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Review

Antiseptic efficacies of waterless hand rub, chlorhexidine scrub, and povidone-iodine scrub in surgical settings: a meta-analysis of randomized controlled trials

Y-H. Ho [a, 1], Y-C. Wang [a, 1], E-W. Loh [b, c], K-W. Tam [b, d, e, f, *]

[a] School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan
[b] Center for Evidence-Based Health Care, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan
[c] Graduate Institute of Clinical Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan
[d] Division of General Surgery, Department of Surgery, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan
[e] Division of General Surgery, Department of Surgery, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan
[f] Cochrane Taiwan, Taipei Medical University, Taipei, Taiwan

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SUMMARY

Background: Presurgical hand washing is crucial for preventing surgical site infections (SSIs). Chlorhexidine gluconate (CHG) and povidone-iodine (PI) products have been conventionally used as hand scrubs for presurgical hand preparation. However, waterless hand rub (WHR) products have been developed for operating room staff.
Aim: The aim of this study was to conduct a systematic review and meta-analysis to compare the antiseptic efficacies of WHR, CHG, and PI in surgical settings.
Methods: PubMed, Embase, and Cochrane Library databases as well as the ClinicalTrials.gov registry were searched for studies published before October 2018. Randomized controlled trials (RCTs) comparing the clinical outcomes of the use of WHRs, CHG, or PI for presurgical hand washing were included. A random effects model was used for meta-analysis. Colony-forming unit (cfu) counts, SSI rates, and preference and compliance were determined to measure efficacies.
Findings: Eleven RCTs involving 5135 participants were included. Residual cfu counts were significantly lower in the WHR and CHG groups than in the PI group. The differences in cfu counts between the WHR and CHG groups were non-significant. No significant differences were observed in the SSI rates between the WHR and traditional hand scrub groups. Moreover, WHRs were considered most favourable and were associated with higher compliance rates than the other products.

* Corresponding author. Address: Center for Evidence-based Health Care, Shuang Ho Hospital, Taipei Medical University, 291, Zhongzheng Road, Zhonghe District, New Taipei City, 23561, Taiwan. Tel.: +886 2 22490088x8860; fax: 886 2 22490088x2507.
E-mail address: kelvintam@h.tmu.edu.tw (K-W. Tam).
[1] Authors contributed equally to this work.

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Conclusion: WHRs and CHG exhibited higher antiseptic efficacies than PI. However, additional studies with consistent outcome measurements and accurate grouping are required to obtain comprehensive results. Moreover, preference, compliance, and the cost determine the selection of hand wash products.

Introduction

Presurgical hand washing is one of the most critical factors affecting the risk of surgical site infections (SSIs), which result in a considerable burden of morbidity, mortality, and avoidable economic costs on hospitals [1,2]. Thorough washing of the hands and forearms with an antiseptic agent, before wearing sterile gowns and gloves, is expected to reduce the number of micro-organisms present on the skin for the duration of a surgical procedure [3].

Traditional methods of presurgical hand washing involve scrubbing by using brushes and antimicrobial solutions for 3–5 min [4,5]. Two widely used (presurgical) traditional hand scrub (THS) products are 4% chlorhexidine gluconate (CHG) and povidone-iodine (PI). Chlorhexidine is a broad-spectrum biocide effective against Gram-positive bacteria, Gram-negative bacteria, and fungi [6]. Despite its long-term use, the development of PI resistance in micro-organisms has not been reported [7]. However, such solutions are applied using a brush or sponge, resulting in skin damage, excessive shedding of superficial skin layers, and microscopic cuts on the skin surface [8,9]. Damaged skin can harbour micro-organisms and cause the spread of infections.

An alcohol-based surgical scrub solution in gel form is also available for surgical hand antisepsis, and its application does not require a brush, sponge, or sterile towel [10]. Two types of solution are available, namely a 75% aqueous alcoholic solution containing propanol-1, propanol-2, and mecetronium ethylsulphate (Sterillium; Rivadis Laboratories, Thouard, France) and a solution of 61% ethyl alcohol containing 1% CHG (Avagard; 3M, St Paul, MN, USA). Some studies have suggested that waterless hand rubs (WHRs) have higher efficacy and more sustained microbicidal effectiveness than THSs [11,12]. Moreover, some studies have shown that the hand-rubbing protocol is better tolerated by the surgical staff than the scrubbing protocol, and that the use of WHRs is associated with higher compliance with guidelines than that of THSs [10,13]. However, cost should be considered a factor when comparing WHRs with THSs [14].

To our knowledge, some studies have reported that the hand-rubbing procedure is more effective than the traditional protocol of scrubbing with PI or CHG due to its antiseptic efficiency [11,15]. Furthermore, other studies have reported that CHG has a stronger antiseptic effect than PI [16,17]. Well-organized articles enabling a systematic comparison of these three products and the effects of potential bias on the evaluation of their efficacies are not currently available. Therefore, we conducted a systematic review and meta-analysis to investigate the efficacy of three antiseptic products, namely WHRs, PI, and CHG, for preoperative hand disinfection.

Methods

Inclusion criteria

Peer-reviewed randomized controlled trials (RCTs) comparing the WHR, PI scrub, and CHG scrub approaches were included in this meta-analysis. The trials were included if they clearly reported the inclusion and exclusion criteria for participants, the protocols of presurgical hand washing, details of the contents of hand-washing products, and the definitions and methods of evaluation for bacterial counts, and related outcomes, such as SSI rates and preferences. Studies that reported non-surgical hand washing, hand washing without standardized protocols, and animal studies were excluded.

Search strategy and study selection

Relevant RCTs published before October 2018 were identified from the databases of PubMed, Embase, and the Cochrane Library. The following medical subject headings were used: 'surgical hand antisepsis' OR 'surgical hand preparation' OR 'surgical hand washing', and 'chlorhexidine' OR 'iodine' OR 'hand rub' OR 'avagard'. The 'related articles' option in PubMed was used to broaden the search, and all abstracts, studies, and citations thus retrieved were reviewed. Finally, unpublished studies were collected from the ClinicalTrials.gov registry (http://clinicaltrials.gov/). No language restrictions were applied. The systematic review described herein has been accepted by PROSPERO (CRD42018103753).

Data extraction

Baseline and outcome data were independently retrieved by two reviewers (Y.H.H. and Y.C.W.). Data regarding study design, study population characteristics, inclusion and exclusion criteria, bacterial counts, SSI rates, and preferences were extracted. The reviewers recorded their decisions individually. The decisions were compared and disagreements were resolved by a third reviewer (K.W.T.).

Appraisal of methodological quality

Two reviewers (Y.H.H. and Y.C.W.) independently assessed the methodological quality of each study by using the Cochrane risk-of-bias tool (RoB 2.0) [18]. Studies were assigned an overall risk-of-bias grade of high, moderate, or low risk. This grade was calculated by assessing the following five domains: bias arising from the randomization process; bias owing to deviations from intended interventions; bias owing to missing outcome data; bias in outcome measurement; and bias in the selection of the reported results.

Outcomes

The primary outcomes were the bacterial cfu counts. The secondary outcomes were SSI rates and preferences.

Statistical analyses

Data were entered and analysed using Review Manager 5.3 (The Cochrane Collaboration, Oxford, UK). A meta-analysis was performed according to the Preferred Reporting Items for Systematic Review and Meta-Analyses guidelines [19]. Standard deviations (SDs) were estimated using the provided confidence interval (CI) limits or standard errors. Continuous and dichotomous variables were analysed using weighted mean differences (WMDs) and odds ratios (ORs), respectively. The precision of the effect sizes was reported at a CI of 95%. A pooled estimate of the WMD and OR was computed using the DerSimonian and Laird random effects model [20]. A statistically significant result was indicated by $P < 0.05$ or the 95% CI not including zero in the WMD and one in the OR.

Statistical heterogeneity and the inconsistency of the treatment effects across studies were evaluated using the Cochran Q-test and I^2-statistic, respectively. Statistical significance was set at $P < 0.10$ for the Cochran Q-tests. Statistical heterogeneity across studies was assessed using the I^2-test, which quantifies the proportion of the total outcome variability across studies. Moreover, subgroup analyses were performed by pooling available estimates for similar subsets of hand antiseptic solution across trials.

Results

Trial characteristics

Figure 1 illustrates the screening and selection of studies. The initial screening yielded 345 citations of which 262 were ineligible based on the criteria used for screening titles and abstracts. Thus, the full texts of 84 studies were retrieved.

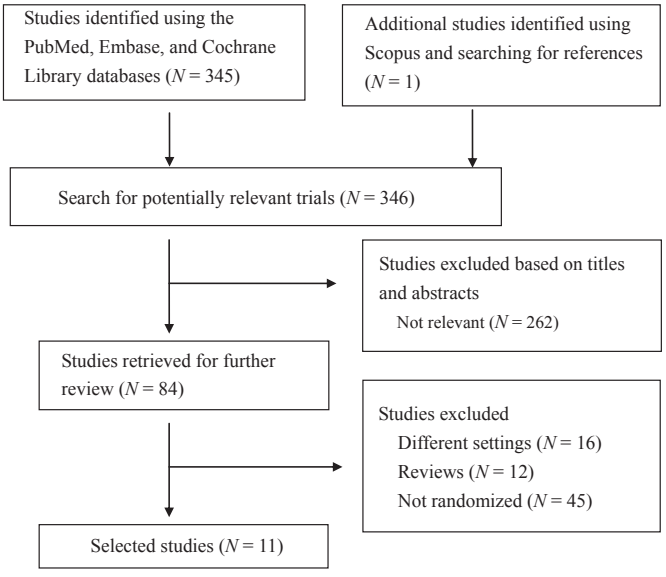

Figure 1. Flow chart for selection of studies.

However, 16 studies featured an inappropriate setting, such as veterinary surgical hand washing; 12 studies were reviews, and 45 studies were not RCTs. Finally, 11 trials were eligible for inclusion in this meta-analysis [3,8,10,13,14,21–26].

These 11 trials were published between 1988 and 2017, including 5135 participants in total. Four RCTs compared alcohol gels and THSs [13,22–24], five RCTs compared alcohol and chlorhexidine gels with THSs [3,8,10,14,21], and six RCTs compared PI and CHG [3,14,22,24–26] in terms of efficacy. To minimize variables during comparison, the participants were surgical staff members in all included RCTs, except for three RCTs [13,25,26]. One trial recruited patients undergoing operations that were conducted by the surgeons enrolled in the experiment [13], and the participants of the other two trials were volunteers [25,26]. The contents and washing protocol of presurgical hand antiseptic agents varied across these 11 trials, and some trials even included other products such as triclosan, Nova Derm, and chloroxylenol [3,10,22,24–26]. Outcome measurement and other detailed information from the 11 trials are shown in Table I.

Regarding the methods of sample collecting, six trials used glove-juice sampling method to collect the bacteria from the volunteers' hands [3,10,11,22,25,26]. However, Forer *et al.* used a modified glove juice method to collect the samples: surgeons put their hands in the sterile bags which were added with some sterile culture fluid and neutralizing medium. The 100 μL samples of suspensions were then cultured on agar plates, thus the authors used cfu/mL as a unit to evaluate the antiseptic results [22]. In Chen *et al.* and Tsai *et al.*, samples were directly imprinted from hands on to the plates without using the glove-juice method [14,21]. In Hajipour *et al.*, each fingertip of each glove was placed on a separate agar plate, and then the samples were collected [23]. In Herruzo-Cabrera *et al.*, the samples were collected via instructing the subjects to place their fingerprints on the surface of the agar plates [24]. However, in Parienti *et al.* the bacterial samples from the surgeons were not collected, since the purpose of this trial was to determine whether different antiseptic products would affect the SSI rate [13].

The methodological quality of the included trials is summarized in Table II. Three trials reported acceptable methods of randomization [8,14,25]. Eight trials were considered to exhibit some risk of bias arising from the randomization process because the trials did not mention the method of randomization [3,10,21,22,26], they exhibited a lack of allocation concealment [13,24], and one had unbalanced surgeon numbers between two groups [23]. Only one trial stated that the participants and supervisors were blinded to the exact identity of the product; this study was considered to have a low risk of bias [25]. Nevertheless, the outcome assessment was objective; therefore, we considered the trials without blinding of participants to have a low risk of performance bias. Two trials used intention-to-treat analysis [21,22]. Among the remaining nine per-protocol analysis trials, the number of participants lost to follow-up in one trial was >20% [3], whereas another trial did not state the loss to follow-up clearly [24]. Five trials were considered to exhibit a high risk of reporting bias owing to unclear description of outcome data [3,10,21,23,26]. Overall, five, three, and three trials showed high risk [3,10,21,23,26], moderate risk [13,24,22], and low risk [8,14,25] of bias, respectively.

Table I
Characteristics of the included trials

Trial	Inclusion criteria	No. of participants (no. of final analysis)	Intervention [Application for scrubbing]	Outcome measurement
Alcohol and CHG gel application versus traditional scrubbing				
Pereira *et al.* [3]	Operating theatre registered nurses	S1: 32 (23) S2: 32 (23) S3: 32 (23) R1: 32 (23) R2: 32 (23) [Crossover design]	S1: 4% CHG × 5 min + 4% CHG × 3.5 min S2: 4% CHG × 3 min + 4% CHG × 2.5 min S3: 5% PI × 3 min + 5% PI × 2.5 min R1: 4% CHG and hibicol × 2.5 min + hibicol × 0.5 min R2: 4% CHG and 0.5% CHG and 70% ethyl alcohol × 2.5 min + 0.5% CHG and 70% ethyl alcohol × 0.5 min [First pump scrubbing solutions on hands and then add solutions on the brushes or sponge to scrub]	Log cfu counts before washing, immediately after initial wash, 2 h after initial wash, and 2 h after consecutive wash
Gupta *et al.* [10]	18 volunteer surgical staff members	S1: 18 (16) S2: 18 (16) R: 18 (16) [Crossover design]	S1: 7.5% povidone-iodine S2: 70% ethyl alcohol + zinc pyrithione × 3 min R: 1% CHG + 61% ethyl alcohol in three 2 mL aliquots [Not mentioned]	Log cfu reduction within 1 min after washing on days 1, 2, and 5
Chen *et al.* [21]	Operating room staff members	S: 50 R: 50	S: 4% CHG in 70% isopropyl alcohol or 10% povidone-iodine × 5 min R: 1% CHG and 61% ethyl alcohol × 3 min [Add scrubbing solutions on the brushes to scrub]	Number of plates with cfu
Tsai *et al.* [14]	Surgical staff members; excluded medical and nursing students	S1: 80 (77) S2: 80 R: 80 (79)	S1: 10% povidone-iodine × 5 min S2: 4% CHG × 5 min R: 1% CHG and 61% ethyl alcohol × 3 min [Add scrubbing solutions on the brushes to scrub]	cfu count before washing, after washing, and after surgery
Larson *et al.* [11]	Full-time surgical staff members	S: 27 (25) R: 27 (25) [Crossover design]	S: 4% CHG R: 1 % CHG + 61% ethyl alcohol [Squeeze the sponge containing the scrubbing agents to work up a lather on hands, and use sterile brush to scrub]	Log cfu count after washing on days 1 and 5 of weeks 1 and 3
Alcohol gel versus traditional scrubbing				
Forer *et al.* [22]	Ophthalmic surgeons	S1: 10 S2: 10 R: 20 [Crossover design]	S1: 4% CHG × 3 min S2: 1% PI × 3 min R: 70% ethanol and 1% glycerine × 1 min [Squeeze the sponge containing the scrubbing agents to work up a lather on hands, and use sterile brush to scrub]	Log cfu count/mL
Hajipour *et al.* [23]	Orthopaedic surgeons	S: 25 R: 57	CHG handwashing for the first case × 5 min S: CHG × 3 min R: alcohol gel × 3 min [Not mentioned]	cfu count
Herruzo-Cabrera *et al.* [24]	Surgical team members (plastic surgery or traumatology)	S1: 49 S2: 50 R: 55	S1: 7.5% iodophors × 3 min S2: 4% CHG × 3 min R: 2.3% *N*-duopropenide in 60% alcohol with emollients × 3 min [Scrub with brushes impregnated with CHG or PI]	cfu count [cfu/5 fingertips] before washing, after washing, and after surgery

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Table I (*continued*)

Trial	Inclusion criteria	No. of participants (no. of final analysis)	Intervention [Application for scrubbing]	Outcome measurement
Parienti *et al.* [13]	Patients with clean and clean-contaminated wound	S: 2135 R: 2252 [Crossover design]	S: 4% CHG or 10% PI R: Sterillium [Squeeze the sponge containing the scrubbing agents to work up a lather on hands, and use sterile brush to scrub]	Surgical site infection within 30 days after surgery
Traditional hand scrub: PI versus CHG				
Faoagali *et al.* [25]	Non-clinical hospital staff members	S1: 33 S2: 33 S3: 33 S4: 33 S5: 33 [Crossover design]	S1: Novaderm R (1% triclosan) S2: Novascrub R (1% triclosan + 5% PI) S3: Betadine (7.5% PI) S4: Hibiclens (4% CHG) S5: Novaderm (liquid soap) [Not mentioned]	Log bacterial count reduction on days 1 and 5 immediately after and 3 h after washing
Aly and Maibach [26]	42 normal, healthy adult volunteers	S1: 14 (13) S2: 14 (12) S3: 14	S1: 4% CHG × 2 min S2: 1% PI × 2 min S3: 3% chloroxylenol × 2 min [Squeeze the sponge containing the scrubbing agents to work up a lather on hands, and use sterile brush to scrub]	Log bacterial count reduction immediately after, 3 h after, and 6 h after washing on days 1, 2, and 5

cfu, colony-forming unit; CHG, chlorhexidine gluconate; PI, povidone-iodine; R, hand rub; S, hand scrub; SSI, surgical site infection; hibicol, 70% isopropanol and 0.5% CHG; Sterillium, 45% w/w of propan-2-ol, 30% w/w of propan-1-ol, and 0.2% w/w of ethylhexadecyldimethyl ammonium ethylsulphate.

Residual cfu counts after washing

Due to inconsistencies in the methods of the included trials for outcome measurement, these trials were divided into seven groups to compare the residual bacterial counts after presurgical hand washing. Different antiseptic solutions were compared. Moreover, due to the different units in outcome assessment, we used the range of bacterial count after washing to compare the antiseptic efficacy in all trials (Figure 2).

Alcohol and CHG gels versus THS (mixed)

Chen *et al.* compared alcohol and CHG gels with THSs, and seven out of 50 plates showed cfu in the gel and THS groups. The microbial cfu count (OR: 1; 95% CI: 0.85–1.71; $P = 1.00$) did not differ significantly between the groups [21].

Alcohol gel versus THS (mixed)

Forer *et al.* compared alcohol gels with THSs. The mean $\log_{10}$ cfu/mL after washing was significantly lower in the alcohol gel group (mean ± SD: 1.59 ± 1.12) than in the THS group (mean ± SD: 3.12 ± 0.60) ($P < 0.0001$) [22].

Alcohol and CHG gels versus CHG scrub

Tsai *et al.* compared alcohol and CHG gels with CHG scrubs. The mean cfu counts after washing were 1.4 ± 0.8 and 0.8 ± 0.8 in the gel and scrub groups, respectively, and no significant difference was observed between the two groups [14]. Larson *et al.* reported that the mean post-scrub $\log_{10}$ cfu counts did not differ significantly between the alcohol and CHG gel group (mean ± SD: 3.86 ± 0.84) and CHG scrub group (mean ± SD: 4.34 ± 1.24) on day 1 of the first week ($P = 0.054$) [8].

The results of Pereira *et al.* are not shown in Figure 2 owing to a lack of raw data. This trial revealed that the gel and scrub groups did not differ significantly at the beginning of the test week. However, at the end of the week, the WHR group showed a significantly lower cfu count than the CHG group (95% CI: 0.401–1.761; $P = 0.003$) [3].

Alcohol gel versus CHG scrub

Forer *et al.* revealed that the mean $\log_{10}$ cfu/mL after washing was 1.59 ± 1.12 in the alcohol gel group and 3.08 ± 0.65 in the CHG scrub group [22]. Herruzo-Cabrera *et al.* reported that after washing, the alcohol gel group (mean: 0) exhibited significantly fewer cfu per five fingertips than the CHG scrub group (mean ± SD: 18 ± 6) ($P < 0.01$) [24]. However, Hajipour *et al.* showed that after washing, the average bacterial cfu count in the alcohol gel group (mean: 16) was significantly higher than that in the CHG scrub group (mean: 2) ($P = 0.002$) [23].

Alcohol and CHG gels versus PI scrub

Tsai *et al.* reported that after washing, the alcohol and CHG gel group (mean ± SD: 1.4 ± 0.8) exhibited a significantly lower mean cfu count than the PI group (mean ± SD: 3.9 ± 0.8) ($P < 0.05$) [14].

Alcohol gel versus PI scrub

Forer *et al.* revealed that the mean $\log_{10}$ cfu/mL after washing was 1.59 ± 1.12 in the alcohol gel group and 3.158 ± 0.58 in the PI group [22]. Herruzo-Cabrera *et al.* showed that after washing, the alcohol gel group (mean: 0)

Table II
Methodological quality assessment of the included trials

Type of bias	Pereira *et al.* [3]	Gupta *et al.* [10]	Chen *et al.* [21]	Tsai *et al.* [14]	Larson *et al.* [11]	Herruzo-Cabrera *et al.* [24]	Parienti *et al.* [13]	Hajipour *et al.* [23]	Forer *et al.* [22]	Aly and Maibach *et al.* [26]	Faoagali *et al.* [25]
Bias arising from the randomization process	Some concerns[a]	Some concerns[a]	Some concerns[b]	Low risk	Low risk	Some concerns	Some concerns	Some concerns	Some concerns[a]	Some concerns[a]	Low risk
Bias due to deviations from intended interventions	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Bias due to missing outcome data	High risk[c]	Low risk	Low risk	Low risk	Low risk	Some concerns[d]	Low risk	Low risk	Low risk	Low risk	Low risk
Bias in measurement of the outcome	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Bias in selection of the reported result	High risk[e]	High risk[e]	High risk[e]	Low risk	Low risk	Low risk	Low risk	High risk[e]	Low risk	High risk[e]	Low risk
Overall risk of bias	High risk	High risk	High risk	Low risk	Low risk	Some concerns	Some concerns	High risk[f]	Some concerns	High risk	Low risk

Methodological quality assessment was based on the Cochrane risk-of-bias tool (RoB 2.0).
[a] The study only stated 'random' without mention the method of randomization.
[b] The subjects were recruited randomly from medical centres in Taiwan and assigned to either a warterless hand rub or a traditional hand scrub.
[c] Loss to follow-up >20%.
[d] No information.
[e] Unclear description of outcome data.
[f] Other bias: unbalanced surgeons number between two groups and not all of the subjects follow the study design.

exhibited significantly fewer cfu per five fingertips than the PI group (mean ± SD: 66 ± 7) ($P < 0.01$) [24].

CHG scrub versus PI scrub

Tsai *et al.* reported that after washing, the mean cfu count was significantly lower in the CHG scrub group (mean ± SD: 0.8 ± 0.8) than in the PI scrub group (mean ± SD: 3.9 ± 0.8) ($P < 0.01$) [14]. Forer *et al.* revealed that after washing, the mean $\log_{10}$ cfu/mL did not differ significantly between the CHG (mean ± SD: 3.08 ± 0.65) and PI scrub groups (mean ± SD: 3.15 ± 0.58) ($P = 0.97$) [22]. Herruzo-Cabrera *et al.* showed that after washing, the CHG scrub group (mean ± SD: 18 ± 6) exhibited significantly fewer cfu per five fingertips than the PI scrub group (mean ± SD: 66 ± 7) ($P < 0.01$) [24].

The results of Pereira *et al.* are not shown in Figure 2 owing to a lack of raw data. This trial revealed no significant differences between the PI and CHG scrub groups immediately after the first scrub and 2 h after the first scrub. However, it indicated a significantly higher increase in the cfu count in the PI group than in the CHG group 2 h after the second scrub ($P = 0.002$) [3].

Meta-analysis of cfu counts between PI and CHG scrub groups

Four trials compared residual cfu counts in the PI and CHG scrub groups after presurgical hand washing [3,14,22,24]. Unlike the other three trials, the trial by Pereira *et al.* did not provide the raw data of residual cfu counts in the two groups; therefore, we could not pool the data from this study with data from the other studies [3]. Our pooling result for the other three trials revealed that the CHG scrub group exhibited a significantly lower cfu count than the PI scrub group (WMD: −16.76; 95% CI: −25.33 to −8.19) (Figure 3) [14,22,24].

Meta-analysis of cfu counts between WHR and PI scrub groups

Three trials compared residual cfu counts in the WHR and PI scrub groups after presurgical hand washing [14,22,24]. The alcohol gel group (WMD: −1.79; 95% CI: −2.01 to −1.56) exhibited a significantly lower cfu count than the PI group in our pooling data [22,24]. The alcohol and CHG gel group (WMD: −2.50; 95% CI: −2.75 to −2.25) exhibited a significantly lower cfu count than the PI scrub group (Figure 4) [14].

Meta-analysis of cfu counts between WHR and CHG scrub groups

Five trials compared residual cfu counts in the WHR and CHG scrub groups after presurgical handwashing [3,8,14,22,24]. Unlike the other four trials, the trial by Pereira *et al.* did not provide the raw data of residual cfu counts in the two groups; therefore, we could not pool the data from this study with data from other studies [3].

The pooling data did not reveal a significant difference between the alcohol gel and CHG scrub groups (WMD: −9.73; 95% CI: −25.91 to 6.45) [22,24]. A moderate level of bias, such as unbalanced and small numbers of participants [22] or an unreasonable mean residual cfu count in the trial [24], resulted in

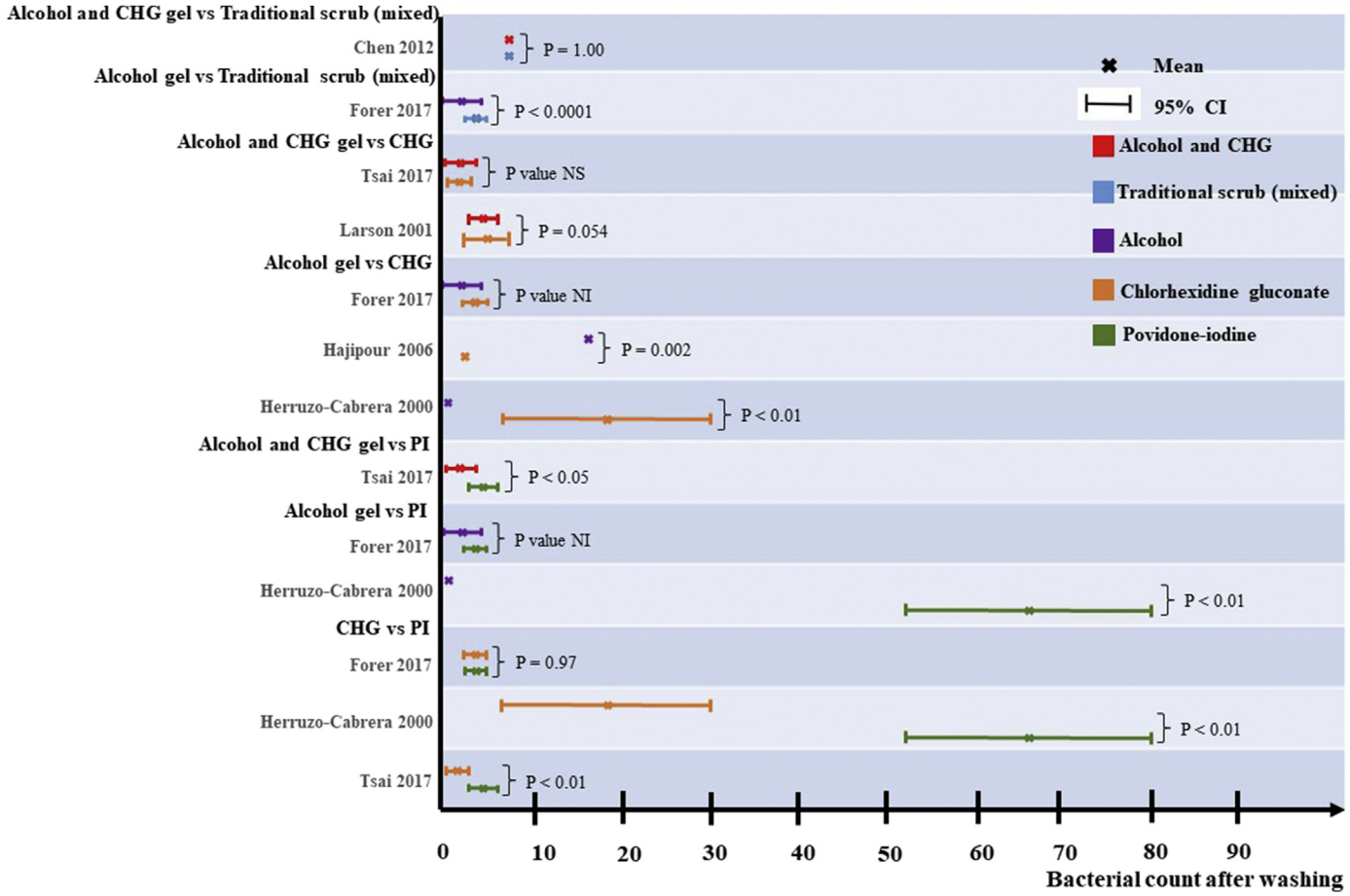

Figure 2. Comparison of bacterial counts after hand washing with different antiseptic solutions. CHG, chlorhexidine gluconate; CI, confidence interval; NS, non-significant; PI, povidone-iodine.

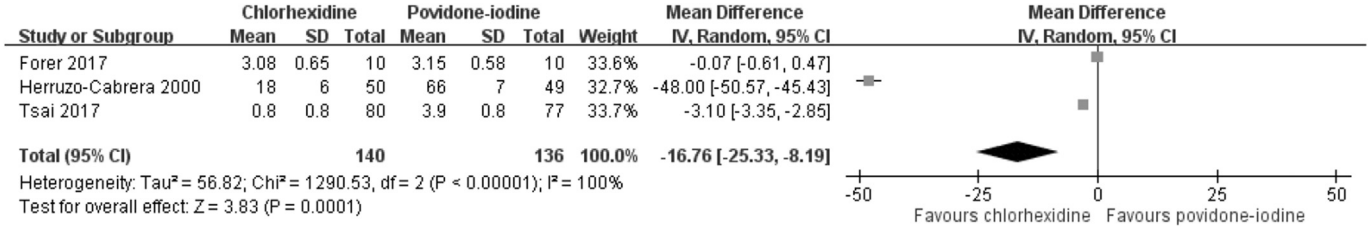

Figure 3. Forest plot of comparison: chlorhexidine gluconate versus povidone-iodine; outcome: residual colony-forming unit count after hand washing.

type 1 error, thereby causing deviation. The pooling data did not reveal significant differences between the alcohol and CHG group and the CHG scrub group (WMD: 0.09; 95% CI: −0.96 to 1.15) (Figure 5) [8,14].

Reduction in cfu counts after washing

Three trials used reduction in cfu counts as an outcome assessment instead of residual cfu counts [10,25,26]. Gupta *et al.* compared the cfu count reduction between the WHR and PI scrub groups. No significant difference was observed between the two groups over the five days of the study ($P = 0.2$); however, the WHR group exhibited a larger reduction in cfu counts within 1 min of the last scrub on day 2 (mean ± SD: 3.1 ± 0.34, $P = 0.02$) and day 5 (mean ± SD: 3.0 ± 0.28, $P = 0.01$) than the PI group (day 2 mean ± SD: 2.4 ± 0.8 and day 5 mean ± SD: 2.3 ± 0.6) [8]. Aly and Maibach and Faoagali *et al.* compared the reduction in cfu count between CHG and PI scrub groups. These two studies revealed larger reductions in cfu counts in the CHG group than in the PI group. Aly and Maibach demonstrated that the reductions in the WHR group were statistically significantly larger than those in the PI group immediately after scrubbing on days 1, 2, and 5, whereas Faoagali *et al.* demonstrated a difference only on day 5 ($P < 0.001$) [25,26].

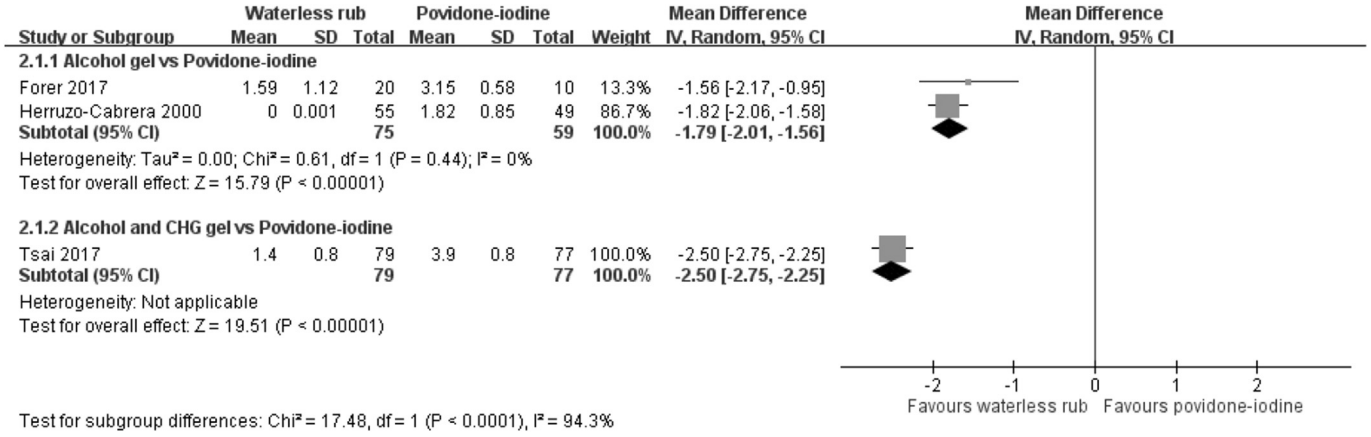

Figure 4. Forest plot of comparison: waterless hand rub versus povidone-iodine; outcome: residual colony-forming unit count after hand washing.

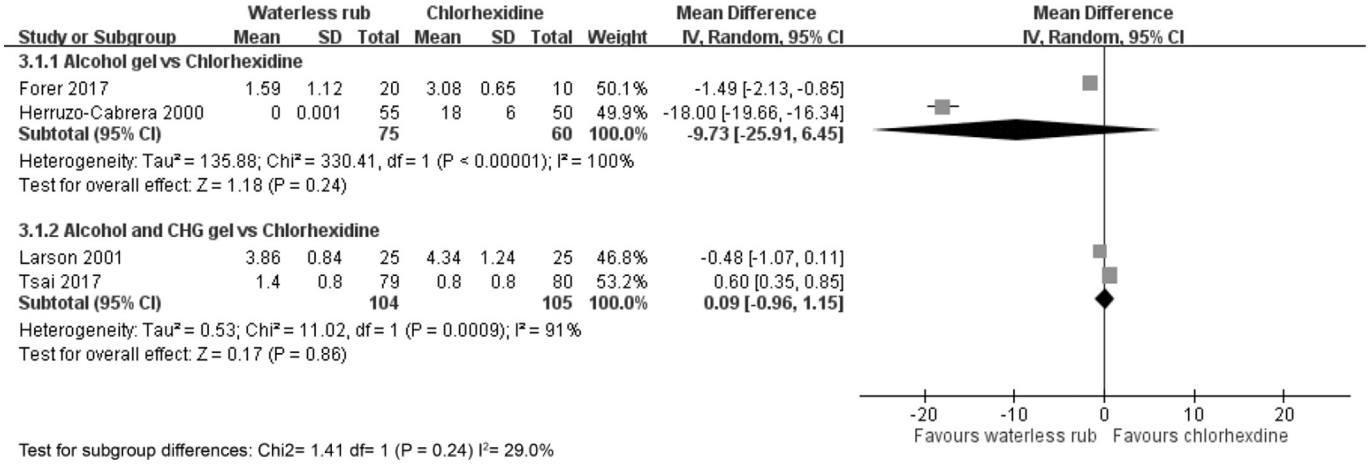

Figure 5. Forest plot of comparison: waterless hand rub versus chlorhexidine gluconate; outcome: residual colony-forming unit count after hand washing.

Surgical site infection

Two trials compared the nosocomial SSI rates after presurgical hand washing [13,21]. Parienti *et al.* reported an SSI rate of 2.48% (53 out of 2135 patients) in the THS group and 2.44% (55 of 2252) in the WHR group. The risk difference of the SSI rate between the THS and WHR groups was 0.04% (95% CI: −0.08 to 0.96), which suggested that the SSI rates did not differ significantly between the two groups [13]. In the study by Chen *et al.*, a statistically significant difference was not observed in the SSIs rates between the WHR and TSH groups [21].

Preference and compliance

Five trials compared product preference and compliance among the WHR, PI, and CHG groups [3,8,10,13,26]. In terms of product preference, the use of the WHR solution was perceived as more favourable than that of the THS solution [8,10]. Moreover, although not significant, the rank order tended to favour the WHR antiseptic protocols as relatively less damaging to hands [3]. Additionally, no statistically significant differences were observed in the mean irritation scores between the PI and CHG groups [26]. The WHR group was significantly more compliant than the THS group (44% vs 28%, $P = 0.008$) [13].

Discussion

The main finding of the study was that the WHR and CHG scrub groups had a significantly lower residual bacterial count after washing than the PI scrub group. Moreover, the antiseptic efficacies of WHR and CHG scrub products did not differ significantly. The SSI rates did not differ significantly between the WHR and THS groups. The operating room staff showed higher preference for and higher compliance with the use of WHR protocols than with the use of THS protocols.

The residual bacterial count immediately after washing was the primary outcome of many studies comparing products of presurgical hand disinfection. Shen *et al.* and Rotter *et al.* compared data on the antimicrobial effectiveness of WHR and THS products [27,28]. Statistical evidence from both the studies supported the superiority of WHR products over THS products. Lai *et al.* reported that the WHR group had a

significantly higher reduction in the cfu count than the PI scrub group [29]. Grabsch *et al.* conducted a crossover study comparing a chlorhexidine in detergent/alcohol regimen with a PI detergent scrub within an orthopaedic operating environment [16]. They reported that the CHG scrub had a stronger antiseptic effect than the PI scrub. Overall, our analysis revealed that WHRs exhibited stronger microbicidal effects than the PI scrub, and that the CHG scrub was significantly more effective than the PI scrub in reducing the bacterial count after hand antisepsis. However, our meta-analysis showed that antimicrobial efficacy did not differ significantly between the WHR and CHG scrub groups. Parienti *et al.* revealed that WHR products are as effective as THS products in controlling nosocomial SSI [13]. Other studies have compared the SSI rates between CHG and PI scrub groups. Doebbeling *et al.* conducted an eight-month prospective multiple-crossover trial involving 1894 adult patients in three intensive care units; they reported that the rate of nosocomial infection was significantly higher after washing with alcohol and soap than with the CHG scrub, possibly due to poor compliance with hand-rubbing instructions [30].

In our included trials, two trials mixed the two THSs, namely PI and CHG solutions, to compare its presurgical antiseptic efficacy with that of WHR products [13,21]. However, several trials have reported that the microbicidal effectiveness of the CHG scrub was higher than that of the PI scrub [3,14,24—26]. Therefore, pooling the data of two conventional scrubs may be a potential bias, which could affect our evaluation, because the antiseptic effect of the CHG scrub might be attenuated by the PI scrub. Consequently, trials comparing WHR and THS products should divide the latter group into PI and CHG subgroups, which will reduce the bias resulting from mixing them together.

Non-surgical members as participants and sampling at different time-points were inconsistent with the real situation in clinical conditions [25,26]. In our included studies, several trials described the residual effect and cumulative effect several hours after hand washing on different days [3,10,25,26]. However, in real clinical settings, the most crucial factor for evaluating the efficacy of hand washing was the residual bacterial count immediately after hand antisepsis. Therefore, study in real scenario, i.e., surgical rooms, should be conducted to understand the exact efficacy of the antiseptic agents.

The cost of the hand antiseptic solution may be a determining factor for selection. Weight *et al.* reported that Avagard's application process costs US$0.59 per application and that antiseptic-impregnated hand brushes cost US$1.04 per application, which excludes the cost of the drying towel or water for scrubbing [31]. Moreover, no waste was generated with the brushless technique, whereas the scrub technique requires water, plus the disposal of the scrub brush, packaging, and drying towel. Larson *et al.* revealed that if manufacturers' instructions are followed, the cost of a regimen per application would be approximately US$60 for THS scrub and US$20 for WHR products [8]. However, Tsai *et al.* revealed that according to the prices provided by the pharmacy department, the cost of (10%) PI product per millilitre is US$0.47; the (4%) CHG product costs US$0.01 per millilitre; and the WHR product costs US$0.10 per millilitre. In practice, 5—10 mL of the 4% CHG product, which costs US$0.06—0.11, is required to complete the scrubbing protocol. Furthermore, 6 mL of WHR solution, which costs US$0.58, is required to complete the rubbing protocol [14]. In summary, the cost of waterless solution was higher, but the other expense in the procedure may differ among countries.

The trials included in our meta-analysis exhibited considerable heterogeneity because of various clinical factors described previously. First, most of the trials included surgical staff as participants, but Faoagali *et al.* and Aly and Maibach included non-surgical team members as participants [25,26]. Second, the concentrations of the hand antiseptic solution differed among the included trials. For example, the concentrations of PI used were 1% [22,26], 5% [3], 7.5% [10,24,25], or 10% [13,14,21]; moreover, various types of WHR solution were used. Finally, the methods of reporting bacterial counts for outcome evaluation differed among the trials. For example, $\log_{10}$ cfu/mL [22], $\log_{10}$ cfu [8], cfu per five fingertips [24], number of plates with bacterial growth [21], reduction in cfu count [10,25,26], or residual cfu count [3,14,23] were reported. Such differences explain the observed heterogeneity among the trials.

Our study has several limitations. First, the participants in our included trials followed standard disinfection procedures. Therefore, the outcome observed may only be extrapolated to surgical staff who scrubbed or rubbed their hands according to standard procedures. Second, our data were reported only for bacteria. Other micro-organisms, such as viruses and fungi, were not included. Finally, owing to inconsistencies in the outcome measurement, our pooling data were used to determine the trend in the residual bacterial count.

In conclusion, three types of presurgical hand washing product were compared in terms of cfu counts, SSI rates, and preference and compliance. The efficacies of WHR products and CHG were higher than the efficacy of PI. The efficacies of WHR and CHG did not differ significantly. Moreover, the WHR protocol was perceived as the most favourable for presurgical hand washing. In summary, additional RCTs with consistent outcome measurement and accurate grouping are necessary to obtain comprehensive results.

Conflict of interest statement
None declared.

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