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# Re-Appraisal for the Protective Effect of Oral Hygiene on Pulmonary Infection in Elderly People

Chang-Hua Chen [a,b,c,d *], Yu-Min Chen [e], Kuan-Min Huang [f], Yu-Jun Chang [g], Hua-Cheng Yen [h]

[a] *Department of Internal Medicine, Changhua Christian Hospital, Changhua, Taiwan,* [b] *Center for Infection Prevention and Control, Changhua Christian Hospital, Changhua, Taiwan,* [c] *Ph.D. Program in Translational Medicine, National Chung Hsing University, Taichung County, Taiwan,* [d] *Rong Hsing Research Center for Translational Medicine, National Chung Hsing University, Taichung County, Taiwan,* [e] *Department of Pharmacy, Changhua Christian Hospital, Changhua, Taiwan,* [f] *Department of Oral & Maxillofacial Surgery, Changhua Christian Hospital, Changhua, Taiwan,* [g] *Epidemiology and Biostatistics Center, Changhua Christian Hospital, Changhua, Taiwan,* [h] *Department of Neurosurgery, Changhua Christian Hospital, Changhua, Taiwan*

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SUMMARY

*Background:* Regular oral care with antiseptics is recommended for patients receiving a ventilator bundle care in intensive care units. It is not clear whether routine oral care with antiseptics be implemented as a daily practice in the elderly. The aim of this study was to re-evaluate the protective effect of routine oral care with antiseptics in the elderly.
*Method:* We selected publications (from inception until July 2018) with studies comparing oral antiseptic use for protective effect of pulmonary infections in the elderly.
*Result:* Six studies out of 42 unique citations, which included 2,345 participants, met our inclusion criteria from inception untill July 2018. The overall odds ratio (OR) of pulmonary infections between the treated group and the control group was 0.586 (95% confidence interval [CI]: 0.341–1.007). The OR of all-cause mortality rate between the treated group and the control group was 0.774 (95% CI: 0.443–1.352). With respect to pulmonary infection, the subgroup analysis showed a favorable OR for professional personnel performing oral care in the treated group (OR, 0.435; 95% CI: 0.233–0.811) and the elderly population in nursing homes (OR, 0.376; 95% CI: 0.204–0.696).
*Conclusion:* Our findings failed to show a benefit of routine oral care with antiseptics for preventing pulmonary infection in the elderly. Further studies are urgently needed to assess the effect of routine oral care with antiseptics on preventing pulmonary infection in the elderly.



## 1. Introduction

An increasingly disabled and aging population has become a major concern in Taiwan,[1] and an urgent demand for long-term care facilities (LTCFs) resulted in the growth of facilities from 246 in 1997 to 1593 in 2015. Among healthcare institutes in Taiwan, a rapid increase in the number of LTCFs has resulted in a focus on the residents' health. Residents of LTCFs are predominantly elderly persons. Institutionalized elderly individuals are susceptible to poor oral health because they have reduced access to dental care and are unable to maintain adequate personal oral care.[2] Chronic low-grade inflammation observed in the elderly indicates that the elderly are prone to pulmonary infections (PIs) and PI-associated mortality.[3,4] Many reports have mentioned that the elderly require adequate oral hygiene care[2,5] which could possibly reduce and prevent elderly from contracting pulmonary infections.[4] El-Solh et al. reported that oral hygiene had positive preventive effects, with a one-tenth reduction in the risk for PIs in elderly hospitalized patients and residents of LTCFs.[6] Furthermore, some studies reported that the number of PI-induced deaths in the control groups was more than three times that in the treated groups.[7,8] However, the study by Juthani-Mehta et al. challenges this viewpoint.[9] Healthcare workers question whether inadequate oral care significantly increases the risk of PI in the elderly and whether oral care should be considered a modifiable risk factor to reduce PI events in the elderly.

Prevention of PIs in institutionalized elderly populations is increasingly viewed as a need to prevent comorbidities and nutritional deficiencies that contribute to the pathogenesis of PIs. In addition to immunizations (with influenza, pneumococcal, and tetanus vaccines),[10] mounting evidence supports the value of adequate nutrition, exercise, social engagement, and continued involvement in productive activities in the attainment of a long and qualitatively rich life,[11] as well as oral care with antiseptics.[12] The report by Klompas et al. showed that regular oral care with chlorhexidine gluconate has become a standard care for the prevention of ventilator-associated pneumonia.[12] Nearly universally adopted ventilator bundle procedures suggests that oral care with chlorhexidine can reduce one-third of ventilator-associated pneumonia.[13,14] Yet, there is a lack of evidence to recommend oral care as a daily practice in the elderly.

Although routine daily oral care with antiseptics is widely recommended, there are two limitations to consider when attempt-

* Corresponding author. Department of Internal Medicine, Changhua Christian Hospital, No. 135, Nanhsiao Street, Changhua 500, Taiwan.
*E-mail address:* 76590@cch.org.tw (C.-H. Chen)

ing to extend this concept to the elderly population. First, current meta-analyses are lacking with only a few studies focused on the elderly.[15,16] Existing meta-analyses are heavily influenced by a few large studies that account for more than half of the patients in prior analyses.[17–19] For example, these studies are problematic due to selection bias since most are post-cardiac surgery patients. Secondly, prior analyses designated ventilator-associated pneumonia as the primary outcome. Rates of ventilator-associated pneumonia are difficult to interpret because of their subjectivity, lack of specificity, high inter-observer variability,[20] and because the elderly are more susceptible to PIs.[3,4] Most importantly, PIs are linked with high-morbidity and high-mortality,[3,4] and prevention of PIs in the elderly is increasingly critical.[21] PI as a patient outcome has more risk associated with it than ventilator-associated pneumonia among the elderly. Regarding these limitations, we re-appraised the evidence base supporting routine antiseptic oral care by evaluating the effect of antiseptic oral care on the incidence of PIs and all-cause mortality in the elderly. We grouped studies into oral reagents, personnel, and target populations, then assessed the potential effect of the study design on reported outcomes.

## 2. Materials and methods

### *2.1. Search strategy and inclusion criteria*

The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the institutional review board of Changhua Christian Hospital (CCH IRB No. 180801). From the earliest record to July 2018, we searched PubMed, Scopus, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, ClinicalTrials.gov, Embase, and Web of Science databases for studies on locking solutions for central venous catheters used in hemodialysis of patients. Full search strategies for each database are available in the Appendix 1. We reviewed the previously published meta-analyses.[3,12–14,22,23] Complete search strategies for each database are available in Appendix 1. The inclusion criteria of the selected articles included (1) usage of antiseptic agents, and (2) evaluation of pulmonary infection or mortality, and (3) elderly population. The exclusion criteria included articles did not be related to elderly population, or articles did not compare the effectiveness of oral antiseptics, or pilot studies only described the methodology nor protocol.

### *2.2. Definition of clinical measures*

The treated group consisted of those who used antiseptics (including chlorhexidine) in their oral care. The control group consisted of those who did not use antiseptics. The primary measured outcome was the presence of a pulmonary infection. The secondary outcome was all-cause mortality during any timeframe. Subgroup analysis included information regarding oral reagents, personnel, target populations, and concentrations of chlorhexidine.

### *2.3. Data extraction and quality assessment*

Two reviewers examined all retrieved articles and extracted data using a pre-determined form and recorded for each study: the first author, publication year, country, study design, double-blind method, preparation of oral regimen, comparator, enrolled participant numbers, type of participant, and quality assessment. The methodological quality of the enrolled studies was evaluated by each reviewer independently, using Jadad scoring[24] for the randomized controlled trials (RCTs) and the Newcastle-Ottawa quality assessment scale[25] for the non-RCT.

### *2.4. Data synthesis and analysis*

The outcomes were measured by determining the odds ratios (ORs). A random effects model was employed to pool individual ORs. All analyses were performed using Comprehensive Meta-Analysis (v.3) statistical software (Biostat, Englewood, NJ, USA). Between-trial heterogeneity was determined using $I^2$ tests; values > 50% were regarded as considerable heterogeneity.[26] Funnel plots was used to examine potential publication bias.[26] Statistical significance was defined as p-values < 0.05, except for the determination of publication bias which employed p < 0.10. This study was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (Appendix 2).[23]

## 3. Results

### *3.1. Main characteristics of all the included studies*

The search strategies yielded 184 citations. Out of 42 unique citations, 6 met our inclusion criteria (Appendix 3). The six eligible studies are summarized in Appendix 4. In brief, the final meta-analysis was comprised of two RCTs,[27] and four observational studies.[17,28,29] The final quantitative analysis included 2,345 participants who were more than 65 years of age. Among these 2,345 participants, 1,821 participants stayed at LTCFs. The study quality was closely aligned with the blinding policy (Appendix 4).

### *3.2. Pooled odds ratios for treated and control group outcomes*

The overall OR of PIs (Figure 1) between the treated group and the control group was 0.586 (95% confidence interval [CI]: 0.341–1.007). The OR of all-cause mortality (Figure 1) between the treated group and the control group was 0.774 (95% CI: 0.443–1.352). With respect to PIs, the subgroup analysis (data not shown) showed a favorable OR for professional personnel performing oral care in the treated group (OR, 0.435; 95% CI: 0.233–0.811) and the elderly population in nursing homes (OR, 0.376; 95% CI: 0.204–0.696). With respect to all-cause mortality, the subgroup analysis (data not shown) showed a favorable OR for participant-based oral care in the treated group (OR, 0.435; 95% CI: 0.233–0.811) and the elderly population in nursing homes (OR, 0.474; 95% CI: 0.279–0.804). A favorable OR was obtained for participant-based oral care in the control group (OR, 1.386; 95% CI: 1.011–1.901).

### *3.3. Publication bias*

The overall OR of PIs (Figure 1), when comparing the treated group and the control group, was 0.586 (95% CI: 0.341–1.007). With regard to OR heterogeneity, the $I^2$ value was 74.1% for both groups in all studies. Egger's test revealed the existence of significant publication bias (p = 0.50) regarding the overall ORs. The funnel plot for the overall OR for PIs is shown in Figure 2a.

The OR of all-cause mortality (Figure 1) between the treated group and the control group was 0.774 (95% CI: 0.443–1.352). With regard to OR heterogeneity, the $I^2$ value was 77.8% for both groups in all studies. Egger's test revealed the existence of significant publication bias (p = 0.50) regarding the overall ORs. The funnel plot for

| Outcomes | No. of Studies | Treat group: No. of Events / No. of Participants | Control Group: No. of Events / No. of Participants | Odds Ratio (95%CI) |
|---|---|---|---|---|
| Pulmonary Infection | 6 | 177 / 1301 | 202 / 1281 | 0.586 (0.341-1.007) |
| All-cause mortality | 5 | 226 / 1113 | 213 / 1101 | 0.774 (0.443-1.352) |

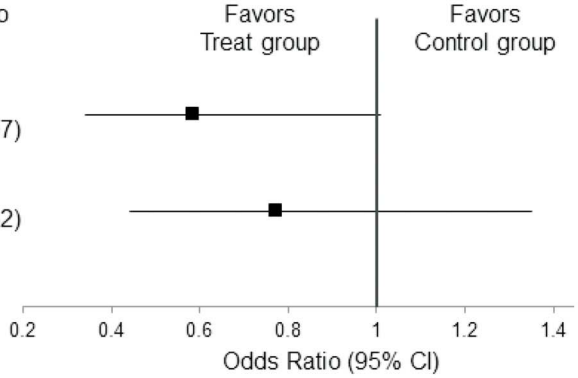


**Figure 1.** Forest plot of the overall odds ratios for pulmonary infection and all-cause mortality in the treated group versus the control group.

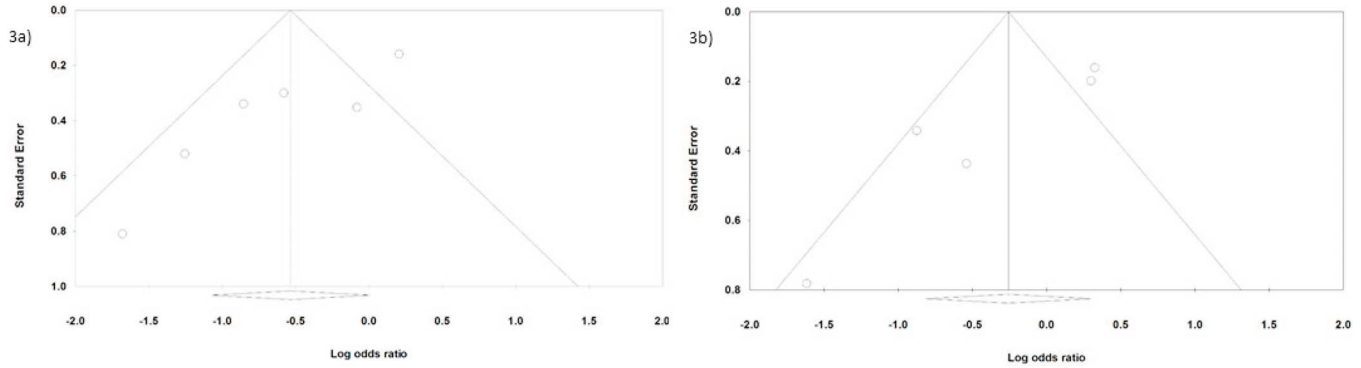


**Figure 2.** Funnel plot of the odds ratio for evaluation event. (a) Funnel plot of the odds ratio of pulmonary infection. (b) Funnel plot of the odds ratio of all-cause mortality.

the overall OR for all-cause mortality rate is shown in Figure 2b.

## 4. Discussion

Our meta-analysis focused on the effects of regular oral care with antiseptics in treating the elderly and included two RCTs and four observational studies. This analysis, based on 6 enrolled studies with a total of 2,345 participants, showed that the PIs and all-cause mortality rates did not change significantly between the treated and control groups. The results were not statistically significant, possibly due to the limited number of enrolled trials. Regular oral care with chlorhexidine is a standard of practice for the elderly in many HCIs; however, our updated review suggests that caution is warranted. Routine oral antiseptics might not prevent PIs according to current meta-analyses. In general, we found no significant difference in the incidence of PI events between the treated group and the control group, and no significant results for increased all-cause mortality between the two groups.

Focusing on PIs, subgroup analysis a favorable OR for professional personnel performing oral care in the treated group (OR, 0.435) and the elderly in nursing homes (OR, 0.376). Concerning the PI event, there is a discrepancy between the current meta-analysis and other reports. El-Solh et al., reported that oral hygiene had positive preventive effects on PIs in the elderly.[6] Furthermore, the study by Bassim et al. found that the odds (OR, 3.57) of mortality due to pneumonia in the control group was more than three times that in the treated group receiving oral care.[8] However, Juthani-Mehta et al. showed no benefit of maintaining oral hygiene.[9] Basic oral health is essential and particularly important for the elderly who might be unable to care for themselves. Juthani-Mehta et al. does suggest that an intervention for oral hygiene was not effective in reducing PIs; thus, the utility of this particular enhanced oral care protocol in LTCFs is still controversial. In the current meta-analysis, we found no significant difference of PI events between the treated group and the control group. In addition, a possible explanation for this lack of significance is that oral care may provide sufficient decontamination in the elderly, but is not adequate to overcome the infectious inoculum load. The lack of clear and strong evidence that adding routine oral care benefits the elderly should prompt a re-examination of LTCFs' policies mandating its use.

No statistical difference was noted between the two groups with respect to all-cause mortality. Subgroup analysis for all-cause mortality showed a favorable OR for participant-based oral care in the treated group (OR, 0.435) and the elderly in nursing homes (OR, 0.474). One potential detriment for the elderly receiving antiseptic oral care involves the aspiration of small amounts of antiseptic which might lead to acute lung injury.[30] In addition, Seguin et al. have raised the possibility that micro-aspiration of oral antiseptics can cause acute respiratory distress syndrome.[31] Another possibility is that oral antiseptic use may mask the PI diagnosis by inhibiting pathogen discovery. Muscedere et al. have reported that culture-negative PIs are associated with higher mortality rates than culture-positive PIs because false-negative PI diagnoses might result in antibiotic withholding.[32] Importantly, Klompas et al. reported no statistical significance in increasing mortality rates among intensive care unit patients who randomly received chlorhexidine oral care.[12] In the current meta-analysis, we found no statistically significant results for increased all-cause mortality between the two groups.

LTCF recommendations often originate from findings in acute care HCIs and may be the consequence of irrelevant and inadequate

evidence. In fact, there are challenges in implementing daily care plans in nursing homes, such as lack of designated health-care workers to perform oral care, limited training in oral care among health-care workers, potential LTCF resident noncompliance due to discomfort, and the health-care workers' inability to performcare procedures with high adherence rates. Patient-care time is limited and precious. Branch-Elliman et al. estimated that nurses spend up to two hours per day per individual providing oral health care.[33] Settling agitated patients using non-pharmacologic means and early mobilization in particular can require substantial time and effort. Oral antiseptics also incur costs, stain teeth, and are stored and administered using formal procedures. It is important to understand that our current meta-analysis only focused on determining whether adding routine oral care provided additional benefits among the elderly. Our current meta-analysis only suggested that adding routine oral care confers little or no additional benefit on the elderly with respect to PI events and all-cause mortality.

However, the present meta-analysis also has several limitations. First, the primary outcome was PIs events. Only a minority of the included trials recorded microbiological results. In order to address the limited data, we also analyzed the OR of the most prevalent PI events to examine whether there were inconsistencies between primary outcome. Secondly, there were significant differences between the trials and studies in participant-inclusion criteria, oral care protocols for applying antiseptics, the use of oral measures such as tooth-brushing, and methods of seeking and defining PIs that may have increased the heterogeneity of the results. The $I^2$ value for OR heterogeneity was approximately 75%, so the influence of measurement precision was considered when reporting on the treatment effectiveness when using ORs. Due to the lack of adjusted data in our selected trials and studies, we compiled the unadjusted ORs. Regardless of these limitations, we have minimized bias throughout the process by our methods of study identification, data selection, and statistical analysis, as well as in our control of publication bias and sensitivity. These steps should strengthen the stability and accuracy of the meta-analysis.

## 5. Conclusions

Routine oral care with antiseptics does not prevent PIs in the elderly. Our current meta-analysis suggests that the ability of antiseptic use to prevent PIs and decrease all-cause mortality rates is questionable. In our meta-analysis, our results were not statistically significant due to the limited amount of available data; therefore, additional RCTs are urgently needed.

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## Ethical approval

The study was approved by the institutional review board of Changhua Christian Hospital (CCH IRB No. 180801).

## Competing interests

All authors declare that they have no competing interests.

## Author contributions

Chen CH, Chen YM, Huang KM, Chang YJ, and Yen HC designed research and performed research; Chen CH, Chen YM and Chang YJ analyzed data; Chen CH wrote the paper; Chen CH, Chen YM, Huang KM, Chang YJ, and Yen HC approved the paper.

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## Appendix

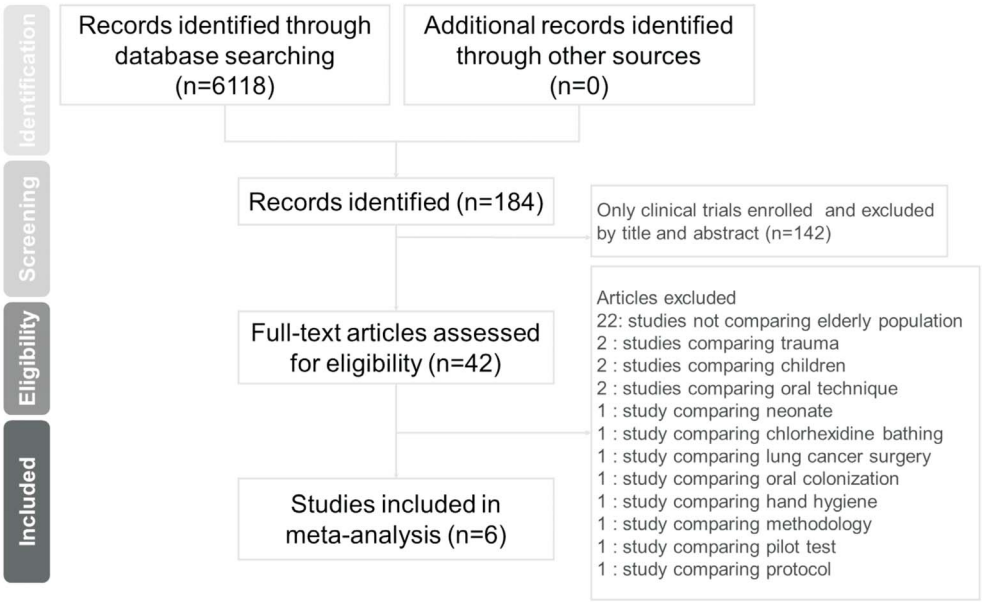
**Appendix 1**
Complete search strategies.

| Search term | Paper number |
|---|---|
| #1 Anti-infective agents or disinfectants or antiseptic agents | 87859 |
| #2 Prophylaxis Antibiotic, Premedication Antibiotic, Antibiotic Premedication, Antibiotic Premedications, Premedications Antibiotic | 1811 |
| #3 #1 or #2 | 88058 |
| #4 Pneumonias, Lobar Pneumonia, Lobar Pneumonias, Pneumonias Lobar, Pneumonia Lobar, Experimental Lung Inflammation, Experimental Lung Inflammations, Inflammation Experimental Lung, Lung Inflammation Experimental, Lung Inflammations Experimental, Pneumonitis, Pneumonitides, Pulmonary Inflammation, Inflammation Pulmonary, Inflammations Pulmonary, Pulmonary Inflammations, Lung Inflammation, Inflammation Lung, Inflammations Lung, Lung Inflammations | 6118 |
| #5 Elderly or aged | 494940 |
| #6 #3 and #5 and #6 | 6118 |

**Appendix 2**
PRISMA 2009 Checklist.

| Section/Topic | # | Checklist item | Reported on Page # |
|---|---|---|---|
| TITLE | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| ABSTRACT | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2 |
| INTRODUCTION | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 3,4 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 4 |
| METHODS | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | - |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 4 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 4 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 4 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 4,5 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 4,5 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 4,5 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 4,5 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 4–6 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | 4–6 |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 4–6 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | 4–6 |
| RESULTS | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 7,8 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 7,8 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see Item 12). | 7,8 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 7,8 |
| Synthesis of results | 21 | Present the main results of the review. If meta-analyses done, include for each, confidence intervals and measures of consistency. | 7,8 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | 7,8 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | 7,8 |
| DISCUSSION | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 8–11 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 11 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 12 |
| FUNDING | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 12 |

*From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med*. 2009;6(6):e1000097. doi:10.1371/journal.pmed1000097




**Appendix 3.** Reporting Items for Systematic Reviews and Meta-Analyses of flow diagram for search and identification of included studies.

**Appendix 4**

Summary of the retrieved trials investigating the treated group and the control group.

| Author, Country (year), Reference | Study design | Double-blind | Preparation of oral regimen | Comparator | Number of participants enrolled | Type of participants | QA |
|---|---|---|---|---|---|---|---|
| DeRiso et al., US (1996) | Observation | No | 0.12% CH | Placebo | 353 | Elderly after cardiac surgery | 3# |
| Yoneyama et al., Japan (1999) | Observation | NM | Receiving oral care | Not receiving oral care | 366 | Nursing home | 3# |
| Yoneyama et al., Japan (2002) | Observation | NM | Receiving POHC | Not receiving POHC | 417 | Older patients in nursing home | 3# |
| Adachi et al., Japan (2007) | Observation | No | Receiving POHC | Not receiving POHC | 190 | Elderly persons in nursing home | 3# |
| Panchabhai et al., India (2009) | RCT | Yes | 0.2% CH | 0.01% PM | 171 | Elderly persons in medical & neurological ICU | 8* |
| Juthani-Mehta et al., US (2015) | RCT | Yes | 0.12% CH | Placebo | 848 | Nursing home elders | 8* |

Abbreviation: CH, chlorhexidine; ICU, intensive care unit; NM, non mentioned; PM, potassium permanganate; POHC, professional oral health care; RCT, randomized control trial; QA, quality assessment. Notes, #, the study was evaluated using the Jadad scale; *, the study was assessed using the Newcastle-Ottawa scale.