appropriate size based on power calculation. Patients were not randomized and outcome assessors were not blinded. Not all patients received their assigned intervention. Conditions at the study hospital changed during the study, which may have altered the characteristics of the population seen and created inequality in the care received in each group.
Boston[27] 2009 USA	Case-control Hospital	Patients were drawn from the same population over the same period and potential confounders were accounted for in the analysis.	No randomization or blinding was performed, given the study design used. Interventions were not clearly described, and adverse events were not reported. It is unclear whether the study was adequately powered.
Incise Drapes			
Jacobson[30] 2005 USA	RCT Clinic	Study was adequately powered to identify clinically important differences, and outcome assessors were blinded to interventions.	The method of randomization was unclear. The study population may not have been representative of the general population. Outcomes were not reported for all patients randomized, and losses to follow-up were not described.

Author Year Country	Study Design, Setting	Study Strengths	Study Limitations
Segal[20] 2002 USA	See above		
Yoshimura[31] 2003 Japan	Cohort Hospital	This study featured a large sample of patients, representative of the general population.	There was no randomization or blinding in this study. Wound infections associated with intra-abdominal infections were omitted and not included in the analysis.
Application Method			
Al-Majaly[32] 2006 Jordan	RCT Hospital	Interventions and outcomes were clearly described.	The study lacked statistical analysis. There was no indication of blinding of patients or outcome assessors, and the randomization method was not described. It is unclear whether the study was adequately powered.
Ellenhorn[33] 2005 USA	RCT Hospital	Study was adequately powered and used a valid method of randomization. Confounding factors were considered in the analysis.	Allocation concealment was unclear. There was no description of blinding. Loss of patients to follow-up was not described and the source of study funding was unclear.
Segal[20] 2002 USA	See above		
Weed[34] 2010 USA	Cohort Hospital	This study featured a large sample of patients, representative of the general population.	There was no randomization or blinding. Study subjects in different groups were recruited over different periods of time.

PI = povidone-iodine; RCT = randomized controlled trial; SSI = surgical site infection.

Appendix 13: Study Results and Authors' Conclusions

Author Year Country	Study Results	Authors' Conclusions
Pre-surgical Showering		
Veiga[13] 2009 Brazil	CHG: 1 *Staphylococcus aureus* (2%) PLC: 2 *Staphylococcus aureus* (4%) Control: 4 *Staphylococcus aureus* (8%) $\chi^2 = 2.10$, P = 0.35 CHG: 1 superficial SSI (2%) PLC: 1 superficial SSI (2%) Control: 0 SSI (0%) $\chi^2 = 1.01$, P = 0.6	CHG showers were effective in reducing skin colonization with coagulase-negative staphylococci and yeasts, but there was no difference in postoperative infection rates.[13]
Veiga[12] 2008 Brazil	PI: 1 *Staphylococcus aureus* (1.8%) No instruction: 12 *Staphylococcus aureus* (21%) P = 0.0019, 95% CI not reported No SSIs were observed in either group.	Single preoperative PI showers are effective in reducing staphylococcal skin colonization before elective clean plastic surgical procedures on thorax and abdomen.[12]
Johnson[15] 2010 USA	Colonization: NR CHG: 0 SSIs (0%) Non-compliant: 14 SSIs (1.6%) P = 0.231, 95% CI not reported	At-home preoperative patient skin preparation is a simple and cost-effective method for reducing periprosthetic hip infection rates.[15]
Zywiel[17] 2010 USA	CHG: 0 SSIs (0%) Partial compliance: 1 SSI (1.5%) Non-compliant: 21 SSIs (3.0%) P-value, 95% CI not reported	Patient-directed use of chlorhexidine-impregnated cloths on evening before and morning of surgery appears to decrease incidence of deep surgical site infection in elective knee arthroplasty.[17]
Dizer[14] 2009 Turkey	CHG: 2 *Escherichiae coli* in SSI (66 %) Control: 2 *Escherichiae coli* in SSI (20%) CHG: 3 SSIs (7%)	Preoperative skin preparation using clipper on nights before an operation and 50 mL CHG bath excluding head area, taken twice in preoperative period, are useful for reducing SSIs during postoperative period.[14]

Author Year Country	Study Results	Authors' Conclusions
	Control: 10 SSIs (25.6%) OR 4.76, 95% CI: 1.2 to 18.8, P = 0.026	
Magera Jr.[16] 2007 USA	4-fold reduction in preoperative perineal colonization with CHG compared with hygiene OR 0.24, 95% CI 0.08 to 0.65 CHG: 0 SSIs (0%) Usual hygiene: 1 SSI (2%)	Preoperative topical antimicrobial scrub resulted in 4-fold reduction in preoperative perineal colonization rate and overall reduction in positive surgical site cultures. Given low cost, safety, and efficacy, topical antimicrobial scrub should be considered before artificial urinary sphincter placement.[16]
Antiseptic Preparation versus Hygiene		
Meier[18] 2001 Nigeria	PI: 6 SSIs (5.9%) Soap: 5 SSIs (5.1%) P = 1.000, 95% CI not reported	Our data demonstrate that PI is no better than market soap and MS for preventing infections in clean, hernia operations. Available funds may better be used for preoperative antibiotics or for improvement in hospital infrastructure, which should result in fewer breaks in optimal operating room technique.[18]
Kalantar-Hormozi[19] 2005 Iran	PI: 0 SSIs Saline: 0 SSIs P = NS	Preoperative surgical scrub or shower with antiseptics is not an obligation in clean wound surgery; equal results can be obtained with the use of normal saline to prepare surgical site for operation if meticulous and careful technique is used.[19]
Comparison of Antiseptics		
Darouiche[24] 2010 USA	CHG: 39 SSIs (9.5%) PI: 71 SSIs (16.1%) P = 0.004, RR 0.59, 95% CI 0.41 to 0.85	Preoperative cleansing of patient's skin with CHG-alcohol is superior to cleansing with PI for preventing SSI after clean-contaminated surgery.[24]
Paochaoroen[21] 2009 Thailand	PI: 8 SSIs (3.2%) CHG: 5 SSIs (2%) OR 1.61, 95% CI 1.40 to 1.81	Colonization of bacterial and postoperative surgical wound infection was significantly reduced in CHG group. CHG antiseptic should be first consideration for preoperative skin preparation.[21]
Kehinde[22] 2009	CHG: 13 (11.4%) positive post-operative cultures CHG + PI: 3 (2.6%) positive post-operative cultures	Addition of PI to CHG-cetrimide mixture-based regimen of perineal skin antiseptic preparation is associated with

Author Year Country	Study Results	Authors' Conclusions
Kuwait	P < 0.001, 95% CI not reported	longer and more effective skin disinfection.[22]
Veiga[23] 2008 Brazil	CHG: 0 SSIs (0%) PI: 4 SSIs (1.6%) P = 0.06, 95% CI not reported	Despite the fact that all patients with postoperative infection were from the PI group, no statistically significant difference in postoperative infection rates was found. However, because staphylococcal skin colonization was significantly lower at end of surgery when CHG 0.5% antisepsis was used, we conclude that it is a better choice for skin antisepsis before elective clean plastic surgery.[23]
Segal[20] 2002 USA	PI paint: 7 SSIs (12.5%) PI scrub then paint: 7 SSIs (13.5%) Film only: 1 SSI (2%) Film plus drape: 3 SSIs (5.9%) χ^2 = 5.889, P = 0.117 Aqueous iodine: 14/108 SSIs (13%) Insoluble iodine: 4/101 SSIs (4%) χ^2 = 5.3, P = 0.02	Incidence of infection was lower in the 2 groups of patients who were prepped with insoluble iodine, indicating that the type of surgical skin preparation could affect whether patients develop surgical site infections. Clinical practice of skin preparation in this hospital changed based on these results.[20]
Levin[25] 2011 Israel	PI: 21 SSIs (14.6%) CHG: 5 SSIs (4.5%) P = 0.011 OR 3.25, 95% CI 1.13 to 9.30	This retrospective study demonstrates that antisepsis with CHG and alcohol was associated with a significant reduction in the rate of SSIs compared with PI in patients undergoing elective gynecological laparotomies. This is of clinical importance, as a change in antisepsis protocol can significantly reduce the morbidity and health care costs associated with patients undergoing elective gynecological surgery.[25]
Swenson[26] 2009 USA	PI: 72 SSIs (4.8%) CHG: 68 SSIs (8.2%) Iodine povacrylex: 38 SSIs (4.8%) P = 0.001 pairwise with CHG	Skin preparation solution is an important factor in the prevention of SSIs. Iodophor-based compounds may be superior to CHG for this purpose in general surgery patients.[26]

Author Year Country	Study Results	Authors' Conclusions
	OR 1.35, 95% CI 0.97 to 1.87, P = 0.073	
Boston[27] 2009 USA	Iodine alone found protective against SSIs OR 0.16, 95% CI 0.06 to 0.45, P < 0.001	Presence of comorbidities and increased surgical duration are risks for postoperative infection. Use of PI only was found to decrease risk of infection.[27]
Incise Drapes		
Jacobson[30] 2005 USA	Positive wound culture: DuraPrep: 23 patients (28%) PI: 32 patients (36.4%) 95% CI –22.4% to 5.6% SSI: No infections reported in either group	Antiseptic skin preparation with DuraPrep solution plus Ioban 2 incise drapes was not different from PI skin preparation plus Ioban 2 drapes for preventing wound contamination during total joint replacement surgery, although improved drape lift, time savings, and cost may influence the choice to use DuraPrep in place of standard iodophor skin preparation kit.[30]
Segal[20] 2002 USA	See above	
Yoshimura[31] 2003 Japan	SSIs: Iodophor only: 21 (12.1%) Iodophor plus drape: 4 (3.1%) P = 0.0096 Regression co-efficient: −0.075 95% CI −0.139 to 0.011 P = 0.0218	Non-use of adherent plastic iodophor drapes is a possible risk factor for wound infection after liver resection for hepatocellular carcinoma, and use of these drapes may be useful for decreasing infection rates, although a prospective study is necessary to reach definitive conclusions.[31]
Application Method		
Al-Majaly[32] 2006 Jordan	SSIs: CHG scrub: 4 (8.82%) CHG paint: 3 (7.42%) P = NS, 95% CI not reported	Simple painting of surgical site is as effective in preventing surgical wound infection as scrubbing for 10 minutes.[32]
Ellenhorn[33] 2005 USA	Wound infection: Scrub and paint: 12 (10%) Paint only: 12 (10%)	For patients undergoing abdominal operations, a PI scrub-and-paint protocol and a PI paint-only protocol do not differ in efficacy for infection prevention.[33]

Author Year Country	Study Results	Authors' Conclusions
	P = 0.078, 95% CI not reported Intra-abdominal infection: Scrub and paint: 4 (3%) Paint only: 2 (2%) P = 0.14 intra-abdominal, 95% CI not reported	
Segal[20] 2002 USA	See above	
Weed[34] 2011 USA	Scrub and paint protocol resulted in 38% reduction in major puerperal infection, 31% reduction in composite wound infection. Puerperal infection incident rate ratio 0.62, 95% CI 0.42 to 0.93, P = 0.02 Composite wound infection incident rate ratio 0.69, 95% CI 0.5 to 0.96, P = 0.03	Scrub and paint protocol is associated with decrease in rate of post-Caesarean delivery infectious complications compared with using PI topical paint alone.[34]

CHG = chlorhexidine gluconate; CI = confidence interval; NS = not significant; NR = not reported; OR = odds ratio; P = probability; PI = povidone-iodine; PLC = placebo; RCT = randomized controlled trial; RR = relative risk; SSI = surgical site infection.