Associations Between Periodontal Disease and Risk for Nosocomial Bacterial Pneumonia and Chronic Obstructive Pulmonary Disease. A Systematic Review

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† Health Sciences Library.

Background: Several recent studies provide evidence that the oral cavity may influence the initiation and/or the progression of lung diseases such as pneumonia and chronic obstructive pulmonary disease (COPD).

Rationale: Studies have shown that poor oral hygiene and periodontal disease may foster colonization of the oropharyngeal region by respiratory pathogens, particularly in hospital or nursing home patients. If aspirated, these pathogens can cause pneumonia, one of the most common respiratory infections, especially in institutionalized subjects. Other cross-sectional epidemiologic studies point to an association between periodontal disease and COPD. This systematic review examines the literature to determine if interventions that improve oral hygiene reduce the rate of pneumonia in high-risk populations.

Focused Question: Do periodontal diseases or other indicators of poor oral health influence the initiation/progression of pneumonia or other lung diseases?

Search Protocol: MEDLINE, pre-MEDLINE, MEDLINE Daily Update, and the Cochrane Controlled Trials Register were searched to identify published studies that related variables associated with pneumonia and other lung disease to periodontal disease. Searches were performed for articles published in English from 1966 through March 2002.

Inclusion criteria: Randomized controlled clinical trials (RCTs), longitudinal, cohort, and case-control studies were included. Study populations included patients with any form of pneumonia or chronic obstructive pulmonary disease (COPD) and periodontal disease, as measured by assessments of gingival inflammation, probing depth, clinical attachment level, and/or radiographic bone loss, or oral hygiene indices.

Exclusion criteria: Limited to studies of humans.

Data Collection and Analysis: The summary statistics used to analyze the RCTs included weighted mean differences in rates of disease between control and intervention groups. For cohort studies that measured differences in rates of disease between groups with and without oral disease, weighted mean differences, relative risks, or odds ratios were compared. A meta-analysis was performed on the 5 intervention studies to determine the relationship between oral hygiene intervention and rate of pneumonia in institutionalized patients.

Main Results
Of the initial 1,688 studies identified, 36 satisfied all inclusion criteria and were read. Of these, 21 (11 case-control and cohort studies [study population 1,413] and 9 RCTs [study population 1,759]) were included in the analysis.

1. A variety of oral interventions improving oral hygiene through mechanical and/or topical chemical disinfection or antibiotics reduced the incidence of nosocomial pneumonia by an average of 40%.
2. Several studies demonstrated a potential association between periodontal disease and COPD.

Reviewers’ Conclusions
1. Oral colonization by respiratory pathogens, fostered by poor oral hygiene and periodontal diseases, appears to be associated with nosocomial pneumonia.
2. Additional large-scale RCTs are warranted to provide the medical community with further evidence to institute effective oral hygiene procedures in high-risk patients to prevent nosocomial pneumonia.
to CAP, the microbiology of nosocomial pneumonia is

tions, with a mortality rate as high as 25%. In contrast
accounts for 10% to 15% of all hospital-acquired infec-
and nursing home patients. Nosocomial pneumonia

viduals such as hospitalized patients admitted to ICUs

Haemophilus influenzae

the oropharynx, such as
caused by aspiration of bacteria that normally reside in

from 12% in the general population to 40% in those

cases that require hospitalization, the mortality rate ranges

geal secretions and intubation are among the best pre-

dictors for pneumonia in the elderly.6

Other conditions predisposing to aspiration include
stroke, Parkinson’s disease, alcohol abuse, and seda-
tive use.5 Multiple defense mechanisms operate within
the healthy respiratory tract to eliminate aspirated bac-
teria from the lower airway, but their effectiveness can
be impaired by a variety of conditions such as malnu-
rition; smoking; chronic obstructive pulmonary disease
(COPD, which includes bronchitis and emphysema);
diabetes; corticosteroid use; and endotracheal or naso-
gastric intubation. Difficulty in coping with oropharyn-
geal mucosa by potential respiratory pathogens,

aspiration of the colonized pathogens into the lower air-

pneumoniae, Escherichia coli, and Enterobacter species.

Rationale

It has become apparent in recent years that the oral
cavity may be an important reservoir for bacterial
pathogens that cause lung disease. The incidence of
respiratory pathogen oropharyngeal colonization by
respiratory pathogens appears to be more common in
patients with teeth or dentures than in edentulous
patients who do not wear dentures.8 Diminished sali-
vation and salivary pH may promote colonization by
respiratory pathogens; these conditions occur in ill
patients and in those receiving various medications.8
Oral colonization by respiratory pathogens is common
in institutionalized patients, especially those admitted
to hospital ICUs and in the elderly who are debilitated,
hospitalized, or in a nursing home.9-11 Poor oral hygiene
and periodontal disease may foster respiratory pathogen
oropharyngeal colonization, and patients who are hos-
pitalized or reside in a nursing home often have poorer
oral hygiene than community-dwelling individuals.11
Finally, several oral interventions that improve oral
hygiene result in a reduction in the rate of pneumonia
in high-risk subjects (see below).

Focused Question

We attempted to answer the following focused ques-
tion: “Do periodontal disease or other indicators of
poor oral health influence the initiation/progression of
pneumonia or other lung diseases?”

Search Protocol

Data Sources and Search Strategy

The search strategy was defined to include randomized
controlled clinical trials (RCTs), longitudinal, cohort
and case-control studies.

Search terms: Searches were run by one of the
reviewers (RB) using Ovid Search software using med-
ical subject headings (MeSH terms) in MEDLINE (1966
to April 2002), and MEDLINE Daily Update through first
quarter 2002. All MeSH terms employed were exploded
to expand retrieval to those records that were assigned
the more narrow related MeSH term. The Cochrane Con-
trolled Trials Register and Pre-MEDLINE required use of
key words (both American and British spellings). All
searches included the term “human.” We also searched
reference lists of previously published review papers to
identify additional articles.

MeSH terms: Lung diseases, or respiratory tract infec-
tions, or respiratory system, or intensive care.

Oral conditions: Periodontal diseases, or tooth dis-
ases, or dental plaque index.
Key words: Lung, or pneumonia, or respiratory, or intensive care.
Oral conditions: Periodontal disease, or periodontitis, or periodontal attachment loss, or alveolar bone loss, or dental plaque, or oral hygiene, or chlorhexidine.

Inclusion criteria: The types of participants recruited for each study included those with pneumonia or COPD (i.e., bronchitis and/or emphysema). Oral conditions considered included periodontal disease as measured by assessments of gingival inflammation, probing depth, clinical attachment loss, and/or radiographic bone loss and oral hygiene indices. The search strategy also considered studies that tested the effect of periodontal or oral hygiene intervention on the initiation or progression of pneumonia or COPD.

Exclusion criteria: The search was limited to human studies.

Outcomes: The following outcome measures were assessed:
1. Primary outcome: reduced rate of pneumonia or other lung diseases.
4. Adverse outcomes: intraoral adverse effects, increased rate of pneumonia.

Data Collection and Analysis
Titles and abstracts of articles obtained using the above described search strategy were screened by two independent readers (FAS and SP) and checked for agreement. The full text of the articles judged by title and abstract to be relevant (by either FAS or SP) were read and independently assessed against the stated inclusion criteria. These studies included patients with pneumonia and/or colonization of the oral cavity by target potential respiratory pathogens or COPD. Intervention studies included were those that tested interventions that improved oral hygiene or periodontal status.

For analysis of RCTs, summary statistics considered included the weighted mean difference in rates of disease compared between control and interven-

Table 1.
Descriptive Epidemiological/Microbiological Studies on Oral Health and Nosocomial Pneumonia

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Population</th>
<th>Oral Assessment</th>
<th>Pulmonary Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chabrand et al.</td>
<td>38 hospitalized patients with bacterial pneumonia,</td>
<td>Clinical periodontal status, panoramic radiological</td>
<td>Bacterial pneumonia, positive blood culture, bacterial/positive</td>
</tr>
<tr>
<td>1986</td>
<td>33 controls hospitalized in the same facility but not</td>
<td>status, number of carious teeth, dental plaque, calculus.</td>
<td>pleural puncture or transtracheal puncture, or (10^8) bacteria in sputum.</td>
</tr>
<tr>
<td></td>
<td>not presenting infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scannapieco et al.</td>
<td>34 noncardiac patients in VA ICU, 25 control outpatients in preventive dentistry clinic.</td>
<td>Oral hygiene status, cultures of dental plaque and buccal mucosa.</td>
<td>None</td>
</tr>
<tr>
<td>1992</td>
<td></td>
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</tr>
<tr>
<td>Trelor et al.</td>
<td>16 intubated patients from medical ICU, no controls.</td>
<td>Oral examination (entry and every other day), plaque index, gingival index, oropharyngeal cultures.</td>
<td>Pneumonia diagnosis: pathogenic bacteria in tracheobronchial secretions, new infiltrates in chest radiographs. Leukocytosis, fever &gt;38.3°C, purulent tracheobronchial secretions.</td>
</tr>
<tr>
<td>1995</td>
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</tr>
<tr>
<td>Bonten et al.</td>
<td>141 adult, mechanically ventilated patients from ICU.</td>
<td>Colonization of enteric Gram-negative bacteria (EGB) and Pseudomonas aeruginosa of oropharynx and trachea.</td>
<td>Temp. &gt;38°C or &lt;35°C, blood leukocytosis/leukopenia, positive culture from tracheal aspirates. Persistent or progressive infiltrate on chest radiograph. Positive broncho-alveolar lavage (BAL), blood culture, or pleural fluid.</td>
</tr>
<tr>
<td>1996</td>
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</tr>
</tbody>
</table>
tion groups. For cohort studies that measured differences in rates of disease between groups with oral disease and groups without oral disease, weighted mean differences, relative risks or odds ratios were compared.

The data from intervention trials were analyzed using a method that was first described by Mantel and Haenszel. This method was later used for a wider class of problems and has been adapted for meta analysis. The results were confirmed by Peto’s method for combining odds ratio.

**Ranking of Studies**

Included papers were graded according to previously reported classifications.

1. Systematic review of randomized controlled clinical trials. RCTs with narrow confidence intervals.
2. Randomized controlled clinical trial. Low quality systematic review.

**RESULTS AND DISCUSSION**

Following the described search strategy, MEDLINE searching yielded 581,756 lung articles, and 115,752 articles including the oral variables. Combining these revealed 1,688 titles. The titles and abstracts were read and the full texts of 35 articles were reviewed, with 24 articles identified as relevant to the objective of this review.

**PNEUMONIA (Table 1)**

<table>
<thead>
<tr>
<th>Major Findings or Odds Ratio (OR) or Risk Ratio (RR)</th>
<th>Conclusions</th>
<th>Study Ranking</th>
</tr>
</thead>
<tbody>
<tr>
<td>No significant differences in the oral status/dental infections between study group of pneumonia patients and non-pneumonia controls.</td>
<td>Dental infections do not affect the formation of bronchopulmonary infections. The controls did not resemble a healthy population which limits the importance of the results.</td>
<td>4</td>
</tr>
<tr>
<td>Oral hygiene of medical ICU patients was poor; mean plaque score was significantly higher than in outpatients (P &lt;0.005). ICU subjects more often colonized by potential respiratory pathogens than the outpatients.</td>
<td>Dental plaque may be an important reservoir for respiratory pathogens in ICU patients.</td>
<td>4</td>
</tr>
<tr>
<td>7/16 (44%) demonstrated pneumonia-associated x-ray changes. No clear relationship between oral conditions and pneumonia was presented.</td>
<td>Systematic oropharyngeal assessment in critically ill orally intubated patients may prevent more serious infections.</td>
<td>5</td>
</tr>
<tr>
<td>Hazard ratio 4.5 for ventilator-associated pneumonia caused by EGB when oropharyngeal colonization with EGB present on admission.</td>
<td>Duration of ventilation and colonization of the upper respiratory tract are the most important risk factors for VAP caused by EGB or Pseudomonasae.</td>
<td>4</td>
</tr>
</tbody>
</table>

(continued)
### Table 1. (continued)

**Descriptive Epidemiological/Microbiological Studies on Oral Health and Nosocomial Pneumonia**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Population</th>
<th>Oral Assessment</th>
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<tbody>
<tr>
<td>Fourrier et al.24</td>
<td>57 ICU patients.</td>
<td>Disease-missing-filled teeth (DMFT) index, dental plaque score, colonization of dental plaque. Edentulous subjects with no prosthesis were excluded.</td>
<td>Blood cultures, BAL. Pneumonia diagnosis: Temp. &gt;38°C or &lt;36°C, infiltrates on chest radiograph, leukocytosis or leukopenia, positive cultures from tracheal aspirate and BAL.</td>
</tr>
<tr>
<td>Terpenning et al.8</td>
<td>134 geriatric patients (34 inpatients, 53 long-term care patients, 47 outpatients). First year of a 5-year study.</td>
<td>Xerostomia, caries, PD, salivary IgA.</td>
<td>Aspiration pneumonia diagnosis: temp &gt;2°C above baseline, clinical deterioration, elevated WBC count, infiltrates on chest radiograph.</td>
</tr>
<tr>
<td>Mojon et al.25</td>
<td>302 nursing home residents, no controls.</td>
<td>Oral examination, periodontal index derived from CPTN.</td>
<td>Incidence of bronchopulmonary infection.</td>
</tr>
<tr>
<td>Langmore et al.26</td>
<td>189 male outpatients, inpatients, and nursing home patients; &gt;60 years old. 4-year follow-up.</td>
<td>Oral/dental status, plaque index, plaque N-benzoyl-DL-arginine-2-naphthylamide score, papillary bleeding score, PD score, etc.</td>
<td>Pneumonia diagnosis: elevated WBC count, fever (temp &gt;100.5°F), new infiltrate on the chest radiograph.</td>
</tr>
<tr>
<td>Preston et al.27</td>
<td>28 elderly patients during acute medical admission.</td>
<td>Clinical oral examination: soft tissues and dentures. Oral (palatal) swab: quantitative bacterial counts and aerobic Gram-negative bacilli (GNB).</td>
<td>Patients admitted to ICU due to cardiac or respiratory illness or for investigation of suspected gastrointestinal problems. No further explanation about the groups.</td>
</tr>
<tr>
<td>Russell et al.11</td>
<td>28 chronic care nursing home residents, 30 dental clinic outpatients; &gt;65 years; gender- and race-matched groups. Cross-sectional study.</td>
<td>Plaque score on tooth, denture, oral mucosal surfaces. Culture of dental plaque.</td>
<td>A history of bronchitis, pneumonia in the preceeding 6 months.</td>
</tr>
<tr>
<td>Terpenning et al.28</td>
<td>358 veterans age 55 and older. Outpatient clinics, inpatient wards, nursing home of VA Medical Center. Longitudinal study with retrospective data.</td>
<td>Personal oral hygiene, dental examination, IgA antibodies from saliva, cultures of saliva, throat, and dental plaque.</td>
<td>Demographic and medical data obtained retrospectively from last 8 years.</td>
</tr>
</tbody>
</table>
### Table 1. (continued)

**Descriptive Epidemiological/Microbiological Studies on Oral Health and Nosocomial Pneumonia**

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<tbody>
<tr>
<td>RR 9.6 when dental plaque colonization on days 0 and 5 associated with the occurrence of nosocomial pneumonia and bacteremia. Mean dental DMFT index did not change during the ICU stay.</td>
<td>A positive dental plaque culture was significantly associated with subsequent nosocomial infections.</td>
<td>5</td>
</tr>
<tr>
<td>27% of dentate inpatients and 19% of dentate long-term care patients developed aspiration pneumonia. Only 2/38 edentulous patients developed pneumonia.</td>
<td>An association between dentate status and pneumonia was noted.</td>
<td>4</td>
</tr>
<tr>
<td>RR 1.7 of respiratory tract infection (RTI) in dentate subjects compared with edentulous subjects. Dentate subjects with a history of RTI had a higher plaque score (P = 0.02) than no-RTI patients. RR 2.5 of having RTI with selected oral disorders such as calculus and generalized gingivitis.</td>
<td>Improvement of the patients’ oral hygiene may reduce the risk of RTI among dependent elderly subjects.</td>
<td>4</td>
</tr>
<tr>
<td>Number of decayed teeth, frequency of brushing teeth, and being dependent for oral care were significantly associated with pneumonia. OR 2.828 (P = 0.0338) prediction for “dependent for oral care” in all patients.</td>
<td>Some predictive oral risk factors for aspiration pneumonia were found but results are based only on male population.</td>
<td>4</td>
</tr>
<tr>
<td>12/28 (43%) of subjects had intraoral GNB.</td>
<td>An oropharyngeal GNB colonization may be associated with infections such as aspiration pneumonia. However, study does not draw a clear correlation between the colonization results and pneumonia.</td>
<td>5</td>
</tr>
<tr>
<td>Plaque scores on teeth and dentures were significantly higher in the chronic care facility (CCF) patients than in outpatient controls (PI 2.3 vs. 1.2 and denture plaque 1.4 vs. 0.3). 14.3% of CCF subjects were colonized with respiratory pathogens in dental plaque vs. 0% of outpatients.</td>
<td>Deficient dental plaque control and the presence of COPD may be related to respiratory pathogen colonization of dental plaque in chronic care facility residents.</td>
<td>4</td>
</tr>
<tr>
<td>Risk factors for aspiration pneumonia: Dentate patients; number of decayed teeth OR = 1.2, P. gingivalis in dental plaque OR = 4.2, S. aureus in saliva OR = 7.4. Dentate and edentulous patients; S. aureus in saliva OR = 8.3. No significant association: plaque index, gingival bleeding score.</td>
<td>Supports the significance of oral and dental factors in aspiration pneumonia incidence.</td>
<td>4</td>
</tr>
</tbody>
</table>
pneumonia with 33 hospitalized controls not presenting with infection. They found no significant differences in the oral status/dental infections between study group of pneumonia patients and non-pneumonia controls.

Scannapieco et al. compared oral hygiene and the rate of dental plaque and/or buccal mucosal colonization by potential respiratory pathogens in ICU patients with age- and gender-matched outpatients upon their initial visit to a dental school clinic. The mean Silness and Löe plaque score was significantly higher in the ICU patients than in the dental subjects (1.9 versus 1.4, respectively, \( P < 0.005 \)). Colonization of dental plaque and/or oral mucosa by potential respiratory pathogens was found in 65% of the ICU patients, but in only 16% of the preventive dentistry clinic patients (\( P < 0.005 \)). The potential respiratory pathogens identified in the ICU patients included \( S. \) aureus, \( P. \) aeruginosa, and a number of different enteric Gram-negative bacteria. Several patients had oropharyngeal colonization by 2 or more potential pathogens. Oral colonization by respiratory pathogens was positively associated with the use of antibiotics.

Treloar et al. provided an oral examination (at entry to the study and every other day thereafter), plaque index, gingival index, and oropharyngeal cultures for 16 intubated patients admitted to a medical ICU. No control subjects were assessed. Pneumonia was diagnosed by quantitation of pathogenic bacteria in tracheobronchial secretions, and new infiltrates on chest radiographs. While 7 of 16 subjects (44%) demonstrated pneumonia-associated x-ray changes, no clear relationship was noted between oral conditions and pneumonia diagnosis.

Bonten et al. reported on the colonization of the oropharynx and trachea by enteric Gram-negative bacteria and \( Pseudomonas \) species in 141 adult, mechanically ventilated ICU patients. They attempted to correlate bacterial colonization with signs and symptoms of lung infection. They found a significant association between potential respiratory pathogen colonization of the oropharynx and ventilator-associated pneumonia (VAP).

Fourrier et al. studied the association of oral health status including dental caries, dental plaque, and colonization of dental plaque by respiratory pathogens, and onset of pneumonia in 57 ICU patients. They reported that the relative risk for pneumonia was increased 9.6-fold when the dental plaque was colonized by a pathogen between days 0 and 5 following ICU admission. Furthermore, they found that the pathogen causing pneumonia first colonized the dental plaque.

**Nursing home and elderly patients.** Terpenning et al. assessed 134 geriatric patients (34 inpatients, 53 long-term care patients, and 47 outpatients). They assessed oral conditions such as xerostomia, caries, periodontal disease, and salivary IgA levels. These were compared to diagnosis of aspiration pneumonia based upon body temperature >2°C above baseline, clinical deterioration,

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Population</th>
<th>Randomization</th>
<th>Appropriate Concealment</th>
<th>Outcome Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pugin et al.³⁰ 1991</td>
<td>52 ICU patients: 25 in test group, 27 in placebo group.</td>
<td>Yes</td>
<td>Unclear</td>
<td>CPIS (clinical pulmonary infection score) based on rectal temp., blood leukocyte count and number of band forms, purulence and quantity of tracheal secretions.</td>
</tr>
<tr>
<td>DeRiso et al.³¹ 1996</td>
<td>Cardiovascular ICU subjects undergoing heart surgery; 173 subjects in test group, 180 in placebo control group. All received systemic antibiotics.</td>
<td>Yes</td>
<td>Yes</td>
<td>Overall nosocomial infection rate, upper and lower respiratory infection rates, in-hospital mortality rate. Pneumonia diagnosis: progressing pulmonary infiltrate, fever, leukocytosis, purulent tracheobronchial secretions.</td>
</tr>
</tbody>
</table>
elevated white blood cell count, and infiltrates on chest radiograph. They noted that 27% of dentate inpatients and 19% of dentate long-term care patients developed aspiration pneumonia, while only 5% of the edentulous patients developed pneumonia.

A study of the relationship of oral health status and lung infection in 302 nursing home residents was reported by Mojon et al. 25 They found an increased risk for respiratory tract infection in subjects with teeth in comparison to edentulous subjects.

Langmore et al. 26 studied 189 male outpatients, hospital inpatients and nursing home patients over 60 years of age. They found significant associations between pneumonia and the number of decayed teeth, the frequency of brushing teeth, and being dependent for oral care.

Preston et al. 27 found the dental plaque of 12 of 28 (43%) elderly patients recently admitted to a hospital were colonized by Gram-negative bacillary pathogens, suggesting the possibility that dental plaque may serve as a reservoir for lung infections.

Russell et al. 11 compared 28 chronic care nursing home residents with 30 dental clinic outpatients over 65 years of age, matched for gender and race. They found that the dental plaque scores were significantly higher in the nursing home residents than in the outpatient controls, and that 14.3% of chronic care subjects showed dental plaque colonization with respiratory pathogens compared to none of the control outpatients.

Terpenning et al. 28 followed 358 veterans age 55 and older. They found that risk for aspiration pneumonia was elevated: in dentate subjects; in subjects with carious teeth; when the periodontopathogen *Porphyromonas gingivalis* was detected in dental plaque; and when the respiratory pathogen *Staphylococcus aureus* was detected in saliva.

**Oral Intervention Trials to Prevent Pneumonia (Table 2)**

**Hospitalized patients.** The findings reviewed above suggest that the oral cavity may serve as a reservoir for lower airway infection, especially in institutionalized subjects. This observation further suggests that improved oral hygiene could reduce or eliminate respiratory pathogens from the mouth and thus prevent the onset of serious respiratory infection in vulnerable subjects. Although oral hygiene measures are a component of nursing care, implementation of such measures is difficult in some patients, such as those who are orally intubated. However, several intervention studies show that improved oral hygiene measures can reduce the incidence of pneumonia.

### Table 2. (continued)

**Intervention Studies of Oral Cleaning and Pneumonia**

<table>
<thead>
<tr>
<th>Oral Intervention</th>
<th>Results (placebo versus control)</th>
<th>Conclusion/Comments</th>
<th>Study Ranking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systematic sanitation (regular cleaning) of the oral cavity, Control: regular oral hygiene.</td>
<td>Children whose oral cavities were systematically sanitized experienced active periods of chronic pneumonia 1.7 times less frequently than children in the control group.</td>
<td>No clear explanation of the oral cleaning method was provided.</td>
<td>1</td>
</tr>
<tr>
<td>Nonabsorbable PNV solution (150 mg of polymyxin B sulfate, 1 g of neomycin sulfate, 1 g of vancomycin hydrochloride per 60 mL of 5% dextrose) or placebo solution 5% dextrose applied to retropharynx every 24 hours, swallowed.</td>
<td>Tracheobronchial colonization by Gram-negative bacteria and <em>S. aureus</em>, as well as pneumonia, occurred less frequently (<em>P = 0.0001</em>) in the PNV group than in the placebo group. Topical oropharyngeal antibiotic application lowered the rate of VAP by a factor 5.</td>
<td>In critically ill patients, topical oropharyngeal antibiotics lowered the rate of ventilator-associated pneumonia and decreased the requirement for IV antibiotics.</td>
<td>3</td>
</tr>
<tr>
<td>0.12% chlorhexidine (CHX) oral rinse (with 11.6% ethanol), 0.5 oz for 30 seconds 2x a day; Placebo (with EtOH 3.2%) 0.5 oz for 30 seconds 2x a day.</td>
<td>69% reduction in the incidence of total respiratory tract infections in the CHX-group (<em>P &lt; 0.05</em>). A reduction in mortality in the CHX-group (1.16% vs. 5.56%).</td>
<td>CHX oral rinse reduces the total nosocomial respiratory infection rate and the use of nonprophylactic systemic antibiotics in patients undergoing heart surgery.</td>
<td>4</td>
</tr>
</tbody>
</table>

(continued)
The first study to assess an oral intervention in the prevention of respiratory infection was reported by Kuriakona in 1977. A group of 295 children (173 experimental and 123 control) with chronic pneumonia were assessed. Respiratory symptoms and the incidence of cold, influenza, and active periods of chronic pulmonary disease were assessed over a 1-year period. The test group received “systematic sanitation” (regular cleaning) of the oral cavity, while the control group received normal oral hygiene (no clear description of the oral cleaning methods were provided). Children whose oral cavities were systematically sanitized experienced active periods of chronic pneumonia 1.7 times less frequently than children in the control group.

Pugin et al. studied 52 ICU patients; 25 in a test group received topical nonabsorbable PNV solution (150 mg of polymyxin B sulfate, 1 g of neomycin sulfate, 1 g of vancomycin hydrochloride in 60 ml of 5% dextrose) and 27 in a placebo group received topical 5% dextrose. Both treatments were applied to the retropharynx every 24 hours and then swallowed. The antibiotic solutions reduced tracheobronchial colonization by Gram-negative respiratory pathogens and *S. aureus*, and the rate of pneumonia by a factor of 5 when compared to the control treatment.

The effectiveness of oral topical chlorhexidine gluconate (CHX) to reduce pneumonia was examined in patients placed on mechanical ventilation after car-

### Table 2. (continued)

<table>
<thead>
<tr>
<th>Reference</th>
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<th>Randomization</th>
<th>Appropriate Concealment</th>
<th>Outcome Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fourrier et al.22,</td>
<td>60 ICU patients requiring mechanical ventilation. 30 patients: 30 controls.</td>
<td>Yes</td>
<td>No</td>
<td>Pneumonia diagnosis: temp. &gt;38°C or &lt;36°C; presence of infiltrates in chest radiographs, leukocytosis or leukopenia, positive culture from tracheal aspirate and/or broncho-alveolar lavage.</td>
</tr>
<tr>
<td>2000</td>
<td></td>
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</tr>
<tr>
<td>Genuit et al.33,</td>
<td>95 surgical ICU patients requiring mechanical ventilation. 39 historic controls from hospital databases. Prospective study.</td>
<td>No</td>
<td>No</td>
<td>Pneumonia documented by bacteriologic etiology via endotracheal suction sputum culture.</td>
</tr>
<tr>
<td>2001</td>
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<tr>
<td>Bergmans et al.34,</td>
<td>Test group: 87 patients. Placebo group: 78 patients. Control group: 61 patients. Prospective study from 3 ICUs over 2-year period.</td>
<td>Yes</td>
<td>Yes</td>
<td>Pneumonia diagnosis: new infiltrate on chest x-ray; temp. &gt;38°C or &lt;36°C; leukocytosis or leukopenia, positive quantitative culture from BAL or protected specimen brush, or a positive culture of blood or pleural fluid.</td>
</tr>
<tr>
<td>2001</td>
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</tr>
<tr>
<td>Yoneyama et al.35,</td>
<td>46 elderly nursing home patients.</td>
<td>No</td>
<td>No</td>
<td>Respiratory infection: cough and/or sputum, temp. &gt;37.5°C; CRP; WBC count; alpha-globulin. Sputum culture.</td>
</tr>
<tr>
<td>1996</td>
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</tr>
<tr>
<td>Yoneyama et al.36,</td>
<td>366 elderly residents from 11 nursing homes. Test group 184, controls 182. Follow-up 2 years.</td>
<td>Yes</td>
<td>Unclear</td>
<td>New pulmonary infiltrate in chest radiograph and cough or temp &gt;37.8°C or subjective dyspnea.</td>
</tr>
<tr>
<td>2002</td>
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</table>
diac surgery. Patients were randomly assigned to receive either 0.12% CHX (treatment) or vehicle alone (placebo), applied twice daily to buccal, pharyngeal, gingival, tongue, and tooth surfaces. Patients in both groups also received standard oral care according to the ICU’s protocol. Exposure to topical CHX reduced the incidence of total respiratory tract infections in the CHX group by 69% (P < 0.05). This intervention also significantly reduced total mortality (1.16% versus 5.56%), and the need for systemic antibiotics.

Another chlorhexidine intervention trial of 60 ICU patients requiring mechanical ventilation was reported by Fourrier et al. A test group of 30 patients received 0.2% CHX gel 3 times a day. The control group received an oral rinse with bicarbonate isotonic serum and oropharyngeal aspiration 4 times a day. The results showed that oral antiseptic decontamination with CHX gel may reduce the incidence of nosocomial infections. The correlation between oral intervention and the incidence of nosocomial pneumonia was, however, not clearly stated.

<table>
<thead>
<tr>
<th>Oral Intervention</th>
<th>Results (placebo versus control)</th>
<th>Conclusion/Comments</th>
<th>Study Ranking</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2% CHX gel 3x a day. Controls: oral rinsing with isotonic bicarbonate and oropharyngeal aspiration 4x a day.</td>
<td>8/30 test patients and 17/30 control patients had nosocomial infections. Number of pneumonia per 1,000 days of mechanical ventilation was significantly lower in the treated group (10.7 vs 32.3 days, respectively, P &lt; 0.05). Trend, but not statistical difference, in a shorter length of stay in the ICU, a shorter duration of mechanical ventilation, and a lower mortality rate in the treated group.</td>
<td>Antiseptic decontamination of dental plaque with 0.2% CHX gel may reduce the incidence of nosocomial infections. The correlation between oral intervention and the incidence of nosocomial pneumonia was, however, not clearly stated.</td>
<td>2</td>
</tr>
<tr>
<td>0.12% CHX oral rinse 2x a day with ventilator weaning protocol (WP). “Placebo control” only WP.</td>
<td>WP and CHX led to significant reduction and delay of occurrence of VAP (37% overall, 75% for late VAP P &lt;0.05).</td>
<td>Improved oral hygiene via topical CHX with the use of WP is effective in reducing the incidence of VAP and the duration of mechanical ventilation in surgical ICU patients.</td>
<td>1</td>
</tr>
<tr>
<td>Topical antimicrobial prophylaxis in the oropharynx: Orabase with gentamicin/colistin/vancomycin 2% every 6 hours. Placebo control: Orabase without antibiotics. Control: no treatment.</td>
<td>Topical prophylaxis prevented acquired oropharyngeal colonization (10% vs. 59% placebo and 63% control, P &lt;0.0001 and P &lt;0.00001, respectively). Incidence of pneumonia was 10% vs. 31% in placebo (P = 0.001) and 23% in control (P = 0.04).</td>
<td>Targeted approach to prevent oropharyngeal colonization is an effective method of pneumonia prevention.</td>
<td>4</td>
</tr>
<tr>
<td>Professional dental care 1x a day, plus gargling/swabbing with 1% povidone iodine.</td>
<td>During oral treatment for 6 months, febrile days did not improve but degradation of febrile days were prevented by oral care in a limited number of patients.</td>
<td>Oral care may be useful in elderly patients to prevent respiratory infections.</td>
<td>1</td>
</tr>
<tr>
<td>Toothbrushing after each meal + in some cases swabbing with povidone iodine 1%, Oral professional care 1x a week.</td>
<td>RR 1.67 of developing pneumonia on no active oral care compared with oral care (P = 0.04).</td>
<td>Oral care may be useful in preventing pneumonia in older patients in nursing homes.</td>
<td>2</td>
</tr>
</tbody>
</table>
A prospective study by Bergmans et al. evaluated 3 groups of patients admitted to 3 ICUs over a 2-year period. The test group of 87 patients received pain reliever with 2% gentamicin/colistin/vancomycin every 6 hours. A placebo group of 78 patients received the pain reliever without antibiotics. A control group of 61 patients received no treatment. The topical antibiotic treatment prevented acquired oropharyngeal colonization (10% vs. 59% placebo and 63% control, \( P < 0.0001 \) and \( P < 0.00001 \), respectively) and the incidence of pneumonia (10% versus 31% in placebo (\( P = 0.001 \)) and 23% in the control group (\( P = 0.04 \)).

**Nursing home and elderly patients.** Yoneyama et al. found in 46 elderly nursing-home patients that professional dental care once a day (supervised tooth brushing, plus oral topical 1% povidone iodine) reduced the number of febrile days in a limited number of patients. This study was followed up with a second study in which 366 elderly residents from 11 nursing-homes were enrolled. A test group of 184 subjects received supervised toothbrushing after each meal, and topical 1% povidone iodine once a day. A control group of 182 subjects received no intervention. A 2-year follow-up found that the relative risk of pneumonia in the group with no active oral care was 67% greater when compared to the oral care group (\( P = 0.04 \)).

**Meta-Analysis**

An analysis of the combined data from 5 oral hygiene intervention trials was performed as described above. A forest plot of these data is presented in Figure 1. As can be seen, oral hygiene intervention significantly reduced the odds of pneumonia in these populations with low heterogeneity. This analysis supports the notion that oral hygiene improvements could dramatically reduce the rate of pneumonia in institutionalized subjects.

**CHRONIC OBSTRUCTIVE PULMONARY DISEASE (Table 3)**

Poor oral hygiene and periodontal disease may also be associated with other respiratory diseases such as COPD, which affects up to 15 million people and is the fourth leading cause of death in the United States. COPD encompasses emphysema and chronic bronchitis, with signs of chronic bronchitis occurring in more than 80% of patients. Although no study has

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Population</th>
<th>Oral Assessment</th>
<th>Pulmonary Outcome Measures</th>
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</thead>
<tbody>
<tr>
<td>Scannapieco et al.17, 1998</td>
<td>77 identified with COPD/309 without disease from a total population of 386 with a reliable history of respiratory status.</td>
<td>Simplified debris index, simplified calculus index, periodontal index.</td>
<td>Self-reported respiratory disease.</td>
</tr>
<tr>
<td>Hayes et al.38, 1998</td>
<td>261 with COPD/1,118 total subjects.</td>
<td>Alveolar bone loss measures from full-mouth radiographs.</td>
<td>Forced expiratory volume in 1 second (FEV1) &lt;65% of predicted volume.</td>
</tr>
<tr>
<td>Scannapieco et al.39, 2001</td>
<td>810 subjects with COPD/1,2982 without COPD.</td>
<td>DMFS/T index (summary of cumulative caries experience), gingival bleeding, gingival recession, gingival PD, and CAL.</td>
<td>A history of bronchitis and/or emphysema was recorded from the medical questionnaire. Subject lung function was estimated by calculating the ratio of forced expiratory volume (FEV) after 1 second (FEV1)/ forced vital capacity (FVC).</td>
</tr>
<tr>
<td>Garcia et al.40, 2001</td>
<td>279 subjects with COPD/833 without COPD.</td>
<td>Alveolar bone loss measures from full-mouth radiographs.</td>
<td>FEV after 1 second.</td>
</tr>
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</table>
established that periodontal disease influences the pathophysiology of COPD, several studies have demonstrated a statistical association between the 2 conditions.

An association between COPD and oral health in community-dwelling populations was first noted in an analysis of the 23,808 individuals in the National Health and Nutrition Examination Survey I (NHANES I) data. Of these, 365 individuals reported a respiratory condition that was assessed by a study physician. These subjects were categorized as having a confirmed chronic respiratory disease (chronic bronchitis, emphysema), acute respiratory disease (influenza, pneumonia, acute bronchitis), or not having a respiratory disease. Logistic regression analysis revealed that poor oral hygiene and smoking status were statistically associated with chronic respiratory disease.

The study of Hayes et al. also found that periodontal disease, measured as alveolar bone loss assessed from periapical radiographs, to be an independent risk factor for COPD in adult males enrolled in the VA Normative Aging Study.

To verify these results, an analysis of data from the National Health and Nutrition Examination Survey III (NHANES III) was performed, which documents the general health and nutritional status of randomly selected United States subjects from 1988 to 1994. This cross-sectional, retrospective study included 13,792 subjects ≥20 years of age having at least 6 natural teeth. Subjects with a history of bronchitis and/or emphysema were considered as having COPD. Subjects with COPD had, on average, more clinical attachment loss (CAL = 1.48 ± 1.35 mm, mean ± SD) than those without COPD (mean CAL = 1.17 mm ± 1.09). To simultane-

<table>
<thead>
<tr>
<th>Reference</th>
<th>N1</th>
<th>N2</th>
<th>Effect</th>
<th>Lower</th>
<th>Upper</th>
<th>P Value</th>
<th>0.1</th>
<th>0.2</th>
<th>0.5</th>
<th>1</th>
<th>2</th>
<th>5</th>
<th>10</th>
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<tbody>
<tr>
<td>Bergmans 2001</td>
<td>87</td>
<td>76</td>
<td>3.852</td>
<td>1.661</td>
<td>8.931</td>
<td>0.001</td>
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<tr>
<td>DeRiso 1991</td>
<td>173</td>
<td>180</td>
<td>3.173</td>
<td>1.384</td>
<td>7.274</td>
<td>0.004</td>
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<tr>
<td>Fournier 2000</td>
<td>30</td>
<td>30</td>
<td>3.696</td>
<td>1.216</td>
<td>10.638</td>
<td>0.018</td>
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<tr>
<td>Pugin 1991</td>
<td>25</td>
<td>27</td>
<td>1.837</td>
<td>4.521</td>
<td>7.486</td>
<td>0.000</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Yoneyama 2000</td>
<td>184</td>
<td>182</td>
<td>1.783</td>
<td>0.991</td>
<td>3.209</td>
<td>0.052</td>
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**Fixed Combined (5) 499 497 3.002 2.064 4.367 0.000**

**Random Combined (5) 499 497 3.678 1.890 7.157 0.000**

**Placebo**

**Treated**

Heterogeneity P = 0.04 (Mantel–Haenszel)

**Figure 1.**

Meta-analysis of 5 oral hygiene intervention trials.

### Table 3. (continued)

<table>
<thead>
<tr>
<th>Major Findings or Odds Ratio (OR) or Risk Ratio (RR)</th>
<th>Conclusions</th>
<th>Study Ranking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals with a confirmed chronic respiratory disease had significantly greater oral hygiene index scores than subjects without respiratory disease (P = 0.0441). Logistic regression analysis of data from that considered age, race, gender, smoking status, and simplified oral hygiene index (OHI), suggested that subjects having the maximum OHI value were 4.5 times more likely to have a chronic respiratory disease than those with an OHI of 0.</td>
<td>These results suggest OHI to have a residual effect on chronic respiratory disease of both practical and statistical significance.</td>
<td>4</td>
</tr>
<tr>
<td>Subjects in the worst population quintile of alveolar bone loss (mean ABL &gt;20% per site) found to be at significantly higher risk (OR = 1.8; 95% CI = 1.3-2.5).</td>
<td>Increased alveolar bone loss is associated with an increased risk for COPD.</td>
<td>3</td>
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<td>After controlling for confounding variables such as age, gender, and smoking, subjects with mean attachment loss (MAL) ≥3.0 mm had a higher risk of COPD than those having MAL &lt;3.0 mm (OR = 1.45; 95% CI = 1.02 to 2.05). Also, lung function appeared to diminish with increasing periodontal attachment loss.</td>
<td>The findings support an association between periodontal disease and COPD.</td>
<td>4</td>
</tr>
<tr>
<td>Worse periodontal health status is associated with an increased risk of COPD (OR ranging from 1.75; 95% CI = 1.33-2.30).</td>
<td>The findings support an association between periodontal disease and COPD.</td>
<td>3</td>
</tr>
</tbody>
</table>
ously control for multiple variables that may confound statistical analysis, gender, age, race, education, income, dental treatment history, alcohol consumption, diabetes status, and smoking status were considered in a logistic regression model against history of COPD. The risk for COPD appeared to be significantly elevated when the mean attachment loss (MAL) was ≥2.0 mm, as compared to the healthy individuals (MAL <2.0 mm) (odds ratio: 1.35; 95% confidence interval: 1.07-1.71). Interestingly, the levels of lung function as related to periodontal status were also considered. A trend was noted in that lung function appeared to diminish as the amount of attachment loss increased. No such trend was apparent when gingival bleeding was considered. These studies provide preliminary evidence that oral disease such as periodontitis may be associated with COPD.

Finally, Garcia and coworkers extended their previous work by conducting a 30-year follow-up of subjects enrolled in the VA Normative Aging Study. They examined the risk of developing COPD assessed by spirometry in 1,112 subjects, 279 of whom developed COPD. They found that subjects in the quintile having the worst periodontal health at baseline (measured by radiographic bone loss or probing depth) had greater risk for developing COPD when compared to all other subjects, after controlling for smoking. Furthermore, worse periodontal status increased the risk for COPD in current smokers, but not in never smokers.

**REVIEWERS’ CONCLUSIONS**

1. Oral colonization by respiratory pathogens appears to be a risk factor for lung infection in high-risk subjects.
2. Oral interventions that improve oral hygiene and possibly reduce oral inflammation may prove to lower risk of lung infection in susceptible populations.
3. Additional multi-center randomized intervention studies are necessary to validate this association and to determine if the association is causal. It is also important that these studies include oral health variables when assessing subjects to prove that improvements in oral health impact respiratory disease sequelae.

**FUTURE DIRECTIONS FOR RESEARCH**

Several rather small-scale interventional trials suggest that improved oral care may reduce the incidence of nosocomial pneumonia. Additional multi-center trials will determine the generalizability of oral intervention in the prevention of pneumonia in the institutional setting. Such studies must monitor appropriate aspects of oral health status to draw proper conclusions regarding the role of oral health in the prevention of pneumonia.

Additional longitudinal epidemiologic studies are required to validate the reported association between periodontal disease and COPD. Randomized controlled intervention studies that test the effect of periodontal treatment on the progression of COPD are needed.

**ACKNOWLEDGMENT**

The authors thank Dr. Nadezhda Shusharina for help in translating reference 29.

**REFERENCES**


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APPENDIX A

CONSENSUS REPORT

Members of the Section read and studied the review titled “Associations Between Periodontal Disease and Risk for Nosocomial Bacterial Pneumonia and Chronic Obstructive Pulmonary Disease: A Systematic Review” by Frank A. Scannapieco, Renee B. Bush, and Susanna Paju. The focused PICO question addressed by this evidence-based systematic review is “Do periodontal diseases or other indications of poor oral health influence the initiation/progression of pneumonia or other respiratory conditions?”

Introduction

Recent studies have shown that the oral cavity serves as a reservoir of infection for nosocomial respiratory pathogens. In addition, several controlled trials have
demonstrated that interventions that reduce the oral microbial burden or oral respiratory pathogen colonization prevent nosocomial pneumonia. Other studies have pointed to an association between periodontal disease and chronic obstructive pulmonary disease.

1. Does the Section agree that the evidence-based systematic review is complete and accurate?
Yes. Members of the Section unanimously agreed that the systematic review was complete and accurate as of April 1, 2002.

2. Has any new information been generated or discovered since the evidence-based search cut-off date?
Adachi et al. reported that utilization of professional oral health care results in a reduction in fever and pneumonia in a high-risk patient group (i.e., elderly nursing home subjects) as compared to a group without dental intervention.1 Houston et al. demonstrated a reduction in the incidence of nosocomial pneumonia in intubated heart surgery patients comparing the use of 2 antiseptic oral rinses.2 Findings of these 2 studies are consistent with previous studies mentioned in the current systematic review.

3. Does the Section agree with the interpretation and conclusion of the reviewers?
As described in the systematic review, recent studies have shown that the oral cavity serves as a reservoir of infection for nosocomial respiratory pathogens. In addition, several controlled trials have demonstrated that interventions that reduce the oral microbial burden or oral respiratory pathogen colonization prevent nosocomial pneumonia. Other studies have pointed to an association between periodontal disease and chronic obstructive pulmonary disease.

Nosocomial pneumonia: The data support an association between nosocomial pneumonia and poor oral health for subjects at high risk (i.e., intensive care unit patients and nursing home residents). Although oral biofilms appear to be an important reservoir for respiratory pathogens, the role of periodontal disease in this association is unclear and needs to be addressed in future studies.

Meta-analysis of RCTs evaluating several oral interventions indicate that therapies aimed at reducing the oral microbial burden in high-risk subjects have been shown to prevent pneumonia and possibly related mortality. The mechanisms need to be elucidated whereby respiratory pathogens colonize oral biofilms and translocate to the lung causing nosocomial pneumonia.

Chronic Obstructive Pulmonary Disease (COPD) (i.e., emphysema, chronic bronchitis): There are 4 epidemiologic studies that have associated periodontal disease with COPD. The role of periodontal disease in the progression of COPD is unclear since prospective epidemiological and randomized controlled trials have not been performed. The investigation of this condition is complicated by the imprecise definition of COPD in the literature and the fact that smoking is a confounding factor in both COPD and periodontal disease.

4. What further research needs to be done relative to the focused questions of the evidence-based review?
Nosocomial Pneumonia: Further randomized controlled trials using oral anti-infective therapy are required to determine the potential beneficial effect on pneumonia-associated morbidity and mortality. Since the at-risk populations acquire infection in different environments and have differing health characteristics such as intubated ICU patients and nursing home care patients, they may each require independent evaluation with regard to efficacy of oral anti-infective therapy in separate RCTs.

COPD (emphysema and bronchitis): In order to determine whether periodontal disease and/or oral microbial burden are associated with chronic obstructive pulmonary disease additional epidemiological and case-control studies are needed.

5. How can the information from the evidence-based review be applied to patient management?
A. Evidence presented in the systematic review suggests that the incidence of nosocomial pneumonia in institutionalized subjects, including those in intensive care units and nursing homes, may be reduced by improving oral hygiene, which can be achieved by both mechanical or chemical approaches.

Level of Evidence:3 Moderate.
Rationale: Assignment of the “moderate” level of evidence was based on the fact that there are 5 level I studies that show consistent positive effects of oral anti-infective therapy on the incidence of nosocomial pneumonia. However, these studies have different study designs, target populations, and therapies. Therefore results from definitive separate RCTs on these 2 target populations are needed to strengthen this recommendation.

B. There is insufficient evidence regarding the potential association between periodontal disease and COPD.

Level of Evidence: Insufficient.
Rationale: Inadequate data.
REFERENCES


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