



Oral care measures for preventing nursing home-acquired pneumonia

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Oral care measures for preventing nursing home-acquired pneumonia

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What's new

Date	Event	Description

History

Date	Event	Description

Abstract

Background

Objectives

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Selection criteria

Data collection and analysis

Main results

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Plain language summary

[Plain language title]

¬[Summary text]

Background

Description of the condition

Residents of nursing homes and long-term care facilities are a predominantly geriatric population. Institutionalised elderly people are prone to poor oral health because they have reduced access to professional dental care and poor maintenance of personal oral hygiene ([Berg 2000](#); [Gaszynska 2014](#)). Many studies have found that elderly people require professional oral hygiene care as well as instruction on personal oral hygiene (e.g. [Frenkel 2000](#); [Gaszynska 2014](#); [Gluhak 2010](#); [Petelin 2012](#)).

The incidence of community-acquired pneumonia (CAP) requiring hospitalisation is 1.96 to 10 times higher amongst elderly nursing home residents than community-dwelling elderly people ([Marrie 2002](#); [Ronald 2008](#); [Ticinesi 2016](#)), with a 2.29 times higher rate of 30-day mortality ([Liapikou 2014](#)). This may be attributable to the particular characteristics of residents of nursing homes and long-term care facilities, as they tend to be older, to have greater functional impairment and to have increased comorbidities, polypharmacy and dependence upon caregivers ([Dudas 2000](#); [Martínez-Moragón 2004](#)). Pneumonia occurring in residents of long-term care facilities and nursing homes can be termed nursing home-acquired pneumonia (NHAP); it closely resembles CAP and usually is caused by multi-drug-resistant bacteria ([Craven 2006](#); [Mylotte 2002](#)), as indicated by data from the United States and Asia ([Micek 2007](#); [Nakagawa 2014](#)), although not confirmed by European data ([Brito 2009](#); [Ewig 2010](#)). Nursing home-acquired pneumonia is the leading cause of mortality among residents ([Cho 2011](#); [Nicolle 1996](#)). Its reported mean incidence ranges from 1 to 3.2 per 1000 patient-days, with 600,000 emergency department admissions ([El-Solh 2010](#); [Medina-Walpole 1999](#); [Muder 1998](#)). It has been suggested that NHAP may be caused by aspiration of oropharyngeal flora into the lung and by failure of host defence mechanisms to eliminate aspirated bacteria ([Scannapieco 2014](#); [Vergheese 1983](#)).

Comorbidities considered as risk factors for NHAP include the following ([Klapdor 2012](#); [Ticinesi 2016](#)):

- Cumulative Illness Rating Scale indexes;
- dementia;
- chronic obstructive pulmonary disease;
- mechanical ventilation; and
- ageing.

A growing body of evidence shows that poor oral hygiene and oral hygiene-related factors (e.g. denture use ([O'Donnell 2016](#)), being edentulous ([Abe 2008](#))) may be additional risk factors for aspiration pneumonia among the elderly, who have an increased rate of dental plaque colonisation as a possible reservoir for pathogenic organisms associated with CAP or NHAP ([Bassim 2008](#); [Janssens 2005](#); [Scannapieco 2003](#)). A systematic review by [Azarpazhooh 2006](#) concluded that there was fair evidence (II-2, grade B recommendation) of an association between pneumonia and oral health, and good evidence (I, grade A recommendation) that better oral health and frequent professional oral care reduce the occurrence or progression of respiratory disease among high-risk elderly living in nursing homes and especially those in intensive care units. However, an RCT by [Juthani-Mehta 2015](#) indicated that advanced oral care measures did not significantly reduce the incidence of first radiographically-confirmed pneumonia or lower respiratory tract infection compared with usual care in residents of nursing homes. Given that NHAP may be linked to oral hygiene, interventions for maintaining good oral hygiene might be of significant interest in this population.

Description of the intervention

It is widely believed that improved oral hygiene and frequent professional oral health care can be effective in reducing the incidence or progression of respiratory infection in residents of nursing homes and long-term care facilities ([Adachi 2007](#); [Azarpazhooh 2006](#); [Scannapieco 2003](#); [Sjögren 2008](#); [Watando 2004](#)). Multiple oral care measures have been reinforced by the National Institute for Health and Care Excellence (NICE) guideline that introduced detailed oral care measures ([NICE guideline 2016](#)). The nature of oral care measures that have been proposed is diverse, but they can be classified broadly as follows.

- Mechanical aids to remove plaque and debris from the oral cavity, for example:
 - toothbrushing;
 - swabbing with water.
- Topical (chemical) disinfection to reduce colonisation, for example:
 - mouthrinses;
 - sprays;
 - liquids;
 - gels.

Antiseptics are broadly defined to include saline, chlorhexidine, povidone-iodine and cetylpyridium and others, but to exclude antibiotics ([Shi 2013](#)).

- Combination of mechanical plaque removal and topical disinfection, for example:
 - swabbing with antiseptic;
 - toothbrushing with antibacterial toothpaste;
 - daily toothbrushing plus antiseptic rinse.
- Professional dental care, for example:
 - aided toothbrushing;
 - suction to remove excess fluid.

Oral care measures can be delivered at any frequency. Oral health measures can be delivered by carers, nurses, dental care professionals or dentists ([Ekstrand 2013](#); [Zuluaga 2012](#)).

How the intervention might work

Increasing evidence suggests a link between colonisation of bacteria and respiratory infection and pneumonia. Gram-negative bacilli (GNB), such as *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Enterobacter* spp., have been suspected as causative pathogens of pneumonia ([Craven 1992](#); [Liapikou 2014](#)). Dependent and frail elderly patients have a higher detection rate of GNB in their oropharyngeal cavities ([Leibovitz 2003](#); [Mylotte 1994](#); [Palmer 2001](#)). [Sumi 2007](#) showed that in a group of 138 dependent elderly, a potential respiratory pathogen colonised the dental plaques of 89 individuals (64.5%). Aspiration of oropharyngeal fluid may cause translocation and colonisation of potential pulmonary pathogens in the lower respiratory tract and lungs ([Gibbons 1989](#); [Munro 2004](#); [Whittaker 1996](#)); the latter may cause aspiration pneumonia ([Van der Maarel-Wierink 2013](#)). Therefore, oral care measures that reduce the colonisation of bacteria could result in decreased risk of pneumonia.

The risk of NHAP might be reduced by measures that mechanically disrupt the biofilm (such as manual or electric toothbrushing) and/or by the use of oral antiseptics that may remain active on oral tissues for several hours after application, reducing the build-up of plaque. For example, chlorhexidine (CHX) gluconate is a broad-spectrum antiseptic agent that reduces both gram-positive and gram-negative bacteria associated with respiratory tract infection; it can remain chemically active on tissue for up to six hours ([Tantipong 2008](#)). Oral conditions of elderly people have been shown to be improved by rinsing with 0.12% CHX solution daily or weekly for six weeks ([DeRiso 1996](#); [Persseon 1991](#)). Similarly, manual oral brushing improves oral hygiene by reducing bacterial pathogen colonisation, and improves the swallowing reflex by stimulating gums ([Yamaya 2001](#); [Yoshino 2001](#)). With removal or disruption of the oral plaque, pneumonia could be significantly reduced ([Shi 2013](#); [Van der Maarel-Wierink 2013](#)). Such oral care measures can be used alone or in combination. For example, [Yoshida 2001](#) found that tooth-brushing after each meal and daily rinsing with 1% povidone-iodine in conjunction with weekly professional dental care significantly decreased the incidence of pneumonia in nursing homes.

Why it is important to do this review

[Cochrane Oral Health](#) undertook an extensive prioritisation exercise in 2014 to identify a core portfolio of clinically important review titles to be maintained in *The Cochrane Library* ([Worthington 2015](#)). The dental public health expert panel (<http://ohg.cochrane.org/priority-reviews>) identified this review as a priority title.

Although good oral hygiene has been shown to play an important role in maintaining the oral health and well-being of institutionalised people, oral care measures have generally been afforded low priority in nursing homes. In some guidelines, such as British Thoracic Society guidance on the prevention of CAP, oral hygiene is not mentioned ([Lim 2009](#)). Moreover, nurses have limited knowledge regarding provision of mouth care in general ([Frenkel 2000](#); [Jablonski 2005](#); [Pyle 2005](#)). [Chiba 2009](#) reported that 32.4% of caregivers hesitated to provide oral care measures, which indicated their lack of knowledge about oral hygiene but bespoke oral health education has been shown to have a positive effect on caregivers' knowledge and attitudes ([Charteris 2001](#); [Frenkel 2001](#); [Frenkel 2002](#); [Sjögren 2010](#)). A systematic review by [Kaneoka 2015](#) found that mechanical oral cleaning significantly reduced the risk of fatal pneumonia in residents in nursing homes. However, no other kinds of oral care measures were evaluated, and no Cochrane systematic review has focused on this issue.

We believe it is important to synthesise the evidence from randomised controlled trials of oral care interventions that have evaluated their effectiveness in reducing NHAP. Identifying effective oral care interventions is also an essential step towards improving oral health and quality of life for nursing home residents.

Objectives

To assess effects of oral care measures for preventing nursing home-acquired pneumonia in residents of nursing homes and other long-term care facilities.

Methods

Criteria for considering studies for this review

Types of studies

We will include parallel randomised controlled trials (RCTs) assessing the effects of oral care measures in residents of nursing and other long-term care facilities. We will include cluster-RCTs, for which the unit of randomisation is the care facility. We will exclude cross-over studies.

[Wu 2009](#) has shown that studies carried out in China often use the terminology of randomisation in a broader way than is usual in other countries, such as the UK. Therefore, we will contact the authors of trials written in Chinese to request a description of the randomisation method used and will include only those trials where participants' allocation to treatment is random.

We will include all trials of oral care in which the purpose of the study is to reduce the incidence of pneumonia. We will exclude trials that report only intermediate outcomes, such as dental plaque and gingivitis, without providing data on pneumonia.

We will not include studies for which the only available information is presented in an abstract with no record of a full-text publication; this would provide insufficient information to enable full assessment of risk of bias.

Types of participants

Residents of any age in nursing homes and other long-term care facilities (e.g. rehabilitation units, medical care facilities), irrespective of oral health status (e.g. edentulous or dentate, using dentures, having physical or intellectual disabilities, being mechanically ventilated, using alternative feeding route). We will exclude participants with pneumonia or respiratory infection at baseline.

Types of interventions

We will include studies comparing oral care measure(s) for prevention of NHAP versus no treatment, placebo, usual care or any other oral care measure(s) used to prevent NHAP (head-to-head studies).

- Intervention group: participant receives clearly defined oral care measure(s), such as professional oral care (dentists/dental hygienists/nurse-assisted tooth brushing), oral rinse or swab and topical decontamination with antiseptics, regardless of frequency, dosage or formulation.
- Control group: participant receives placebo or another specific oral care measure(s) or no treatment or usual care, including self-care.

Use of topical antibiotics in the intervention group only makes a study ineligible for inclusion in the review.

Types of outcome measures

Primary outcomes

- Incidence, incidence proportion or prevalence of NHAP of any severity (diagnosis of NHAP should be based on radiological results, clinical signs and symptoms, bacterial culture or some synthetic criteria ([American Thoracic Society 2005](#)))
- Mortality (pneumonia-associated death)
- Mortality (all-cause death)

Secondary outcomes

- Change in systemic antibiotic use: This parameter includes both number of participants who have used systemic antibiotics and length of antibiotic use
- Adverse reactions to the interventions (both local and systemic): This parameter refers to both numbers of participants who have adverse reactions and numbers of adverse reactions
- Incidence or prevalence of fever: This will include proportions of participants with fever higher than 37.8°C and prolonged length of febrile days
- Change in data on economics and quality of life
- Oral health indices, such as gingival index, plaque index, bleeding index, periodontal index, etc.

Search methods for identification of studies

Cochrane Oral Health's Information Specialist will conduct systematic searches for randomised controlled trials and for controlled clinical trials. We will place no restrictions on the language or date of publication when searching electronic databases.

Electronic searches

We will search the following databases.

- Cochrane Oral Health Group Trials Register.
- Cochrane Central Register of Controlled Trials (CENTRAL), in *The Cochrane Library*.
- MEDLINE Ovid (from 1946 onwards) (see [Appendix 1](#)).
- Embase Ovid (1980 onwards).
- Cumulative Index to Nursing and Allied Health Literature (CINAHL) EBSCO (from 1937 onwards).
- Chinese Biomedical Literature Database (1978 to present).
- China National Knowledge Infrastructure (1994 to present).

Searching other resources

We will search the following trials registries and databases.

- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (<http://clinicaltrials.gov/>).
- World Health Organization International Clinical Trials Registry Platform (<apps.who.int/trialsearch>).
- Sciencepaper Online.

We will search the reference lists of included studies and review articles for additional papers.

We will not perform a separate search for adverse effects of interventions. We will consider adverse effects described in included studies only.

Review authors will scan records from 19 Chinese dental and nursing journals (2000 to 2010), as listed below.

- *Chinese Journal of Stomatology.*
- *Journal of Practical Stomatology.*
- *Shanghai Journal of Stomatology.*
- *Journal of Clinical Stomatology.*
- *West China Journal of Stomatology.*
- *Journal of Modern Stomatology.*
- *Journal of Stomatology.*
- *Journal of Oral Science Research.*
- *Journal of Dental Prevention and Treatment.*
- *International Journal of Stomatology.*
- *Beijing Journal of Stomatology.*
- *Chinese Journal of Geriatric Dentistry.*
- *Chinese Journal of Nursing.*
- *Chinese Nursing Management.*
- *Nursing Journal of Chinese People's Liberation.*
- *Journal of Nursing Science.*
- *Chinese Journal of Practical Nursing.*
- *Chinese Nursing Research.*
- *Modern Clinical Nursing.*

Data collection and analysis

Selection of studies

Two review authors will independently screen the titles and abstracts retrieved from the searches. We will independently assess eligibility according to the inclusion criteria and will obtain full-text copies of studies that appear to meet the inclusion criteria, or when information in the title or the abstract is insufficient to permit a clear judgement of eligibility. We will resolve disagreements by discussion within the review author team.

From the retrieved full-text articles, we will discard studies that clearly do not meet the inclusion criteria and will record the reasons for exclusion in the 'Characteristics of excluded studies' tables.

Data extraction and management

Two review authors will carry out data extraction independently and will resolve disagreements by discussion.

We will create a data extraction form and will pilot it on three of the included studies. Two review authors will extract the following data independently and will record them in the 'Characteristics of included studies' tables.

- Trial design with inclusion and exclusion criteria, duration, setting and location of the study.
- Demographic data of participants and risk factors for NHAP, including proportions of non-oral feeding, dysphagia, xerostomia, tongue coating, mechanical ventilation and MRSA.
- Diagnostic criteria of CAP or NHAP: outcomes such as incidence of NHAP and mortality; oral, dental and respiratory health status before and after treatment; any adverse reactions potentially relevant to the interventions; and timing of measurement.
- Management and intensity of specific interventions.

If any important data are missing, we will contact the authors of the study to request it. We will collect data from duplicated studies and will analyse these findings as from a single study.

Assessment of risk of bias in included studies

Two review authors will independently carry out risk of bias assessments and will resolve disagreements by discussion. We will use the tool for risk of bias assessment of The Cochrane Collaboration ([Higgins 2011a](#)).

We will use seven domains to assess the risk of bias in included studies. For each domain, we will provide information from the trial report on what measures were taken to address possible bias and a judgement of 'low risk', 'unclear risk' and 'high risk' of bias. We present the seven domains and their descriptions below.

- Random sequence generation: selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence. We will consider low risk of bias only if the generation of random numbers is clearly described. We will consider an unclear description of random sequence generation with the phrase "stratified randomisation", "block randomisation scheme" or "randomisation completed by statistician or nurse" as having unclear risk of bias.
- Allocation concealment: selection bias (biased allocation to interventions) due to inadequate concealment of the allocation.
- Blinding of participants and personnel: performance bias due to knowledge of the allocated interventions by participants and personnel during the study. We will judge studies with completely different treatment arms when blinding was apparently impossible as having high risk of performance bias, even if details of blinding were not reported.

- Blinding of outcome assessment: detection bias due to knowledge of allocated interventions by outcome assessors.
- Incomplete outcome data: attrition bias due to quantity, nature or handling of incomplete outcome data.
- Selective reporting: reporting bias due to selective outcome reporting.
- Other bias: bias due to problems not covered elsewhere in the table, such as baseline imbalance, contamination and co-intervention.

We will classify the overall risk of bias in included studies as in the following table, and we will present this information as a 'Risk of bias' summary graphic.

Risk of bias	Interpretation	In outcome	In included studies
Low risk of bias	Plausible bias unlikely to seriously alter the results	Low risk of bias for all key domains	Most information is from studies at low risk of bias.
Unclear risk of bias	Plausible bias that raises some doubt about the results	Unclear risk of bias for one or more key domains	Most information is from studies at low or unclear risk of bias.
High risk of bias	Plausible bias that seriously weakens confidence in the results	High risk of bias for one or more key domains	The proportion of information from studies at high risk of bias is sufficient to affect interpretation of results.

Blinding of outcome assessment is less important for our objective outcomes all-cause mortality and pneumonia-associated mortality. We will consider this when assessing the quality of evidence on mortality in 'Summary of findings' tables.

Measures of treatment effect

We will treat the incidence proportion and prevalence of NHAP as dichotomous data (presence/absence) and the incidence of NHAP and mortality as time-to-event data when this has been reported, or as dichotomous data when time to event is not reported. The effect estimate for dichotomous outcomes will be the risk ratio (RR) with 95% confidence interval (CI).

For time-to-event data, we will express the treatment effect as a hazard ratio (HR) or a rate ratio. If HR is not reported, we will calculate the log HR and the standard error from available summary statistics or Kaplan-Meier curves, according to the methods proposed by [Parmar 1998](#), or we will request the data from study authors. If all measures fail, we will consider RR for time-to-event data presented as one-year survival, two-year survival and so on.

For continuous outcomes, when studies use the same scale, we will use mean values and standard deviations (SDs) to express the estimate of effect as mean difference (MD) with 95% confidence interval (CI). When different scales are used to measure the same outcome, we will use the standardised mean difference (SMD) with 95% CI as the effect measure.

We consider it likely that few participants will have adverse reactions; we will adopt the Peto odds ratio and the 95% CI as measures of treatment effect.

Unit of analysis issues

The unit of analysis adopted in this review will be the individual, and we will analyse only participant-level data. For cluster-RCTs analysed and reported by statistical measures that take clustering into account, we will use the reported effect estimate and the standard error. When clustering has been ignored, we will attempt to re-analyse study data using approximate analyses with an 'effective sample size.' We will calculate and use external estimates of the intracluster correlation coefficient (ICC) from similar studies (when available) to calculate the design effect ([Deeks 2011](#)).

Dealing with missing data

We will contact the first and corresponding authors of the study to request missing details. If these are not forthcoming, we will use standard methods provided in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011b](#)) to extract approximate summary statistics from primary studies.

Assessment of heterogeneity

For each meta-analysis, we will assess clinical heterogeneity by examining characteristics of studies and similarities between types of participants, interventions and outcomes. We will use Cochran's Q test to determine the presence of statistical heterogeneity at a significance level of 0.1. We will use the I^2 statistic (plus 95% confidence interval) to quantify the degree of statistical heterogeneity as follows.

- 0% to 40% may indicate slight heterogeneity.
- 30% to 60% may indicate moderate heterogeneity.
- 50% to 90% may indicate substantial heterogeneity.
- 75% to 100% may indicate very substantial heterogeneity.

If substantial or very substantial heterogeneity exists, we will provide a narrative description of the results instead of pooling data.

Assessment of reporting biases

To assess whether results are influenced by publication bias, we will construct a funnel plot to assess asymmetry (assuming we have at least 10 studies). We will use tests for funnel plot asymmetry, such as Egger's methods for continuous data ([Egger 1997](#)), and Begg's methods for dichotomous and time-to-event data ([Begg 1994](#)).

Data synthesis

We will undertake meta-analysis only when studies of similar comparisons report the same outcomes. Our general approach to evidence synthesis will be to use a random-effects model. With this approach, the CI for the average intervention effect is wider than the value that would be obtained if a fixed-effect approach were used, leading to a more conservative interpretation.

In an additional table, we will report the results from studies not suitable for inclusion in meta-analysis.

Subgroup analysis and investigation of heterogeneity

To decide whether intervention effect is consistent across participants or interventions with specific characteristics, we will conduct subgroup analyses. The main subgroup analysis will include types of oral care measures. We will also consider study design (cluster or parallel), length of follow-up, characteristics of participants (dentate or edentulous, with or without physical/intellectual disabilities), characteristics of oral care measures (e.g. concentrations of the solutions used, mechanical or topical intervention) and diagnostic criteria of the outcome (clinical or radiological).

Sensitivity analysis

To test stability of judgements made during the review process, we will undertake sensitivity analyses that include only studies at low risk of bias or only studies using intention-to-treat (ITT) analysis.

Assessing the quality of the evidence

We will assess the quality of the body of evidence for comparisons of clinical importance, such as different oral care drugs versus placebo; oral care measures versus no treatment; and nurse/dentist-aided oral measures versus confrontational oral measures. At least two of the review authors, with no conflicts of interest, will use GRADE criteria and GRADE profiler software to independently judge the quality of the evidence ([Atkins 2004](#); [Guyatt 2008](#); [Schünemann 2011](#)). Evidence from randomised controlled trials is initially judged to be of high quality, but our confidence in the body of evidence may be decreased owing to study limitations (risk of bias), indirectness of the evidence, heterogeneity, imprecision of effect estimates and risk of publication bias (see above [Assessment of reporting biases](#)). We will classify the quality of a body of evidence into one of four categories: high, moderate, low or very low ([Guyatt 2008](#)).

Summarising findings

We will present all important comparisons and primary outcomes in the 'Summary of findings' (SoF) table(s), together with illustrative comparative risks (which will be based on epidemiological data on the prevalence of NHAP if robust data are available, or will be based on the included studies); relative effect; numbers of participants and studies involved; quality of the evidence; and related comments. We will also include information pertaining to adverse events.

Results

Description of studies

Results of the search

Included studies

Excluded studies

Risk of bias in included studies

Allocation (selection bias)

Blinding (performance bias and detection bias)

Incomplete outcome data (attrition bias)

Selective reporting (reporting bias)

Other potential sources of bias

Effects of interventions

Discussion

Summary of main results

Overall completeness and applicability of evidence

Quality of the evidence

Potential biases in the review process

Agreements and disagreements with other studies or reviews

Authors' conclusions

Authors' conclusions

Implications for practice

Implications for research

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Contributions of authors

Chunjie Li and Qi Zhang wrote and revised the protocol. Linda Ng, Ian Needleman and Jie Lin were involved in revising the protocol. Tanya Walsh revised the protocol and provided important guidance.

Declarations of interest

Chunjie Li: none known

Qi Zhang: none known

Linda Ng: none known

Ian Needleman has received funding for lectures and research from industry related to oral hygiene products and prevention of ventilator-associated pneumonia. Professor Needleman is an editor with Cochrane Oral Health.

Tanya Walsh: none known. Tanya Walsh is an editor with Cochrane Oral Health.

Jie Lin: none known

Differences between protocol and review

Published notes

Characteristics of studies

Characteristics of included studies

Footnotes

Characteristics of excluded studies

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

Additional tables

References to studies

Included studies

Excluded studies

Studies awaiting classification

Ongoing studies

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Data and analyses

Figures

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Feedback

Appendices

1 MEDLINE via Ovid Search Strategy

1. exp Preventive dentistry/
2. exp Dentifrices/
3. Mouthwashes/

4. Oral health/
5. Anti-infective agents, local/
6. Cetylpyridinium/
7. Chlorhexidine/
8. Povidone-iodine/
9. ((oral or mouth or dental) adj3 (care or hygiene or health)).ti,ab.
10. (care adj3 teeth).ti,ab.
11. (denture\$ adj5 (clean\$ or clens)).ti,ab.
12. (plaque adj3 (control\$ or remov\$)).ti,ab.
13. (mouthwash\$ or mouth-wash\$ or mouthrins\$ or mouth-rins\$ or oral-rins\$ or toothpaste\$ or "tooth paste\$" or dentifrice\$ or toothbrush\$ or "tooth brush\$" or fluorid\$ or chlorhexidine or betadine\$ or triclosan or cepacol or Corsodyl or Peridex or Hibident or Prexidine or Parodex or Chlorexil or Peridont or Eludril or Peroxidin or Chlorohex or Savacol or Periogard or Chlorhexamed or Nolvasan or Sebidin or Tubulicid or hitbitane).ti,ab.
14. (antiseptic\$ or antiinfect\$ or "local microbicide\$" or "topical microbicide\$").ti,ab.
15. ((oral or mouth or dental) adj5 (foam\$ or gel\$)).ti,ab.
16. (floss\$ or "interdental brush\$" or (tooth adj5 clean\$) or (teeth adj5 clean\$) or (denture\$ adj5 hygien\$) or (tongue\$ adj5 scrap\$)).ti,ab.
17. "professional oral health care".ti,ab.
18. or/1-17
19. exp Pneumonia/
20. pneumonia.ti,ab.
21. ("gram negative bacilli" or "pseudomonas aeruginosa" or "pseudomonas aruginosa" or enterobacter\$ or pneumonitis or "pulmonary inflammation" or "lung inflammation").ti,ab.
22. or/19-21
23. 18 and 22

The above subject search will be linked to the Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomised trials in MEDLINE: sensitivity-maximising version (2008 revision) as referenced in Chapter 6.4.11.1 and detailed in box 6.4.c of *The Cochrane Handbook for Systematic Reviews of Interventions*, Version 5.1.0 [updated March 2011] ([Lefebvre 2011](#)).

1. randomized¬controlled¬trial.pt.
2. controlled¬clinical¬trial.pt.
3. randomized.ab.
4. placebo.ab.
5. drug¬therapy.fs.
6. randomly.ab.
7. trial.ab.
8. groups.ab.
9. or/1-8
10. exp¬animals/¬not¬humans.sh.
11. 9¬not¬10