

University of Dundee

**Antimicrobial mouthwashes (gargling) and nasal sprays to protect healthcare workers when undertaking aerosol-generating procedures (AGPs) on patients without suspected or confirmed COVID-19 infection**

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## **Antimicrobial mouthwashes (gargling) and nasal sprays to protect healthcare workers when undertaking aerosol-generating procedures (AGPs) on patients without suspected or confirmed COVID-19 infection (Review)**

Burton MJ, Clarkson JE, Goulao B, Glenny AM, McBain AJ, Schilder AGM, Webster KE, Worthington HV

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[Intervention Review]

# Antimicrobial mouthwashes (gargling) and nasal sprays to protect healthcare workers when undertaking aerosol-generating procedures (AGPs) on patients without suspected or confirmed COVID-19 infection

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## ABSTRACT

### Background

COVID-19 infection poses a serious risk to patients and – due to its contagious nature – to those healthcare workers (HCWs) treating them. The risks of transmission of infection are greater when a patient is undergoing an aerosol-generating procedure (AGP). Not all those with COVID-19 infection are symptomatic, or suspected of harbouring the infection. If a patient who is not known to have or suspected of having COVID-19 infection is to undergo an AGP, it would nonetheless be sensible to minimise the risk to those HCWs treating them.

If the mouth and nose of an individual undergoing an AGP are irrigated with antimicrobial solutions, this may be a simple and safe method of reducing the risk of any covert infection being passed to HCWs through droplet transmission or direct contact. Alternatively, the use of antimicrobial solutions by the HCW may decrease the chance of them acquiring COVID-19 infection. However, the use of such antimicrobial solutions may be associated with harms related to the toxicity of the solutions themselves or alterations in the natural microbial flora of the mouth or nose.

### Objectives

To assess the benefits and harms of antimicrobial mouthwashes and nasal sprays administered to HCWs and/or patients when undertaking AGPs on patients without suspected or confirmed COVID-19 infection.

### Search methods

Information Specialists from Cochrane ENT and Cochrane Oral Health searched the Central Register of Controlled Trials (CENTRAL 2020, Issue 6); Ovid MEDLINE; Ovid Embase and additional sources for published and unpublished trials. The date of the search was 1 June 2020.

## Selection criteria

This is a question that urgently requires evidence, however at the present time we did not anticipate finding many completed RCTs. We therefore planned to include the following types of studies: randomised controlled trials (RCTs); quasi-RCTs; non-randomised controlled trials; prospective cohort studies; retrospective cohort studies; cross-sectional studies; controlled before-and-after studies. We set no minimum duration for the studies.

We sought studies comparing any antimicrobial mouthwash and/or nasal spray (alone or in combination) at any concentration, delivered to the patient or HCW before and/or after an AGP.

## Data collection and analysis

We used standard Cochrane methodological procedures. Our primary outcomes were: 1) incidence of symptomatic or test-positive COVID-19 infection in HCWs or patients; 2) significant adverse event: anosmia (or disturbance in sense of smell). Our secondary outcomes were: 3) COVID-19 viral content of aerosol (when present); 4) change in COVID-19 viral load at site(s) of irrigation; 5) other adverse events: changes in microbiome in oral cavity, nasal cavity, oro- or nasopharynx; 6) other adverse events: allergy, irritation/burning of nasal, oral or oropharyngeal mucosa (e.g. erosions, ulcers, bleeding), long-term staining of mucous membranes or teeth, accidental ingestion. We planned to use GRADE to assess the certainty of the evidence for each outcome.

## Main results

We found no completed studies to include in this review.

## Authors' conclusions

We identified no studies for inclusion in this review, nor any ongoing studies. The absence of completed studies is not surprising given the relatively recent emergence of COVID-19 infection. However, we are disappointed that this important clinical question is not being addressed by ongoing studies.

## PLAIN LANGUAGE SUMMARY

**Does the use of antimicrobial mouthwash or nasal spray by people who are not actively suspected of having COVID-19 - or by their healthcare workers - protect their healthcare workers when they undertake 'aerosol-generating procedures' on them?**

### Why is this question important?

COVID-19 is an infectious disease caused by the SARS-CoV-2 virus. Most people infected with COVID-19 develop a mild to moderate respiratory illness, and some may have no symptoms (asymptomatic infection). Others experience severe symptoms and need specialist treatment and intensive care.

COVID-19 spreads from person to person primarily through droplets that are produced when an infected person coughs, sneezes or talks. A person can also become infected by touching a surface or object that has viral droplets on it, and then touching their own mouth or nose.

Some people with COVID-19 do not have any symptoms, therefore they might not be known to be or suspected of being infected. However, they might still be able to pass the infection on to others. This means that healthcare workers who are treating them may be at risk of catching the infection. Risk of infection may be particularly high when healthcare workers undertake 'aerosol-generating procedures', which are medical procedures that cause the patient to produce many small droplets. For example, people who have surgery under general anaesthesia, or people with a lung disease that makes breathing difficult (such as pneumonia), may need to be placed on a ventilator (artificial breathing machine) to help them breathe. This requires a healthcare worker to insert a tube through the patient's mouth, into their airway – a procedure during which many small droplets are likely to be produced by the patient. Similar droplets can be produced during routine dental procedures, such as drilling or scaling of teeth.

Patient or healthcare worker use of antimicrobial mouthwash (to rinse the mouth) or nasal spray (sprayed into the nose) might help to protect healthcare workers against infection by COVID-19. Antimicrobial mouthwash and nasal spray are liquids that kill or stop the growth of micro-organisms such as viruses or bacteria.

As with any medical treatment, antimicrobial mouthwash and nasal spray have potential risks as well as benefits. It is possible that using mouthwash or nasal spray could cause a variety of unwanted (adverse) effects, including irritation, allergic reactions or loss of smell. It may also remove micro-organisms from the mouth or nose that are useful for protecting the body against infection.

We set out to assess the benefits and risks of self-administration of antimicrobial mouthwashes and nasal sprays by patients without a known or suspected COVID-19 infection, or the healthcare workers who treat them with aerosol-generating procedures, by reviewing the research evidence.

### How did we search for evidence?

Our team of researchers searched the medical literature for studies that compared the effects of patients or healthcare workers self-administering any antimicrobial mouthwash or nasal spray against using no treatment, water or a salt solution.

**What did we find?**

We found no completed, or ongoing, studies to include in this review.

**What does this mean?**

There is currently no evidence relating to the benefits and risks of healthcare workers' or patients' use of antimicrobial mouthwashes or nasal sprays to protect healthcare workers who undertake aerosol-generating procedures on patients without a known or suspected COVID-19 infection.

We need studies to be conducted so that we can answer this important clinical question.

**How-up-to date is this review?**

We last searched for evidence on 1 June 2020. This review covered research that was available up to that date, but did not consider any evidence that may have been produced since then.

## SUMMARY OF FINDINGS

### Summary of findings 1. Antimicrobial mouthwashes (gargling) and nasal sprays to protect healthcare workers when undertaking aerosol-generating procedures (AGPs) on patients without suspected or confirmed COVID-19 infection

Antimicrobial mouthwashes (gargling) and nasal sprays to protect healthcare workers when undertaking aerosol-generating procedures (AGPs) on patients without suspected or confirmed COVID-19 infection

**Patient or population:** patients without suspected or confirmed COVID-19 infection, undergoing aerosol-generating procedures (AGPs) and those healthcare workers (HCWs) treating them

**Setting:** any healthcare setting

**Intervention:** any antimicrobial mouthwash and/or nasal spray

**Comparison:** no treatment or saline or water

Outcomes	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)		Certainty of the evidence (GRADE)	What happens
		Without mouth-wash or nasal spray	With mouth-wash or nasal spray		
Incidence of symptomatic or test-positive COVID-19 infection in HCWs or patients	No data available (no included studies)				
Anosmia	No data available (no included studies)				
COVID-19 viral content of aerosol	No data available (no included studies)				
Change in COVID-19 viral load at site(s) of irrigation	No data available (no included studies)				
Changes in microbiome in oral cavity, nasal cavity, oro-or nasopharynx	No data available (no included studies)				
Other adverse events	No data available (no included studies)				

\***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

**CI:** confidence interval; **RR:** risk ratio; **OR:** odds ratio

#### GRADE Working Group grades of evidence

**High certainty:** We are very confident that the true effect lies close to that of the estimate of the effect

**Moderate certainty:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

**Low certainty:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

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**Very low certainty:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect



## BACKGROUND

### Description of the condition

The emergence of a novel coronavirus (SARS-CoV-2) in late 2019 has resulted in a global pandemic of an infectious condition - COVID-19. To date, almost 19.9 million people have been reported to be infected, with close to 732,000 deaths. Patients may be asymptomatic, or they may have an illness with symptoms varying from mild to very severe. Not all those who have the condition are tested for the presence of the virus. Multiple therapeutic interventions and vaccines are in development. The steroid dexamethasone has been shown to reduce the mortality rate of people requiring invasive ventilation for COVID-19 by a third (Horby 2020), and the antiviral drug remdesivir can reduce the time to recovery of patients in hospital (Beigel 2020). Prevention efforts have focused on measures of social distancing and isolation in many countries.

Healthcare workers are at the forefront of this crisis, with repeated exposure to individuals who are, or may be, infected, and are therefore at risk themselves. Access to and proper use of personal protective equipment (PPE) is a key intervention that should reduce the frequency of transmission of the infection to healthcare workers.

These workers may be especially at risk when undertaking 'aerosol-generating procedures' (AGPs). This is any medical, dental or patient-care procedure that results in the production of airborne particles (aerosols) from the upper aerodigestive tract (mouth, nose, throat, oesophagus) and lower respiratory tract where the virus is shedding. These can remain suspended in the air and travel over a distance. They may cause infection if they are inhaled. Such procedures therefore create the potential for airborne transmission of infection.

This review is one of a set of three which consider two measures that may protect healthcare workers and patients - both for their own benefit, and to reduce the frequency of onward transmission. These two measures are 1) the pre-procedural use of mouthwashes and nasal sprays by patients, to reduce the risk that any aerosol that they generate will infect healthcare workers, and 2) the use of mouthwashes and nasal sprays by healthcare workers pre- and post-exposure to patients with confirmed or suspected infection to reduce the risk of acquiring such infection through their mouth or nose. This particular review focuses on the **protection of HCWs** when they are undertaking AGPs on patients who are *not* known to have, or suspected of having, COVID-19 infection. It evaluates the use of mouthwashes and nasal sprays by either the patients (1) above) or the HCWs treating them (2) above) or both. (The other two reviews will focus on a) the use of antimicrobial mouthwashes and nasal sprays by HCWs treating patients with suspected or confirmed COVID-19 infection (Burton 2020a) and b) the use of antimicrobial mouthwashes and nasal sprays by patients with suspected or confirmed COVID-19 infection (Burton 2020b)).

### Description of the intervention

Mouthwashes are oral rinsing solutions: many are in common use to manage halitosis, prevent tooth decay and reduce plaque formation. In some countries they are recommended as a hygiene measure during the regular cold and flu season. Many mouthwashes with some antimicrobial activity can be purchased

over the counter, and others are available on prescription. The antimicrobial agents and effectiveness vary and whilst most have some antibacterial properties a few are also antiviral.

Similar topical antimicrobial solutions may be administered via the nose using a nasal spray, or by direct irrigation or douching (administered by sniffing a solution through each nostril and spitting it out).

### How the intervention might work

There has been considerable interest in the use of nasal irrigation or oral rinses to prevent transmission of upper respiratory tract infections (URTI) caused by viruses, or to alleviate their symptoms. Transmission of such disease occurs by the inhalation of small droplets containing viral particles, or by transfer (for example, from surfaces to hands, and then to the face, mouth and nose). Rinsing the mouth and/or nose may eradicate viral particles completely - preventing transmission to that individual - or reduce the viral load that the individual is exposed to. This may prevent the disease developing in that individual or reduce the severity of it. Gargles that have been investigated for their ability to reduce viral transmission include tea (or components of tea) (Ide 2016), water (Goodall 2014) and povidone iodine (Kitamura 2007; Satomura 2005). Other mouthwashes in common use, including hydrogen peroxide and chlorhexidine, may also have antiviral activity (Bernstein 1990).

Nasal irrigation with topical antimicrobial solutions similar to those used as mouthwashes has also been investigated. Carrageenan, a carbohydrate found in red seaweed, has been trialled as an antiviral nasal spray. Studies have identified a decrease in the nasal viral load from URTI, but results on symptomatic improvement have been mixed (Eccles 2010; Eccles 2015; Fazekas 2012; Ludwig 2013).

Given the new emergence of COVID-19, the efficacy of nasal or oral irrigation fluids against this disease is not yet known. However, activity against similar novel coronaviruses (such as those responsible for severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS)) has been demonstrated for some preparations (Eggers 2015; Kariwa 2006). Gargle solutions of povidone iodine have been shown to be active against the coronaviruses causing both MERS and SARS in vitro (Eggers 2018; Kariwa 2006).

### How the intervention might cause harm

Use of mouthwash or nasal irrigation has the potential to cause a variety of adverse effects. In common with many treatments, there is the possibility of irritation or allergic reaction to components of the product. A key concern for any agent used intranasally is the potential for long-term damage resulting in anosmia (loss of sense of smell). However, anosmia may also be a symptom of COVID-19 infection.

There is also a concern that local application of antimicrobials will disrupt the normal nasal and oral microbiota. The microbiome is increasingly recognised as playing a vital role in preventing colonisation with invading pathogens, supporting the host immune system and a variety of other functions (Kilian 2016; Man 2017). Alteration of this delicate environment by exposure to antimicrobial compounds could alter the composition and/or activities of the oral and nasal microbiotas. This may occur through reduced total microbial abundance and/or via the selective

suppression of commensal micro-organisms with the greatest susceptibility to the treatment. Potential health problems resulting from this include an increased risk of infection due to the suppression of colonisation resistance, by which commensal micro-organisms inhibit extrinsic pathogens, the overgrowth of species within the microbiota with pathogenic potential, and interference with beneficial host-microbe interactions that prime the immune system.

Other potential harms are related to specific irrigation fluids. These include the risk of excess iodine ingestion from iodine-containing gargle solution or staining of teeth with chlorhexidine.

## OBJECTIVES

To assess the benefits and harms of antimicrobial mouthwashes and nasal sprays administered to healthcare workers (HCWs) and/or patients when undertaking aerosol-generating procedures (AGPs) on patients without suspected or confirmed COVID-19 infection.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

This is a question that urgently requires evidence, however at the present time we did not anticipate finding many completed RCTs. We therefore included the following types of studies:

- randomised controlled trials (RCTs);
- quasi-RCTs;
- non-randomised controlled trials;
- prospective cohort studies;
- retrospective cohort studies;
- cross-sectional studies;
- controlled before-and-after studies.

There was no minimum duration for the studies.

#### Types of participants

Patients without suspected or confirmed COVID-19 infection, undergoing aerosol-generating procedures (AGPs) and those healthcare workers (HCWs) treating them.

#### Setting

- Any healthcare setting.

#### Types of interventions

##### Interventions

Any antimicrobial **mouthwash** and/or **nasal spray** (alone or in combination) at any concentration, delivered to the patient or HCW before and/or after an AGP.

##### Comparator

No treatment or saline or water.

#### Types of outcome measures

We analysed the following outcomes in the review, but we did not use them as a basis for including or excluding studies.

We assessed the primary outcomes at a minimum of two weeks. For all other outcomes, there was no minimum follow-up.

For all outcomes we planned to accept the method of measurement used by the trialists but we would take a critical approach to the value of each measure.

#### Primary outcomes

- Incidence of symptomatic or test-positive COVID-19 infection in HCWs or patients.
- Significant adverse event: anosmia (or disturbance in sense of smell).

#### Secondary outcomes

- COVID-19 viral content of aerosol (when present).
- Change in COVID-19 viral load at site(s) of irrigation.
- Other adverse events: changes in microbiome in oral cavity, nasal cavity, oro- or nasopharynx.
- Other adverse events: allergy, irritation/burning of nasal, oral or oropharyngeal mucosa (e.g. erosions, ulcers, bleeding), long-term staining of mucous membranes or teeth, accidental ingestion.

#### Search methods for identification of studies

The Cochrane ENT and Cochrane Oral Health Information Specialists conducted systematic searches for all human studies. There were no language, publication year or publication status restrictions. We contacted original authors for clarification and further data when trial reports were unclear and arranged translations of papers where possible. The date of the search was 1 June 2020.

#### Electronic searches

The Information Specialist searched:

- the Cochrane Central Register of Controlled Trials (CENTRAL 2020, Issue 6) (searched via the Cochrane Register of Studies);
- Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) (1946 to 1 June 2020);
- Ovid EMBASE (1974 to 1 June 2020);
- World Health Organization (WHO) COVID-19 Global literature on coronavirus disease <https://search.bvsalud.org/global-literature-on-novel-coronavirus-2019-ncov> (searched to 1 June 2020);
- Cochrane COVID-19 Study Register <https://covid-19.cochrane.org/> (search via the Cochrane Register of Studies to 1 June 2020).

The Information Specialists modelled subject strategies for databases on the search strategy designed for Ovid MEDLINE. Search strategies for major databases including CENTRAL are provided in [Appendix 1](#).

#### Searching other resources

We did not perform a separate search for adverse effects. We planned to consider adverse effects described in the included studies only.

We did not perform a separate search for pre-print publications. We planned to identify and report as awaiting assessment any we identified from the sources above that met our inclusion criteria but we would not extract the data until their publication in a peer-reviewed journal.

We planned to make efforts to identify full-text papers regardless of language of publication and to endeavour to seek help with translation; however, we would not hold up the rapid review process. Any papers that we were unable to source quickly or were unable to get translated would be listed as awaiting assessment.

## Data collection and analysis

### Selection of studies

AMG, HW (and others) performed screening using [Covidence](#).

Two review authors independently screened all titles and abstracts identified through the searching. Discrepancies were discussed and, where necessary, a third review author was included. Where uncertainties remained, we retrieved the full text for clarification. Two review authors again independently screened the full text of potentially relevant articles.

We documented and outlined in the final report all decisions regarding exclusion of studies, taken during screening, with a list of excluded studies.

### Data extraction and management

We planned that AMG, HW (and others) would perform data extraction using a predefined data extraction form (Word/Excel). Data were limited to a minimal set of required data items following input from content experts and methodologists.

A single review author would undertake data extraction and a second review author would check the completeness/accuracy of the data extraction. Discrepancies would be discussed and taken to a third review author as required.

We planned to contact study authors for missing outcome data, or where there were conflicting data reported across multiple sources for a single study.

### Assessment of risk of bias in included studies

We planned to undertake 'Risk of bias' assessment at the same time as data extraction. We planned to use the Cochrane RCT 'Risk of bias' tool and the ROBINS-I tool for non-randomised studies. We planned to exclude studies judged to be at critical risk of bias from analysis.

As for data extraction, all judgements were to be checked by a second review author. Discrepancies would be discussed and taken to a third review author as required.

### Measures of treatment effect

We planned to present dichotomous data as risk ratios (RR) with corresponding 95% confidence intervals (CIs). However, if we identified case-control studies relevant to the review questions, we would have considered the use of odds ratio as the appropriate estimate of effect.

We planned to present continuous data as a mean difference (MD) with corresponding 95% CIs. Where necessary, we would have converted outcome data to the same unit of measurement.

Where data were extracted from non-RCTs, we planned to use adjusted effects where available. If multiple adjusted effects were reported, then we would have chosen the one judged to minimise the risk of bias due to confounding.

### Unit of analysis issues

The unit of analysis was the participant. Any cluster-RCTs would need to have analysed results taking account of the clustering present in the data, otherwise we would have used the methods outlined in Section 16.3.4 of the *Cochrane Handbook for Systematic Reviews of Interventions* in order to perform an approximately correct analysis ([Higgins 2011](#)). We planned to include studies with multiple treatment arms as appropriate, ensuring that there was no double counting of patients in any meta-analysis.

### Dealing with missing data

We planned to contact study authors for missing outcome data. Where appropriate, we would have used the methods outlined in Section 7.7.3 of the *Cochrane Handbook for Systematic Reviews of Interventions* in order to estimate missing standard deviations ([Higgins 2011](#)). We would not have used any further statistical methods or carried out any further imputation to account for missing data.

### Assessment of heterogeneity

We planned to assess statistical heterogeneity initially through inspection of forest plots. We would use the  $\text{Chi}^2$  for heterogeneity, with  $P = 0.10$ , to indicate substantial heterogeneity (acknowledging that this has low power if there is a small sample size or few studies).

We also planned to use the  $I^2$  statistic, following the interpretation recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (0% to 40% might not be important; 30% to 60% may represent moderate heterogeneity; 50% to 90% may represent substantial heterogeneity; 75% to 100% considerable heterogeneity) ([Handbook 2019](#)). We would be cautious in interpreting the  $I^2$  value, as this may be uncertain when there are few studies.

We planned to explore potential sources of heterogeneity among study results. Sources may include: clinical setting and clinical procedure.

### Assessment of reporting biases

Where there were 10 or more studies in a meta-analysis, we planned to assess possible publication bias by visually inspecting a funnel plot for asymmetry.

### Data synthesis

We planned to make a judgement regarding the clinical and methodological heterogeneity; only where there was deemed to be reasonable homogeneity across studies would we consider statistical pooling of data. If appropriate, we would have conducted statistical pooling of data from RCTs, followed by data from non-RCTs. We would not have undertaken pooling across different types of study designs.

We planned to use a random-effects model.

Lastly, we planned to undertake a narrative synthesis, encompassing findings from both RCT and non-RCT studies.

#### **Subgroup analysis and investigation of heterogeneity**

Where data were available, we planned to conduct subgroup analyses, where possible, according to clinical procedure and clinical setting (e.g. inpatient, outpatient, dental, ENT).

#### **Sensitivity analysis**

We planned to undertake sensitivity analysis excluding studies at high risk of bias.

#### **Summary of findings and assessment of the certainty of the evidence**

We planned to use the GRADE approach and present 'Summary of findings' tables for all comparisons and all outcomes.

## **RESULTS**

### **Description of studies**

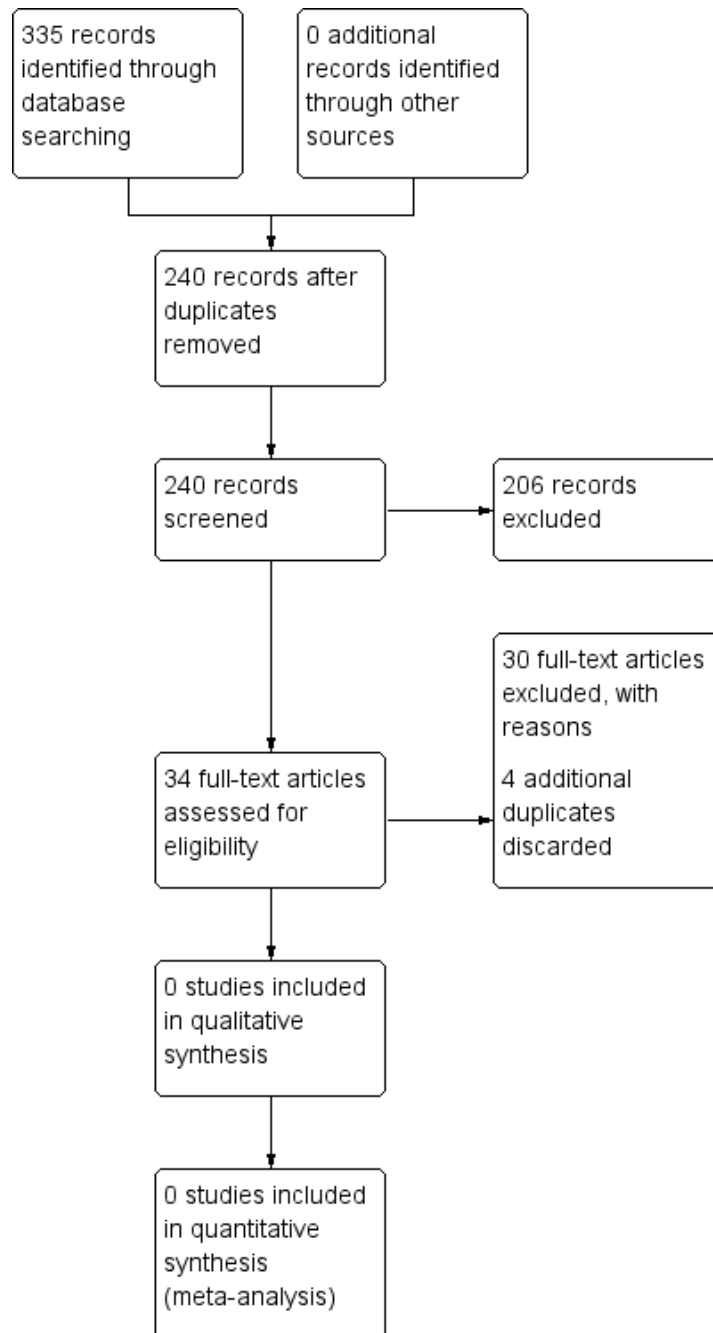
#### **Results of the search**

The searches retrieved a total of 335 references. This reduced to 240 after the removal of duplicates. We screened the title and abstracts of the remaining 240 references. We discarded 206 references and assessed 34 full-text articles. We identified four additional duplicates, which we discarded. We excluded all 30 remaining references with reasons recorded in the review (see [Excluded studies](#)).

We did not identify any completed or ongoing studies that met the inclusion criteria for this review.

The PRISMA diagram in [Figure 1](#) shows our study search and selection process.

**Figure 1. Process for sifting search results and selecting studies for inclusion**



**Included studies**

We did not include any studies.

**Excluded studies**

We excluded 30 papers after reviewing the full text. Further details for the reasons for exclusion can be found in the [Characteristics of excluded studies](#) table. These are the main reasons for exclusion:

We excluded eight references that were narrative review articles, which did not report any data of relevance to this review (Carrouel 2020; Dexter 2020; Ham 2020; Hamid 2020; Henwood 2020; Leboulanger 2020; Parhar 2020).

We also excluded four references as they were letters to the editor of a journal, providing a comment rather than reporting on a study (Challacombe 2020; Loftus 2020; Mady 2020; Maguire 2020).

We excluded 18 studies as the intervention was used in an incorrect population - the trial considered the use of nasal sprays and gargles to treat individuals who have the virus, or as routine prophylaxis for healthcare workers (rather than at the time of aerosol-generating procedures) (ACTRN12620000470998p; AMPoL (NCT04409873); BBCovid (NCT04352959); ChiCTR2000030539; ELVIS-COVID-19 (NCT04382131); GARGLES (NCT04341688); GARGLESb (NCT04410159); KILLER (NCT04371965); KONS-COVID-19 (NCT04357990); NCT04344236; NCT04347538;

NCT04347954; NCT04382040; NCT04408183; NOCOVID (NCT04337918); PICO (ISRCTN13447477); PIIPPI (NCT04364802); SINUS WASH (NCT04393792)).

Finally, we excluded one study as it was conducted in an incorrect population - although participants were infected with a coronavirus, this was not COVID-19 (Ramalingam 2020).

### Risk of bias in included studies

We did not include any studies.

### Effects of interventions

See: [Summary of findings 1](#) Antimicrobial mouthwashes (gargling) and nasal sprays to protect healthcare workers when undertaking aerosol-generating procedures (AGPs) on patients without suspected or confirmed COVID-19 infection

No studies are included in the review. See [Summary of findings 1](#).

## DISCUSSION

### Summary of main results

We identified no studies for inclusion in this review, nor any ongoing studies. The absence of completed studies is not surprising given the relatively recent emergence of COVID-19 infection. However, we are disappointed that this important clinical question is not being addressed by ongoing studies.

### Overall completeness and applicability of evidence

As no studies are included in the review and the searches did not identify any relevant ongoing studies, there remains a lack of evidence regarding the potential benefits or harms of mouthwashes and nasal sprays when used at the time of AGPs.

### Quality of the evidence

We did not include any studies.

### Potential biases in the review process

Given the recent emergence of COVID-19 infection, we aimed to design a protocol that would be inclusive, to encompass as much relevant information as possible.

The search strategy was designed and run by qualified Cochrane Information Specialists so any bias here should be minimal. The search was not limited to the English language. It is possible that suitable studies have been carried out and the results published elsewhere in another language; however, we feel that this is unlikely, as all applicable studies are likely to have been registered with one of the central trial registries.

All studies that we discarded during our search and selection process were rejected based on a lack of relevant data (e.g. they were letter to the editor of a journal, or narrative review articles) or because they did not address the relevant population.

### Agreements and disagreements with other studies or reviews

We are not aware of any other published reviews that address the use of antimicrobial mouthwashes and nasal sprays at the time of AGPs.

## AUTHORS' CONCLUSIONS

### Implications for practice

No studies are included in this review, therefore we are unable to ascertain the relative benefits and harms of the use of antimicrobial mouthwashes and nasal sprays at the time of aerosol-generating procedures (AGPs).

### Implications for research

We are concerned that no ongoing studies were identified that address this important question. Evidence regarding the efficacy and safety of methods to reduce the risk of COVID-19 transmission at the time of AGPs is urgently required to ensure that routine medical and dental procedures may be undertaken without exposing healthcare professionals to unnecessary risk.

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NCT04344236. Gargling and nasal rinses to reduce oro- and nasopharyngeal viral load in patients with COVID-19 [A phase II, randomized, open-label, single-institution study of the effects of povidone iodine oral gargles and nasal rinses on viral load in patients with COVID-19]. <https://clinicaltrials.gov/show/NCT04344236> (first received 14 April 2020). [CENTRAL: CN-02091597] [13367550] [13367550]

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## CHARACTERISTICS OF STUDIES

### Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
<a href="#">ACTRN12620000470998p</a>	Incorrect population. This trial considers treatment of individuals who are positive for COVID-19, and is relevant for another review in this suite (Antimicrobial mouthwashes (gargling) and nasal sprays administered to patients with suspected or confirmed COVID-19 infection to improve patient outcomes and to protect healthcare workers treating them; <a href="#">Burton 2020b</a> ).
<a href="#">AMPoL (NCT04409873)</a>	Incorrect population. This trial considers treatment of individuals who are positive for COVID-19, and is relevant for another review in this suite (Antimicrobial mouthwashes (gargling) and nasal sprays administered to patients with suspected or confirmed COVID-19 infection to improve patient outcomes and to protect healthcare workers treating them; <a href="#">Burton 2020b</a> ).
<a href="#">BBCovid (NCT04352959)</a>	Incorrect population. This trial considers treatment of individuals who are positive for COVID-19, and is relevant for another review in this suite (Antimicrobial mouthwashes (gargling) and nasal sprays administered to patients with suspected or confirmed COVID-19 infection to improve patient outcomes and to protect healthcare workers treating them; <a href="#">Burton 2020b</a> ).
<a href="#">Carrouel 2020</a>	Review article, no relevant data.
<a href="#">Challacombe 2020</a>	Letter to the editor - no relevant data.
<a href="#">ChiCTR2000030539</a>	Incorrect population. This trial considers treatment of individuals who are positive for COVID-19, and is relevant for another review in this suite (Antimicrobial mouthwashes (gargling) and nasal sprays administered to patients with suspected or confirmed COVID-19 infection to improve patient outcomes and to protect healthcare workers treating them; <a href="#">Burton 2020b</a> ).
<a href="#">Dexter 2020</a>	Review article, no relevant data.
<a href="#">ELVIS-COVID-19 (NCT04382131)</a>	Incorrect population. This trial considers treatment of individuals who are positive for COVID-19, and is relevant for another review in this suite (Antimicrobial mouthwashes (gargling) and nasal sprays administered to patients with suspected or confirmed COVID-19 infection to improve patient outcomes and to protect healthcare workers treating them; <a href="#">Burton 2020b</a> ).
<a href="#">GARGLES (NCT04341688)</a>	Incorrect population. This trial considers treatment of individuals who are positive for COVID-19, and is relevant for another review in this suite (Antimicrobial mouthwashes (gargling) and nasal sprays administered to patients with suspected or confirmed COVID-19 infection to improve patient outcomes and to protect healthcare workers treating them; <a href="#">Burton 2020b</a> ).
<a href="#">GARGLESb (NCT04410159)</a>	Incorrect population. This trial considers treatment of individuals who are positive for COVID-19, and is relevant for another review in this suite (Antimicrobial mouthwashes (gargling) and nasal sprays administered to patients with suspected or confirmed COVID-19 infection to improve patient outcomes and to protect healthcare workers treating them; <a href="#">Burton 2020b</a> ).
<a href="#">Ham 2020</a>	Review article, no relevant data.
<a href="#">Hamid 2020</a>	Review article, no relevant data.
<a href="#">Henwood 2020</a>	Review article, no relevant data.
<a href="#">KILLER (NCT04371965)</a>	Incorrect population. This trial considers treatment of individuals who are positive for COVID-19, and is relevant for another review in this suite (Antimicrobial mouthwashes (gargling) and nasal sprays administered to patients with suspected or confirmed COVID-19 infection to improve patient outcomes and to protect healthcare workers treating them; <a href="#">Burton 2020b</a> ).

Study	Reason for exclusion
KONS-COVID-19 (NCT04357990)	Incorrect population. This trial considers treatment of individuals who are positive for COVID-19, and is relevant for another review in this suite (Antimicrobial mouthwashes (gargling) and nasal sprays administered to patients with suspected or confirmed COVID-19 infection to improve patient outcomes and to protect healthcare workers treating them; <a href="#">Burton 2020b</a> ).
Leboulanger 2020	Review article, no relevant data.
Loftus 2020	Letter to the editor, no relevant data.
Mady 2020	Letter to the editor, no relevant data.
Maguire 2020	Letter to the editor, no relevant data.
NCT04344236	Incorrect population. This trial considers treatment of individuals who are positive for COVID-19, and is relevant for another review in this suite (Antimicrobial mouthwashes (gargling) and nasal sprays administered to patients with suspected or confirmed COVID-19 infection to improve patient outcomes and to protect healthcare workers treating them; <a href="#">Burton 2020b</a> ).
NCT04347538	Incorrect population. This trial considers treatment of individuals who are positive for COVID-19, and is relevant for another review in this suite (Antimicrobial mouthwashes (gargling) and nasal sprays administered to patients with suspected or confirmed COVID-19 infection to improve patient outcomes and to protect healthcare workers treating them; <a href="#">Burton 2020b</a> ).
NCT04347954	Incorrect population. This trial considers treatment of individuals who are positive for COVID-19, and is relevant for another review in this suite (Antimicrobial mouthwashes (gargling) and nasal sprays administered to patients with suspected or confirmed COVID-19 infection to improve patient outcomes and to protect healthcare workers treating them; <a href="#">Burton 2020b</a> ).
NCT04382040	Incorrect population. This trial considers treatment of individuals who are positive for COVID-19, and is relevant for another review in this suite (Antimicrobial mouthwashes (gargling) and nasal sprays administered to patients with suspected or confirmed COVID-19 infection to improve patient outcomes and to protect healthcare workers treating them; <a href="#">Burton 2020b</a> ).
NCT04408183	Incorrect population. This trial considers prophylaxis to prevent acquisition of COVID-19 and is relevant for another review in this suite (Use of antimicrobial mouthwashes (gargling) and nasal sprays by healthcare workers to protect them when treating patients with suspected or confirmed COVID-19 infection; <a href="#">Burton 2020a</a> ).
NOCOVID (NCT04337918)	Incorrect population. This trial considers treatment of individuals who are positive for COVID-19, and prophylaxis for healthcare professional during routine clinical care. It is relevant for two other reviews in this suite (Antimicrobial mouthwashes (gargling) and nasal sprays administered to patients with suspected or confirmed COVID-19 infection to improve patient outcomes and to protect healthcare workers treating them; <a href="#">Burton 2020b</a> ; and Use of antimicrobial mouthwashes (gargling) and nasal sprays by healthcare workers to protect them when treating patients with suspected or confirmed COVID-19 infection; <a href="#">Burton 2020a</a> ).
Parhar 2020	Review article, no relevant data.
PICO (ISRCTN13447477)	Incorrect population. This trial considers treatment of individuals who are positive for COVID-19, and is relevant for another review in this suite (Antimicrobial mouthwashes (gargling) and nasal sprays administered to patients with suspected or confirmed COVID-19 infection to improve patient outcomes and to protect healthcare workers treating them; <a href="#">Burton 2020b</a> ).
PIIPPI (NCT04364802)	Incorrect population. This trial considers prophylaxis to prevent acquisition of COVID-19 and is relevant for another review in this suite (Use of antimicrobial mouthwashes (gargling) and nasal sprays by healthcare workers to protect them when treating patients with suspected or confirmed COVID-19 infection; <a href="#">Burton 2020a</a> ).

Study	Reason for exclusion
Ramalingam 2020	Incorrect population - participants did not have COVID-19.
SINUS WASH (NCT04393792)	Incorrect population. This trial considers treatment of individuals who are positive for COVID-19, and is relevant for another review in this suite (Antimicrobial mouthwashes (gargling) and nasal sprays administered to patients with suspected or confirmed COVID-19 infection to improve patient outcomes and to protect healthcare workers treating them; <a href="#">Burton 2020b</a> ).

## APPENDICES

### Appendix 1. Search strategies

CENTRAL	Ovid MEDLINE	Ovid Embase
1 ("2019 nCoV" or 2019nCoV or "COVID 19" or COVID19 or "new coronavirus" or "novel coronavirus" or "novel corona virus" or "SARS CoV-2" or "2019- novel CoV" or ncov19 or ncov-19) AND CENTRAL:TARGET	1 ("2019 nCoV" or 2019nCoV or "COVID 19" or COVID19 or "new coronavirus" or "novel coronavirus" or "novel corona virus" or "SARS CoV-2" or "2019- novel CoV" or ncov19 or ncov-19).ab,ti.	1. ("2019 nCoV" or 2019nCoV or "COVID 19" or COVID19 or "new coronavirus" or "novel coronavirus" or "novel corona virus" or "SARS CoV-2" or "2019- novel CoV" or ncov19 or ncov-19).ab,ti.
2 (Wuhan and (coronavirus or "corona virus")) AND CENTRAL:TARGET	2 (Wuhan and (coronavirus or "corona virus")).ab,ti.	2. (Wuhan and (coronavirus or "corona virus")).ab,ti.
3 ((coronavirus near3 2019) or ("corona virus" near3 2019)) AND CENTRAL:TARGET	3 ((coronavirus or "corona virus") adj3 "2019").ab,ti.	3. ((coronavirus or "corona virus") adj3 "2019").ab,ti.
4 ((wuhan near2 disease) or (wuhan near2 virus)) AND CENTRAL:TARGET	4 (wuhan adj2 (disease or virus)).ab,ti.	4. (wuhan adj2 (disease or virus)).ab,ti.
5 ("LAMP assay" or "COVID-19" or "COVID-19 drug treatment" or "COVID-19 diagnostic testing" or "COVID-19 serotherapy" or "COVID-19 vaccine" or "severe acute respiratory syndrome coronavirus 2" or "spike glycoprotein, COVID-19 virus") AND CENTRAL:TARGET	5 ("LAMP assay" or "COVID-19" or "COVID-19 drug treatment" or "COVID-19 diagnostic testing" or "COVID-19 serotherapy" or "COVID-19 vaccine" or "severe acute respiratory syndrome coronavirus 2" or "spike glycoprotein, COVID-19 virus").os.	5. ("LAMP assay" or "COVID-19" or "COVID-19 drug treatment" or "COVID-19 diagnostic testing" or "COVID-19 serotherapy" or "COVID-19 vaccine" or "severe acute respiratory syndrome coronavirus 2" or "spike glycoprotein, COVID-19 virus").ti,ab.
6 #1 OR #2 OR #3 OR #4 OR #5	6 1 or 2 or 3 or 4 or 5	6. or/1-5
7 MESH DESCRIPTOR Mouthwashes EXPLODE ALL AND CENTRAL:TARGET	7 exp Animals/	7. mouthwash/
8 MESH DESCRIPTOR Nasal Sprays EXPLODE ALL AND CENTRAL:TARGET	8 exp Humans/	8. nose spray/
9 MESH DESCRIPTOR Nasal Lavage EXPLODE ALL AND CENTRAL:TARGET	9 7 not 8	9. nasal lavage/
10 (mouthwash* or gargl* or mouthrins*) AND CENTRAL:TARGET	10 (editorial or comment or letter or newspaper article).pt.	
11 (oral near3 (spray* or douch* or irrigat* or lavag* or wash or rins* or decontaminat* or aerosol or mist or clean*)) AND CENTRAL:TARGET	11 9 or 10	
	12 6 not 11	
	13 exp Mouthwashes/	
	14 exp Nasal Sprays/	
	15 exp Nasal Lavage/	
	16 (mouthwash* or gargl* or mouthrins*).ab,ti.	
	17 ((oral or mouth or nasal or nose or nasopharyngeal or larynx* or pharynx* or intranasal) adj3 (spray* or	

(Continued)

- 12 (mouth near3 (spray\* or douch\* or irrigat\* or lavag\* or wash or rins\* or decontaminat\* or aerosol or mist or clean\*)) AND CENTRAL:TARGET
- 13 (nasal near3 (spray\* or douch\* or irrigat\* or lavag\* or wash or rins\* or decontaminat\* or aerosol or mist or clean\*)) AND CENTRAL:TARGET
- 14 (nose near3 (spray\* or douch\* or irrigat\* or lavag\* or wash or rins\* or decontaminat\* or aerosol or mist or clean\*)) AND CENTRAL:TARGET
- 15 (nasopharyngeal near3 (spray\* or douch\* or irrigat\* or lavag\* or wash or rins\* or decontaminat\* or aerosol or mist or clean\*)) AND CENTRAL:TARGET
- 16 (larynx\* near3 (spray\* or douch\* or irrigat\* or lavag\* or wash or rins\* or decontaminat\* or aerosol or mist or clean\*)) AND CENTRAL:TARGET
- 17 (pharynx\* near3 (spray\* or douch\* or irrigat\* or lavag\* or wash or rins\* or decontaminat\* or aerosol or mist or clean\*)) AND CENTRAL:TARGET
- 18 (intranasal near3 (spray\* or douch\* or irrigat\* or lavag\* or wash or rins\* or decontaminat\* or aerosol or mist or clean\*)) AND CENTRAL:TARGET
- 19 MESH DESCRIPTOR Chlorhexidine EXPLODE ALL AND CENTRAL:TARGET
- 20 MESH DESCRIPTOR Povidone-Iodine EXPLODE ALL AND CENTRAL:TARGET
- 21 MESH DESCRIPTOR Cetylpyridinium EXPLODE ALL AND CENTRAL:TARGET
- 22 MESH DESCRIPTOR Hexetidine EXPLODE ALL AND CENTRAL:TARGET
- 23 MESH DESCRIPTOR Anti-Infective Agents, Local EXPLODE ALL AND CENTRAL:TARGET
- 24 MESH DESCRIPTOR Hydrogen Peroxide EXPLODE ALL AND CENTRAL:TARGET
- 25 MESH DESCRIPTOR Carbamide Peroxide EXPLODE ALL AND CENTRAL:TARGET
- 26 MESH DESCRIPTOR Triclosan EXPLODE ALL AND CENTRAL:TARGET
- 27 MESH DESCRIPTOR Oils, Volatile EXPLODE ALL AND CENTRAL:TARGET
- 28 MESH DESCRIPTOR Plant Oils EXPLODE ALL AND CENTRAL:TARGET
- douch\* or irrigat\* or lavag\* or wash or rins\* or decontaminat\* or aerosol or mist or clean\*).ab,ti.
- 18 exp Chlorhexidine/
- 19 exp Povidone-Iodine/
- 20 exp Cetylpyridinium/
- 21 exp Hexetidine/
- 22 exp Anti-Infective Agents, Local/
- 23 exp Hydrogen Peroxide/
- 24 exp Carbamide Peroxide/
- 25 exp Triclosan/
- 26 exp Oils, volatile/
- 27 exp Plant oils/
- 28 Menthol/
- 29 Lavandula/
- 30 Thymus plant/
- 31 Mentha piperita/
- 32 Eugenol/
- 33 Cinnamomum verum/
- 34 Muramidase/
- 35 Lactoferrin/
- 36 Glucose oxidase/
- 37 Lactoperoxidase/
- 38 (povidone or chlorhexidine or CHX or PVP or Polyvinylpyrrolidone or Betadine\* or Providine\* or Disadine\* or Isodine\* or Pharmadine\* or Alphadine\* or Betaisodona or Tubulicid or Novalsan or Sebidin or MK-412A or MK412A).ab,ti.
- 39 (Chlorhexamed or Corsodyl or Curasept or Dyna-Hex or Eludril or Gibitan or Hexidine or Hibiclen or Hibident or Hibiscrub or Hibisol or Hibitane or Peridex or avagard).ab,ti.
- 40 (Hexadecylpyridinium or Cetylpyridium or Biosept or Ceepryn or Cetamium or Catamium or Sterogenol or Dobendan or Merocets or Pristacin or Pyrisept or Angifonil or Cetylyre).ab,ti.
- 41 (Vagi-Hex or Vagi Hex or VagiHex or Oraldene or Hexigel or Steri-sol or Steri sol or Hextril or Oraldine or Oralspray or Hexoral or Bactidol or Elsix or Duranil or Doreperol or Hexetidine).ab,ti.
10. (mouthwash\* or gargl\* or mouthrins\*).ab,ti.
11. ((oral or mouth or nasal or nose or nasopharyngeal or larynx\* or pharynx\* or intranasal) adj3 (spray\* or douch\* or irrigat\* or lavag\* or wash or rins\* or decontaminat\* or aerosol or mist or clean\*).ab,ti.
12. chlorhexidine/
13. povidone iodine/
14. cetylpyridinium salt/
15. hexetidine/
16. exp topical antiinfective agent/
17. hydrogen peroxide/
18. carbamide peroxide/
19. triclosan/
20. essential oil/
21. menthol/
22. lavender/
23. thymus extract/
24. Mentha piperita/
25. eugenol/
26. Cinnamomum zeylanicum/
27. lysozyme/
28. lactoferrin/
29. Glucose oxidase/
30. Lactoperoxidase/
31. (povidone or chlorhexidine or CHX or PVP or Polyvinylpyrrolidone or Betadine\* or Providine\* or Disadine\* or Isodine\* or Pharmadine\* or Alphadine\* or

(Continued)

- 29 MESH DESCRIPTOR Menthol AND CENTRAL:TARGET
- 30 MESH DESCRIPTOR Lavandula AND CENTRAL:TARGET
- 31 MESH DESCRIPTOR Thymus Plant AND CENTRAL:TARGET
- 32 MESH DESCRIPTOR Mentha piperita AND CENTRAL:TARGET
- 33 MESH DESCRIPTOR Cinnamomum zeylanicum AND CENTRAL:TARGET
- 34 MESH DESCRIPTOR Muramidase AND CENTRAL:TARGET
- 35 MESH DESCRIPTOR Lactoferrin AND CENTRAL:TARGET
- 36 MESH DESCRIPTOR Glucose Oxidase AND CENTRAL:TARGET
- 37 MESH DESCRIPTOR Lactoperoxidase AND CENTRAL:TARGET
- 38 (povidone or chlorhexidine or CHX or PVP or Polyvinylpyrrolidone or Betadine\* or Providine\* or Disadine\* or Isodine\* or Pharmadine\* or Alphadine\* or Betaisodona or Tubulicid or Novalsan or Sebidin or MK-412A or MK412A) AND CENTRAL:TARGET
- 39 (Chlorhexamed or Corsodyl or Curasept or Dyna-Hex or Eludril or Gibitan or Hexidine or Hibiclens or Hibident or Hibiscrub or Hibisol or Hibitane or Peridex or avagard) AND CENTRAL:TARGET
- 40 (Hexadecylpyridinium or Cetylpyridium or Biosept or Ceepryn or Cetamium or Catamium or Sterogenol or Dobendan or Merocets or Pristacin or Pyrisept or Angifonil or Cetylyre) AND CENTRAL:TARGET
- 41 (Vagi-Hex or Vagi Hex or VagiHex or Oraldene or Hexigel or Steri-sol or Steri sol or Hextril or Oraldine or Oralspray or Hexoral or Bactidol or Elsix or Duranil or Doreperol or Hexetidine) AND CENTRAL:TARGET
- 42 (Hydrogen Peroxide or H2O2 or Hydroperoxide or Superoxol or Oxydol or Perhydrol or Urea Peroxide or Perhydrol Urea) AND CENTRAL:TARGET
- 43 (Methyl salicylate or methylsalicylate or Rheumabal or Metsal Liniment or Hewedolor or Linsal) AND CENTRAL:TARGET
- 44 (Tricolsan or Hydroxydiphenyl or trichlorodiphenyl or Clearasil or Cliniclean or Irgasan or Trisan or Oxy Skin Wash or pHiso-Hex or Sapoderm or
- 42 (Hydrogen Peroxide or H2O2 or Hydroperoxide or Superoxol or Oxydol or Perhydrol or Urea Peroxide or Perhydrol Urea).ab,ti.
- 43 (Methyl salicylate or methylsalicylate or Rheumabal or Metsal Liniment or Hewedolor or Linsal).ab,ti.
- 44 (Tricolsan or Hydroxydiphenyl or trichlorodiphenyl or Clearasil or Cliniclean or Irgasan or Trisan or Oxy Skin Wash or pHisoHex or Sapoderm or Tersaseptic or Aquasept or Ster-Zac or Manusept or Microshield).ab,ti.
- 45 ((Spray\* or douch\* or irrigat\* or rins\* or wash\* or lavag\* or intranasal\* or topical) adj3 (antimicrobial or anti-microbial or disinfect\* or antisept\* or anti-infect\*)).ab,ti.
- 46 ("essential oil\$" or "plant oil\$" or menthol or menthyl or (mint adj2 oil\$) or lavender or thyme or peppermint or "mentha piperita" or eugenol o eucalyptus or "blue gum\$" or cajeput or clove or cinnamon).ab,ti.
- 47 (muramidase or lysozyme\$ or leftose or lactoferrin or lactotransferrin or "glucose oxidase" or lactoperoxidase or "saliva substitute").ab,ti.
- 48 (Listerine or Biotene).ab,ti.
- 49 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48
- 50 12 and 49
- Betaisodona or Tubulicid or Novalsan or Sebidin or MK-412A or MK412A).ab,ti.
32. (Chlorhexamed or Corsodyl or Curasept or Dyna-Hex or Eludril or Gibitan or Hexidine or Hibiclens or Hibident or Hibiscrub or Hibisol or Hibitane or Peridex or avagard).ab,ti.
33. (Hexadecylpyridinium or Cetylpyridium or Biosept or Ceepryn or Cetamium or Catamium or Sterogenol or Dobendan or Merocets or Pristacin or Pyrisept or Angifonil or Cetylyre).ab,ti.
34. (Vagi-Hex or Vagi Hex or VagiHex or Oraldene or Hexigel or Steri-sol or Steri sol or Hextril or Oraldine or Oralspray or Hexoral or Bactidol or Elsix or Duranil or Doreperol or Hexetidine).ab,ti.
35. (Hydrogen Peroxide or H2O2 or Hydroperoxide or Superoxol or Oxydol or Perhydrol or Urea Peroxide or Perhydrol Urea).ab,ti.
36. (Methyl salicylate or methylsalicylate or Rheumabal or Metsal Liniment or Hewedolor or Linsal).ab,ti.
37. ((spray\* or douch\* or irrigat\* or rins\* or wash\* or lavag\* or intranasal\* or topical) adj3 (antimicrobial or anti-microbial or disinfect\* or antisept\* or anti-infect\*)).ab,ti.
38. (Tricolsan or Hydroxydiphenyl or trichlorodiphenyl or Clearasil or Cliniclean or Irgasan or Trisan or Oxy Skin Wash or pHiso-Hex or Sapoderm or

(Continued)

Hex or Sapoderm or Tersaseptic or Aquasept or Ster-Zac or Manusept or Microshield) AND CENTRAL:TARGET	Tersaseptic or Aquasept or Ster-Zac or Manusept or Microshield).ab,ti.
45 ((spray* or douch* or irrigat* or rins* or wash* or lavag* or intranasal* or topical) and (antimicrobial or anti-microbial or disinfect* or antisept* or anti-infect*)) AND CENTRAL:TARGET	39. ("essential oil\$" or "plant oil\$" or menthol or menthyl or (mint adj2 oil\$) or lavender or thyme or peppermint or "mentha piperita" or eugenol or eucalyptus or "blue gum\$" or cajeput or clove or cinnamon).ab,ti.
46 ("essential oil*" or "plant oil*" or menthol or menthyl or (mint near2 oil*) or lavender or thyme or peppermint or "mentha piperita" or eugenol or eucalyptus or "blue gum*" or cajeput or clove or cinnamon) AND CENTRAL:TARGET	40. (muramidase or lysozyme\$ or leftose or lactoferrin or lactotransferrin or "glucose oxidase" or lactoperoxidase or "saliva substitute") AND CENTRAL:TARGET
47 (muramidase or lysozyme* or leftose or lactoferrin or lactotransferrin or "glucose oxidase" or lactoperoxidase or "saliva substitute") AND CENTRAL:TARGET	41. (Listerine or Biotene).ab,ti.
48 (Listerine or Biotene) AND CENTRAL:TARGET	42. or/7-41
49 #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48	43. 6 and 42
50 #49 AND #6	

**WHO COVID-19 Register**
**Cochrane COVID-19 Register**

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(tw:((oral or mouth or nasal or nose or nasopharyngeal or larynx* or pharynx* or intranasal) ) AND (tw:(spray* or douch* or irrigat* or lavag* or wash or rins* or decontaminat* or aerosol or mist or clean*))	1 (mouthwash* or gargl* or mouthrins*) AND INREGISTER	—
(tw:((mouthwash* or gargl* or mouthrins*)))	2 (oral near3 (spray* or douch* or irrigat* or lavag* or wash or rins* or decontaminat* or aerosol or mist or clean*)) AND INREGISTER	
(tw:((spray* or douch* or irrigat* or rins* or wash* or lavag* or intranasal* or topical))) AND (tw:((antimicrobial or anti-microbial or disinfect* or antisept* or anti-infect*)))	3 (mouth near3 (spray* or douch* or irrigat* or lavag* or wash or rins* or decontaminat* or aerosol or mist or clean*)) AND INREGISTER	
(povidone or chlorhexidine or CHX or PVP or Polyvinylpyrrolidone or Betadine* or Providine* or Disadine* or Isodine* or Pharmadine* or Al-phadine* or Betsodona or Tubulicid or Noval-san or Sebidin or MK-412A or MK412A)	4 (nasal near3 (spray* or douch* or irrigat* or lavag* or wash or rins* or decontaminat* or aerosol or mist or clean*)) AND INREGISTER	
	5 (nose near3 (spray* or douch* or irrigat* or lavag* or wash or rins* or decontaminat* or aerosol or mist or clean*)) AND INREGISTER	
	6 (nasopharyngeal near3 (spray* or douch* or irrigat* or lavag* or wash or rins* or decontaminat* or aerosol or mist or clean*)) AND INREGISTER	
	7 (larynx* near3 (spray* or douch* or irrigat* or lavag* or wash or rins* or decontaminat* or aerosol or mist or clean*)) AND INREGISTER	

(Continued)

8 (pharynx\* near3 (spray\* or douch\* or irrigat\* or lavag\* or wash or rins\* or decontaminat\* or aerosol or mist or clean\*)) AND INREGISTER

9 (intranasal near3 (spray\* or douch\* or irrigat\* or lavag\* or wash or rins\* or decontaminat\* or aerosol or mist or clean\*)) AND INREGISTER

10 (povidone or chlorhexidine or CHX or PVP or Polyvinylpyrrolidone or Betadine\* or Providine\* or Disadine\* or Isodine\* or Pharmadine\* or Alphadine\* or Betaisodona or Tubulicid or Novalsan or Sebidin or MK-412A or MK412A) AND INREGISTER

11 (Chlorhexamed or Corsodyl or Curasept or Dyna-Hex or Eludril or Gibitan or Hexidine or Hibiclens or Hibident or Hibiscrub or Hibisol or Hibitane or Peridex or avagard) AND INREGISTER

12 (Hexadecylpyridinium or Cetylpyridium or Biosept or Ceepryn or Cetamium or Catamium or Sterogenol or Dobendan or Merocets or Pristacin or Pyrisept or Angifonil or Cetylyre) AND INREGISTER

13 (Vagi-Hex or Vagi Hex or VagiHex or Oraldene or Hexigel or Steri-sol or Steri sol or Hextril or Oraldine or Oralspray or Hexoral or Bactidol or Elsix or Duranil or Doreperol or Hexetidine) AND INREGISTER

14 (Hydrogen Peroxide or H2O2 or Hydroperoxide or Superoxol or Oxydol or Perhydrol or Urea Peroxide or Perhydrol Urea) AND INREGISTER

15 (Methyl salicylate or methylsalicylate or Rheumabal or Metsal Liniment or Hewedolor or Linsal) AND INREGISTER

16 (Tricolsan or Hydroxydiphenyl or trichlorodiphenyl or Clearasil or Cliniclean or Irgasan or Trisan or Oxy Skin Wash or pHisoHex or Sapoderm or Tersaseptic or Aquasept or Ster-Zac or Manusept or Microshield) AND INREGISTER

17 ((Spray\* or douch\* or irrigat\* or rins\* or wash\* or lavag\* or intranasal\* or topical) and (antimicrobial or anti-microbial or disinfect\* or antisept\* or anti infect\*)) AND INREGISTER

18 ("essential oil\*" or "plant oil\*" or menthol or menthyl or (mint near2 oil\*) or lavender or thyme or peppermint or "mentha piperita" or eugenol or eucalyptus or "blue gum\*" or cajeput or clove or cinnamon) AND INREGISTER

19 (muramidase or lysozyme\* or leftose or lactoferrin or lactotransferrin or "glucose oxidase" or lactoperoxidase or "saliva substitute") AND INREGISTER

20 (Listerine or Biotene) AND INREGISTER

21 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20



## HISTORY

Protocol first published: Issue 5, 2020

Review first published: Issue 9, 2020

## CONTRIBUTIONS OF AUTHORS

The initial idea for these reviews was conceived by Janet Clarkson and Martin Burton. All authors were involved in the development of the protocols and reviews, responding to feedback and agreed the final drafts.

## DECLARATIONS OF INTEREST

Martin J Burton: none known.

Janet E Clarkson: none known.

Beatriz Goulao: none known.

Anne-Marie Glenny: none known.

Andrew McBain: Andrew McBain conducts research and advises companies in the areas of antimicrobials, microbiome and microbial control.

Anne GM Schilder: in her roles of Director of NIHR UCLH BRC Hearing Theme and National Specialty Lead of NIHR CRN ENT, Professor Schilder advises companies in the hearing field about design and delivery of clinical trials. Her evidENT research team at UCL receives support from various funders, including NIHR, EU Horizon 2020 and Wellcome.

Katie E Webster: none known.

Helen V Worthington: none known.

Professors Martin Burton, Anne Schilder, Janet Clarkson and Anne-Marie Glenny are Co-ordinating Editors for Cochrane ENT and Cochrane Oral Health but had no role in the editorial sign-off process for these reviews.

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## DIFFERENCES BETWEEN PROTOCOL AND REVIEW

There are no differences between the published protocol and the review.