# Oral Care for Intensive Care Unit Patients Without Mechanical Ventilation: Protocol for a Systematic Review and Meta-Analysis

**Xiaoxia Tang**
Kunming Municipal Hospital of Traditional Chinese Medicine
**Yunxia Shen**
Kunming Municipal Hospital of Traditional Chinese Medicine
**Xuejiao Pan**
Kunming Municipal Hospital of Traditional Chinese Medicine
**Jianglong Liao**
Kunming Municipal Hospital of Traditional Chinese Medicine
**Yanfei Xu**
Kunming Municipal Hospital of Traditional Chinese Medicine
**Wen Luo**
Kunming Municipal Hospital of Traditional Chinese Medicine
**Xiaolin Zhang**
Kunming Municipal Hospital of Traditional Chinese Medicine
**Chun'e Li**
Kunming Municipal Hospital of Traditional Chinese Medicine
**Qing Wan**
Kunming Municipal Hospital of Traditional Chinese Medicine
**Xin Cai**
Kunming Municipal Hospital of Traditional Chinese Medicine
**Xiaomei Zhang**
Kunming Municipal Hospital of Traditional Chinese Medicine
**Tao Wang** ( taowang0871@126.com )
Kunming Municipal Hospital of Traditional Chinese Medicine https://orcid.org/0000-0003-3111-3932
**Guilan Zhang**
Kunming Municipal Hospital of Traditional Chinese Medicine

**Protocol**

**Keywords:** oral care, intensive care unit, nosocomial pneumonia, review, protocol

**Posted Date:** December 8th, 2020

**DOI:** https://doi.org/10.21203/rs.3.rs-121895/v1



**Version of Record:** A version of this preprint was published at Systematic Reviews on January 5th, 2022.
See the published version at https://doi.org/10.1186/s13643-021-01878-0.

# Abstract

Background

Infection is a common problem and a major cause of morbidity and mortality for patients in intensive care units (ICUs). Oral care has been found to reduce the risk of nosocomial pneumonia according to published meta-analysis, and has been recommended to improve the oral environment for the patients in ICUs. However, relatively little information is available about the effects of oral care in patients without ventilatory support in ICUs. Therefore, this study was designed to evaluate the effectiveness of oral care in preventing pneumonia in non-ventilated ICUs patients.

Methods

The literature source will be gained from eight databases including four Chinese online databases and four English online databases from their inception to December 31, 2020. Records obtained will be managed and screened via Endnote X7a widely used reference management software. The duplicate literature will be removed. All literature will be selected in accordance with pre-established inclusion criteria by two independent review authors to obtain quality trials. The quality of the included records will be evaluated according to “Risk of table”, recommended by Cochrane Handbook for Systematic Reviews of Interventions. All the data will be extracted by one author and checked by another. If there is any disagreement, a final agreement will be reached with a third reviewer via consulting. The data obtained will be managed via Microsoft Excel. If there is missing data, the original authors will be emailed to ask for it. If enough data was collected, the data synthesis will be performed using Review Manager (RevMan5.3). Otherwise, only the qualitative analysis will be carried out. The overall effect will be estimated on oral care for intensive care unit patients without mechanical ventilation to prevent nosocomial pneumonia using random effect model or fixed effect model base on the heterogeneity results. The sources of heterogeneity will be performed using Meta-regression and subgroup analysis if there is significant heterogeneity. The funnel plot will be used to assess the publish bias, if there are enough records included. The Cochrane Handbook for Systematic Reviews of Interventions will be followed throughout the system evaluation process.

Conclusion

This study will provide evidence of oral care for intensive care unit patients without mechanical ventilation to prevent nosocomial pneumonia.

PROSPERO Research registration identifying number

CRD42020146932

# 1. Background

## 1.1 Description of condition

Infection is a common problem and a major cause of morbidity and mortality for patients in intensive care units (ICUs) [1-4]. It is the leading cause of death in non-cardiac ICUs [1,5]. Pneumonia is the most common site of infection according to an international study of the prevalence and outcomes of infection in intensive care units, which include 13,796 patients [6]. Nosocomial pneumonia (NP) is among the main causes of mortality in patients at ICU. Importantly, the incidence of nosocomial pneumonia is increasing, and the number of infection-related death that follows is also increasing. Thus, to prevent nosocomial pneumonia is a cost-reducing and life-saving healthcare practice, especial in ICUs.

Nosocomial pneumonia (NP), also called hospital-acquires pneumonia or health-care associated pneumonia, was defined as an infection of the lower respiratory tract which do not exist at the time of admission and do not have the incubation period of infection, but occur 48 hours after admission[7]. The most important cause of the development of nosocomial pneumonia is oral environment [8]. The oral cavity of ICU patients is an important reservoir for bacteria and provides a habitat for microorganisms leads to nosocomial pneumonia [7]. Patients in ICUs acquire pneumonia by aspirating oral bacteria that have been colonized in the oral cavity into the lower respiratory tract. Due to advanced age, limited mobility, illness, cognitive dysfunction, patients in ICUs often have difficulty to maintain oral hygiene by themselves. Poor dental hygiene has been linked to respiratory pathogen colonization in ICUs patients. Therefore, respiratory pathogens tend to colonize dental plaque and oral mucosa in these populations [9]. So strategies to eliminate respiratory pathogens from the oral cavity may improve oral hygiene and decrease the development of nosocomial pneumonia.

### 1.2 Description of the intervention

Oral care has been defined as “science and technology that is aimed at the prevention of oral diseases, improvement of the treatment effect, promote the rehabilitation of patients, improvement the quality of life (QOL), protection the health”.[10] Oral care has been found to reduce the risk of nosocomial pneumonia according to published meta-analysis [11,12], and has been recommended to improve the oral environment for the patients in ICUs [7]. The aim of oral care is to remove plaque and debris from the oral cavity. Mouth rinses including saline, water, antiseptics maybe applied as sprays, liquids during the oral care. During the oral care, mouth rinses including water, antiseptic agents sprays maybe applied. Antiseptic agents sprays include povidone iodine, saline, chlorhexidine, cetylpyridium, and possibly others, (but exclude antibiotics) [13]. Possible tools include swab or tooth brushing (either manual or powered) which can provide mechanical cleaning [14,15].

### 1.3 How the intervention might work

Patients in ICUs often have difficulties to complete their own oral hygiene due to dysfunction, illness, and old age, which can responsible for poor oral environment. Poor oral environment results the colonization of respiratory pathogen in ICUs patients, which is the primary cause of the development of hospital acquired pneumonia (HAP).

In oral care, manual or electric toothbrushes can be used to provide mechanical cleaning to remove plaque and debris, as well as to replace certain functions of saliva to moisturize and gargle. It can remove plaque on teeth and gum, destroy the biofilm in which plaque bacteria multiply, thereby enhancing the effect of oral care.

### 1.4 Why it is important to do this review

There are a number of systematic reviews focused on the effect of oral care in high-risk patients with ventilator-associated pneumonia (VAP). Oral decontamination with antiseptic [15-18] and antibiotic agents[19] had been reported significantly reduce the risk of VAP. There is a systematic review and meta-analysis of randomized controlled trials showed that a preventive effect of oral care on pneumonia in non-ventilated individuals. But this study included the patients in hospitals or long-term care facilities, which leads to the high heterogeneity between the participants [20]. A study was also performed to investigate the preventive effect of oral care for non-VAP elderly people in nursing homes and hospitals. It included 4 RCTs, in which the results of 3 studies indicated that oral care can effectively reduce the incidence of HAP. However, because of clinical heterogeneity among the 3 studies, meta-analyses were not performed. Another limitation of this study is that the literature searches were conducted only in the Cochrane library databases and the Medline database. Therefore, the evidence strength of the research results is insufficient [21]. Furthermore, relatively little information is available about the effects of oral care in patients without ventilatory support in ICUs. To address this limitation, this study was designed to evaluate the effectiveness of oral care in preventing pneumonia in non-ventilated ICUs patients.

## 2. Methods

### 2.1 Study design and program registration

This design was registered in the international prospective register of systematic reviews (https://www.crd.york.ac.uk/PROSPERO/ID = CRD42020146932). The detail of this protocol was conducted follow the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocols (PRISMA-P) statement [22]. Since this study is a secondary study of the literature, formal ethical approval is not applicable.

### 2.2. Including criteria

#### 2.2.1. Types of studies

Only the clinical randomized controlled trials (RCT) of oral care interventions will be included in this study. The quasi-RCTs and non-RCTs will be excluded. If there are cross-cover randomized controlled trials, the first period will be included as a parallel group trial.

#### 2.2.2. Types of patients

ICUs patients did not receive mechanical ventilation, without infection of the lower respiratory tract at admission will be included. Hospital-acquired pneumonia must be diagnosed as following: temperature >37.8°C, and chest radiograph, cough or subjective dyspnea. If ICUs patients with and without mechanical ventilation are involved in a study, only these RCTs with over 50% of patients without mechanical ventilation will be included in this review. If different setting patients such as rehabilitation unit, nursing home, community were included in RCTs, only these RCTs with over 50% of patients without mechanical ventilation from ICUs will be included in this study.

### 2.2.3. Interventions

Patients in the experimental group received clearly-defined oral care procedures, including decontamination of oropharyngeal cavities with antiseptics, oral and pharyngeal cavity rinse, nurse-assisted tooth brushing. Patients in the control group received no treatment, 'usual care', or placebo. Studies which compared different types of oral care will not be included. These studies in which oral care used as one part of whole treatment protocols will be excluded.

### 2.2.4. Outcomes

#### 2.2.4.1. Primary outcomes

The incidence of nosocomial pneumonia defined as the primary outcome of this study. Nosocomial pneumonia was defined as an infection of the lower respiratory tract that is diagnosed at least 48 h after the patient has been admitted to hospital, which is not present or incubating at the time of hospital admission [23].

#### 2.2.4.2. Secondary outcomes

Other outcomes such as mortality, 30-day mortality, duration of ICU stay, oral health indices (including periodontal index, plaque index, bleeding index, gingival index, etc.), the usage of antibiotic, adverse effects of the intervention, economic data were defined as secondary outcomes.

### 2.2.5. Search strategy

#### 2.2.5.1. Online electronic databases

Four English online electronic databases including Embase (via embase.com), Medline (via PubMed), CINAHL (via EBSCOhost), and Cochrane Central Register of Controlled Trials (CENTRAL) will be systematic searched without language restrictions from their inception to December 31, 2020. Four Chinese-language databases include WanFang Database, Sino-Med Database, Chinese Science and Technology Periodical (VIP) Database, and China National Knowledge Infrastructure (CNKI) database will be searched from their inception to December 31, 2020. The English terms were used individually or combined "intensive care" "nosocomial infection" "oral care" "mouth care" and the Chinese searching terms were "zhong zheng jian hu (intensive care)," "yi yuan huo de xing fei yan(nosocomial infection)," "

kou qiang hu li oral care)". The search strategy we have built for Medline via PubMed was showed in Table 1, which was performed according to Cochrane Handbook for Systematic Reviews of Interventions [24]. Some adaptive changes will be made when searching in other databases.

#### 2.2.5.2. Additional resources

Although there are no full-text articles in Chinese or English, articles with Chinese or English titles or abstracts will also be screened.

### 2.3. Data collection and analysis

#### 2.3.1. Research management and screening.

The literature management software, EndNoteX7, will be used in this study to manage all records collected. Before two independent reviewers read the title and abstract of the trials, duplicate records will be removed from the literature database. Then obviously unqualified records will be identified. For potentially eligible records, full text of these records will be read by two independent reviewers. Finally, qualified literature was selected according to the pre-determined inclusion criteria. All records included must fit the type of study, type of patients, intervention, design (PIS) strategy of this review. Original author will be contacted via email when there is more information is needed to make a decision. If there is any disagreement, the final consensus is generated through discussion with a third reviewer. Details of the literature screening will be reported following the PRISMA flow diagram (Fig. 1).

#### 2.3.2. Data extraction and management.

First, all data will be extracted according to the data table previously prepared by one researcher. Then all data extracted will be verified by another researcher. The information we will extract is multifaceted. The information will be extracted from each included trial as following: (1) Basic information of studies including the journal, publish year, author, author institutions, title; (2) The characteristics of participants of RCTs including sex, age, inclusion/exclusion criteria; (3) Intervention used in groups, including the intensity, frequency, and period; (4) The methodological information of each trial including random sequence generation, allocation concealment, blinding of participants, and blinding of outcomes assessment; (5) Outcomes including instruments, drop-out, follow-up, and adverse events. If there is any missing data, original author will be emailed to ask for it. The measurement data will be described using mean and standard deviation (SD) or standard error (SE). The count data will be described using the number of events. The two arms' data that most fit our aims of this review will be extracted rather than all arms if there are more than two arms in study. Before entering the data into the RevMan5.3 for analysis, necessary data conversion will be performed via spreadsheet software (Microsoft Excel). If there is any disagreement, the final consensus is generated through discussion with a third review author.

### 2.4. The risk of bias assessment for included studies

The quality of included studies will be assessed using “Risk of bias” (ROB) table, which was recommended by Cochrane Handbook for Systematic Reviews of Interventions[24]by two reviewers independently. This tool is a two-part tool, addressing the following six specific domains when defining the quality of an RCT: (1) sequence generation; (2) allocation concealment; (3) blinding of participants, personnel and outcome assessors; (4) incomplete outcome data; (5) selective outcome reporting; (6) Other sources of bias. Each domain consists of one or more specific entries. Within each entry, the first part is to describe what happened in the study. The second part is a judgment of the risk of bias for that entry. This is achieved by answering a pre-specified question for each entry. In all cases, if there is insufficient information about the part description, the judgment as will usually be “unclear” risk of bias. An answer “No” indicates high risk of bias and an answer“Yes” indicates low risk of bias. If there is any disagreement, the final consensus is generated through discussion with a third review author.

### 2.5. Handling of missing data

If there is any missing data, original authors will be contacted to request it. If the missing data is not obtained, the analysis will be performed only using the available data. Effect of missing data on the final results will be discussed in the discussion section.

### 2.6. Assessment of heterogeneity

Heterogeneity across trials will be detected by χ2 test with a 0.10 level as the cut-off value ($P$<0.1). Heterogeneity across trials will be quantified using $I^2$ statistic. Studies with an $I^2$ value of more than 75% will be considered to have high degree heterogeneity. If the included studies have good homogeneity, the overall effect will be synthesized [25]. Otherwise, the sources of heterogeneity will be explored via subgroup and analysis meta-regression [25].

### 2.7. Evaluation of publication bias

If there are more than ten studies in an outcome, a funnel plots will be structured to funnel plot used to investigate publication bias [25]. Asymmetry in the funnel plot indicates possible publication bias.

### 2.8. Data synthesis

If there are sufficient studies focusing on similar comparison and the same outcomes, meta-analysis will be undertaken using fixed-effect model or the random-effect model dependent on heterogeneity results. Otherwise, only the qualitative analysis will be carried out.

### 2.9. Subgroup analyzes

Subgroup analysis will be undertaken according to whether toothbrush was used or not. Subgroup analysis will also be undertaken according to the different types of mouthwash.

### 2.10. Sensitivity analysis

The studies that with a low methodological quality adversely affect the strength of the evidence, so sensitivity analysis will be performed to investigate the effect of these trials on the evidence. It will be performed via excluding a study and comparing the results changes. The results will be reported and discussed the discussion part.

### 2.11. Grading the quality of evidence

The quality of evidence for outcomes will be evaluated according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system, which rates the quality the quality of evidence into four levels (high, moderate, low, very low levels) [26].

## 3. Discussion

It was reported that pneumonia is the most common site of infection in intensive care units. The occurrence of nosocomial pneumonia is closely related to the mortality for the ICUs patients. The main mechanism of hospital-acquired pneumonia is inhalation of bacteria which is multiplied in the mouth and entered the lower respiratory tract. Patients in ICUs often cannot effectively remove bacteria from their mouths due to illness, elderly age or dysfunction. Therefore, to help ICUs patients clear the bacteria from the mouth effectively can significantly improve their oral environment, thereby reducing the incidence of hospital acquired pneumonia.

Oral care has been recommended to improve the oral environment. Several studies demonstrated that oral care can significantly reduce the incidence of mechanical ventilator-associated pneumonia (VAP). Unlike the VAP, the effect of the oral care for hospital acquired pneumonia in ICUs patients without ventilatory support has not been well established. Only two review focus on the effect of oral care for the patients without ventilatory support. But there are significant clinical heterogeneity between included studies because they included patients from different institutions including ICUs, Nursing institute, rehabilitation setting, ect [20,27]. Another limitation is the limited database the sources obtained. Thus, it is necessary to conduct this review to investigate the effect of oral care for hospital acquired pneumonia in ICUs patients without ventilatory support.

We believed that this study results will provide comprehensive and systemic evidence for the effect of oral care for the ICUs patients without ventilatory support. It will also give help to make decisions regarding future practice of oral care for ICUs patients without ventilatory.

Strengths of the study include rigorous design and the clear definition of participants and intervention. However, there are also some limitations we should note. Firstly, the diversity of oral care media may be one of the sources of clinical heterogeneity. Secondary, different interventions in the control group between studies may affect the results. Finally, the intervention frequency and operator of oral care may contribute to clinical heterogeneity.

## Abbreviations

ICU, intensive care unit; QOL, quality of life; HAP, hospital -acquired pneumonia; NP, Nosocomial pneumonia; RCTs, randomized controlled trials; VAP, ventilator-associated pneumonia; CNKI, China National Knowledge Infrastructure; VIP, Chinese Science and Technology Periodical; ROB, Risk of bias.

# Declarations

**Ethical approval**: Formal ethical approval of this systematic review is not required because there is no direct human data involved.

**Consent for publish:** Not applicable.

**Availability of data and materials:** Not applicable.

**Competing interests:** All authors declare that they have no conflict of interest.

**Funding:** This study is supported by Kunming health science and technology talent training project (No. 2016-sw-13, 2018-sw-64, 2020-sw-23), Kunming Science and technology project (No. 2019-1-S-2531800000139), Yunnan health science and technology program (No. 2018NS0188), and Medical and health science and technology plan project of Kunming municipal health and family planning commission (No. 2018-14-05-009). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Authors' contributions:** T.W. and G.L.Z conceived and designed the study; X.X.T and Y.X.S. made the manuscript preparation and wrote the draft manuscript; X.J.P, J.L.L, and Y.F.X., developed the search strategy; W.L. X.L.Z. and C.E.L. made the manuscript preparation; Q.W., X.C., and X.M.Z. performed preliminary literature search. All authors contributed to draft the manuscript and have read and approved the final manuscript.

**Research registration unique identifying number:** CRD42020146932

**Guarantor:** Tao Wang and Guilan Zhang are the guarantors of the article.

**Acknowledgements:** This study is supported by Kunming health science and technology talent training project (No. 2016-sw-13, 2018-sw-64, 2020-sw-23), Kunming Science and technology project (No. 2019-1-S-2531800000139), Yunnan health science and technology program (No. 2018NS0188), and Medical and health science and technology plan project of Kunming municipal health and family planning commission (No. 2018-14-05-009).

# References

1. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. *Critical care medicine.* 2001;29(7):1303-1310.

2. Vincent JL, Sakr Y, Sprung CL, et al. Sepsis in European intensive care units: results of the SOAP study. *Critical care medicine.* 2006;34(2):344-353.
3. Esteban A, Frutos-Vivar F, Ferguson ND, et al. Sepsis incidence and outcome: contrasting the intensive care unit with the hospital ward. *Critical care medicine.* 2007;35(5):1284-1289.
4. Harrison DA, Welch CA, Eddleston JM. The epidemiology of severe sepsis in England, Wales and Northern Ireland, 1996 to 2004: secondary analysis of a high quality clinical database, the ICNARC Case Mix Programme Database. *Critical care (London, England).* 2006;10(2):R42.
5. Vincent JL, Abraham E, Annane D, Bernard G, Rivers E, Van den Berghe G. Reducing mortality in sepsis: new directions. *Critical care (London, England).* 2002;6 Suppl 3(Suppl 3):S1-18.
6. Vincent JL, Rello J, Marshall J, et al. International study of the prevalence and outcomes of infection in intensive care units. *Jama.* 2009;302(21):2323-2329.
7. Vilela MC, Ferreira GZ, Santos PS, Rezende NP. Oral care and nosocomial pneumonia: a systematic review. *Einstein (Sao Paulo).* 2015;13(2):290-296.
8. Amaral SM, Cortês Ade Q, Pires FR. Nosocomial pneumonia: importance of the oral environment. *Jornal brasileiro de pneumologia : publicacao oficial da Sociedade Brasileira de Pneumologia e Tisilogia.* 2009;35(11):1116-1124.
9. Scannapieco FA, Stewart EM, Mylotte JM. Colonization of dental plaque by respiratory pathogens in medical intensive care patients. *Critical care medicine.* 1992;20(6):740-745.
10. Fernandez Rodriguez B, Peña Gonzalez L, Calvo MC, Chaves Sanchez F, Pallas Alonso CR, de Alba Romero C. Oral care in a neonatal intensive care unit. *The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet.* 2017;30(8):953-957.
11. Zhang Z, Hou Y, Zhang J, et al. Comparison of the effect of oral care with four different antiseptics to prevent ventilator-associated pneumonia in adults: protocol for a network meta-analysis. *Systematic reviews.* 2017;6(1):103.
12. Gu WJ, Gong YZ, Pan L, Ni YX, Liu JC. Impact of oral care with versus without toothbrushing on the prevention of ventilator-associated pneumonia: a systematic review and meta-analysis of randomized controlled trials. *Critical care (London, England).* 2012;16(5):R190.
13. Tada A, Miura H. Prevention of aspiration pneumonia (AP) with oral care. *Arch Gerontol Geriatr.* 2012;55(1):16-21.
14. Pace CC, McCullough GH. The association between oral microorgansims and aspiration pneumonia in the institutionalized elderly: review and recommendations. *Dysphagia.* 2010;25(4):307-322.
15. Chan EY, Ruest A, Meade MO, Cook DJ. Oral decontamination for prevention of pneumonia in mechanically ventilated adults: systematic review and meta-analysis. *Bmj.* 2007;334(7599):889.
16. Labeau SO, Van de Vyver K, Brusselaers N, Vogelaers D, Blot SI. Prevention of ventilator-associated pneumonia with oral antiseptics: a systematic review and meta-analysis. *The Lancet. Infectious diseases.* 2011;11(11):845-854.

17. Li J, Xie D, Li A, Yue J. Oral topical decontamination for preventing ventilator-associated pneumonia: a systematic review and meta-analysis of randomized controlled trials. *The Journal of hospital infection.* 2013;84(4):283-293.
18. Chlebicki MP, Safdar N. Topical chlorhexidine for prevention of ventilator-associated pneumonia: a meta-analysis. *Critical care medicine.* 2007;35(2):595-602.
19. Price R, MacLennan G, Glen J. Selective digestive or oropharyngeal decontamination and topical oropharyngeal chlorhexidine for prevention of death in general intensive care: systematic review and network meta-analysis. *Bmj.* 2014;348:g2197.
20. Kaneoka A, Pisegna JM, Miloro KV, et al. Prevention of Healthcare-Associated Pneumonia with Oral Care in Individuals Without Mechanical Ventilation: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Infection control and hospital epidemiology.* 2015;36(8):899-906.
21. Sjögren P, Nilsson E, Forsell M, Johansson O, Hoogstraate J. A systematic review of the preventive effect of oral hygiene on pneumonia and respiratory tract infection in elderly people in hospitals and nursing homes: effect estimates and methodological quality of randomized controlled trials. *J Am Geriatr Soc.* 2008;56(11):2124-2130.
22. Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *Bmj.* 2015;350:g7647.
23. Lanks CW, Musani AI, Hsia DW. Community-acquired Pneumonia and Hospital-acquired Pneumonia. *The Medical clinics of North America.* 2019;103(3):487-501.
24. Higgins J, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. 2011; https://www.cochrane.org/search/manuals/handbook?manual=Handbook. Accessed 04 Sep 2018.
25. Copas J, Shi JQ. Meta-analysis, funnel plots and sensitivity analysis. *Biostatistics.* 2000;1(3):247-262.
26. Guyatt GH, Oxman AD, Vist GE, et al. GRADE:an Emerging Consensus on Rating Quality of Evidence and Strength of Recommendations. *Bmj British Medical Journal.* 2008;336(7650):924-926.
27. Emery KP, Guido-Sanz F. Oral care practices in non-mechanically ventilated intensive care unit patients: An integrative review. *J Clin Nurs.* 2019;28(13-14):2462-2471.

# Tables

**Table 1 Search strategy for Medline via PubMed**

| No. | Search items |
|---|---|
| #1 | “CRITICAL ILLNESS”[Mesh] |
| #2 | (“critical$” adj5 “ill$”)[tw] |
| #3 | (“depend$” adj5 “patient$”)[tw] |
| #4 | ( “INTENSIVE CARE”)[Mesh] |
| #5 | (“intensive care” OR “intensive-care” OR “critical care” OR “critical-care”) [Mesh] |
| #6 | ICU[Mesh] or CCU[tw] |
| #7 | ((“intubat$” or “ventilat$”) adj5 “patient$”) [tw] |
| #8 | #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 |
| #9 | ( “PNEUMONIA, VENTILATOR-ASSOCIATED”)[Mesh] |
| #10 | pneumonia[tw] |
| #11 | VAP[tw] |
| #12 | “nosocomial infection”[tw] |
| #13 | #9 OR #10 OR #11 OR #12 |
| #14 | (“ORAL HYGIENE”)[Mesh] |
| #15 | (DENTIFRICES)[Mesh] |
| #16 | (MOUTHWASHES)[Mesh] |
| #17 | (“ANTI-INFECTIVE AGENTS, LOCAL”)[Mesh] |
| #18 | “Cetylpyridinium”[Mesh] |
| #19 | “Chlorhexidine”[Mesh] |
| #20 | “Povidone-Iodine”[Mesh] |
| #21 | (“oral care” OR “mouth care” OR “oral hygien$” OR oral-hygien$ OR “dental hygien$”)[tw] |
| #22 | (“mouthwash$” OR “mouth-wash$” OR “mouth-rins$” OR “mouthrins$” OR “oral rins$” OR “oral-rins$” OR “toothpaste$” OR “dentifrice$” OR “toothbrush$” OR “chlorhexidine$” OR “betadine$” OR “triclosan$” OR “cepacol” OR “Corsodyl” OR “Peridex” OR “Hibident” OR “Prexidine” OR “Parodexor Chlorexil” OR “Peridont” OR “Eludril” OR “Perioxidin” OR “Chlorohex” OR “Savacol” OR “Periogard” OR “Chlorhexamed” OR “Nolvasan” OR “Sebidin” OR “Tubulicid” OR “hibitane”) [tw] |
| #23 | (“antiseptic$” OR “antiinfect$” OR “local microbicide$” OR “topical microbicide$”) [tw] |
| #24 | #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 |
| #25 | randomized controlled trial [pt] |
| #26 | controlled clinical trial [pt] |

| | |
|---|---|
| #27 | randomized [tiab] |
| #28 | placebo [tiab] |
| #29 | clinical trials as topic [mesh: noexp] |
| #30 | randomly [tiab] |
| #31 | trial [ti] |
| #32 | #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 |
| #33 | #8 AND #13 AND #24 AND #32 |

# Figures

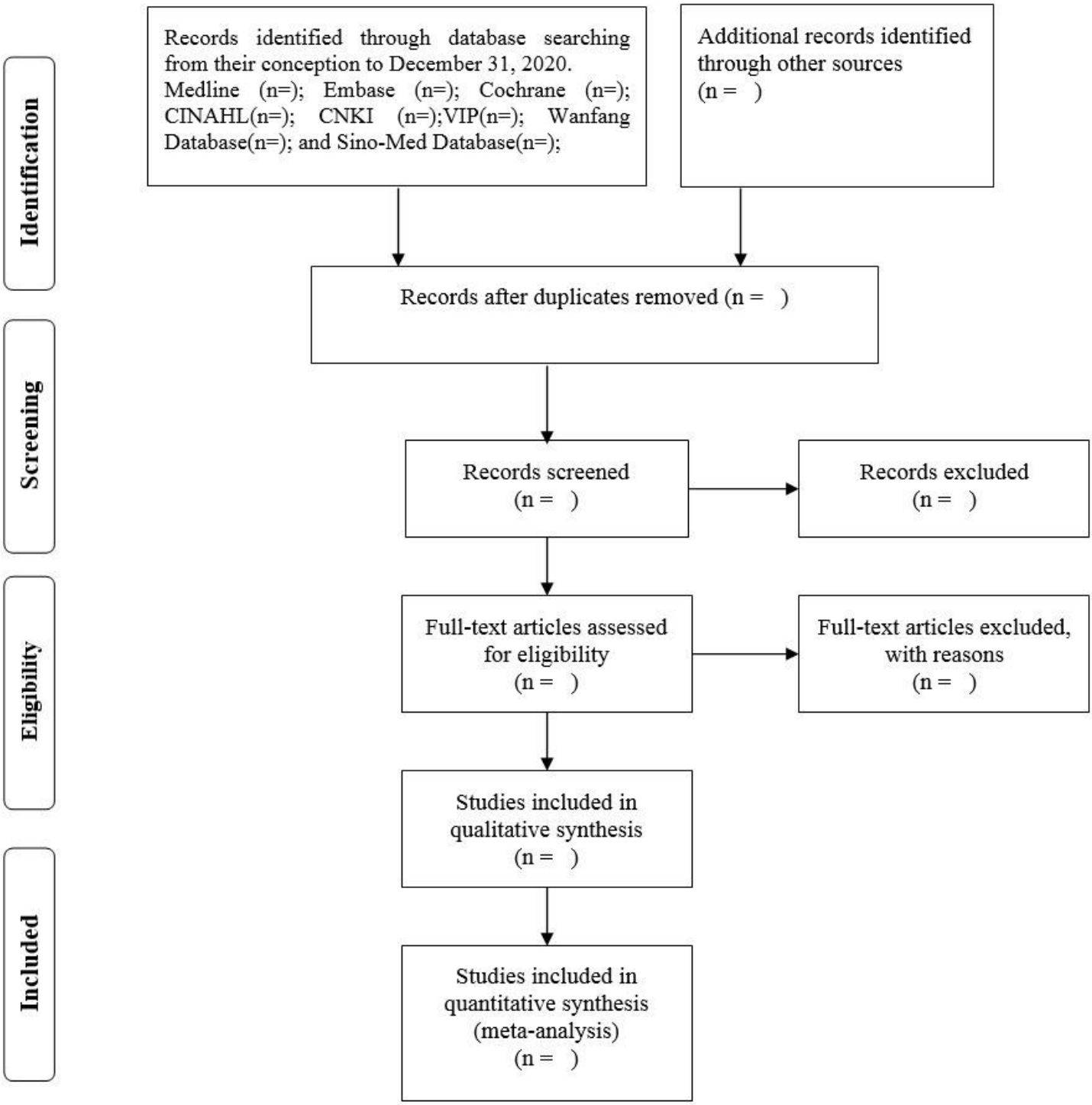


**Figure 1**

Flow diagram of the study selection process

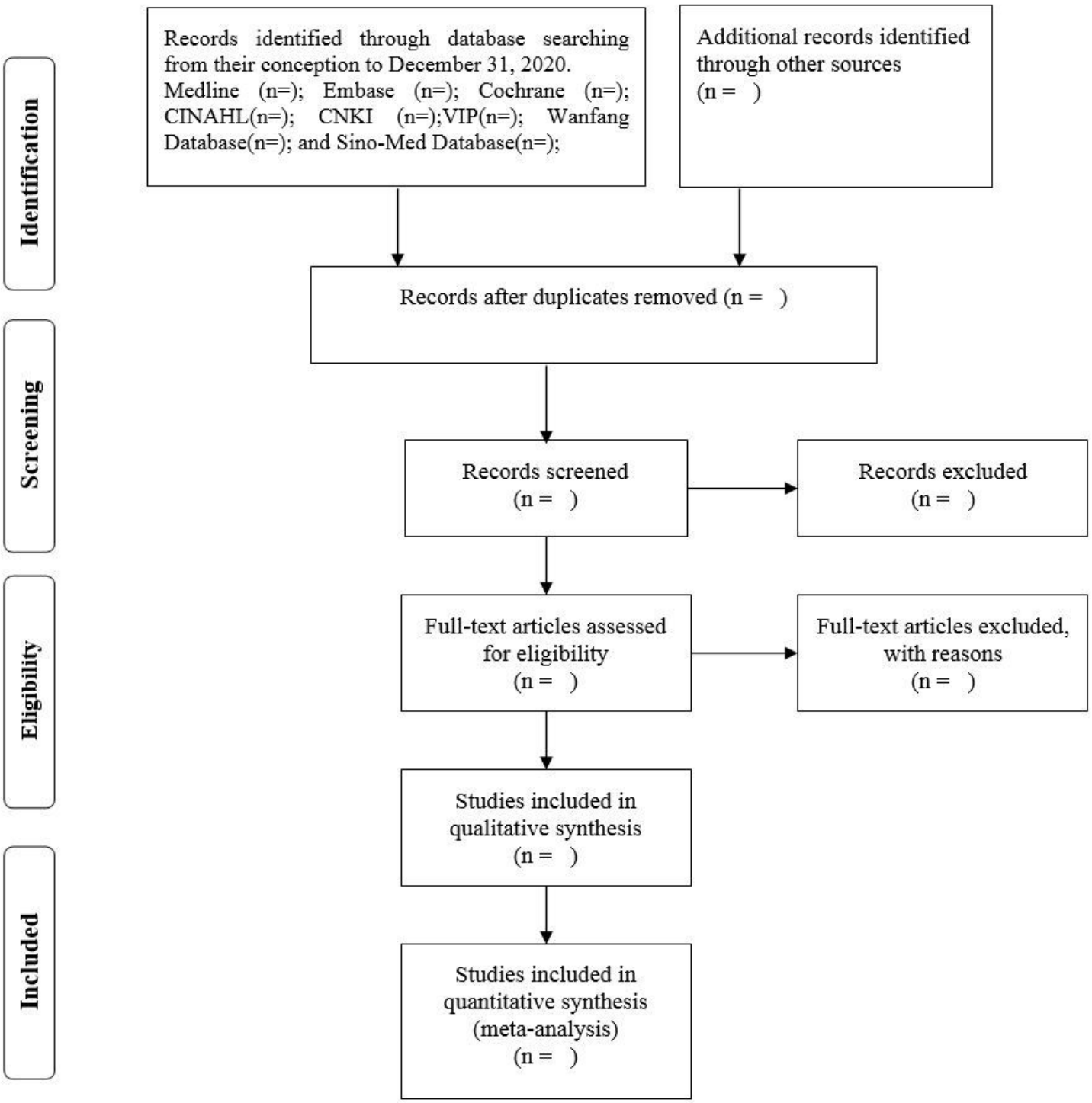


**Figure 1**

Flow diagram of the study selection process

# Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- PRISMAPchecklist.doc

- PRISMAPchecklist.doc