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Efficacy of antimicrobial washes before shoulder surgery against *Cutibacterium*: a systematic review and meta-analysis

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Background: *Cutibacterium acnes* is a commensal intradermal microorganism that is commonly isolated at revision shoulder arthroplasty. Standard practice chlorhexidine gluconate (CHG) skin preparation agents have limited effectiveness at eradicating *C. acnes* in the dermis. Benzoyl peroxide (BPO) has demonstrated effectiveness against *C. acnes*. This meta-analysis compares the efficacy of at-home shoulder decolonization before surgery using CHG vs. BPO to reduce shoulder *C. acnes* burden.

Methods: This was a Preferred Reporting Items for Systematic Reviews and Meta-Analyses systematic review. PubMed and MEDLINE databases were searched for studies evaluating the effects of CHG and BPO in reducing *C. acnes* at the shoulder. Trial results were extracted and pooled using a random effects model, separating data from randomized controlled trials (RCTs) and non-RCTs. Methodologic quality of studies was assessed using the Cochrane Risk of Bias Assessment Tools.

Results: Ten studies (589 patients) were included. RCTs showed that both BPO and CHG led to significant reductions in culture positivity compared with negative controls (risk ratio [RR] with 95% confidence interval [CI] = 0.20 [0.13, 0.30], $P < .0001$ and 0.46 [0.37, 0.57], $P < .0001$, respectively). Non-RCT data demonstrated similar results comparing BPO and CHG to the control (RR with 95% CI = 0.34 [0.21, 0.57], $P < .0001$ and 0.31 [0.20, 0.49], $P < .0001$, respectively). Comparing BPO and CHG, RCT data showed a significant reduction in culture positivity with BPO (RR with 95% CI = 0.46 [0.27, 0.77], $P < .009$). Of RCTs, 5 were low and one was of moderate risk of bias. Of non-RCTs, 3 had low risk of bias, whereas one had moderate risk of bias.

Conclusion: This review demonstrated that preoperative CHG and BPO can reduce *C. acnes* at the shoulder. However, BPO exhibits greater efficacy than CHG, potentially because of the compound's ability to penetrate the dermis. BPO is a simple and economical agent that may reduce joint exposure to *C. acnes* in shoulder surgery.

Cutibacterium acnes (previously named *Propionibacterium acnes*) is a gram-positive aerotolerant anaerobic bacterium that is commensal on the skin surface but also resides deeper in the sebaceous glands of hair follicles because of its lipophilic characteristics. *C. acnes* is the pathogen associated with facial and truncal inflammatory acne vulgaris and is predominantly found in the shoulder, axilla, and chest regions of younger, male patients, illustrating the importance of this bacterium in shoulder surgery.[36] Although initially thought to be a culture contaminant, *C. acnes* is now recognized to be the leading cause of periprosthetic joint infection in the shoulder.[2]

Increased bacterial load with *C. acnes* has been implicated in many postsurgical complications, including arthroplasty failure, indolent shoulder pain and stiffness, and septic arthritis.[21,32,36] The risk factors for bacterial growth in the shoulder include prior ipsilateral shoulder surgery and corticosteroid injections, which are thought to seed the bacterium into the deep tissues.[29] The ability of *C. acnes* to produce a biofilm on the surface of implants is an important virulence factor in prosthetic joint infections. *C. acnes* has been cited as the most commonly isolated bacteria from cultures taken during revision surgery of failed arthroplasties.[1,20]

Skin preparation before surgical incision is one of many ways to reduce infection risk.[7,8] Standard skin preparation of the shoulder consists of 3 phases: at-home decolonization, presurgical preparatory decolonization, and sterile surgical preparation. As institutional guidelines and surgeon preferences vary, a consistent standard for skin preparation has yet to be developed. Commonly,

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at least 2 applications of at-home chlorohexidine gluconate (CHG) washes or benzoyl peroxide (BPO) gels and ointments beginning 48 hours preoperatively are recommended.[14] Presurgical preparatory decolonization often uses 70% isopropyl alcohol (IPA) solution at the site before sterile surgical preparation using ChloraPrep 2% CHG and 70% IPA (BD, Care Fusion, San Diego, CA, USA).

Investigations have shown that standard surgical skin preparation agents, such as 2% chlorhexidine gluconate (CHG) and 70% IPA are effective in eradicating Staphylococcal species but are less effective at eradicating *C. acnes*.[20,29] Up to 70% of healthy male patients have positive *C. acnes* cultures after standard sterile preps.[1] The limited ability of these standard agents to penetrate the deeper layers of the skin where *C. acnes* resides in sebaceous glands makes this bacterium difficult to eradicate. Thus, current standard surgical skin preparation agents may place patients at risk of developing prosthetic joint infection.

Peroxide-based skin preparation agents have shown promise in decreasing epidermal *C. acnes* in multiple studies.[10,16,22,33,44] Various applications of topical skin preparation with 5% and 10% BPO and 3% hydrogen peroxide (H_2O_2) have been studied in the perioperative period, including application by the patient in the 24-72 hours leading up to surgery.[9,17,22,33-35,44] BPO is a sterilizing agent adopted from its use of eradicating *C. acnes* for the dermatological condition acne vulgaris.[22] H_2O_2 is an inexpensive and readily available antimicrobial agent that creates free radicals through oxidative species. Both agents have shown substantial efficacy in significantly reducing *C. acnes* burden in patients undergoing shoulder surgery.[31,41] The superior efficacy of peroxide-based agents is likely because of their lipophilic structure, which allows deeper follicular penetration into the sebaceous glands of the dermis where the bacteria reside, which may be out of reach of traditional surgical skin preparations.[3,13]

The purpose of this study is to systematically review the literature and perform a meta-analysis comparing the effectiveness of at-home shoulder decolonization using standard agents alone (CHG and IPA) to BPO in reducing bacterial culture positivity in the superficial and deep tissues of the shoulder at the time of surgery. As prior studies have described the efficacy of BPO to eradicate *C. acnes* from the dermal layers and poorer response to CHG, in the present study, we seek to determine the clinical efficacy of each agent with respect to reducing shoulder culture positivity to define BPO's superiority over CHG for *C acnes* specifically. Although a previous review[31] has assessed the use of at-home applications of CHG and BPO, additional recent studies have been released that have significant clinical impact.[17,25,34,35] This meta-analysis will present high-level evidence and assess the quality of included studies by their risk of bias to assist clinical decision-making of surgical skin preparation techniques and help reduce periprosthetic joint infections caused by *C. acnes*.

Methods

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)

This systematic literature review and meta-analysis was performed in accordance with the guidelines published by Preferred Reporting Items for Systematic Reviews and Meta-Analyses.[23]

Search strategy and eligibility criteria

The primary literature search was conducted using the MEDLINE and PubMed databases for published research studies analyzing the efficacy of skin preparatory methods to reduce *C. acnes* culture positivity from dermal layers in shoulder surgery through May 21, 2021. Boolean operators were used in the PubMed database, and similar search terms were used in MEDLINE. The initial search produced 173 studies, which were assessed by 2 independent reviewers for eligibility criteria. Disagreement over eligibility was resolved by including a third independent reviewer to assess the study eligibility. The reference lists of included studies were screened for inclusion eligibility to identify articles not originally populated in the database searches.

Inclusion criteria for this study were based on preoperative or sterile preparatory methods to reduce *C. acnes*, shoulder or axillary culture location, outcome measured by culture positivity or bacterial load, and use of at least one common solution of interest (CHG or BPO). Exclusion criteria included articles not available in English, inclusion of patients aged <18 years, nonresearch trial–based methods, and case reports.

Data extraction

Data extraction was performed independently by 2 reviewers and was cross-referenced to determine discrepancies, which were resolved by consensus. Study data were extracted on publication date, study type, level of evidence, skin preparatory method, and type of surgery. Patient information, including diagnosis, sample size, preoperative antibiotics used, patient demographics, including age, gender, ethnicity, body mass index, previous steroid injections, and previous surgery, were collected to describe the included study population. Outcome data were collected using sample locations, operative timing of samples, culture durations, culture positivity (superficial, dermal, deep, suture, and negative control), shoulder infection rate, and culture positivity of other samples (surgeon's gloves, tools, controls, etc.).

The primary outcome assessed was the presence of *C. acnes* in the superficial skin, dermis, and deep cultures, measured by the incidence of positive cultures. These outcomes were evaluated among various treatment groups (no antimicrobial treatment, CHG, and BPO) and compared with determine statistically significant differences.

Risk of bias assessment

To assess the methodologic quality of included studies, independent reviewers used the Cochrane risk of bias tool for randomized trials (RoB-2) for randomized controlled trials (RCTs),[40] whereas the Cochrane risk of bias tool for nonrandomized studies of interventions (ROBINS-I) was used for non-RCT studies.[39] The domains assessed via RoB-2 were random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases to determine the overall risk of bias. The domains assessed via ROBINS-I were biases because of confounding, participant selection, classification of intervention, deviation from intended intervention, missing data, measurement of outcomes, and reported results. Using these tools, the studies were classified as low overall risk if they were deficient in only one domain, moderate risk if deficient in 2-3, and high risk if unsatisfactory in 4 or more.

Statistical analyses

Investigators analyzed the incidence of culture positivity from each study separately and categorized the data by intervention type (none, CHG, or CHG with BPO). Pooled risk ratios (RRs) with 95% confidence intervals (CIs) were determined for each subgroup analysis using the comparison group of unprepared shoulder culture positivity. To determine potential sources of heterogeneity in

the included RCTs, we conducted a one-at-a-time sensitivity analysis. All statistical analyses were run using Cran R version 4.1.0 (R Foundation for Statistical Computing, Vienna, Austria) and the Cochrane Review Manager 5.4 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2020).

Results

Study selection

We located 164 articles from our searches in the PubMed and MEDLINE databases (Fig. 1). Additional articles identified from reviewing references of articles in the search yielded 17 more articles. In total, our assessment began with 173 articles after removing duplicates. From these 173 articles, 111 were excluded based on title and abstract incongruence with study objectives. The remaining 62 articles were assessed for inclusion and exclusion criteria; 50 were excluded, as they did not assess CHG or peroxide-based agents, and another 2 articles were excluded for lacking a comparison group. Thus, our meta-analysis consisted of 10 total studies. All studies were assessed by 2 independent investigators, and no discrepancies were found in the abstracted data.

Study characteristics

Table I depicts the characteristics of the 10 included studies. Of these studies, 6 are RCTs, 2 are prospective cohort studies, and 2 are case series. The included RCTs represent level I evidence, the prospective cohort studies represent level II evidence, and the case series represents level IV evidence. These trials included a total of 589 participants. The CHG- and BPO treated subgroups consisted of 255 and 294 patients, respectively. The average reported age of patients enrolled in the RCTs was between 49.0 and 65.5 years, whereas the non-RCTs noted an average age ranging from 26.0 to 63.0 years. Of the 10 studies, 2 assessed CHG efficacy, 4 assessed BPO efficacy, and 4 assessed both CHG and BPO efficacy. Three of the non-RCT included studies assessed BPO, whereas only one used CHG. Eight of the included studies' outcomes were culture positivity for *C. acnes*, whereas 2 assessed the bacterial load with colony-forming unit quantification. Culture duration varied among the included trials, ranging from 5 to 21 days. Although some authors have reported mean anaerobic culture times of 6.8 days for *C acnes* growth, others favor incubation periods of up to 14-21 days to increase anaerobic culture load.[24,42] There were no studies comparing BPO or CHG to H_2O_2 with the primary outcome of culture positivity; thus, this relationship was not assessed in the present study.

The included studies each used an at-home application of antimicrobial agents (either CHG or BPO) in the days leading up to surgery, with adherence to protocol assessed by patient journals. All 6 studies that assessed CHG followed a treatment schedule of application of the solution the night prior and again on the morning of skin culturing. Four of these studies used a 4% CHG solution, 1 used a 2% solution, and 1 used a 0.5% solution. Of the 8 studies assessing BPO efficacy, 7 used a 5% BPO solution, and 1 used a 10% solution; each of these studies used a similar application schedule as the CHG studies. In all 10 included studies, before sampling in both CHG and BPO groups, the superficial skin of the shoulder was

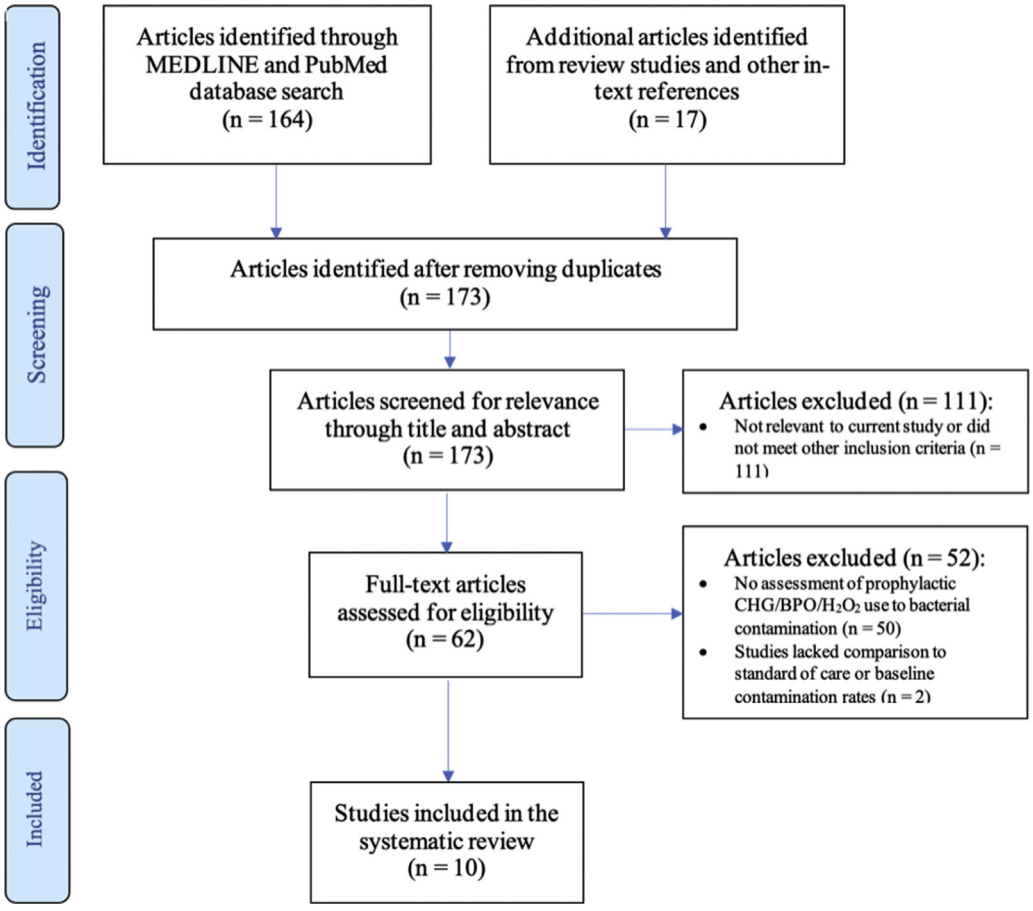

Figure 1 PRISMA flowchart depicting trial selection for inclusion.

Table I
Characteristics of studies comparing CHG and BPO efficacy to reduce *C. acnes*.

Study, year	Study type	Level of evidence	Study size	CHG Group size	Peroxide group size	Age (years)	Antimicrobial assessed	Culture duration	Primary study findings for *C. acnes*
Murray, 2011[30]	RCT	I	100	50	-	Experimental: 49 ± 16.2 Control: 52 ± 16.7	CHG	7 d	At-home CHG wash is not significantly superior to standard soap ($P = .32$)
Kolakowski, 2018[22]	RCT	I	80	39	41	CHG: 51 (mean) BPO: 51 (mean)	CHG and BPO	7 d	BPO is significantly superior to CHG at anterior ($P = .03$) and posterior ($P = .005$) deltoid
Scheer, 2018[34]	RCT	I	40	20	20	Range: 20-66	CHG and BPO	5 d	BPO significantly reduces colony-forming units compared with CHG ($P = .044$)
Hsu, 2020[17]	RCT	I	49	25	24	CHG: 65.5 ± 11.1 BPO: 63.4 ± 11.1	CHG and BPO	21 d	BPO is not significantly superior to CHG for bacterial load ($P = .681$) or presence ($P = .369$)
Van Diek, 2020[44]	RCT	I	42	-	15	Overall: 57.2 ± 8.6	BPO	18 d	BPO significantly reduces culture positivity compared with placebo gel ($P = .01$)
Scheer, 2021[35]	RCT	I	100	55	45	Experimental: 63 ± 13 Control: 65 ± 13	CHG and BPO	12 d	BPO significantly reduces culture positivity compared with standard soap ($P = .0001$)
Sabetta, 2015[33]	Case series	IV	50	-	50	Overall: 52.3 (mean)	BPO	14 d	BPO is not significantly superior to CHG to reduce culture positivity ($P = .375$)
Dizay, 2017[9]	Prospective cohort	II	65	-	65	Overall: 56.9 (mean)	BPO	21 d	BPO significantly reduces culture positivity and multiple applications are beneficial ($P = .006$)
Duvall, 2020[10]	Case series	IV	102	-	34	Overall: 26.0 (mean)	BPO	7 d	BPO leads to significant reductions in bacterial load at the deltoid ($P = .0047$)
Matsen, 2020[25]	Prospective cohort	II	66	66	-	Overall: 63 ± 12	CHG	21 d	CHG does not significantly reduce bacterial load of the skin ($P = .585$)

BPO, benzoyl peroxide; *CHG*, chlorhexidine gluconate; *RCT*, randomized controlled trials.

prepared with a standard preoperative solution of 2% CHG with 70% IPA. The positive control samples in each study were defined as superficial skin cultures taken from the shoulder before the use of any antimicrobial agent.

The treatment randomization among the 6 included RCTs was not uniform. Three of the studies used simple randomization of the participants into treatment groups. Two used block randomizations to ensure balanced sample sizes in each group. One study randomized treatment allocation by sending participants a random blank envelope filled with either CHG (experimental) or normal soap (control). Although these treatment allocation methods varied among trials, conclusions were likely not significantly impacted, as a method of blinded and randomized allocation was adapted by each study.

Risk of bias assessment

Independent assessment of the 6 RCTs using the Cochrane RoB-2 tool (Table II) determined that 5 studies were classified as low overall risk of bias, and 1 study was classified as moderate risk. Other biases primarily consisted of treatment compliance validity, as they were self-reported by patients, thus difficult to confirm. Five studies relied on patient self-reporting for treatment compliance, whereas one study did not assess compliance.

Independent assessment of the 4 non-RCTs using the Cochrane ROBINS-I tool (Table III) determined that 1 study was classified as moderate risk of bias, whereas the other 3 studies were classified as low risk of bias. The study classified as moderate risk was found to be deficient in classification of intervention (because of treatment duration being determined by number of days preoperatively a patient was evaluated in clinic) and measurement of outcome (because of contracting issues necessitating the use of multiple laboratories during the study). Similar to the RCTs, all studies relied on patient self-reporting of treatment compliance.

Culture positivity meta-analysis

The assessment of RCT use of CHG at-home treatment to the unprepared superficial skin for culture positivity consisted of 4 RCTs for 334 total participants (Fig. 2). The associated RR with 95% CI = 0.46 (0.37, 0.57), $P < .0001$, demonstrated a statistically significant decrease in culture positivity using CHG. The associated number needed to treat (NNT) to reduce 1 incident of contamination is 2.14 patients.

RCT use of BPO at-home treatment compared with the unprepared superficial skin for culture positivity included 4 RCTs for 280 patients (Fig. 3). In this group, the RR with 95% CI = 0.20 (0.13, 0.30), $P < .0001$, yielding a statistically significant reduction in *C. acnes* presence using BPO. The NNT to reduce one incident of contamination for this analysis is 1.48 patients. Comparing the pooled RCT outcomes for BPO to the pooled RCT results of CHG, at-home treatment (Fig. 4) revealed a statistically significant difference with BPO being associated with lower rates of positive culture with the RR 95% CI = 0.46 (0.27, 0.77), $P < .009$.

Non-RCT comparison of CHG to unprepared superficial skin included 132 patients, but only a single study assessed the CHG efficacy (Fig. 5). This analysis demonstrated a RR with 95% CI = 0.31 (0.20, 0.49), $P < .0001$, a statistically significant difference between the groups. The associated NNT from this study was 3.34 patients.

Non-RCT comparison of BPO to the unprepared superficial skin consisted of 2 studies for 230 participants (Fig. 6). The associated RR with 95% CI = 0.34 (0.21, 0.57), $P < .0001$, with a NNT of 2.49 patients, demonstrating another statistically significant difference between the groups. This result did not define a statistically significant difference between the non-RCT assessments of CHG and BPO.

The RCT by Kolakowski et al[22] did not detail specific culture results for analysis with other RCTs but did report that shoulders treated with 5% BPO had fewer positive *C. acnes* cultures than the CHG group at the anterior and posterior portal sites ($P = .03$ and $P = .005$, respectively). The case series by Duvall et al[10] assessed *C. acnes* bacterial load from sebaceous gland cultures using BPO. This study reported a statistically significant reduction in anterior ($P = .003$), lateral ($P = .003$), and posterior ($P = .008$) *C acnes* burden in the dermal layer.

Sensitivity analyses

To investigate for heterogeneity in the RCTs examining CHG and BPO efficacy against *C. acnes*, sensitivity analyses were performed. The results from a one-at-a-time sensitivity analysis of the RCT

Table II
Cochrane risk of bias (RoB-2) tool assessment for included randomized controlled trials (RCTs).

Study, year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias	Overall risk of bias judgment
Murray, 2011[30]	+	+	+	+	+	+	?	Low
Kolakowski, 2018[22]	+	+	+	+	+	+	?	Low
Scheer, 2018[34]	+	+	+	+	+	+	?	Low
Hsu, 2020[17]	+	+	+	+	+	+	–	Low
Van Diek, 2020[44]	+	+	+	+	+	+	?	Low
Scheer, 2021[35]	+	+	?	+	+	+	?	Moderate

Table III
Cochrane risk of bias assessment for included non-RCT studies (ROBINS-I).

Study, year	Confounding	Participant selection	Intervention classification	Deviation from intended intervention	Missing data	Measurement of outcomes	Reported results	Overall risk of bias judgment
Sabetta 2015[33]	+	+	+	+	+	+	+	Low
Dizay, 2017[9]	+	+	–	+	+	–	+	Moderate
Duvall, 2020[10]	+	+	+	+	+	+	+	Low
Matsen, 2020[25]	+	+	+	+	+	+	+	Low

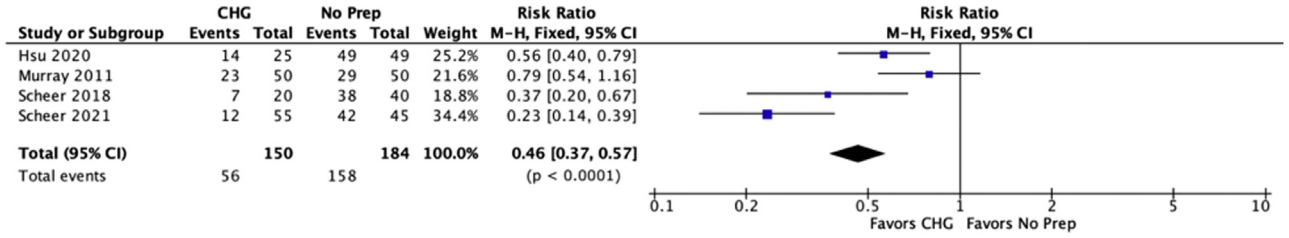

Figure 2 Analysis of culture positivity in RCTs comparing CHG to no skin preparation.

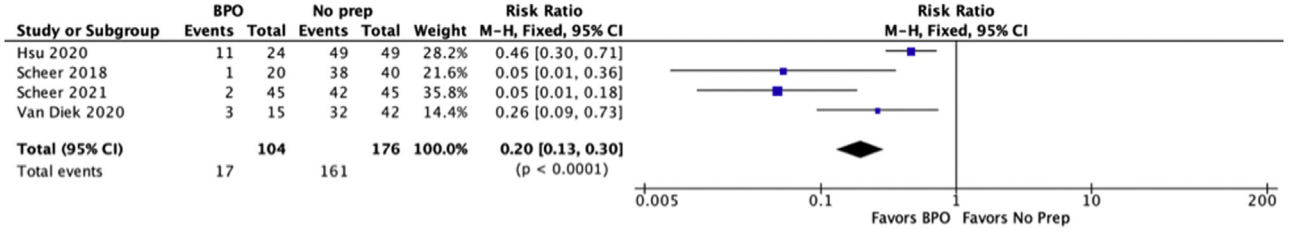

Figure 3 Analysis of culture positivity in RCTs comparing BPO to no skin preparation.

results showed no difference in statistical significance when excluding studies from Hsu 2020,[17] Scheer 2018,[34] and Van Diek 2020.[44] The sensitivity analyses excluding Murray 2011[30] and Scheer 2021[35] did indicate that they may be the predominant source of result heterogeneity in this meta-analysis. For these studies, although the reported CHG and BPO efficacy to reduce positive cultures compared with unprepared skin (negative control) maintained statistical significance, CHG vs. BPO RR comparison yielded nonsignificant results. Excluding the Scheer 2021 study when assessing agent efficacy compared with negative controls, the CHG RR with 95% CI = 0.57 (0.45, 0.71) and the BPO RR with 95% CI = 0.31 (0.20, 0.48). Without the Murray 2011 results, the CHG RR with 95% CI 0.36 (0.27, 0.48) and the BPO RR with 95% CI 0.19 (0.13, 0.30).

Discussion

This meta-analysis of RCTs has found that preoperative BPO is significantly more effective than CHG at eradicating *C. acnes* from superficial and dermal cultures. Our findings identified greater than a 2-fold difference in *C. acnes* culture positivity using BPO rather than the standard CHG method. Although both CHG and BPO are unsurprisingly more effective than no skin preparation, the findings demonstrate BPOs were associated with a lower risk of positive C. acnes culture when compared with CHG.

In addition to the preoperative and at-home use of BPO, peroxide-based preparations have been increasingly used in surgical skin preparation before the standard CHG and IPA solution application.[11,15] The peroxide-based skin preparations have been supported as an economically warranted practice for infection prevention in shoulder arthroplasty.[28] CHG and BPO are the most studied sterile preparatory agents used in shoulder surgery because of their relative efficacy in relation to cost and adverse reaction profiles. The included studies analyzing CHG used a 2% or 4% solution through a variety of application methods, including CHG soaps, soaked cloths, or topical solutions. The studies evaluating BPO used either 5% or 10% gels or ointments. At these concentrations, both agents report few adverse effects, most often dryness, erythema, or pruritus, and much less commonly skin burns or anaphylaxis.[37,45]

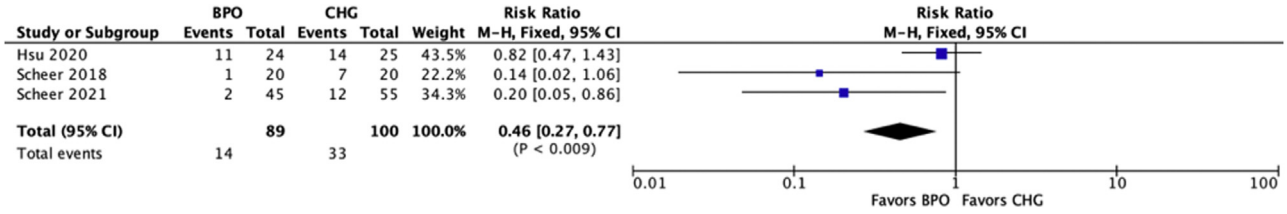

Figure 4 Analysis of culture positivity in RCTs comparing BPO to CHG.

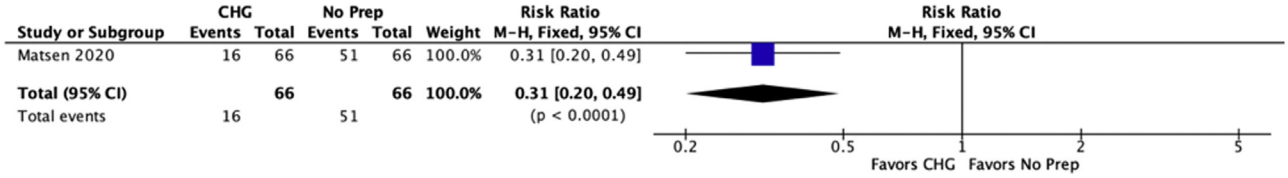

Figure 5 Analysis of culture positivity in non-RCTs comparing CHG to no skin preparation.

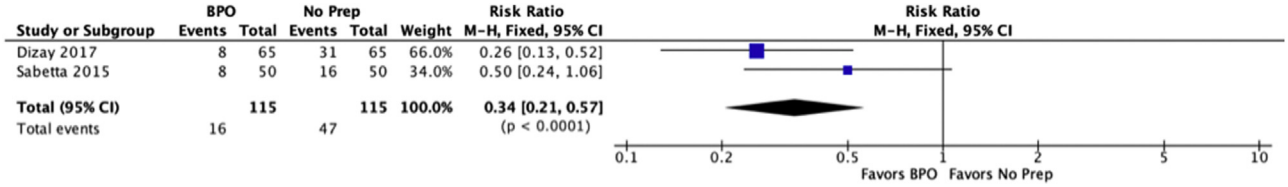

Figure 6 Analysis of culture positivity in non-RCTs comparing BPO to no skin preparation.

Prophylaxis against *C. acnes* contamination has been difficult because of the commensal bacterium residing in the dermal sebaceous glands, out of reach of standard sterile preparation solutions. Peroxide-based agents are theorized to have improved dermal penetration because of the compound's lipophilicity.[10,33] Although CHG has excellent coverage against the superficial staphylococcal bacterial load, the agent has limited ability to penetrate the dermis.[29,30,32] This property of BPO allows decreased bacterial contamination of the deep structures when incising the dermis. Reducing the presurgical and intraoperative volume of *C. acnes* is important to consider, as these skin preparation techniques may reduce the risk of clinical joint infection after shoulder surgery. Prior studies have quantified *C. acnes* volume or load as a factor in deep shoulder samples at the time of revision surgery.[43] However, because of the indolent nature of the bacterium and often prolonged time from exposure to infection, the clinical implications of positive cultures to shoulder infection have not been determined.[27] Furthermore, recent studies have demonstrated a high false-positive rate for *C. acnes* cultures from both open and arthroscopic procedures, which may vary among institutions and culturing methods.[26] Several of the included studies in this meta-analysis did assess clinical shoulder infection; however, the follow-up time was either undisclosed or short, at 2-3 months. The results were predominantly infection free, which may be expected because of the low overall rate of shoulder infection after surgery.[5] Nonetheless, we deemed this follow-up period either inconsistent or too short to diagnose the often indolent shoulder infection.

The risk of bias assessment of RCTs using the RoB-2 determined that of the 6 trials, 5 were of low overall risk. The deficiency found in all 6 of the trials was a lack of patient compliance confirmation. Most studies assessed the at-home treatment compliance with patient-logged journals, whereas one did not assess compliance. Although these studies were likely accurate for treatment adherence, the solution application schedules were unable to be reviewed. The non-RCTs, assessed using the ROBINS-I tool, deemed 3 studies as low risk or bias and only one as moderate risk. Although the included studies in this review were mostly of low risk of bias, a previous study analyzing orthopedic journal RCTs demonstrated that the articles are at a higher risk of bias than other trial types and rarely satisfy all criteria to be deemed low risk.[6]

This meta-analysis does have limitations. The included studies were heterogeneous in their use of control swabs and culturing methods. Culture methods varied by duration and culture medium. Although there are opposing reports in the literature defining *C acnes* culture durations,[24,42] it is important to note that although longer incubation periods increase the number of positive samples, it may also result in higher incidence of false-positive cultures.[12] Prior studies have noted that when excluding for cases with false-positive results, the time to culture positivity was only 5 days, and cultures with true bacterial load had significantly shorter time-to-positivity than false-positive cultures.[4] This variation in culture duration among the included trials may have presented variable results. Trial controls varied as well; some used the contralateral shoulder as control, whereas others used another study cohort with a separate preparatory solution. The preparatory solutions were mostly similar but had some variation in concentration of CHG and BPO and method of application (cloth, soap, ointment, and so on). However, the studies were consistent in their sampling of the skin swabs before and after the at-home application of CHG or BPO, allowing a reasonable unbiased comparison among the included trials. As previously mentioned, the trial outcomes were assessed as superficial culture positivity to analyze the presence of *C. acnes*, which has an unknown clinical causative effect on shoulder infection. In addition, the studies that did report infection rates were often at too short an interval from surgery to appropriately

determine infection. Few studies reported adverse effects of the at-home CHG and BPO application. Although this is likely because of the rarity of adverse reactions with such a short treatment course, analysis of these effects may help guide their future use or application protocol. Finally, the non-RCT data in Figs. 5 and 6 do not have the same robust level of evidence as the RCT data in Figures 2–4.

Further studies may strengthen the pool of evidence by using reproducible evidence-based methods to assess the efficacy of these preparatory agents at each stage of the sterilization protocol (at-home decolonization, presurgical preparatory decolonization, and sterile surgical preparation). In addition, these studies should aim to correlate agent use to clinical infection with appropriate follow-up duration, analyzing other treatment types (combinations of CHG and BPO or novel agents such as PCA),[18,19,38,46,47] assessing specific application methods (frequency, concentration, and timing), and culturing sites from the deep tissues and dermis.

Conclusions

Based on data from this meta-analysis, the study has demonstrated the effectiveness of BPO against *C. acnes* and the agent's lower risk for positive *C. acnes* cultures compared with CHG. BPO may be recommended for at-home preoperative preparation to reduce the *C. acnes* load of the skin at the site of shoulder surgery, in conjunction with a standard CHG and IPA skin preparation at the time of surgery. The challenge for at-home use of BPO is patient compliance, which warrants future research. BPO decreases the bacterial load of Cutibacterium and may be a cost-effective and well-tolerated prophylactic measure to reduce shoulder contamination in surgery. Although bacterial load and culture positivity of Cutibacterium are decreased with BPO application, the effect on clinical shoulder infection has not been determined.

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