Association Between Oral Health and Cognitive Status: A Systematic Review

Bei Wu, PhD, Gerda G. Fillenbaum, PhD, Brenda L. Plassman, PhD, and Liang Guo, BS

OBJECTIVES: To systematically review longitudinal studies examining the association between oral health and cognitive decline.

DESIGN: Studies published between January 1993 and March 2013 were identified by search of English language publications in PubMed/Medline using relevant Medical Subject Heading terms and title and abstract keywords and from CINAHL using relevant subject headings. After applying eligibility criteria and adding four studies identified from article references, 56 of the 1,412 articles identified remained; 40 were cross-sectional, and 16 were longitudinal; 11 of the latter examined the effect of oral health on change in cognitive health or dementia incidence, five examined the reverse.

SETTING: Sources of information included administrative data, subject evaluations in parent studies, medical and dental records, self-reports, and in-person evaluations.

PARTICIPANTS: Older adults.

MEASUREMENTS: Most studies used subjects whose oral or cognitive status was known, using standard approaches to impute for missing information. The oral health information most frequently studied included number of teeth, periodontal and caries problems, and denture use. Cognition was most frequently evaluated using the Mini-Mental State Examination or according to a diagnosis of dementia.

RESULTS: Some studies found that oral health measures such as number of teeth and periodontal disease were associated with risk of cognitive decline or incident dementia, whereas others did not find an association. Similarly, cognitive decline was not consistently associated with greater loss of teeth or number of decayed teeth. It is likely that methodological limitations play a major role in explaining the inconsistent findings.

CONCLUSION: It is unclear how or whether oral health and cognitive status are related. Additional research is needed in which there is greater agreement on how oral health and cognitive states are assessed to better examine the linkages between these two health outcomes. J Am Geriatr Soc 2016.

Key words: oral health; dementia; cognitive decline

In the past 2 decades, an increasing number of studies have examined the relationship between cognitive impairment and oral health in older adults, because the question has arisen as to whether there is an association, possibly through a common inflammatory pathway. This question is of considerable relevance given the rapid increase in the proportion and number of older persons in the population, an increasing number of whom are retaining their natural teeth. Furthermore, approximately 36% of individuals aged 70 and older are cognitively impaired, and the prevalence of cognitive impairment and dementia increases with age. Up to 3.1 million Americans currently have a dementing disorder, with an expected doubling by 2050.

Concomitantly, evidence from clinical samples suggests that elderly adults have an greater incidence of oral disease, with the frequency of oral health problems being significantly greater in cognitively impaired elderly adults, particularly those with dementia. Any intervention that might help delay the onset or progression of dementia, including improvement of oral hygiene and dental services, could have a significant effect on personal and family well-being and healthcare costs.

In order to examine the association between oral health and cognition in the elderly adult, and provide direction for future studies, we conducted a systematic review of the existing literature. Our focus is on longitudinal studies, since they may be informative with respect to causation.
METHODS

Search Strategy
The time frame considered was from the first relevant publication found in 1993 to March 1, 2013. Human study publications in English were searched for in the PubMed/Medline database, using the Medical Subject Heading terms (memory disorders or cognition or cognition disorders or or dementia) AND (oral health or mouth diseases or tooth diseases), which identified 515 articles; a title and abstract keyword search using (mouth or tooth or oral AND cogni* or Alzheimer or demen*), which identified 790 articles; and the CINAHL database using the subject headings (dementia+ or Alzheimer’s diseases or cognition+ or cognition disorders+ or memory disorders+) AND (mouth diseases or tooth loss or dental caries), which identified 107 articles. After removing 41 duplicates from the 1,412 articles identified, 1,371 unique articles remained (Figure 1).

Two exclusionary criteria were applied to identify nonqualifying articles. The first criterion excluded 1,273 articles that, according to the title or abstract, did not examine the association between cognition and oral health diseases and conditions in adults, leaving 98 articles. The second criterion excluded articles that, based on review of the abstract by two readers, had inadequate information on oral health or cognitive status. A third reviewer resolved any disagreement. In consequence, an additional 46 articles were excluded and 52 retained. Four articles culled from article reference lists were added to these, resulting in 56 articles, based on 55 studies. Of these, 40 articles reported on cross-sectional studies and 16 on longitudinal studies.

Data Extraction
Two reviewers independently extracted information from each longitudinal article on first author and date of publication, study name, location, study date(s), sample demographics, cognitive and oral health measures, covariates, and key findings. Disagreements on data extraction were resolved by consensus with the assistance of a third person.

RESULTS
The characteristics of the 16 longitudinal studies are summarized in Table 1. The first section summarizes the 11 studies of oral health predicting cognitive decline, the second section summarizes the five studies of cognitive status or dementia predicting oral health.

Several developed countries are represented (United States, n = 8; Japan, n = 3; Australia, n = 1; France, n = 1;
Table 1. Characteristics of Longitudinal Studies of Oral Health and Cognitive Status

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<tr>
<th>Author, Location, Study Title</th>
<th>Sample and Study Design</th>
<th>Cognitive Measures</th>
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<tr>
<td>Shimazaki et al., 2001&lt;sup&gt;11&lt;/sup&gt;</td>
<td>Baseline: 10/1988–02/1989 N = 1,929 (87% of residents) Follow-up: 10/1994–03/1995 N = 719 (856 died, 167 status unknown, 187 hospitalized) M = 169; F = 550 Age: range 59–107; mean 79.7 ± 7.5</td>
<td>From medical records Mental health status: good, fair, poor regarding symptoms of dementia or cognitive disability Follow-up: deterioration = symptoms of dementia, or cognitive disability status at lower level</td>
<td>Baseline: 2 dentists trained in use of epidemiological indices for oral health Number of teeth (excluding retained roots) categorized, denture use for eating</td>
<td>From medical records Age, sex, mobility, type of institution, chronic diseases</td>
<td>Logistic regression adjusted for age, physical health, type of institution, cerebrovascular disorder Number of teeth, denture use, not associated with decline in mental health status. Reference = 20 + teeth (OR, 95% CI) 1–19 teeth + dentures (OR = 1.9, 95% CI = 0.8–4.6) teeth-dentures (OR = 2.3, 95% CI = 0.9–5.8) 0 teeth + dentures (OR = 1.0, 95% CI = 0.7–4.0) 0 teeth-dentures (OR = 2.4, 95% CI = 0.9–6.5)</td>
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<td>Kitakyushu City, Japan 29 institutions for elderly adults</td>
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<td>Yoneyama et al., 2002&lt;sup&gt;12&lt;/sup&gt;</td>
<td>Baseline: 9/1996, followed at 6, 12, 18, 24 months N = 366, randomized: 184 oral care (M = 36, F = 148; mean age 82.0 ± 7.8) 182 no oral care (M = 37, F = 145; mean age 82.1 ± 7.5) Oral intervention—brush teeth for 5 minutes after each meal or clean oral cavity. Clean dentures daily. Plaque and calculus control as necessary.</td>
<td>MMSE score at baseline, 24 months Debris index for plaque score</td>
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<td>Survivors only. 24-month change in MMSE score: Oral care: −1.5 ± 4.9 No oral care: −3.0 ± 5.9 P &lt; .05</td>
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<td>Japan 11 nursing homes</td>
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<td>Gatz M et al., 2006&lt;sup&gt;15&lt;/sup&gt;</td>
<td>Questionnaires mailed 1961, 1963, 1967 (1970 if no response in 1967) 1998 survivors aged ≥65 of same-sex twins born before 1926 and contacted for HARMONY study N = 310 dementia (M = 85, F = 225) average onset age 78.9 ± 7.0 N = 3,063 no dementia (M = 1,200, F = 1,863) mean age 79.2 ± 4.7</td>
<td>Dementia determined from Swedish Inpatient Discharge Registry and Swedish Cause of Death Registry (sensitivity 63%, specificity 98% for dementia)</td>
<td>Self-report of own teeth at age 35 (all or most, half, few or none)</td>
<td>Age, sex, education, CVD Lifestyle before age 40: mental activity (reading, cultural activities, studies) Physical exercise Adult height (&gt;1 standard deviation shorter than the rest) Parents’ social class (upper, middle, lower)</td>
<td>Analyses adjusted for all covariates. Loss of all teeth Case control analysis predicting (1) all dementias, (2) Alzheimer’s disease: OR = 1.49, 95% CI = 1.14–1.95 OR = 1.68, 95% CI = 1.21–2.32 Monozygotic co-twin control analyses: OR = 3.60, 95% CI = 1.34–9.70 OR = 5.50, 95% CI = 1.22–24.80</td>
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<td>Sweden Swedish Twin Registry HARMONY study</td>
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<td>Stein et al., 2007&lt;br&gt;Milwaukee, WI Nun Study (Snowdon, 1997)</td>
<td>Baseline: 1991–1992  N = 144 nuns with cognitive assessment and known APOE ε4 status  Age range 75–98  n = 32 with dementia  n = 112 without dementia  n = 101 with adequate follow-up data  Neuropathology data on 118/129 decedents  Follow-up: annual, 12 years</td>
<td>CERAD neuropsychology battery, 30 administered annually for 12 years  Dementia criteria: NINCDS-ADRDA  Braak staging for AD neuropathology</td>
<td>40 years of dental records  Number of teeth excluding non-third molars present at first cognitive evaluation  Presence of periodontal damage</td>
<td>Age, education, APOE ε4 status  Medical history in dental records (n = 133)  Medical conditions associated with inflammatory process</td>
<td>Incident dementia over 12 years:  Adjusted for age, education, APOE ε4: 0–9 versus 10–28 teeth (HR = 2.20, 95% CI = 1.1–4.5)  Further adjusted for periodontal damage, no association (HR = 2.4, 95% CI = 0.86–6.6)  For 118 deceased, adjusted for age, education, APOE ε4:  No association between number of teeth and severity of AD neuropathology (Braak stage) (HR = 1.1, 95% CI = 0.49–2.7) or brain infarcts (HR = 1.14, 95% CI = 0.49–2.86)</td>
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<td>Kaye et al., 2010&lt;br&gt;U.S. Department of Veterans Affairs Dental Longitudinal Study Boston, MA, metropolitan area</td>
<td>Baseline: 1968  Original N = 1,231  Race: 97% white, 3% black  Current study: n = 597 men with necessary dental and cognitive data  Aged 24–84  Convenience sample, community dwellers  Follow-up: up to 32 years (until 2002)</td>
<td>Given at each dental examination (~every 3 years)  MMSE (low score &lt;25, or &lt;90% of age- and education-specific median)  SCT</td>
<td>Dental examination ~every 3 years by calibrated periodontist, reliability of measurements determined: number of teeth, maximum probing pocket depth for each tooth, alveolar bone loss, caries or restoration (5 tooth surfaces examined)</td>
<td>Age, education, smoking, aspirin use, nonsteroidal anti-inflammatory drugs, BMI, coronary heart disease, stroke, hypertension, CVD, cancer, diabetes mellitus, alcohol, coffee, tea, folate, B6, B12</td>
<td>Adjusted analyses  Additional tooth loss/decade associated with low:  MMSE (HR = 1.09, 95% CI = 1.01–1.18)  SCT (HR = 1.12, 95% CI = 1.05–1.18)  Greater alveolar bone loss associated with low:  MMSE (HR = 1.03, 95% CI = 1.00–1.07)  SCT (HR = 1.03, 95% CI = 1.01–1.06)  Deeper pocket depth associated with low:  MMSE (HR = 1.04, 95% CI = 1.01–1.09)  SCT (HR = 1.04, 95% CI = 1.01–1.06)  New caries, restoration associated with low:  MMSE (HR = 1.02, 95% CI = 0.97–1.08)  SCT (HR = 1.05, 95% CI = 1.01–1.08)</td>
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<td>Stein et al., 2010 Milwaukee, WI</td>
<td>Same sample as Stein et al., 2007</td>
<td>Delayed word recall (from CERAD neuropsychology battery)</td>
<td>Same as Stein et al., 2007</td>
<td>Education (&lt; vs &gt; high school) APOE e4</td>
<td>Persons with APOE e4 allele, ≤ 9 teeth, or both had poorer delayed recall scores at baseline and declined faster than those with one or neither of these risk factors.</td>
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<td>Arrivé et al., 2012 PAQUIDENT, substudy of PAQUID study (Dartigues et al., 1992)</td>
<td>PAQUIDENT baseline: 1989–1990 N = 406 Aged 66–80 Median age 70 M = 184, F = 221 No dementia Median follow-up 10 years</td>
<td>MMSE, Benton Visual Retention Test, Wechsler Paired Associates, verbal fluency, visuospatial attention, digit symbol Dementia criteria: Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised NINCDS-ADRDA (for AD) Hachinski score (vascular dementia) Dementia status ascertained after in-person assessment by neurologist (dementia vs normal)</td>
<td>In-home oral examination by 10 trained, calibrated dentists Number of decayed, missing, filled teeth (for 28 teeth) Number of missing teeth (denture substitution counts as own teeth) Plaque, calculus Periodontal examination for Community Periodontal Index</td>
<td>Sex, education (lower vs higher, years not specified), living condition, tobacco, alcohol use Health status: Center for Epidemiologic Studies Depression Scale, BMI, vascular risk factors</td>
<td>Adjusted for sex, BMI, vascular risk factors Predicting incident dementia Higher education ≥11 vs &lt;11 missing teeth (HR = 1.07, 95% CI = 0.57–2.02) Bleeding, calculus (HR = 0.71, 95% CI = 0.31–1.63) Pockets (HR = 0.42, 95% CI = 0.15–1.15) No eligible sextant (HR = 1.51, 95% CI = 0.63–3.57) Lower education ≥11 vs &lt;11 missing teeth (HR = 0.30, 95% CI = 0.11–0.79) Bleeding, calculus (HR = 1.24, 95% CI = 0.39–3.88) Pockets (HR = 0.97, 95% CI = 0.29–3.19) No eligible sextant (HR = 0.02, 95% CI = 0.02–3.66)</td>
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<td>Paganini-Hill et al., 2012 Leisure World Laguna Hills, CA</td>
<td>Study dates: 1992–2010 N = 5,468 Age: median 81, range 52–105 M = 1,733; F = 3,735 Number with incident dementia: 1,145 (followed up to 18 years) Retirement community</td>
<td>Dementia determined according to: In-person evaluation for aged ≥ 90 (n = 519 with dementia, identified by different study). Self-report (n = 90), hospital records (n = 46), death certificates (n = 490) Date of diagnosis = date dementia first mentioned</td>
<td>Self-report: number of natural teeth: ≤16, 16–25, ≥26 Adequate natural dentition (10 in upper jaw, 6 in lower jaw) Inadequate natural dentition: further categorized as does or does not wear dentures Oral health habits</td>
<td>1992—Self-reported education, head injury, first-degree relative with AD, senility, or dementia 1983/1985—smoke, alcohol, caffeine, BMI, hypertension, angina pectoris, heart attack, rheumatoid arthritis, cancer, high blood pressure, stroke, diabetes mellitus Active/sedentary</td>
<td>Fully adjusted, predicting incident dementia; separate analyses for men and women Number of natural teeth: NS (men and women) Inadequate natural dentition, no dentures, men (HR = 1.91, 95% CI = 1.13–3.21), women (HR = 1.22, 95% CI = 0.86–1.73) Inadequate dentition, alone or with dentures: NS (men + women) Oral health habits (40 comparisons): no daily tooth brushing (HR = 1.65, 95% CI = 1.05–2.62) women only No dental visits last 12 months (HR = 1.89, 95% CI = 1.21–2.95) men only</td>
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<td>Yamamoto et al., 2012 Aichi Gerontological Evaluation Study (AGES) Six municipalities in Aichi province, Japan</td>
<td>Baseline: 2003 N = 4,425 (from mail survey of random sample of 9,783 community residents) Aged ≥65 M = 2,158; F = 2,267 Race and ethnicity: Asian</td>
<td>Dementia onset: from administrative data Certified to receive insurance benefits, based on Ministry questionnaire on functional, cognitive, behavioral, communication problems in dementia. Graded I (can still live independently) to IV (consistent care needed) or M (severe psychiatric symptoms, specialized medical service needed)</td>
<td>Self-report ≥20 vs &lt;20 teeth Few teeth + denture use Few teeth no dentures Data missing Mastication: Chew anything/cannot chew at all Have regular dentist (yes/no) Personal dental care good (yes/no)</td>
<td>Age, sex, adjusted household income, BMI, current illnesses (up to 18 conditions), smoking history, alcohol use, exercise, forgetfulness</td>
<td>Adjusted for all characteristics excluding “forgetfulness”; predicting incident dementia Only significant findings reported Oral health status. Reference: ≥20 teeth Few teeth no dentures (HR = 1.85, 95% CI = 1.04–3.29) Mastication: Can’t chew very well (HR = 1.47, 95% CI = 0.95–2.25) No regular dentist (HR = 1.44, 95% CI = 1.04–2.01) Poor personal dental care (HR = 2.01, 95% CI = 1.11–3.63)</td>
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<td>Batty et al., 2013 ADVANCE trial Effect of reducing blood pressure, intensive glucose control, on Type II diabetes mellitus 215 centers, 20 countries</td>
<td>Baseline: 2001–2003 N = 11,140 M = 6,407; F = 4,733 Aged 55–88 (all with type II diabetes mellitus and history of major macro- or microvascular disease or ≥1 other cardiovascular risk factor) White (67%) (other ethnicities not reported) Follow-up: 5 years</td>
<td>MMSE (3 assessments over 5 years) If MMSE score &lt;24 or doctor- or nurse-suspected dementia, referred to specialist for dementia evaluation, DSM-IV criteria Cognitive decline = drop ≥ 3 MMSE points by 3rd assessment</td>
<td>Baseline: self-reported number of natural teeth connected to gum or jawbone Number of days bleeding gums in past 12 months</td>
<td>Age, sex, EQ-5D, socioeconomic, CVD risk factors: -behavioral -physiological -psychological</td>
<td>Fully adjusted Incident dementia (N = 109) Number of of teeth (reference ≥22 teeth) 0 teeth (HR = 1.48, 95% CI = 1.24–1.78) 1–21 teeth (HR = 1.24, 95% CI = 1.05–1.46) Bleeding gums ≥12 days (HR = 1.19, 95% CI = 0.51–2.75) &lt;12 days (HR = 0.42, 95% CI = 0.10–1.71) Cognitive decline (N = 1,806) Number of of teeth 0 teeth (HR = 1.39, 95% CI = 1.21–1.59) 1–21 teeth (HR = 1.23, 95% CI = 1.10–1.36) Bleeding gums ≥12 days (HR = 0.94, 95% CI = 0.77–1.15) &lt;12 days (HR = 0.92, 95% CI = 0.75–1.13)</td>
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<td>Stewart et al., 2013 Memphis and Pittsburgh</td>
<td>Baseline: 1997/1998 N = 947 (with cognitive data, y5) Aged 70–79 M=50%; F=50%</td>
<td>Cognitive assessment: 1997/1998 (Year 1), 1999/2000 (Year 3), 2000/2001 (Year 5) Cognitive impairment: 3MS score</td>
<td>Dental examination 1998/99 (Year 2) Number of of teeth Number of occluding tooth</td>
<td>Age, sex, education, race Self-reported cardiovascular disease and risk factors Center for Epidemiologic</td>
<td>Change in Year 1 to Year 3 3MS cognitive impairment and decline; stratified according to APOE ε4 genotype to ascertain</td>
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<td>Health, Aging and Body Composition study</td>
<td>Race or ethnicity: black 34%, white 66% Healthy Medicare community residents in local area, unimpaired basic ADL or mobility. Included all blacks, and random sample of whites Sample based on Year 2 oral health participants Follow-up: Year 5</td>
<td>&lt;80 (bottom 10%) Cognitive decline: Decline ≥5 points (~20%) Year 3—DSST, clock drawing Cognitive impairment = bottom 10%</td>
<td>pairs Probing depth Attachment loss (number and proportion of sites) Mean gingival index Mean plaque score Number of sites bleeding on probing All measures categorized into quartiles</td>
<td>Studies Depression Scale score C-reactive protein, interleukin-6 at Year 1; weight loss Year 1 to Year 3 Anticholinergic medication APOE e4</td>
<td>No significant association between any dental measure and cognitive decline on 3MS Closest association: number of teeth (OR = 0.88, 95% CI = 0.77–1.00), gingival index (OR = 1.17, 95% CI = 0.99–1.38) DSST decline: no association Dichotomized gingival index (Q4/rest): associated with decline in 3MS, fully adjusted (OR = 2.28, 95% CI = 1.60–3.25) No association with DSST</td>
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<td>Cognitive impairment predicts oral disease</td>
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<td>Jones et al., 1993</td>
<td>Baseline: 1986–1989 Dementia (AD)</td>
<td>AD cases drawn from VA-LDS, with previously determined diagnosis MMSE</td>
<td>Initial caries examination: after teeth scaled and polished 50-month follow-up: caries examination (teeth not scaled or polished) NIDR criteria Katz criteria for root caries evaluation Annualized net caries increment (% per 100 available surfaces)</td>
<td>Demographic (from medical records)</td>
<td>Annualized follow-up: Veterans with AD had greater coronal caries increment (2.29 ± 4.29 vs 0.88 ± 1.14); root caries (2.38 ± 5.57 vs 0.31 ± 0.69 per 100 available surfaces) than control group. All findings NS.</td>
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<td>VA Longitudinal Study of Dementia VA Medical Center, Bedford, MA VA-DLS (subset of VA Normative Aging Study). Boston VA</td>
<td>Baseline: Age: 67.4 ± 7.5 Controls (matched on age, number of teeth, education) N = 46 male veterans (VA-DLS) Aged 65 ± 12 Follow-up: 23, 50 months Retrospective data</td>
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<td>Ship and Puckett, 1994</td>
<td>Baseline: AD: N = 21; M = 13; F = 8 Aged 64 ± 9 Controls (age, sex matched) N = 21; M = 13; F = 8 (from National Institute on Aging Normative Aging Program Also, Clinical Center, National Institutes of Health, Bethesda, MD</td>
<td>NINCDS-ADRDA criteria for AD (vigorously screening) MMSE</td>
<td>Unstimulated and stimulated major salivary gland flow rates Extensive assessment of gingival, periodontal (NIDR criteria), dental and oral mucosal tissues. Standard criteria and scales used in assessment. Test–retest reliability of assessment determined. Annualized change</td>
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<td>No association between change in salivary flow rate and change in MMSE Gingival health: Poorer MMSE scores associated with greater gingival bleeding and plaque. Periodontal health: no difference between groups Number of teeth, restored surfaces: no difference Loss of tooth attachment: findings unclear Intraoral mucosal tissue: no difference between groups, but lower MMSE scores related to poorer mucosal health</td>
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<td>Chalmers et al., 200221</td>
<td>Baseline: 1998/99</td>
<td>Physician-confirmed diagnosis Dementia: 76% AD, 24% other MMSE: ≥26 no dementia, 21–25 mild, 11–20 moderate, ≤10 severe dementia GDS</td>
<td>Two calibrated dentists NIDR protocol Tooth status (present, absent, replaced, root status) Caries (initial, incident): coronal, root surface; sound, decayed, treated; gingival recession Assessed as CCI, NCI, ADJC</td>
<td>ADL (Katz) Instrumental ADL (Lawton Brody) Number of medical conditions Anticholinergics: (severity: none, low, high) Dental care problems Zarit Burden Scale Medical status, medication status, cognitive status</td>
<td>Caries increments (dementia vs no dementia): Coronal: CCI = 3.7 vs 1.5 NCI = 3.5 vs 1.4 ADJC = 3.6 vs 1.4, all P &lt; .01. Incidence: 71.8% vs 48.7%, P &lt; .01. Root surfaces: CCI = 1.9 versus 0.9 NCI = 1.7 versus 0.8 ADJC = 1.8 versus 0.9, all P &lt; .01. Incidence: 62.1% versus 44.2%, P &lt; .01. Greater root caries incidence in high-maintenance patients Dementia group—coronal caries increment: 3.5 (for 1 increment in nondemented) (P = .001) GDS moderate-severe dementia—additional 1.78 coronal increments (P = .01) 0.95 root caries increment (P = .001)</td>
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<td>“Oral health of community dwelling older adults with dementia” South Australian Dental Longitudinal Study Adelaide, Australia</td>
<td>Age (≤79, n = 91, ≥80, n = 25) Follow-up: 1999-2000</td>
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<td>South Australian Dental Longitudinal Study</td>
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<td>Ellefsen et al., 200922</td>
<td>Baseline: 2002-2004 N = 106 (AD, n = 61; OD, n = 26; no dementia, n = 19) M = 37, F = 69</td>
<td>MMSE Dementia criteria: ICD-10 AD versus OD versus no dementia</td>
<td>Oral evaluation in home NIDR criteria for coronal and root decayed surfaces and filled surfaces, gingival recession. Calculated Adjusted Caries and filling Increments (ADJCIs) Number of teeth present, dental prostheses</td>
<td>Demographic, functional, social variables from structured questionnaire</td>
<td>No statistically significant differences for decayed and filled coronal and root surfaces, although rates higher for AD and OD than for no dementia. ADJCIs higher for aged ≥80 but not always significant; no difference for MMSE ≤24 versus ≥24. Predicting coronal caries AD (OR = 0.64, 95% CI = 0.09–4.50) OD (OR = 4.13, 95% CI = 0.44–39.05) Predicting root caries AD (OR = 0.08, 95% CI = 0.01–0.79) OD (OR = 1.01, 95% CI = 0.11–9.56)</td>
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<td>Copenhagen, Denmark Two hospital memory clinics</td>
<td>Follow-up: ~1 year later N = 77 (AD, n = 49; OD, n = 15; no dementia = 13) M = 28, F = 49 Mean age 81.9 (no information on age range)</td>
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<th>Author, Location, Study Title</th>
<th>Sample and Study Design</th>
<th>Cognitive Measures</th>
<th>Oral Health Measures</th>
<th>Primary Covariates</th>
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<tr>
<td>Chen et al., St. Paul, Minnesota 2010 24</td>
<td>Study years: 10/1999–12/2006, follow-up 1–90 months, mean 38.8 months</td>
<td>Medical history from dental records; diagnosis of AD, other dementia, chronic brain syndrome, or ICD-9-CM-R codes 290.x, 294.1, 331.2</td>
<td>From dental records Follow-up treatment focused on continued treatment as needed</td>
<td>Charlson Comorbidity Index Anticholinergic Drug Scale to measure medication-related anticholinergic burden</td>
<td>Fully adjusted models Number of teeth lost (HR = 0.92, 95% CI = 0.59–1.63, $P = .99$) Rate of tooth loss ($P = .52$), slightly higher in individuals with dementia (NS)</td>
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<tr>
<td>Geriatric dental clinic affiliated with University of Minnesota School of Dentistry, for aged ≥55, persons with disabilities, community and nursing home residents</td>
<td>N = 491 Dementia: N = 119 M = 30, F = 89 Age, mean 81.5 ± 9.2, range 49–102</td>
<td>Medical, cognitive, functional assessment from dental records</td>
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<tr>
<td></td>
<td>No dementia (propensity score matched) N = 372 M = 110, F = 262 Age, mean 73.8 ± 10.7, range 44–103</td>
<td>New patients, dentate after initial treatment, returned for routine care at least once</td>
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Psychological measures for which results are not reported have been excluded to reduce space. If there was no indication of race, or of number of men or women, the information was not mentioned in the paper.

3MS = Modified Mini-Mental State Examination; AD = Alzheimer’s disease; ADJCI = Adjusted Caries Increment, determined as CCI [crude caries increment number of surfaces] (1 – examiner reversals/examiner reversals + x [decayed/recurrent/filled/filled unsatisfactory/root sound]); ADL = activities of daily living APOE = apolipoprotein E; BMI = body mass index; CCI = crude caries increment; CERAD = Consortium to Establish a Registry for Alzheimer’s Disease; CVD = cerebrovascular disease; DSST = Digital Symbol Substitution Test; GDS = Global Deterioration Scale; HR = hazard ratio; MMSE = Mini-Mental State Examination; NCI = net caries increment; NIDR = National Institute of Dental Research; NINCDS-ADRDA = National Institute of Neurological, Communicative Disorders, and Stroke-Alzheimer’s Disease and Related Disorders Association; OD = other dementia; OR = odds ratio; PAQUID= Personnes Agées QUID; PAQUIDENT = PAQUID Dental study; SCT = Spatial Copying Task; VA = Department of Veterans Affairs; VA-DLS = Veterans affairs Dental Longitudinal Study; VA-LSD = VA Longitudinal Study of Dementia. M = male; F = female; N = total number; CI = confidence interval; NS = not stated
Denmark, n = 1; Sweden, n = 1; and a European consortium, n = 1). Two studies used the same sample but different outcomes and statistical analyses.9,10 All but four studies9–12 were conducted in community residents, but some community-based studies may have included nursing home residents. Sample sizes ranged from small (N = 42) to large (N = 11,140, from 215 centers in 20 European countries).14

Subject selection and source of data reflected several creative, overlapping approaches. These included use solely of administrative data,15 use of data already gathered in longitudinal studies (often designed for other purposes),9,10,16–20 selecting subjects for whom cognitive status or oral health status had been established and adding an oral or cognitive evaluation,8,11,13,21,22 and linking subject data to administrative records.21

Study design varied: intervention studies of good oral care,12,24 samples matched on demographic characteristics using randomization8,12,13,21 or propensity scores,24 and natural history studies.7

Measures of Oral Health Status

Oral health status measures are summarized in online Table S1. Nine of the 16 studies used oral health evaluation, and seven used dental records. In studies gathering oral health data, examiners were trained, they were calibrated if more than one participated, and interexaminer reliability for assessing a variety of oral health measures was determined. The amount of oral health information gathered in person or from records and used in analyses varied from extensive and highly detailed, particularly in studies of oral health predicting cognitive impairment (number of decayed, missing, filled teeth; plaque; periodontal disease)8,13,20 to minimal (self-reported approximate number of teeth currently or when younger).14,15,19,23 Subject-provided information included pain or discomfort,17 bleeding gums,14 and denture use.11,19,23 Information from dental records was used in three studies,9,10,24 two of which relied on up to 40 years of records.9,10,25

Tooth loss was the most common measure of oral health, recorded in 14 of the 16 studies, with a significant relationship to cognition reported in 11.9,11,13,15–17,19,20,22,23 When used in analysis, the number of teeth present was typically categorized, with categorization varying from study to study, and sometimes linked to denture use.9,11,15,17

Eleven studies used clinical evaluation to assess oral health status.8,13,16,17,20,21,24 Standard oral health indices were used in some studies: Debris Index for plaque score,12 Community Periodontal Index,17 Gingival Index,20 Plaque Index,22 Katz criteria for roots and adjusted caries increment,21 and National Institute for Dental Research criteria.5,13,21,22

In examining periodontal disease, attention was paid to extent of gingival bleeding on probing (ratio of examined sites), proportion of examined sites with loss of attachment greater than 3 mm, and mean pocket depth. Periodontal diseases were assessed in five studies, four on the effect of oral health on cognitive impairment (three studies used clinical assessment,16,17,20 one used self-report14) and one on the effect of cognitive impairment on oral health.13 Two studies assessed periodontal damage based on decades of dental records.7,10

Measures of Cognitive Assessment

Assessment of the presence of dementia included self-reported diagnosis; use of standard clinical diagnostic criteria; neuropathological diagnostic criteria; and information from medical, dental, and administrative records. (See summarized information in online Table S2.) Cognitive status was based on a variety of neuropsychology measures, ranging from use of a substantial battery to reliance on a single brief measure.

The standard diagnostic criteria for dementia included Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised (DSM-III-R), DSM-IV, International Classification of Diseases, Ninth Revision, Clinical Modification, Revised (ICD-9-CM-R), and ICD-10, reflecting the date of evaluation.13–15,17,22 At times these criteria were supplemented by the National Institute of Neurological and Communicative Disorders and Stroke—Alzheimer’s Disease and Related Disorders Association (Alzheimer’s disease (AD));8,13,15,17 National Institute of Neurological Disorders and Stroke—Association Internationale pour la Recherche et l’Enseignement en Neurosciences (vascular dementia);15 Hachinski scale (vascular dementia);17 Lund and Manchester (frontal lobe dementia);15 Geriatric Mental State examination;17 and Global Deterioration Scale,26 which assesses presence and severity of dementia.21,22 Neuropathological criteria27 were also used but were available for only one dataset.9

Non-AD dementias15,17,22 were rarely analyzed separately because of limited numbers. The validity of administrative records, which were frequently used, was evaluated for only one study.15 Cognitive batteries and individual measures were used to assess cognitive change and ascertain the presence of dementia. The most popular single measure was the Mini-Mental State Examination (MMSE),28 used in 10 studies—in eight as a single measure (four of which examined the effect of oral condition on cognitive state12,14,16,19 and four the reverse8,13,21,22 and in two as part of a larger neuropsychology battery.9,17 All neuropsychology measures had established validity and reliability. Criteria used to assess cognitive change included self-perceived deterioration, change in score on neuropsychology measures, specific decline (which differed across studies), crossing a cut-point (with cut-points differing across studies), or reaching an administrative criterion indicating need for assistance.

Covariates Used in Analysis

The covariates used varied widely across studies and included demographic characteristics (sex, race, education, income—none uniformly reported), specific health conditions and associated risk factors or number of health conditions present (12 studies), and the Charlson Index14 (Online Table S3). biomarker and genetic information (interleukin (IL)-6, C-reactive protein, apolipoprotein E ε4, first-degree kin with dementia);9,10,19,20 prescription and over-the-counter medications, particularly anticholinergics;16,20,21,24
scales of depression and caregiver burden, and life style and health behavior measures (included by 10 studies) were also considered. No study included all these areas.

**FINDINGS**

**Effect of Oral Health on Cognitive Status (11 Articles)**

Two studies indicated that having fewer teeth at baseline or decline in number of teeth was not associated significantly with cognitive decline, whereas other studies that found an association with cognitive decline or dementia contradicted this. Findings are further sent. Development of caries or the presence of new of dementia but not when periodontal damage was present. Another study reported that having fewer teeth increased the hazard of dementia but not when periodontal damage was present. Development of caries or the presence of new restoration was associated with poorer performance on the MMSE and a spatial copying task. Mastication difficulty was not associated with incident dementia.

Five studies examined the effect of periodontal disease on incident dementia, cognitive decline, or low level of cognitive functioning. Two found some indication of a relationship; alveolar bone loss and pocket depth were associated with poor cognitive functioning, the other found a significant decline on the Modified Mini-Mental State Examination (which assesses several areas of cognition) with gingival inflammation but only when the continuous form of the gingival index was categorized and the bottom quartile was compared with the rest; no significant decline was found on the Digit Symbol Substitution Test.

Three studies asked about or provided personal dental care. An intervention in nursing homes to make sure that teeth, dentures, and the oral cavity were cleaned and plaque and calculus controlled found a significantly smaller decline in MMSE score in the group receiving this oral care, although variation was large, and the number of participants present at study end were unclear. In one study, poor oral hygiene and no regular visits to the dentist predicted incident dementia. Similar findings were reported in another study but were sex-specific—no daily tooth brushing (women only) and no dental visits in the previous 12 months (men only) predicted incident dementia.

**Effect of Cognitive Status on Oral Health (5 Articles)**

Sample sizes tended to be small when examining the effect of cognitive status on longitudinal oral status, and the number of oral outcomes of interest was large. One study that provided routine dental care and treatment focused specifically on tooth loss; neither number of teeth lost nor rate of loss differed significantly between the groups with and without dementia. Other studies also found no statistically significant differences in number of teeth or restored surfaces.

Considerable attention was paid to increase in the number of decayed teeth, which was variously higher in individuals with dementia, higher but not significant because of small sample size, or not significantly different. Poorer MMSE scores were associated with gingival bleeding, plaque, and poorer mucosal health, but because sample sizes were small, these findings were only suggestive.

**Assessment of Strength of Eligible Studies**

A set of criteria was used to assess each of the studies, including sample selection, adequate sample size, description of the sample, validated assessment of exposure (e.g., cognitive status or oral health measure) and outcome (e.g., cognitive status or oral health measure), length of follow-up, attrition, controls for confounding, and appropriate analytical approach. The evidence suggests that there are methodological deficiencies in this area, most notably due to small sample size or lack of representativeness of the population, inadequate assessment of cognitive function, and lack of clinical evaluation of oral health. Thus, there was insufficient evidence of a causal association between cognitive function and oral health.

**DISCUSSION**

This systematic review of 20 years of longitudinal studies designed to examine the association between oral health and cognitive status identified 16 studies, 11 of which examined the effect of oral health status on change in cognitive status and five the reverse. It is likely that the uneven distribution reflects the costs and difficulties of performing oral health assessments. It is easier and cheaper to add cognitive assessments to a study for which oral health has already been measured than to do the reverse.

It is unclear how or whether oral health conditions and cognitive status are related. Findings based on number or change in number of teeth or decayed teeth are conflicting or, because of inadequate sample size, do not reach statistical significance. Limited studies (2 of 5) found that periodontal conditions (e.g., gingival health, pocket depth) were associated with poorer cognitive status or cognitive decline, with findings possibly sensitive to the neuropsychology assessments used. There are indications, albeit weak, that better oral hygiene and regular dental visits may reduce the rate of cognitive decline and the hazard of incident dementia. With good dental care, the dental status of individuals with dementia remained comparable with that of individuals without dementia. These findings may reflect that incipient cognitive decline or dementia leads to decline in hygiene but that oral health can be maintained with self or assisted oral hygiene and dental appointments.

Although the argument of a common underlying cause associated with inflammation may be enticing, it was examined directly in only one study and found to be only marginally relevant. Current studies are not adequate to indicate whether poor oral health and cognitive decline have a common underlying cause in inflammation, but with the increase in major surveys with biomarker data, testing of this hypothesis is becoming more feasible.

Because of the costs of detailed dental examination, there may be a temptation to conduct small sample studies.
As seen in the current review, this results in a lack of power. There is also a temptation to match cases and controls, but matching must be considered carefully. Doing so eliminates the possibility of examining the “matching” conditions (e.g., demographic characteristics), which may be associated with oral health and cognitive status. With an older population, the duration of a study becomes a challenge because of incidence of additional chronic conditions that may affect oral health and cognition, attrition due to sickness, and death.

To better compare findings of studies, agreement is needed regarding the oral health factors to be explored, oral health and neuropsychological measures to use, and covariates for which to adjust. In particular, to reduce the costs of dental studies, additional information is needed on the extent to which self-report accurately determines oral health, oral hygiene behavior, and dental visits. Although it appears that self-assessment of obvious conditions (e.g., number of teeth) and those that are salient (e.g., root canal, dentures) can be reported reliably (with accuracy varying according to demographic status), self-report is less reliable for conditions requiring oral health expertise (e.g., caries, periodontal disease), but because no studies have been conducted to examine the reliability of self-reported data in individuals with cognitive impairment, how reliable self-reported oral health data from such individuals is unclear.

There is considerable literature on assessment of cognitive state, with agreement on preferred measures to use in memory disorders clinics to assess dementing disorders and procedures to follow in epidemiological studies, such as diagnostic adjudication. With increasing information on dementia, diagnostic criteria are changing, and diagnosis at an earlier stage of disease is becoming possible. Consequently, the characteristics of diagnosed subjects may change, with findings on an association between oral health and dementia changing as well.

Standardization of assessment of cognitive status should be considered. The most frequently used measure has been the MMSE, indicating preference for a brief, easy-to-administer assessment. The MMSE has several drawbacks: multiple versions with unknown equivalence, age-, race-, and education-biased performance, as with many brief cognitive screens; a ceiling effect; and payment required for use. Better screens such as the Montreal Cognitive Assessment have become available since data were gathered for many of the current studies, and these screens should be considered. Agreement on use of a brief screen would facilitate comparison of findings and aggregation of data.

Covariates varied from study to study, with a large variety reported: demographic, health conditions (in particular cardiovascular conditions and risk factors), medications (anticholinergics), health behaviors, and an assortment of other characteristics (e.g., scales of depression, caregiver burden). Certain relevant information was rarely included (e.g., nutrition, which affects oral health and general health, and environmental characteristics (dental insurance, access to dentists, cultural expectations regarding dentition)). Although many studies have found self-report of medical conditions to be valid, care should be taken regarding medical and dental records and administrative data. Diagnosis of dementia based on administrative records that determine level of care to be provided may yield overdiagnosis, whereas dementia may be underreported in administrative medical records and death certificates. Agreement is needed on which covariates to include in analysis and the manner in which they should be handled, in particular, regarding categorization of age, and education.

Current studies that capitalize on already available information on oral health, cognition, or biomarkers illustrate how sample size and possibly representativeness can be increased and costs reduced. In addition to secondary analysis of data, some studies have used administrative records with known sensitivity and specificity for diagnosis of dementia, whereas others have linked the main study data to dental records. Although there is no report as to whether those dental records were evaluated, studies that have examined preexisting radiographs have found them to be usable for assessment of periodontal disease.

This is the first systematic review to examine longitudinal studies focused on oral health and cognition. As such, it shows substantial diversity across studies with regard to data and sample sources, sample size, and variety of oral health and cognitive data obtained. In summary, the strength of the evidence is weak, and findings were often inconsistent. For example, some studies found a significant association, albeit relatively weak, between periodontal disease and cognitive decline, but other studies found no association. Similarly the association between dental caries and cognition was inconsistent across studies. Findings are even more complex for the association between tooth loss and cognitive decline, ranging from a positive association to no association to a negative association (only in the group with a lower level of education) in different studies. Nevertheless, these studies lay the groundwork for future longitudinal work.

Although research in the field appears to be moving in the right direction, some specific suggestions are offered, operationalization of which may permit more-accurate determination of the grounds for an association, if one is present, between oral health and cognitive status. In the current studies, cognitive function has been evaluated using a great variety of cognitive measures. Information could be better evaluated if there were agreement on a uniform set of cognitive assessments. When change in cognition is assessed, it may be preferable to examine decline in cognitive function (which is more straightforward to assess) instead of development of dementing disorders, with attendant complexities in diagnosis. Regarding the assessment of oral health status, several studies used standardized oral health examination protocols, such as the U.S. National Institute of Dental Research protocol, a standard procedure that researchers should follow. Future research should pay more attention to calibration of dental assessment, between and within dental evaluators. The oral health outcomes used should reflect oral health status, which can change during the study period. With respect to other aspects of study design, use of standard covariates, samples sized adequately for the number and type of outcomes to be measured and better representative of the study population, study duration appropriate to the
planned outcome, and sophisticated statistical approaches already in use should be encouraged.

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REFERENCES


