

The Utility of Chlorhexidine Cloth Use for the Prevention of Surgical Site Infections in Total Hip Arthroplasty and Surgical as well as Basic Science Applications

A Meta-Analysis and Systematic Review



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KEYWORDS

• Infection • Prevention • Total joint arthroplasty • Chlorhexidine cloth • Outcomes

KEY POINTS

- Skin antisepsis is one of the fundamental cornerstones for reducing infections of primary lower extremity total joint arthroplasties.
- Found an almost universal benefit of the ready-to-use, no-rinse, 2% chlorhexidine-impregnated cloths.
- Applies to various surgical applications, such as total knee and hip arthroplasty as well as other surgical specialties.
- Recommend that dual application with use the night before and the morning of surgery should be the standard of care.

INTRODUCTION

The United States has the highest annual reported number of primary lower extremity total joint arthroplasties, with more than 658,000 performed.¹⁻³ Although knee and hip arthroplasties are highly successful elective surgical procedures with greater than 95% survivorship at 10-year mean follow-ups, there are still estimated to be approximately 80,000 revision procedures performed each year, with the most common reason now being periprosthetic infections.²⁻⁶ Despite the prevention efforts, the infection rates in total knee and hip arthroplasty (TKA and THA) remain at approximately 1.5% or higher.^{7,8} Their approximate cost is \$75,000

per year per infection,⁹ making it close to a \$2 billion or more annual problem.

Despite substantial infection prevention efforts, there are reports that demonstrate that the incidence of infection has been increasing.^{2,10} Springer and colleagues studied infection among knee and hip arthroplasties¹¹ in six national arthroplasty registries (ie, American Joint Replacement Registry, Australian Orthopedic Association National Joint Replacement Registry, National Joint Registry of England, Wales, Northern Ireland, and the Isle of Man, New Zealand Joint Registry, Swedish Hip Arthroplasty Register, and the Swedish Knee Arthroplasty Register). Between 2010 and 2015, the incidence of periprosthetic infections

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increased for both knee (0.88%–1.03%) and hip arthroplasty (0.79%–0.97%). Thus, it is imperative that new or improving strategies to reduce infections continue to be advanced.

Surgical site infections (SSIs) are affected by the density of microbes that may contaminate wounds during operations.¹² The endogenous flora of patients' skin is the most common cause of SSIs.^{13,14} Although it takes as little as 100 microbes per gram of soft tissue to cause infections, the natural density on the skin may be as great as 2×10^6 bacteria per square centimeter.^{13–16} Therefore, prevention protocols implemented for decreasing microorganisms on the skin should decrease rates of SSIs.³

There are a multitude of preoperative skin preparation methodologies currently available.³ One method is ready-to-use, disposable, 2% chlorhexidine-impregnated cloths. These are quick and simple to apply. They only need to be wiped on, and the antiseptic solution rapidly dries without having to be rinsed off. It has been demonstrated that skin treated in this manner retains antimicrobial activity for approximately 6 hours.¹⁷

Therefore, a basic overview and analysis of antiseptic disinfectants and chlorhexidine cloths is warranted. The authors first describe a comparison of chlorhexidine to other antiseptics and then a comparison of the cloths to solutions. This will then be followed by the main purpose of this study, which is a systematic review of chlorhexidine cloth applications in: (1) surgically relevant basic science studies; (2) knee arthroplasties; (3) hip arthroplasties; and (4) other surgical specialties. In addition, a meta-analysis of the qualifying knee and hip arthroplasty reports will be performed.

This summary of all surgeries will include every report on chlorhexidine cloth applications in TKAs. Although it is expected that TKAs and THAs cannot always be separated in studies, this thorough review will be valuable to knee surgeons.

COMPARISON TO OTHER ANTISEPTICS

Chlorhexidine has been shown to be effective as an antiseptic agent.^{18,19} It is a broad-spectrum bactericidal antimicrobial agent with activity against gram-positive and gram-negative bacteria. The mechanism of action is that the chlorhexidine salts dissociate and release cationic ions. These cations bind to the negatively charged bacterial cell walls, disrupting cell membrane integrity and lipid formation, and at high concentrations are bactericidal.^{20,21}

The Association of Registered Nurses recommends that patients receive preoperative scrubbing or antiseptic wash the night before or on the day of surgery. The Department of Health and Human Services recommends using an appropriate antiseptic agent for skin preparation and approved the use of preoperative showering or bathing with agents such as chlorhexidine.¹² Kapadia and colleagues investigated the incidence of SSIs in THA patients who used chlorhexidine cloths preoperatively compared with patients who did not.¹⁸ Through a review of their institution's database, 557 patients who used the cloths and 1901 patients who did not use the cloth were studied. They found that a statistically significant lower incidence of infections occurred in patients who were cleaned with cloths (0.5%) when compared with patients who were not (1.7%) at approximately 1 year follow-up ($P = .04$), thus demonstrating the efficacy of chlorhexidine (Fig. 1). Darouiche and colleagues studied whether chlorhexidine and alcohol were superior to povidone-iodine in patients undergoing clean-contaminated surgery (ie, colorectal, small intestinal, gastroesophageal, biliary, thoracic, gynecologic, or urologic operations performed under controlled conditions without substantial spillage or unusual contamination).²² A total of 849 patients (409 in the chlorhexidine–alcohol group and 440 in the povidone–iodine group) from six hospitals were analyzed. Their outcome of interest was any SSIs within approximately 30 days after surgery and they found that the rate was significantly lower in the chlorhexidine–alcohol group than in the povidone–iodine group (9.5 vs 16.1%; $P = .004$). Thus, this study further suggests the superiority of chlorhexidine compared with povidone-iodine.

ADVANTAGES OF CHLORHEXIDINE CLOTH APPLICATION VERSUS SOLUTIONS

Although there are many studies supporting the efficacy of preoperative chlorhexidine, there are two different ways to dispense the product.^{23–30} It can be applied as a solution or in no-rinse impregnated polyester cloth. Edmiston and colleagues supported the efficacy of showering with the solution, but also noted that the cloths might be a superior option.¹⁷ They studied the effect of chlorhexidine solution showering on skin surface concentrations. In a randomized prospective study conducted at a single institution, they analyzed 120 subjects. All of these participants were equally randomized into two groups, two applications (at night and then in

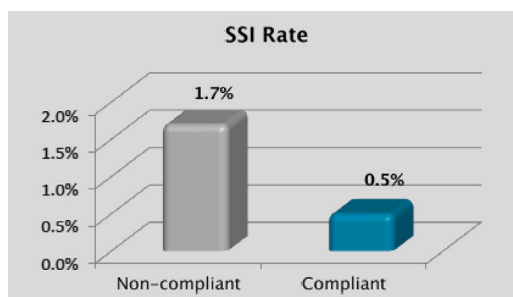


Fig. 1. Surgical site infection (SSI) rates within approximately 1 year follow-up in total hip arthroplasty patients who used chlorhexidine preoperatively (compliant) compared with patients who did not (non-compliant).

the morning), or three applications (two consecutive nights and then in the morning). Each of these groups was also equally subdivided into groups that paused for 0, 1, or 2 minutes before rinsing. Their outcome of measure was chlorhexidine skin surface concentration at approximately 4 hours after the morning application. They found that the mean chlorhexidine concentrations were significantly higher in the 1- and 2-min pause groups compared with the no-pause group in participants taking 2 (978.8 ± 234.6 , $1,042.2 \pm 219.9$, and 265.6 ± 113.3 $\mu\text{g/mL}$, respectively) or 3 ($1,067.2 \pm 205.6$, $1,017.9 \pm 227.8$, and 387.1 ± 217.5 $\mu\text{g/mL}$, respectively) showers ($P < 0.001$). They also investigated the activity of 2% chlorhexidine impregnated preoperative skin preparation cloth compared with an application of 4% chlorhexidine solution.¹⁷ They studied 30 subjects by randomizing their right and left inguinal skin sites into either cloth or solution treatment, respectively. They demonstrated that microbial reduction was significantly greater for the sites treated with the cloths at approximately 10 minutes, 30 minutes, and 6 hours after preparation ($P < 0.01$). The log(10) reductions for cloth-prepped sites at 10 minutes, 30 minutes, and 6 hours were 2.50, 2.33, and 2.54 for the abdominal sites as well as 3.45, 3.50, and 3.64 for the inguinal sites, respectively. However, the log(10) reductions for solution-prepped sites at 10 minutes, 30 minutes, and 6 hours were 2.18, 2.19, and 2.77 for the abdominal sites as well as 2.78, 2.63, and 3.15 for the inguinal sites, respectively. Therefore, this suggested that the cloth application is more advantageous than the solution. There are also many other potential advantages of the cloth application in addition to its superior efficacy compared with solution, such as ease of use and consistent dosing. There

is also no need to rinse it off after usage. As noted in the above study, if the chlorhexidine solution is left on to dry, antimicrobial activity is sustained for approximately 6 hours.¹⁷ In the following review, the authors specifically focus on the use of chlorhexidine cloths and not solutions.

METHODS

A literature search of the PubMed, EMBASE, and Cochrane Library was performed to identify studies evaluating the outcomes of chlorhexidine cloth use in surgeries. Search terms included "chlorhexidine," "gluconate," "wipe," "cloth," "antimicrobial," "antiseptic," "surgery," "hip," and "knee." An exhaustive review of the literature was further generated by looking at the reference list of the found articles.

Our initial search returned a total of 790 records. The products—cloths and solutions—were then clearly delineated. Inclusion criteria included: studies in English language, studies with greater than five cases, and articles reporting on the results of chlorhexidine cloths. Studies reporting only on the outcomes of chlorhexidine solutions were excluded. Other exclusion criteria included: narrative reviews, case reports of individual patients, and series with less than five total patients.

Studies were analyzed regarding their level of evidence. They were classified into: level of evidence I (high-quality prospective cohort studies with adequate power or systematic reviews or meta-analyses of these studies); II (lesser quality prospective cohort studies, retrospective cohort studies, untreated controls from randomized control studies, or systematic reviews of these studies); III (case-control studies or systematic reviews of these studies); IV (case series); and V (expert opinions, unpublished abstracts, case reports or clinical examples, or evidence based on physiology, bench research, or "first principles").³¹

After applying our criteria, 26 studies were deemed eligible and included in our review (Fig. 2).

Eligible knee and hip articles underwent a full-text systematic review of relevant outcome parameters with the primary outcome of interest (decreased rates of infection) coded as a binary variable (decreased vs not decreased). Demographics and infection rates stratified by patient risk were also tabulated. The tabulated results were stratified by surgically relevant basic science studies, TKAs, THAs, and other surgical specialties.

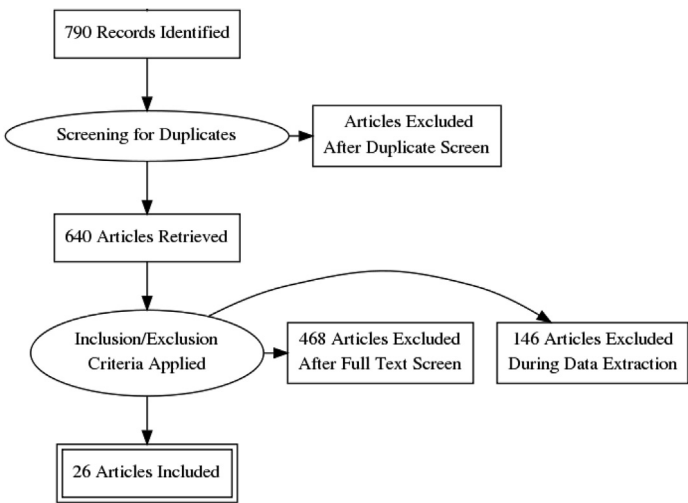


Fig. 2. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) diagram for study selection.

A further meta-analysis was performed to qualify relevant lower extremity joint arthroplasty studies from the above list. The inclusion criteria for the meta-analysis included: studies in English language, those with greater than five cases, and articles reporting on the comparison results of dual application chlorhexidine cloths on lower extremity total joint arthroplasties.

Data were extracted, compiled in a database, and analyzed using Microsoft Excel (Microsoft Corporation, Redmond, WA).

RESULTS
Surgically Relevant Basic Science Studies

A total of seven articles (one level of evidence I and six level of evidence II studies), detailed below, studied chlorhexidine cloth effectiveness from a basic science standpoint.

Edmiston and colleagues studied the superiority of chlorhexidine cloths compared with solution when they investigated the activity of 2% chlorhexidine-impregnated preoperative skin preparation cloth compared with an application of 4% chlorhexidine solution¹⁷ as described in detail above. They demonstrated that the antibacterial effect was greater for the sites treated with the cloths. When it is left on to dry, its antimicrobial activity persists for approximately 6 hours.

A study by Ryder investigated whether 2% no-rinse chlorhexidine cloths improved antiseptic persistence on patients' skin compared with 4% chlorhexidine rinse-off solutions.³² A total of 24 subjects were equally randomized (level of evidence II) into groups that either used the applications just the morning of the test or the

night before and the morning of the test. Testing of the different methods occurred 1 week apart. The outcome of interest was chlorhexidine residual 3 hours after the morning application. The results showed that in both groups, the 2% chlorhexidine cloth subjects had more residual chlorhexidine on their skin than the 4% chlorhexidine solution subjects. Two applications of the 2% chlorhexidine cloth showed more residual chlorhexidine than one ($P = 0.016$).

Rhee and colleagues investigated whether no-rinse 2% chlorhexidine-impregnated polyester cloth skin application yields greater residual chlorhexidine concentrations and lower bacterial densities on skin versus non-antiseptic cloths or cotton washcloths.³³ In a level of evidence II evidence prospective, randomized 2-center study, 63 participants (126 forearms) received chlorhexidine cloth skin cleansing on 1 forearm, whereas 33 participants received a non-antiseptic-impregnated cellulose/polyester cloth application on the contralateral forearm, and 30 participants were washed with a cotton washcloth dampened with sterile water. Immediately and 6 hours after application, chlorhexidine cloths yielded the highest residual chlorhexidine concentrations (2,500 and 1,250 $\mu\text{g/mL}$, respectively) and significantly lower bacterial densities compared with non-antiseptic cloths or cotton washcloths ($P < 0.001$).

Makhni and colleagues prospectively analyzed the effectiveness of chlorhexidine gluconate cloths for decreasing bacterial counts of patients on their posterior neck region.³⁴ There were 16 healthy adults who participated, where their right side of their neck was wiped twice

(ie, the night before and the morning of the experiment) with chlorhexidine gluconate cloths and the left side was used as a control region. Their outcomes of interest were bacterial growth at baseline on enrollment in the study, then on arrival at the hospital, and finally, after both sides of the neck had received standard preoperative scrubbing. All patients had positive bacterial growth at baseline (median > 1000 colonies/mL). When chlorhexidine gluconate cloths were used, bacterial counts were noted to be decreased (mean decrease in bacterial counts was 536 colonies for control and the mean decrease was 790 colonies for the intervention group) before the preoperative scrub, but this finding was not statistically significant ($P = 0.059$). All patients (100%) had no bacteria identified on either side of their neck after completion of the preoperative scrub. Thus, the authors suggested that at-home use of chlorhexidine gluconate cloths may not decrease the topical bacterial burden. However, their results suggested a decrease in bacterial counts with chlorhexidine cloth use, and its insignificance may have been due to the study being underpowered because there were only 16 participants.

Edmiston and colleagues performed a larger study to determine the skin concentrations of chlorhexidine after preoperative showering/skin cleansing using 4% soap compared with application via 2% impregnated polyester cloths.³⁵ A total of 60 participants were equally randomized into three groups: evening application only; morning application only; or evening and morning after application (level of evidence II). All groups showered with the soap first before a 1-week wash period before applying with the cloths. Their outcomes of interest were chlorhexidine skin surface concentrations at five selected skin sites (right/left antecubital fossa, right/left popliteal fossa, and abdomen) the morning after their respective applications. They found that the chlorhexidine cloths yielded significantly higher skin concentrations of the antiseptic as the mean values ranged from 12.7 to 27.4 times higher in that arm of the study compared with the antiseptic soap group ($P < 0.0001$). Thus, this study further supported the superiority of chlorhexidine cloths compared with solutions.

Whitman and colleagues evaluated the impact of 2% chlorhexidine-impregnated cloths on methicillin-resistant *Staphylococcus aureus* (MRSA) colonization.³⁶ In a randomized, double-blind, controlled trial, they studied 1,562 US Marine Corps recruits (level of evidence I). A total of 781 were randomized into

the chlorhexidine cloth group and 781 into the control cloth group. Subjects applied their respective cloths three times weekly, with the outcome of interest being the incidence of MRSA colonization during a minimum 6-week follow-up. Their results demonstrated that 77 subjects (4.9%) acquired MRSA and there were significantly fewer in the chlorhexidine group, 26 (3.3%), compared with 51 (6.5%) in the control group ($P = 0.004$).

Edmiston and colleagues investigated the benefit of an electronic alert system for enhancing compliance of preadmission application of 2% chlorhexidine gluconate and the effect of five applications on concentration levels.³⁷ A total of 100 participants from a single institution were equally randomized to five skin application groups: 1, 2, 3, 4, or 5 consecutive applications (level of evidence II). Subsequently, participants were also further equally randomized into two subgroups: with or without an electronic alert. Their outcome of interest was chlorhexidine skin-surface concentration measured approximately 10 days after final application. They found that the mean composite skin surface chlorhexidine concentrations in participants receiving electronic alerts following 1, 2, 3, 4, and 5 applications were: 1,040.5, 1,334.4, 1,278.2, 1,643.9, and 1,803.1 $\mu\text{g/mL}$, respectively, whereas composite skin surface concentrations in the no-electronic alert group were: 913.8, 1,240.0, 1,249.8, 1,194.4, and 1,364.2 $\mu\text{g/mL}$, respectively ($P < 0.001$). Therefore, this demonstrated the efficacy of electronic alerts and patient compliance as well as the sequential increase in chlorhexidine skin concentration with each additional application.

In summary, six of seven basic science articles (level of evidence I, 1 study, level of evidence II, five studies) demonstrated the positive antibacterial results of chlorhexidine cloths (Table 1). Although one other level of evidence II study only trended toward decreased bacterial counts with chlorhexidine cloth use ($P = 0.059$), the insignificant result was possibly due to its low power.

Knee Arthroplasty

The following section evaluates the outcomes of "TKA" using chlorhexidine cloths. In some articles, results combined TKAs and THAs where they could not be separated, and the data will be presented in this section. There were a total of 10 studies, 2 were level of evidence I reports, 6 were level of evidence II, and 2 were unpublished lower level studies (Table 2).

Table 1
 Results of basic science reports

Report	Subjects	Results
Edmiston, et al ¹⁷ 2007	30	Microbial reduction was significantly greater for the sites treated with the cloths at approximately 10 min, 30 min, and 6 h after preparation ($P < 0.01$)
Ryder, ³² 2007	24	Chlorhexidine cloth subjects had more residual chlorhexidine on their skin than the 4% chlorhexidine solution subjects
Edmiston, et al ³⁵ 2008	60	Chlorhexidine cloths yielded significantly higher skin concentrations (mean values ranged from 12.7 to 27.4 times higher) compared with the antiseptic soap group ($P < 0.0001$)
Whitman, et al ³⁶ 2012	1,562	Significantly less MRSA colonization in the chlorhexidine group, 26 (3.3%), compared with 51 (6.5%) in the control group ($P = 0.004$)
Edmiston, et al ³⁷ 2015	100	Mean skin surface chlorhexidine concentrations in participants receiving electronic alerts following 1, 2, 3, 4, and 5 applications were 1,040.5, 1,334.4, 1,278.2, 1,643.9, and 1,803.1 $\mu\text{g/mL}$, respectively, whereas concentrations in the no-electronic alert group were 913.8, 1,240.0, 1,249.8, 1,194.4, and 1,364.2 $\mu\text{g/mL}$, respectively ($P < 0.001$)
Rhee, et al ³³ 2018	63	Immediately and 6 h after cleansing, chlorhexidine cloths yielded higher residual chlorhexidine concentrations (2,500 and 1,250 $\mu\text{g/mL}$, respectively) and significantly lower bacterial densities compared with non-antiseptic cloths or cotton washcloths ($P < 0.001$)
Makhni, et al ³⁴ 2018	16	When chlorhexidine gluconate cloths were used, bacterial counts were noted to be decreased, but this finding was not statistically significant ($P = 0.059$)

Abbreviation: MRSA, methicillin-resistant *Staphylococcus aureus*.

Zywiel and colleagues evaluated the incidence of deep SSIs in knee arthroplasty patients who used six chlorhexidine-impregnated cloths the evening before surgery and the morning of surgery without rinsing (dual application).³⁸ A single institution’s database was reviewed in this level of evidence II study. A total of 136 patients who completed this protocol were compared with 711 who underwent standard in-hospital preparation only. The investigators defined a deep SSI as either a deep incisional or joint space infection occurring within 1 year of the surgical procedure and with the infection appearing to be related to the surgical procedure (ie, defined as an absence of a focus of infection or precipitating event unrelated to the index arthroplasty). They found that patients who complied with the skin preparation protocol had a considerably lower incidence of SSIs compared with those who underwent in-hospital preparation only. The 136 patients who used the dual-application protocol had no

SSIs compared with 21 infections in the 711 patients (3%).

Johnson and colleagues evaluated the incidence of surgical infections in TKA patients at a single institution using a preadmission dual-application chlorhexidine cloth protocol compared with a cohort of patients undergoing standard in-hospital perioperative preparation only.¹⁹ In a level of evidence II study, a total of 478 patients who underwent the protocol were compared with 1,735 patients who did not. They found that the incidence of SSIs was significantly lower at approximately 1 year follow-up in patients who used the full at-home advance 2% chlorhexidine gluconate protocol when compared with the comparison group (ie, 0.6 compared with 2.2%, $P = 0.021$).

Kapadia and colleagues in a level of evidence II study further investigated the incidence of surgical infections in TKA patients at a single institution using a preadmission chlorhexidine cloth dual-application protocol compared with a

Table 2
Results of total knee arthroplasty studies

Report	Subjects	Results
Eiselt, ⁴² 2009	736	Lower incidence of infections following total joint arthroplasty after implementation of chlorhexidine cloth use compared with before (1.59 vs 3.19%)
Zywiell, et al ³⁸ 2011	847	Patients who used chlorhexidine cloths had a 0% incidence of SSIs compared with 3% for those who underwent in-hospital preparation only
Hogenmiller, ⁴⁴ 2011	341	Found zero SSIs in the 7-month time period following implementation of chlorhexidine cloth use
Kapadia, et al ⁹ 2013	per 1,000	Annual net savings of approximately \$2.1 million with use of chlorhexidine cloths at their institution, and annual US health care savings of potentially \$3.18 billion
Johnson, et al ¹⁹ 2013	2,213	Patients who used chlorhexidine cloths had a 0.6% incidence of SSIs compared with 2.2% for those who did not ($P = 0.021$)
Farber, et al ⁴³ 2013	3,715	Incidence of SSIs was similar in patients receiving (1.0%, 18 of 1,891) and

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Table 2
(continued)

Report	Subjects	Results
		not receiving (1.3%, 24 of 1,824) chlorhexidine cloth, though only one cloth application
Kapadi, et al ⁴⁰ 2015	4,751	A total of 1,035 patients were compliant with a chlorhexidine cloth disinfection protocol (22%) compared with 3,716 who were not (78%)
Kapadia, et al ³⁹ 2016	3,717	Patients who used chlorhexidine cloths had a 0.03% incidence of periprosthetic infections compared with 1.9% for those who did not ($P = 0.002$)
Kapadia, et al ⁴¹ 2016	554	There were seven infections in the non-chlorhexidine group (2.9%) vs one in the chlorhexidine group (0.4%)
Worden, et al ⁴⁵ 2017	N/A	Found a marked reduction in the SSI rate from 1.28% to 0.78%

Abbreviations: N/A, not available; SSIs, surgical site infections.

cohort of patients undergoing standard in-hospital perioperative preparation only.³⁹ In their study of 3717 total patients who underwent primary or revision TKA and either used chlorhexidine cloths before surgery (991 patients) or did not (2,726 patients), the use of the cloths was found to be associated with a significantly reduced relative risk (RR) of periprosthetic infection at approximately 1 year surveillance (0.03 compared with 1.9%, $P = 0.002$).

The same investigators also studied the annual health care cost savings of implementing a preoperative chlorhexidine cloth treatment

protocol.⁹ In a level of evidence II study, they determined the rates of SSIs following TKA and the cost per revision procedure by analyzing reports from the National Healthcare Safety Network and previously published reports. They concluded that the cost-benefit of using chlorhexidine cloths at their institution per 1,000 TKA patients was a net savings of approximately \$2.1 million and this was extrapolated to be greater than \$2 billion in annual health care savings for the United States (ie, two-thirds reduction of periprosthetic annual cost of \$3.18 billion).

Kapadia and colleagues evaluated the compliance with a chlorhexidine cloth disinfection protocol at their institution.⁴⁰ They reviewed their institutional database (level of evidence II) and analyzed 2,458 patients who underwent primary or revision THA as well as 2,293 patients who underwent primary or revision TKA. Compliance was assessed by instructing patients to remove adhesive stickers from the cloth packages at the time of disinfection and to affix them to the instruction sheet presented on the day of surgery. Their results demonstrated that a total of 1,035 patients were compliant (22%) compared with 3,716 who were not (78%). The demographics of the two groups were not found to be greatly different. This low compliance demonstrates the need to overly emphasize to patients the need to use these cloths.

These same investigators conducted a prospective randomized study to better assess the effect of the chlorhexidine cloths.⁴¹ In analyses of primary hips, primary knees, revision hips, and revision knees (level of evidence I) with 275 patients in the chlorhexidine group and 279 in the non-chlorhexidine group, they found that there were seven deep periprosthetic infections in the non-chlorhexidine group (2.9%) versus one in the chlorhexidine group (0.4%). Thus, their prospective randomized study demonstrated the advantage of using chlorhexidine cloths.

A level of evidence I study by Eiselt confirmed the effects of the chlorhexidine cloths.⁴² The implementation of a protocol wherein chlorhexidine cloths were applied the evening before and the morning of the surgery was evaluated at a single institution with a total of 736 joint arthroplasty procedures analyzed. The investigator found a lower incidence after patients started to use chlorhexidine cloths compared with patients who did not (1.59 vs 3.19%). This represented a greater than 50% decrease in the rate of SSIs. The study further demonstrated that this trend continued through the year after implementation.

One study did not demonstrate a statistically significant effect of chlorhexidine cloths.⁴³ In a one-application study (level of evidence II) without mention of compliance, Farber and colleagues retrospectively compared the SSI rates between total joint arthroplasty patients who used chlorhexidine cloths to those who did not. They reviewed 3,715 patients (1,660 THAs and 2,055 TKAs) from their institution. They did not see a positive effect of using the chlorhexidine-impregnated cloths as part of a preoperative preventative measure for patients undergoing primary lower extremity total joint arthroplasty. The 1-year incidence of SSIs was similar in patients receiving (1.0%, 18 of 1,891) and not receiving (1.3%, 24 of 1,824) chlorhexidine cloths. However, this study only used a single chlorhexidine application, which differed from all of the other studies that used a dual application technique.

Hogenmiller presented an investigation of whether 2% chlorhexidine cloths used the night before and morning of surgery prevented total joint arthroplasty SSIs.⁴⁴ A total of 341 patients were analyzed in a level of evidence III single-institution study. They found no SSIs in the 7-month time period following implementation of chlorhexidine cloth use.

Worden and colleagues reported on whether the use of chlorhexidine cloths the day of surgery decreased SSIs in TKA or THA patients as well as spine surgery patients.⁴⁵ All patients who underwent TKA or THA as well as spine surgery from April 1 through October 31, 2016 in a 168-bed acute care community hospital were included (level of evidence III). They found a marked reduction in the SSI rate, from 1.28% to 0.78% for the 6-month observation period.

In summary, 10 studies analyzing chlorhexidine cloths and their relationship with knee arthroplasty (or combined lower extremity arthroplasty with hip) were evaluated (see [Table 2](#)). Seven of 8 outcome studies showed a decreasing incidence of SSIs with the use of the cloths. The one report that did not still had a lower infection rate for the chlorhexidine cloth group (1.0 vs 1.3%, not significant), but this may not have been an appropriate comparison to the other seven studies, because they only used a single application. The remaining two reports discussed the substantial economic impact of chlorhexidine cloths and the need to improve on patient compliance.

Hip Arthroplasty

In the following section, the authors review the outcomes from three level of evidence II reports

Table 3
Results of hip arthroplasty studies

Report	Subjects	Results
Johnson, et al ⁴⁶ 2010	954	No surgical site infections in the chlorhexidine cloth users, whereas there were 14 (1.6%) for those receiving only standard preoperative skin preparation
Kapadia, et al ¹⁸ 2013	2,458	Statistically significant lower incidence of infections occurred in patients who used chlorhexidine cloths (3 infections, 0.5%) compared with patients who did not (32 infections, 1.7%) at approximately 1 year follow-up ($P = 0.04$)
Brown, et al ⁴⁸ 2014	3,517	Rate of infections fell from 1.17 (25 of 2,130) to 0.5% (7 of 1,387) ($P = 0.045$)
Kapadia, et al ⁴⁷ 2016	3,844	Patients who did not have preoperative chlorhexidine gluconate disinfection were shown to have a significantly higher risk of infections vs those who received chlorhexidine (1.62 compared with 0.6%, $P = 0.0226$)

Abbreviation: THAs, total hip arthroplasties.

and a lower level study on THA. Other combined knee and hip studies were discussed above in the knee arthroplasty section.

Johnson and colleagues evaluated the effectiveness of chlorhexidine-impregnated cloths in decreasing the incidence of deep periprosthetic hip arthroplasty infections in a multi-surgeon single-institution study.⁴⁶ In a level of evidence II study, a total of 954 patients were analyzed with 157 performing applications of chlorhexidine cloths the night before and the morning of surgery and the remaining 897 receiving only the standard preoperative skin preparation. There were no SSIs in the chlorhexidine cloth users, whereas 14 (1.6%) had infections in the comparison group.

Kapadia and colleagues investigated the incidence of SSIs in THA patients who used a dual application of chlorhexidine-impregnated cloth compared with patients who did not.¹⁸ A total of 557 patients who used the chlorhexidine cloths and 1901 patients who did not were studied through a review of their institution's database (level of evidence II). They found a statistically significant lower incidence of infections occurring in patients who used the chlorhexidine cloths (3 infections, 0.5%) when compared with patients who did not (32 infections, 1.7%) ($P = .04$), thus, demonstrating the efficacy of the chlorhexidine-impregnated cloths.

The above investigators also performed a larger level of evidence II study to determine if preadmission dual application of chlorhexidine cloths decreased the risk of SSIs in patients undergoing THA. A total of 3844 THA patients who either used chlorhexidine cloths before surgery (998 patients) or only underwent standard perioperative disinfection (2,846 patients) were

studied. Patients who did not use the preoperative chlorhexidine disinfection protocol were shown to have a significantly higher risk of infections for 1 year after surgery (1.62 compared with 0.6%, $P = 0.0226$).⁴⁷

Brown and colleagues evaluated the effects of preoperative chlorhexidine use at home.⁴⁸ A total of 3,517 THA patients from a single center were investigated (level of evidence III). They compared the infection rates after implementation of this protocol to the rate of infection in the preceding 34 months. Their results demonstrated that the rate of hip infections fell from 1.17 (25 of 2,130) to 0.5% (7 of 1,387) ($P = 0.045$). They also found that the rate of infections caused by *S aureus* decreased from 0.66% to 0.22% over the same time period.

In summary, three level of evidence II articles and a lower level study all showed the positive effect of chlorhexidine cloth use for the prevention of SSIs after THAs (Table 3). Note that four other studies reporting on positive results of cloths after combined hip and knee arthroplasties were discussed in the preceding section.

Further Summary of Hip and Knee Arthroplasty Reports

In total, there were nine knee and hip arthroplasty clinical outcome studies (two level of evidence I and seven level of evidence II) on the effects of preoperative chlorhexidine cloth use. The specifics of the demographics (Table 4) and infection rates (Table 5) are detailed below.

Meta-Analysis

The meta-analysis included eight studies (15,323 patients) and demonstrated overall significant reductions with the dual application use of

Table 4
Demographics

Study	Combined Number of Patients	Age in Years, Mean (Range)	Sex: M:F	Mean Body Mass Index (kg/m ²) (Range)
Eiselt, ⁴² 2009	736	N/A	N/A	N/A
Johnson, et al ⁴⁶ 2010	954	58 (26–89)	1:1	29 (15–60)
Zywiell, et al ³⁸ 2011	847	63 (20–90)	1:2	34 (17–39)
Johnson, et al ¹⁹ 2013	2213	63 (18–90)	1:1	34 (15–74)
Kapadia, et al ¹⁸ 2013	2,458	57 (12–106)	2:3	34 (15–77)
Farber, et al ⁴³ 2013	3,715	64	4:5	N/A
Kapadia, et al ³⁹ 2016	3,717	62	2:3	34
Kapadia, et al ⁴¹ 2016	554	62 (41–104)	1:2	32 (19–41)
Kapadia, et al ⁴⁷ 2016	3,844	59	9:11	30

Abbreviations: F, female; M, male; N/A, not available

chlorhexidine cloths (0.42 vs 1.98%, $P < 0.05$) (Table 6). In addition, a meta-analysis was performed on six studies (14,033 patients) analyzing the infection incidence stratified by patient risk (Table 7). It found that the dual application of chlorhexidine cloths significantly reduced the rate in low- (0.5 vs 1%), medium- (0.3 vs 2.1%), and high-(0.7 vs 4.6%) risk patients ($P < 0.05$).

Other Surgical Specialties

Chlorhexidine cloth use has been analyzed in five studies (two level of evidence I, two level of evidence II, and one lower level unpublished study) in other surgical fields, which will now be summarized.

Murray and colleagues tested whether the home application of a 2% chlorhexidine gluconate cloth before shoulder surgery would be more efficacious than a standard shower of

soap and water at decreasing the preoperative cutaneous levels of pathogenic bacteria on the shoulder.⁴⁹ In a multi-surgeon single-institutional randomized, prospective study (level of evidence I), they evaluated 100 consecutive patients, equally assigned to use 2% chlorhexidine gluconate-impregnated cloths (treatment group) or to shower with soap and water before surgery (control group). Their outcomes of interest were overall positive culture rates and the positive culture rates for coagulase-negative *Staphylococcus* at a minimum of 2 months follow-up. They found that the treatment group had an overall positive culture rate of 66%, whereas it was 94% in the control group ($P = 0.0008$). The positive culture rate for coagulase-negative *Staphylococcus* was 30 versus 70% for the treatment and control cohorts, respectively ($P = 0.0001$).

Table 5
Infection prevention success of chlorhexidine cloths stratified by patient risk

Study	Combined Number of Patients	Overall Infection Incidence	Low Risk	Medium Risk	High Risk
Eiselt, ⁴² 2009	736	1.59 vs 3.19%	N/A	N/A	N/A
Johnson, et al ⁴⁶ 2010	954	0 vs 1.6%	0 vs 1.6%	0 vs 2.7%	0 vs 7.3%
Zywiell, et al ³⁸ 2011	847	0 vs 3%	0 vs 1.6%	0 vs 2.4%	0 vs 7.3%
Johnson, et al ¹⁹ 2013	2,213	0.6 vs 2.2%	0.9 vs 1.1%	0.5 vs 2.4%	0 vs 4%
Kapadia, et al ¹⁸ 2013	2,458	0.5 vs 1.7%	0.6 vs 0.8%	0 vs 1.7%	2.5 vs 5.6%
Farber, et al ⁴³ 2013	3,715	1.0 vs 1.3%	N/A	N/A	N/A
Kapadia, et al ³⁹ 2016	3,717	0.03 vs 1.9%	0.5 vs 1%	0.2 vs 2.1%	0 vs 3.5%
Kapadia, et al ⁴¹ 2016	554	0.4 vs 2.9%	N/A	N/A	N/A
Kapadia, et al ⁴⁷ 2016	3,844	0.6 vs 1.62%	0.5 vs 0.9%	0.6 vs 1.8%	1 vs 4.1%

Abbreviation: N/A, not available.

Table 6
Meta-analysis of overall infection incidence

Study	Combined Number of Patients	Overall Infection Incidence
Eiselt, ⁴² 2009	736	1.59 vs 3.19%
Johnson, et al ⁴⁶ 2010	954	0 vs 1.6%
Zywiell, et al ³⁸ 2011	847	0 vs 3%
Johnson, et al ¹⁹ 2013	2,213	0.6 vs 2.2%
Kapadia, et al ¹⁸ 2013	2,458	0.5 vs 1.7%
Kapadia, et al ³⁹ 2016	3,717	0.03 vs 1.9%
Kapadia, et al ⁴¹ 2016	554	0.4 vs 2.9%
Kapadia, et al ⁴⁷ 2016	3844	0.6 vs 1.62%
Pooled effect	15,323	0.42 vs 1.98% ($P < 0.05$)

Graling and colleagues conducted a prospective cohort study on the effectiveness of preoperative chlorhexidine gluconate cloths at reducing SSIs.⁵⁰ They implemented a practice change to use 2% chlorhexidine cloths preoperatively on all patients older than 2 months of age who were admitted through the main operating room preoperative area during a 4-month period. These patients were compared with baseline patients undergoing general and vascular surgery found in the National Surgical Quality Improvement Program database maintained by their surgery department (level of evidence II). A total of 335 patients who received the chlorhexidine cloths were compared with 284 patients who did not receive chlorhexidine cloth application. They defined a deep surgical wound infection as occurring at the operative site within 30 days of surgery if no implant was left in place or within 1 year if an implant was left in place. The infections also had to seem to be related to the surgery and involve tissue or

spaces at or beneath the fascial layer. Their results indicated a statistically significant overall reduction of infections in the group that received a 2% chlorhexidine cloth application before surgery (7 infections (2.1%) compared with 18 (6.3%) without chlorhexidine cloths, $P = 0.01$).

Bak and colleagues evaluated the rate of SSIs after their institution implemented chlorhexidine gluconate-impregnated cloths as a preoperative antiseptic preparation in elective vascular surgery.⁵¹ They reviewed 250 patients who used the chlorhexidine cloths preoperatively and compared them with 252 control patients who received chlorhexidine showers preoperatively before the implementation (level of evidence II). They evaluated SSIs within 30 days of operation and found no difference in the overall rate (5.6 vs 5.6%, $P = 1.00$), but the chlorhexidine shower group trended toward deeper infections (4 deep incisional and 2 organ space vs 0 and 1, respectively). In addition, the shower group had

Table 7
Meta-analysis of infection incidence stratified by patient risk

Study	Combined Number of Patients	Low Risk	Medium Risk	High Risk
Johnson, et al ⁴⁶ 2010	954	0 vs 1.6%	0 vs 2.7%	0 vs 7.3%
Zywiell, et al ³⁸ 2011	847	0 vs 1.6%	0 vs 2.4%	0 vs 7.3%
Johnson, et al ¹⁹ 2013	2,213	0.9 vs 1.1%	0.5 vs 2.4%	0 vs 4%
Kapadia, et al ¹⁸ 2013	2,458	0.6 vs 0.8%	0 vs 1.7%	2.5 vs 5.6%
Kapadia, et al ³⁹ 2016	3,717	0.5 vs 1%	0.2 vs 2.1%	0 vs 3.5%
Kapadia, et al ⁴⁷ 2016	3,844	0.5 vs 0.9%	0.6 vs 1.8%	1 vs 4.1%
Pooled effect	14,033	0.5 vs 1% ($P < 0.05$)	0.3 vs 2.1% ($P < 0.05$)	0.7 vs 4.6% ($P < 0.05$)

Table 8
Results of other surgical specialty studies

Report	Subjects	Results
Baxter et al, ⁵³ 2009	1,098 orthopedic cases	Significant reduction in the SSI rate from 3.05% to 1.04% ($P = 0.015$)
Murray et al, ⁴⁹ 2011	100 shoulder surgeries	Group treated with 2% chlorhexidine gluconate-impregnated cloths had an overall positive culture rate of 66%, whereas it was 94% in the control group ($P = 0.0008$)
Graling et al, ⁵⁰ 2013	619 general and vascular surgery cases	Reduction of infection in the group that received a 2% chlorhexidine cloth application before surgery (7 infections (2.1%) compared with 18 (6.3%), $P = 0.01$)
Bak et al, ⁵¹ 2017	502 vascular surgery cases	Chlorhexidine shower group trended toward deeper infections and had significantly more dirty or infected surgical wounds (21.4 vs 10%, $P < 0.01$), antibiotic errors, including their redosing and timing ($P < 0.02$), and frequent perioperative hypothermia (22.2 vs 10%, $P < 0.01$)
Stone et al, ⁵² 2020	1,309 cesarean deliveries	A total of 10 of 516 (1.9%) patients in the chlorhexidine group and 17 of 502 (3.4%) patients in the placebo group were diagnosed with SSIs at 6 wk after cesarean delivery (relative risk, 0.57; 95% confidence interval, 0.26–1.24)

Abbreviation: SSI, surgical site infection.

significantly more dirty or infected surgical wounds (21.4 vs 10%, $P < 0.01$), antibiotic errors, including redosing and timing ($P < 0.02$), and frequent perioperative hypothermia (22.2 vs 10%, $P < 0.01$), suggesting that the use of chlorhexidine cloths led to shallower and cleaner infections.

Stone and colleagues investigated whether preadmission application of chlorhexidine gluconate-impregnated cloths may decrease SSIs after cesarean delivery.⁵² In a single-institution level of evidence I study, they randomized 662 patients to use chlorhexidine cloths and 647 to use a placebo the night before and after a shower in the morning of the scheduled cesarean delivery. They found no significant difference in

SSIs by 6 weeks between the two groups (2.6 in the chlorhexidine group compared with 3.7% in the placebo group, $P = 0.24$). However, they found that the absolute difference in the rate of SSIs between the chlorhexidine and the placebo groups was -1.14% . In addition, when adjusting for full adherence to the protocol and those who were available for assessment, 10 of 516 (1.9%) patients in the chlorhexidine group and 17 of 502 (3.4%) patients in the placebo group were diagnosed with SSIs at 6 weeks after cesarean delivery (RR, 0.57; 95% confidence interval (CI), 0.26–1.24). The low RR and wide range of the CIs suggested to the authors that greater compliance may lead to enough power to achieve clinical significance.

Baxter and colleagues, in a level of evidence III study, investigated the effect of implementing 2% chlorhexidine non-rinse cloths for the “night-before and morning-of” site-specific skin preparation on orthopedic SSIs.⁵³ They analyzed 1,098 cases performed at a single institution. Their data analyses revealed a significant reduction in the SSI rates per 100 surgeries from 3.05% to 1.04% ($P = 0.015$).

In summary, five studies in other surgical fields also reported on the efficacy of chlorhexidine cloths in decreasing SSIs (Table 8). A total of three of the studies reported significant reductions in infections with the use of the chlorhexidine cloths. The remaining two both showed improved outcomes and positively trending results regarding the cloth applications reducing SSIs. However, they did not achieve significance, possibly due to their low power.

DISCUSSION

One of the most devastating complications after primary lower extremity total joint arthroplasties is periprosthetic infections.³⁻⁶ Unfortunately, despite substantial infection prevention efforts, their rate has been increasing.^{2,10} Ready-to-use, no-rinse, 2% chlorhexidine-impregnated cloths have shown excellent results for infection prophylaxis. Thus, the authors endeavored to conduct a literature review of studies on chlorhexidine cloths relating to the relevant surgical basic science studies, knee and hip arthroplasties, and other surgical fields. Almost every study that had reasonable power ($>90\%$) and used a dual application approach showed positive results and improvement. All other studies demonstrated decreases in SSI rates or severity. A further meta-analysis of relevant studies comparing the results of dual application chlorhexidine cloths on lower extremity joint arthroplasties (15,323 patients) demonstrated significant reduction in SSI incidence (0.42 vs 1.98%, $P < 0.05$). In addition, a meta-analysis analyzing the infection incidence stratified by patient risk (14,033 patients) found that the dual application of chlorhexidine cloths significantly reduced the rate in low- (0.5 vs 1%), medium- (0.3 vs 2.1%), and high- (0.7 vs 4.6%) risk patients ($P < 0.05$).

This comprehensive review of surgeries contained all literature on chlorhexidine cloth applications in TKAs. Some TKA data were combined with THA results, but nevertheless, these findings should provide guidance for the audience.

This study is not without limitations. Some reports were underpowered and there is still the

need for more level of evidence I studies. In addition, compliance was not always reported and, as particularly noted in one study, can be a major problem.⁴⁰ If compliance were optimized, even better results may have been achieved. Further work in this area is warranted.

SUMMARY

Based on the reports included in this review, it seems that the use of chlorhexidine cloths is appropriate for prophylaxis in a wide variety of surgeries. In knee and hip arthroplasties, preoperative use of chlorhexidine cloths has demonstrated favorable clinical outcomes in the systematic reviews. In addition, a detailed meta-analysis showed favorable outcomes in all arthroplasty studies. Also, there were similar favorable outcomes in reducing SSIs found in other general surgical fields. Further investigation into those specialties as well as even more medical applications would be appropriate for future studies. In summary, chlorhexidine cloths have demonstrated a reduction in SSIs, and the authors believe that their dual application with use the night before and the morning of surgery should be the standard of care.

CLINICS CARE POINTS

- use of chlorhexidine cloths is appropriate for prophylaxis in a wide variety of surgeries, especially lower extremity arthroplasties.
- Dual application use the night before and the morning of surgery should be the standard of care.
- Further investigation into other specialties as well as even more medical applications would be appropriate for future studies.

DISCLOSURE

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