

BRIEF REPORT OF RAPID REVIEW

Is dilute sodium hypochlorite (bleach) solution for hand-washing safe and effective for reducing transmission of SARS-CoV-2 compared to alcohol hand sanitizer or soap and water handwashing?

Date: 27 July 2020

Reviewers: South African Medical Research Council (SAMRC) Health Systems Research Unit, College of Public Health Medicine Evidence-based COVID-19 Task Team and SAMRC Cochrane South Africa

Declaration of interests: None of the authors have any interests to declare in respect of sodium hypochlorite solution, alcohol or soap and water for hand-washing for preventing transmission of SARS-CoV-2 in the community.

Key findings

EFFICACY

- ➔ A small cross-over trial of 18 healthy volunteers evaluated the efficacy of handwashing protocols using the bacteriophage Phi6 as a proxy for the enveloped virus, Ebola
- ➔ There is low certainty evidence that there is no difference between washing hands with 0.05% sodium hypochlorite solution compared to alcohol-based sanitizer to reduce viral contamination
- ➔ There is low certainty evidence that washing hands with soap and water may reduce viral contamination more than 0.05% sodium hypochlorite solution, but the magnitude of handwashing efficacy differences was small

SAFETY

- ➔ A single trial in which participants washed their hands ten times daily for 28 days indicated very low certainty that there may be a reduction in the Hand Eczema Score Index (HECSI) score in the NaOCl group compared to that in the soap and water group; for other safety outcomes including dermatitis and specific signs of transmission risk derived from the HECSI score, there was low certainty that there was no difference

SUMMARY

- ➔ Comparative data on the efficacy and safety of NaOCl solutions for handwashing is sparse. No major differences were observed compared to soap and water and alcohol-based sanitizers.

BACKGROUND

The disease, COVID-19, is caused by the transmission from person to person of the enveloped RNA virus, SARS-CoV-2, either via respiratory droplet spread or via contaminated surfaces (<https://www.who.int/news-room/commentaries/detail/transmission-of-sars-cov-2-implications-for-infection-prevention-precautions>). UNICEF states that the virus envelope (covering) can be disrupted through regularly and thoroughly cleaning your hands by washing them with soap or water or using an alcohol-based hand rub (<https://www.unicef.org/coronavirus/everything-you-need-know-about-washing-your-hands-protect-against-coronavirus-covid-19>).

Dilute sodium hypochlorite at a concentration of 1:1000ppm (0.1%) is recommended by the National Institute of Communicable Disease as an effective disinfectant to wipe (not spray) surfaces to decontaminate where virus may be present (<https://www.nicd.ac.za/wp-content/uploads/2020/05/ipc-guidelines-covid-19-version-2-21-may-2020.pdf>). A more dilute solution (usually 0.05%) has been used for hand-washing in the context of other viral epidemic contexts such as for Ebola Virus (Wolfe, Wells et al. 2016, Wolfe, Gallandat et al. 2017). A 2014 WHO rapid advice guideline, based on a systematic review, recommended that bleach/chlorine solutions currently in use for hand hygiene and glove disinfection for filoviruses (such as Ebola) may be used in the interim period in emergency situations until alcohol-based handrubs or soap and water become available (<https://www.who.int/csr/resources/publications/ebola/hand-hygiene/en/>). This was noted to be based on low quality evidence and was intended to be an interim measure.

Current World Health Organization interim guidance (1st April 2020) - specifically for prevention of transmission of SARS-CoV-2 - recommends against chlorine hand washing solutions because of potential harm to users and those making the solutions, as well as degradation of chlorine exposed to sunlight or heat. The guidance recommends handwashing with soap and water a hand rubbing with an alcohol-based hand rub and notes that soap is generally cheap and easy to find, and liquid soap solutions can also be used.

In South Africa, NICD guidelines stipulate that the percentage of alcohol in a sanitizer should not be less than 70% alcohol (<https://www.nicd.ac.za/wp-content/uploads/2020/05/Clinical-management-of-suspected-or-confirmed-COVID-19-Version-4.pdf>). Where water is in short supply, such as in rural schools, the use of alcohol sanitizers are advised as a substitute to soap and water hand-washing. The high cost of alcohol sanitizers has raised concerns about the longer-term sustainability of the use of these. Some communities have expressed concerns regarding the use of alcohol based on religious or cultural grounds (Lu and Heacock 2014) (Ng, Shaban et al. 2019). UNICEF notes that while alcohol-based hand sanitizer kills the coronavirus, it does not kill all kinds of bacteria and viruses, such as the norovirus and rotavirus. This rapid review aimed to evaluate the use of dilute bleach solution for handwashing as an alternative to handwashing with soap and water and rubbing with alcohol sanitizer.

OBJECTIVES

To assess the safety and effectiveness of sodium chlorite solution for handwashing compared to handwashing with soap and water or alcohol-based sanitizer for preventing transmission of SARS-CoV-2 to inform College of Public Health Medicine guidance.

METHODS

We conducted a rapid review of the evidence. We formulated the research question using the PICO format:

Population: Any human populations

Intervention: Handwashing with dilute sodium chlorite solution

Comparators: Handwashing with soap and water or alcohol-based sanitizer (at least 60% alcohol)

Outcomes: Skin and respiratory irritation and conditions
Viral decontamination

Study designs: Randomised Controlled Trials (RCTs)
Comparative observational studies
Systematic Reviews

Search Strategy

We conducted systematic searching of two electronic databases (PubMed and *The Cochrane Library*) as well as the following trials registries www.clinicaltrials.gov and WHO ICTRP (<https://www.who.int/ictrp/en/>), on 23 April 2020. See **Appendix 1**.

The search strategy was developed and conducted by an experienced information specialist (JO). All records were uploaded into EndNote. Each record was screened independently by two assistant reviewers to identify possible eligible studies. The lead reviewer (JtWN) screened all possible eligible studies to create a final list for which full-text articles were obtained. Two reviewers (NS and WC) independently conducted eligibility assessment on each full-text article.

Data extraction and quality appraisal

NS and WC conducted independent, duplicate critical appraisal and risk of bias assessment of included RCTs using the Cochrane Risk of Bias 2.0 tool; NS and JtWN conducted quality evaluation of the systematic review using the ROBIS tool for systematic reviews.

NS extracted numerical data from the 2 RCT reports and entered the data into REVMAN where reporting permitted. For the data on reduction of Phi6 contamination we determined means and 95% confidence intervals from the graphs as these were not reported in the text, and determined the Standard Deviations from the 95% confidence intervals using an assumed t distribution given the small sample size. We extracted data on compliance directly from the trial reports. The data was checked by WC.

No meta-analysis was possible given that the trials evaluated different outcomes. For the N = 1 trial, we report the results narratively.

NS conducted GRADE assessment and all reviewers checked and approved the final report.

RESULTS

1305 records were screened and 37 full-text studies were checked for eligibility of which 1 systematic review, 2 RCTs and one comparative trial with an N = 1 met inclusion criteria. **Appendix 3** contains the PRISMA flow diagram of the search.

No additional studies were identified from www.clinicaltrials.gov or the dedicated COVID-19 WHO ICTRP platform (<https://www.who.int/ictcp/en/>).

Characteristics of included studies

1. Systematic Review

The Kampf et al. review was judged to be highly relevant to our PICO (Kampf, Todt et al. 2020). We judged the overall risk of bias to be high due to the limited search, the potential for publication and language bias, and the lack of reporting of study design and quality assessment, which overall reduced our confidence in the review results. Given the high risk of bias, and the finding that there were no handwashing studies identified in this review, we were not able to draw any conclusions from this review.

See **Appendix 3** for ROBIS.

2. Randomised Controlled Trials

Two trials conducted in healthy volunteers in the USA evaluated the effectiveness and safety of several different handwashing protocols which could be used during an Ebola outbreak (Wolfe, Wells et al. 2016, Wolfe, Gallandat et al. 2017).

The Wolfe 2017 was a crossover RCT in which reduction in the concentration of an Ebola surrogate organism (bacteriophage Phi6) was tested in the absence and presence of a soil load to simulate bodily fluids on the same of 18 participants at different times, and in which the order of application of the handwashing protocols was randomized for each participant at each time to evaluate six handwashing protocols including those of interest to our PICO (namely; soap and water, alcohol-based hand sanitizer, stabilized sodium hypochlorite solution) (Wolfe, Gallandat et al. 2017).

Similar handwashing protocols were evaluated in Wolfe 2016 with 6 groups of 18 participants each who were instructed to wash their hands ten times daily for 28 days according to protocol. The safety outcomes assessed were irritation as measured by the Hand Eczema Score Index (HECSI) and signs of transmission risk derived from the HECSI (e.g. skin cracking) and dermatologist-diagnosed dermatitis (Wolfe, Wells et al. 2016).

3. Comparative observational study

Ma (Ma, Shan et al. 2020) evaluated the efficacy of instant hand wiping using a towel soaked in water containing soap powder or sodium hypochlorite, in removing Avian Influenza Virus (AIV) from a single individual's hands. In this study, the AIV was used to imitate the enveloped SARS-CoV-2 virus. The palm was wiped three times from the root of the palm to the tips of the fingers, using a towel soaked in water containing soap or sodium hypochlorite and then wrung to remove most of the water inside. Each treatment and a control without wiping were conducted independently three times.

Evidence of effectiveness and safety

See **Appendix 4** for the Risk of Bias results, **Appendix 5** for the forest plots and **Appendix 6** for GRADE table. Note that no formal risk of bias assessment was conducted on the Ma comparative study as it was judged to be at high risk given it was conducted in a single individual with no randomization and was therefore prone to selection, performance, detection and attrition bias.

1. Sodium hypochlorite NaOCl (0.05% solution) versus alcohol-based sanitizer

1.1 Removal and inactivation of virus (mean log reduction in Phi6) with and without soil load

There is low certainty evidence that there was no difference between NaOCl compared to alcohol-based sanitizer for reducing the mean log reduction in Phi6 concentrations with soil load (Mean Difference (MD) = 0.1 lower (96% Confidence Interval (CI): 1.02 lower to 0.82 higher) and without soil load (Mean Difference (MD) = 0.40 higher (95% Confidence Interval (CI): 0.69 lower to 1.49 higher).

1.2 Dermatitis

There was very low certainty evidence that the risk of dermatitis was greater in the NaOCl group than the alcohol-based sanitizer group (RR = 1.38 (CI: 0.15 to 77.12)). Given that only 1 event was recorded, this result should be viewed with caution.

1.3 HECSI score and signs of transmission from HECSI score

There was low certainty evidence that there were no differences between NaOCl and alcohol-based hand sanitizers for both the HECSI score (OR = 1.06; CI: 0.73 to 1.39) and the specific signs of transmission risk derived from the HECSI score (Beta coefficient = 0.15 (CI: -0.36 to 0.66) p value > 0.05).

2. Sodium hypochlorite NaOCl (0.05% solution) versus soap and water

2.1 Removal and inactivation of virus

From the Wolfe 2017 trial, there is low certainty evidence that NaOCl reduced the mean log reduction in Phi6 concentrations with soil load less than soap and water (MD 1.15 lower (1.95 lower to 0.35 lower compared to the control)). For the condition without soil load, there was low certainty evidence that there was no difference between NaOCl and soap and water (MD = 0.41 higher (CI: 0.51 lower to 1.33 higher)) compared to the control.

The article reports that for the condition with soil load, handwashing with soap and water resulted in greater log reduction than both NaOCl (p = 0.001) and alcohol-based sanitizer (p = 0.002) compared to control.

There is very low certainty evidence that in the small N = 1 trial conducted by Ma et al., the virus on the palm declined by 98.36% and 96.62% through wiping using the wet towel soaked in water containing soap powder and 0.05% sodium hypochlorite, compared to a control respectively. The mean difference in Ct values (a measure showing that if the virus amount declines by 50%, the Ct value of the RT-PCR shall increase by 1) indicated no difference between soap powder and 0.05% active chlorine (MD = -1.04; CI: -3.87 to 1.79).

2.2 Dermatitis

There was very low certainty evidence that the risk of dermatitis was no different in the NaOCl group than from the soap and water group (RR = 1.07 (CI: 0.07 to 15.57)). Given that only 1 event was recorded in each group, this result should be viewed with caution.

2.3 *HECSI score and signs of transmission from HECSI score*

There was low certainty evidence that there may be a reduction in the HECSI score in the NaOCl group compared to that in the soap and water group (OR = 0.68; CI: 0.36 to 1.00). For the specific signs of transmission risk derived from the HECSI score, there was low certainty that there was no difference (beta coefficient = 0.46(CI: -0.98 to 0.06; p = 0.084).

3. Compliance

1.4 *Compliance*

The handwashing protocols for the trial evaluating efficacy outcomes were carried out in 18 volunteers under supervision in the laboratory so compliance was likely high (Wolfe, Gallandat et al. 2017).

For the trial evaluating the safety of handwashing protocols, participants self-reported handwashing an average of 8.8 to 9.2 times/day according to their designated protocol with no significant differences in compliance noted by the group found by linear regression.

CONCLUSION

Comparative data on the efficacy and safety of NaOCl solutions for handwashing is sparse. No major differences were observed between NaOCl solutions compared to soap and water and alcohol-based sanitizers. While the evidence is of low or very low certainty due to the relatively few and small studies identified, the data indicates that NaOCl solutions may be a reasonable alternative to current practices should availability, cost or cultural concerns preclude the use of either alcohol-based sanitizer or soap and water for hand-washing.

REFERENCES

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- Ma, Q. X., H. Shan, H. L. Zhang, G. M. Li, R. M. Yang and J. M. Chen (2020). "Potential utilities of mask-wearing and instant hand hygiene for fighting SARS-CoV-2." J Med Virol.
- Ng, W. K., R. Z. Shaban and T. van de Mortel (2019). "The effect of a hand hygiene program featuring tailored religion-relevant interventions on healthcare workers' hand rubbing compliance and beliefs in the United Arab Emirates: A cohort study." Infect Dis Health **24**(3): 115-123.
- Wolfe, M. K., K. Gallandat, K. Daniels, A. M. Desmarais, P. Scheinman and D. Lantagne (2017). "Handwashing and Ebola virus disease outbreaks: A randomized comparison of soap, hand sanitizer, and 0.05% chlorine solutions on the inactivation and removal of model organisms Phi6 and E. coli from hands and persistence in rinse water." PLoS One **12**(2): e0172734.
- Wolfe, M. K., E. Wells, B. Mitro, A. M. Desmarais, P. Scheinman and D. Lantagne (2016). "Seeking Clearer Recommendations for Hand Hygiene in Communities Facing Ebola: A Randomized Trial Investigating the Impact of Six Handwashing Methods on Skin Irritation and Dermatitis." PLoS One **11**(12): e0167378.

Appendix 1: Search strategy of 23 April 2020

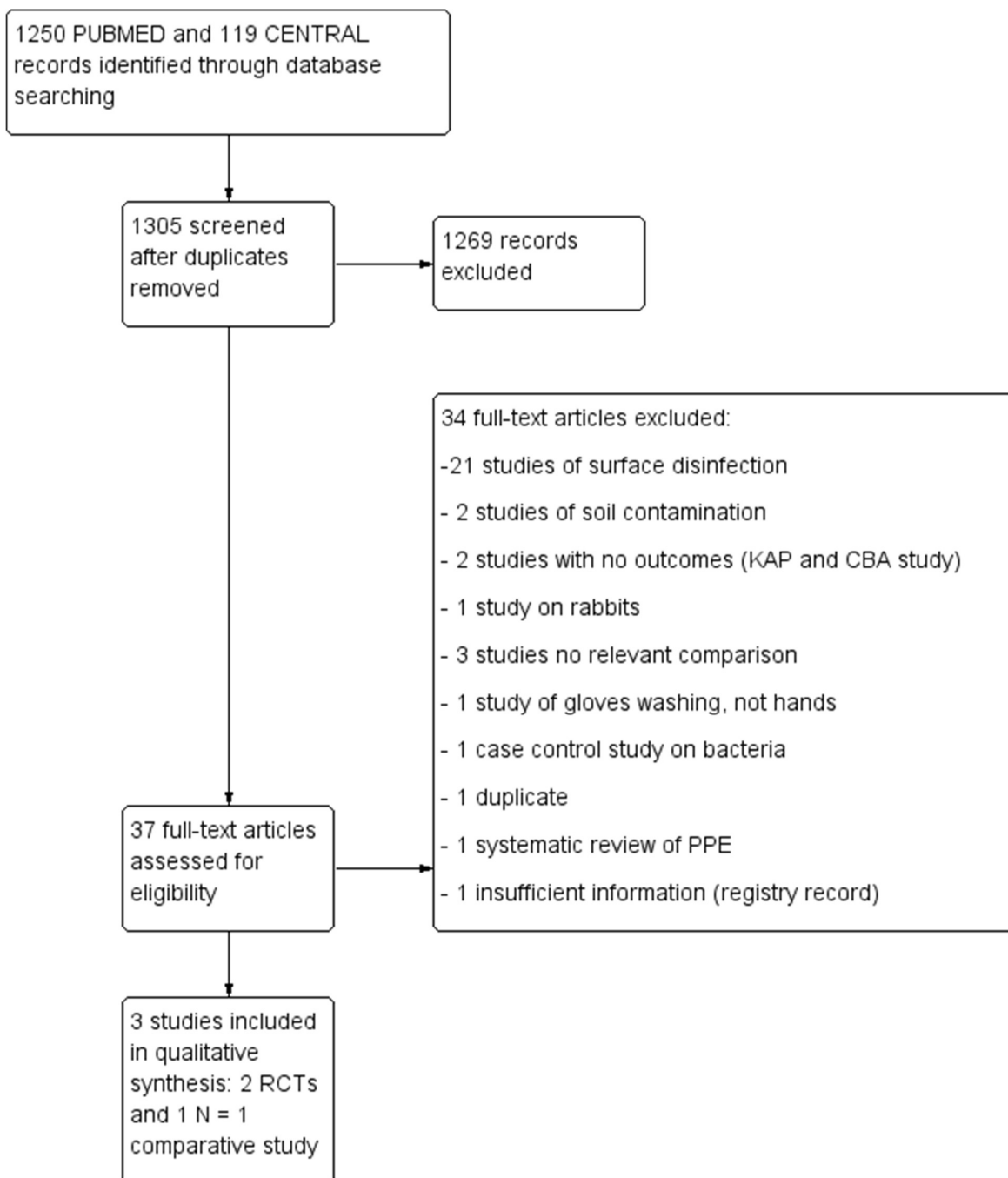
PubMed

Search	Query	Items found
#27	Search (#22 AND #26)	1250
#26	Search (#23 OR #24 OR #25)	47641
#25	Search (handwash*[tiab] OR handsaniti*[tiab] OR handrub*[tiab])	2157
#24	Search (surface*[tiab] AND (clean*[tiab] OR disinfectants[mh] OR disinfect*[tiab] OR wash*[tiab] OR sanitis*[tiab] OR sanitiz*[tiab] OR wipe*[tiab]))	29041
#23	Search (hand disinfection[mh] OR hand sanitizers[mh] OR hand hygiene[mh] OR (hand[tiab] OR hands[tiab]) AND (disinfect*[tiab] OR sanitis*[tiab] OR sanitiz*[tiab] OR antiseptic[tiab] OR antiseptics[tiab] OR hygiene[tiab] OR wash*[tiab] OR wipe*[tiab] OR gel[tiab] OR gels[tiab] OR rub[tiab] OR rubs[tiab] OR foam*[tiab])	18570
#22	Search (sodium hypochlorite[mh] OR sodium hypochlorite[tiab] OR clorox[tiab] OR antiformin[tiab] OR bleach[tiab] OR jik[tiab] OR eusol[tiab] OR chloride of soda[tiab] OR carrel-dakin solution[tiab] OR dakin's solution[tiab])	9853

Cochrane Library CENTRAL (Issue 4 of 12, April 2020)

ID	Search	Hits
#1	[mh "sodium hypochlorite"] or "sodium hypochlorite":ti,ab,kw or Clorox:ti,ab,kw or antiformin:ti,ab,kw or bleach:ti,ab,kw or jik:ti,ab,kw or eusol:ti,ab,kw or "chloride of soda":ti,ab,kw or "carrel-dakin solution":ti,ab,kw or "dakin's solution":ti,ab,kw (Word variations have been searched)	1682
#2	[mh "hand disinfection"] or [mh "hand sanitizers"] or [mh "hand hygiene"] or (hand OR hands) near/6 (disinfect* or sanitis* or sanitiz* or antiseptic or antiseptics or hygiene or wash* or wipe* or gel or gels or rub or rubs or foam*):ti,ab,kw (Word variations have been searched)	1502
#3	handwash*:ti,ab,kw or handsaniti*:ti,ab,kw or handrub*:ti,ab,kw (Word variations have been searched)	475
#4	(surface* near/6 (clean* or disinfect* or wash* or sanitis* or sanitiz* or wipe*)):ti,ab,kw (Word variations have been searched)	360
#5	surface*:ti,ab,kw and [mh disinfectants]	177
#6	#2 or #3 or #4 or #5	2065
#7	#1 and #6 in Trials	117

Appendix 2: Flow diagram of search



Appendix 3: Risk of Bias for Systematic Review (ROBIS) for Kampf 2020

ID	Publication year	Number and type of studies	Publication limits	Language limits	ROBIS Domains				
					1	2	3	4	Overall
Influenza-like Illness									
Kampf	2020	2 laboratory studies of sodium hypochlorite for inanimate surface disinfection and 0 in vitro studies on the efficacy of hand washing against coronavirus contaminations on hands	Yes ¹	Yes ²	Some Concerns	High risk	High Risk	Some concerns	High risk ³

1 Only one databases searched – MEDLINE

2 Assumed to only include English-language as only a single database searched, and for example, no Chinese-specific literature searched

3 The limited search, potential for publication and language bias and the lack of reporting of study design and quality assessment, reduce our confidence in the review results.

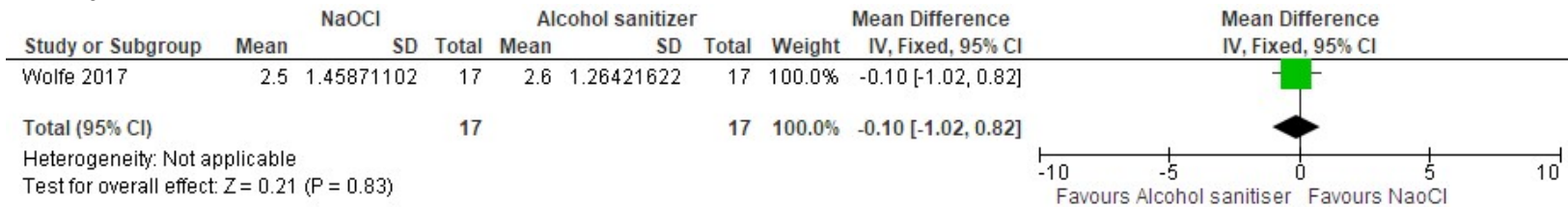
Appendix 4: Risk of Bias Assessment for RCTs

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Wolfe 2016	+	?	-	+	+	+	+
Wolfe 2017	+	?	-	+	+	+	+

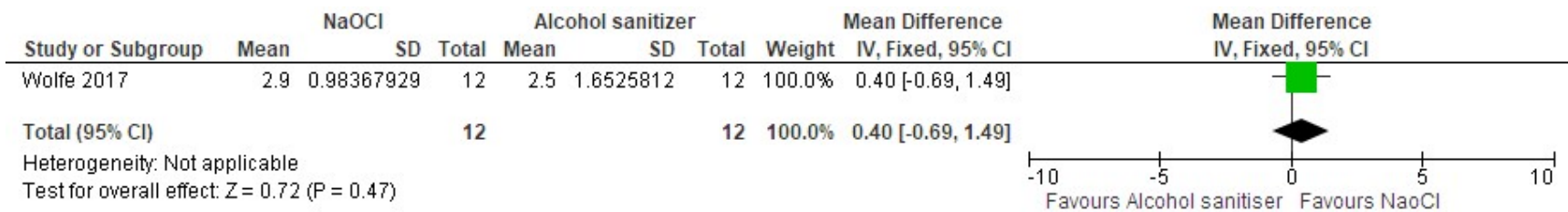
Appendix 5: Forest plots

1. Sodium hypochlorite (0.05% solution) versus alcohol-based sanitizer

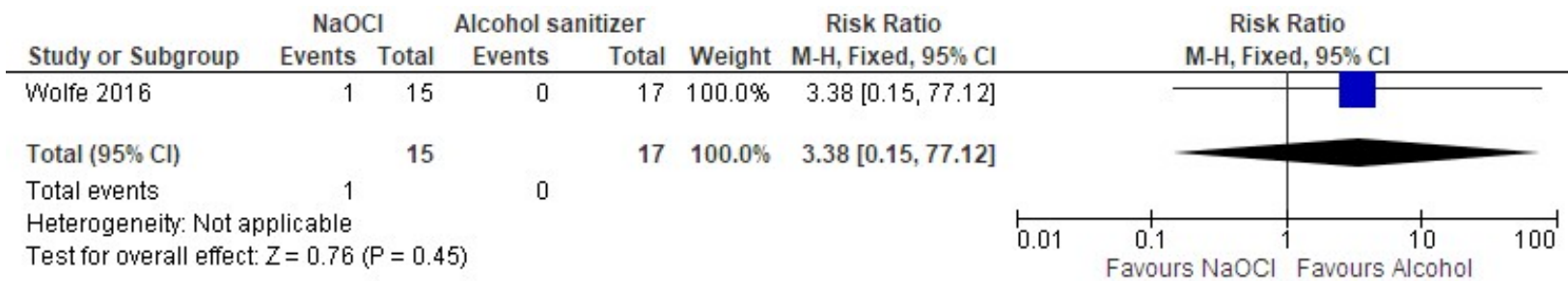
1.1. Mean Log reduction *Phi6* with soil load



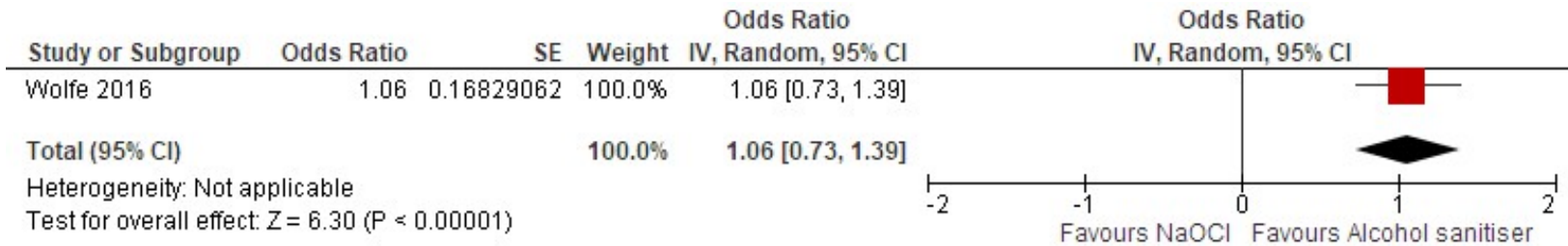
1.2. Mean Log reduction *Phi6* without soil load



1.3. Dermatitis

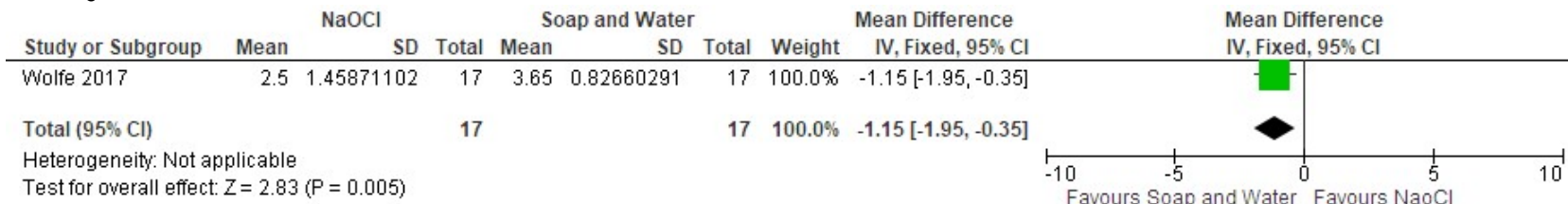


1.4. Signs of Transmission from HECSI score

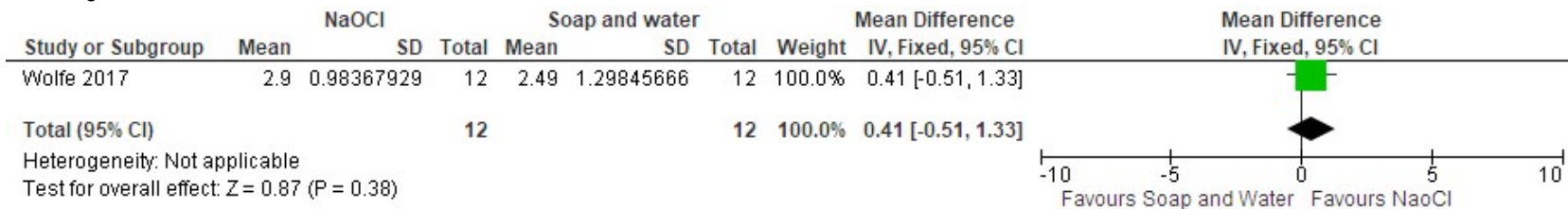


2. Sodium hypochlorite (0.05% solution) versus soap and water

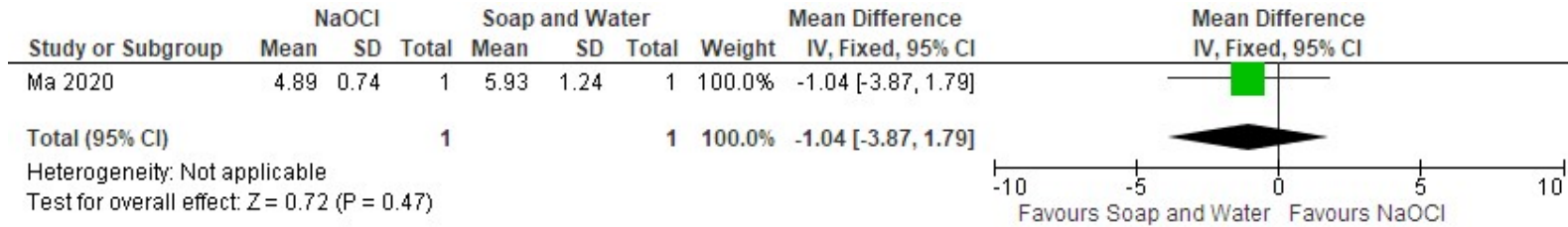
2.1. Mean Log reduction Phi6 with soil load



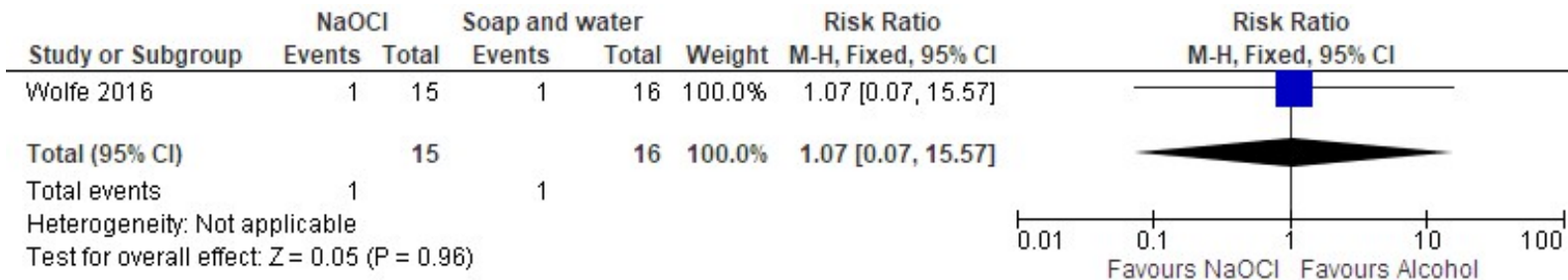
2.2. Mean Log reduction Phi6 without soil load



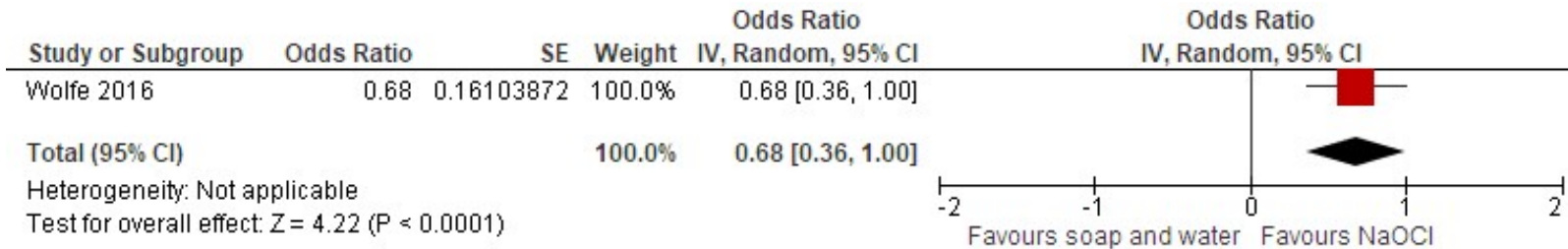
2.3. Mean Ct increase in removal of AIV



2.4. Dermatitis



2.5. Signs of Transmission from HECSI score



Appendix 6: GRADE table

Sodium hypochlorite 0.05% stabilized solution compared to alcohol sanitizer for hand-washing for SARS-CoV-2

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sodium hypochlorite 0.05% stabilized solution	Alcohol sanitizer	Relative (95% CI)	Absolute (95% CI)		
Mean Log reduction Phi6 with soil load												
1	randomised trials	not serious ^{US}	not serious	serious ^a	serious ^b	none	17	17	-	MD 0.1 lower (1.02 lower to 0.82 higher)	⊕⊕○○ LOW	CRITICAL
Mean Log reduction Phi6 without soil load												
1	randomised trials	not serious	not serious	serious ^a	serious ^b	none	12	12	-	MD 0.40 higher (0.69 lower to 1.49 higher)	⊕⊕○○ LOW	CRITICAL
Dermatitis												
1	randomised trials	not serious	not serious	serious ^a	very serious ^c	none	1/15 (6.7%)	0/17 (0.0%)	RR 3.38 (0.15 to 77.12)	0 fewer per 1,000 (from 0 fewer to 0 fewer)	⊕○○○ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sodium hypochlorite 0.05% stabilized solution	Alcohol sanitizer	Relative (95% CI)	Absolute (95% CI)		

HECSI score

1	randomised trials	not serious	not serious	serious ^a	serious ^b	none	Beta coefficient = 0.15 (-0.36 to 0.66) p value > 0.05			⊕⊕○○ LOW	CRITICAL
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Signs of Transmission from HECSI score

1	randomised trials	not serious	not serious	serious ^a	serious ^b	none	-/0	-/0	OR 1.06 (0.73 to 1.39)	1 fewer per 1,000 (from 1 fewer to 1 fewer)	⊕⊕○○ LOW	CRITICAL
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CI: Confidence interval; MD: Mean difference; RR: Risk ratio; OR: Odds ratio

Explanations

a. Indirectness: Rated as serious and downgraded once as the intervention was tested in the laboratory, not in the field and a surrogate marker, Phi6, for Ebola virus was used. This was then used as a proxy for SARS-CoV-2 given that it is also an enveloped virus.

b. Imprecision: Rated as Serious and downgraded once. Sample size and event rates are very small and confidence interval is wide.

c. Imprecision: Rated as Very Serious and downgraded twice. Sample size and event rates are very small and confidence interval is very wide.

Sodium hypochlorite 0.05% stabilized solution compared to soap and water for hand-washing for SARS-CoV-2

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sodium hypochlorite 0.05% stabilized solution	soap and water	Relative (95% CI)	Absolute (95% CI)		

Mean Log reduction Phi6 with soil load

1	randomised trials	not serious	not serious	serious ^a	serious ^b	none	17	17	-	MD 1.15 lower (1.95 lower to 0.35 lower)	⊕⊕○○ LOW	CRITICAL
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Mean Log reduction Phi6 without soil load

1	randomised trials	not serious	not serious	serious ^a	serious ^b	none	12	12	-	MD 0.41 higher (0.51 lower to 1.33 higher)	⊕⊕○○ LOW	CRITICAL
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Dermatitis

1	randomised trials	not serious	not serious	serious ^a	serious ^c	none	1/15 (6.7%)	1/16 (6.3%)	RR 1.07 (0.07 to 15.57)	4 more per 1,000 (from 58 fewer to 911 more)	⊕○○○ VERY LOW	CRITICAL
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Signs of Transmission from HECSI score

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sodium hypochlorite 0.05% stabilized solution	soap and water	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	not serious	not serious	serious ^a	serious ^b	none	-/0	-/0	OR 0.68 (0.36 to 1.00)	1 fewer per 1,000 (from 1 fewer to 0 fewer)	⊕⊕○○ LOW	CRITICAL

HECSI score

1	randomised trials	not serious	not serious	serious ^a	serious ^b	none	Beta coefficient = -0.46 (95% CI: -0.98 to 0.06). P = 0.084	⊕⊕○○ LOW	CRITICAL
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CI: Confidence interval; **MD:** Mean difference; **RR:** Risk ratio; **OR:** Odds ratio

Explanations

a. Indirectness: Rated as serious and downgraded once as the intervention was tested in the laboratory, not in the field and a surrogate marker, Phi6, for Ebola virus was used. This was then used as a proxy for SARS-CoV-2 given that it is also an enveloped virus.

b. Imprecision: Rated as Serious and downgraded once. Sample size and event rates are very small and confidence interval is wide.

c. Imprecision: Rated as Very Serious and downgraded twice. Sample size and event rates are very small and confidence interval is very wide.