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Cognitive function and oral health among ageing adults

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Keywords:	cognition, memory, Tooth loss, English longitudinal study of ageing, Oral health
Abstract:	<p>OBJECTIVES: There is inconclusive evidence that cognitive function is associated with oral health in older adults. This study investigated the association between cognitive function and oral health among older adults in England.</p> <p>METHODS: This longitudinal cohort study included 4,416 dentate participants aged 50 years or older in the English Longitudinal Study of Ageing during 2002-2014. Cognitive function was assessed at baseline in 2002/2003 using a battery of cognitive function tests. The self-reported number of teeth remaining and self-rated general oral health status were reported in 2014/2015. Ordinal logistic regression was applied to model the association between cognitive function at baseline and tooth loss or self-rated oral health.</p> <p>RESULTS: Cognitive function at baseline was negatively associated with the risk of tooth loss (per each 1-standard-deviation lower in cognitive function score, OR: 1.13, 95% CI: 1.05-1.21). When cognitive function score was categorized into quintiles, there was a clear gradient association between cognitive function and tooth loss (P-trend=0.003); people in the lowest quintile of cognitive function had higher risk of tooth loss than those in the highest quintile (OR: 1.39, 95% CI: 1.12-1.74). A similar magnitude and direction of association was evident between cognitive function and self-rated oral health.</p> <p>CONCLUSION: This longitudinal study in an English ageing population has demonstrated that poor cognitive function at early stage was associated with poorer oral health and higher risk of tooth loss in later life. The gradient relationship suggests that an improvement in cognitive function could potentially improve oral health and reduce the risk of tooth loss in the ageing population.</p>

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3 **Title:** Cognitive function and oral health among ageing adults
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6 **Short running title:** Cognitive function and oral health
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ABSTRACT

OBJECTIVES: There is inconclusive evidence that cognitive function is associated with oral health in older adults. This study investigated the association between cognitive function and oral health among older adults in England.

METHODS: This longitudinal cohort study included 4,416 dentate participants aged 50 years or older in the English Longitudinal Study of Ageing during 2002-2014. Cognitive function was assessed at baseline in 2002/2003 using a battery of cognitive function tests. The self-reported number of teeth remaining and self-rated general oral health status were reported in 2014/2015. Ordinal logistic regression was applied to model the association between cognitive function at baseline and tooth loss or self-rated oral health.

RESULTS: Cognitive function at baseline was negatively associated with the risk of tooth loss (per each 1-standard-deviation lower in cognitive function score, OR: 1.13, 95% CI: 1.05-1.21). When cognitive function score was categorized into quintiles, there was a clear gradient association between cognitive function and tooth loss (P-trend=0.003); people in the lowest quintile of cognitive function had higher risk of tooth loss than those in the highest quintile (OR: 1.39, 95% CI: 1.12-1.74). A similar magnitude and direction of association was evident between cognitive function and self-rated oral health.

CONCLUSION: This longitudinal study in an English ageing population has demonstrated that poor cognitive function at early stage was associated with poorer oral health and higher risk of tooth loss in later life. The gradient relationship suggests that an improvement in cognitive function could potentially improve oral health and reduce the risk of tooth loss in the ageing population.

Key words: Cognition, Memory, Tooth loss, Oral Health, English Longitudinal Study of Ageing, ELSA

INTRODUCTION

Cognitive impairment and its neuropathological manifestations, such as Alzheimer's disease and dementia in an ageing population, place significant burdens on health systems.¹ Many studies have proposed that poor oral health, specifically periodontal disease and tooth loss, is an important risk factor for cognitive impairment and increases the risk of dementia.²⁻⁷ Conversely, some studies also suggested that people with poor cognitive function or dementia might have poorer oral hygiene and experience more dental caries, periodontal disease, and more tooth loss than those with normal cognition.⁸⁻¹⁴ The possible reciprocal association between cognitive function and oral diseases might be explained by inflammatory and immune pathways in the pathogenesis, with inflammation being in this case a physiological response to oral bacterial infection. This is evidenced by a higher level of antibody to organisms (e.g. *P. gingivalis*, *Fusobacterium nucleatum* and *Prevotella intermedia*) observed in people with both oral diseases and cognitive impairment.¹⁵⁻¹⁷ The dysregulation of inflammatory and immune pathways leads to chronic inflammation, tissue destruction and disease manifestations.¹⁸ Whilst the evidence of a causal association between cognitive status and oral health, especially the impact of cognitive function on oral health, is still inconclusive from existing population studies^{3, 7}, it warrants further investigation.

The impact of cognitive function on oral health in existing longitudinal studies is weak or not evident due to small sample sizes, short follow-up, lack of representativeness, or inadequate assessment of cognitive function^{8-10, 19, 20}, while the association is more likely to be observed in the large representative cross-sectional studies.^{12, 13, 21-23} To date, evidence from a large representative longitudinal study with a long-term follow up to investigate the association between cognitive function and oral health, is lacking. The prospective national English Longitudinal Study of Ageing (ELSA)²⁴ is an ideal database to investigate the association between cognitive function and oral health.

This study used the ELSA database to investigate whether the cognitive function at early stage is associated with oral health outcomes later in life in an ageing population. We assessed whether tooth loss and self-rated general oral health status were affected by cognitive function at baseline during the 12-year follow-up, after adjusting for

sociodemographic characteristics, health conditions and behaviours, and relevant biomarkers.

METHODS

Study design and participants

This 12-year longitudinal cohort study included study participants from the ELSA, an ongoing, prospective cohort study of older, noninstitutionalized persons in England.²⁴

The first phase of data collection took place in 2002/2003, when the study recruited participants aged 50 years or older from three cross-sectional Health Surveys for England (HSE) conducted between 1998 and 2001.²⁵ A total of 11,391 participants, broadly representative of the English population, were surveyed in the first wave of data collection.²⁴ Between 2002 and 2014, there have been 7 biennial face-to-face examinations of study participants, and the study was replenished with new participants from HSE to maintain the size and representativeness of the cohort.

Therefore, not all participants at baseline survey in 2002/2003 were followed up at the 7th survey in 2014/2015. For the present analyses, we included only study participants who were surveyed at baseline in 2002/2003 and then had a follow-up survey in 2014/2015. Participants without any dentition or cognitive function data at baseline were excluded from the study. The flow chart of study participants is presented in Supplementary Figure S1. Ethical approval for ELSA was granted by the London Multicentre Research Ethics Committee. The study is reported in accordance with the STROBE guidelines.

Cognitive Function

Cognitive function at baseline was assessed using a battery of tests.²⁴ We selected three cognitive tests from three domains widely associated with age-related decline: memory, executive function, and processing speed. Memory was measured using the Delayed Word Recall Test.²⁶ Executive function was measured using the Verbal Fluency Test.²⁷ Processing speed was assessed using the Digit Symbol Substitution Test.²⁸ All scores were normally distributed with no evidence of ceiling or floor effects. A summed score from all three domains was calculated to represent cognitive function, which was a validated measure of general cognitive function in the field of cognitive epidemiology.²⁹ The ELSA also included other cognitive measurements within these three cognitive domains, but they were either objective or not discriminable, and therefore excluded in the analyses.²⁹

Oral Health Outcomes

The outcome variables were self-reported number of teeth remaining and self-rated general oral health status during face-to-face nurse interview at the 7th biennial survey in 2014/2015. Self-reported number of teeth remaining was obtained from the following question: “Adults usually have up to 32 natural teeth but over time people lose some of them. How many natural teeth have you got? Is it 1. None at all, 2. Between 1 and 9 natural teeth, 3. Between 10 and 19 natural teeth, 4. 20 or more natural teeth?” Self-rated general oral health status was obtained from the following question: “Would you say your dental health (mouth, teeth and/or dentures) is 1. excellent, 2. very good, 3. good, 4. fair, 5. or, poor?”

Covariates

Sociodemographic characteristics included age, sex, education qualification, marital status, and total net wealth. Health conditions included self-reported doctor diagnosed cardiovascular conditions (abnormal heart rhythm, angina, congestive heart failure, diabetes mellitus, heart attack, heart murmur, hypertension, and stroke), self-reported doctor diagnosed non-cardiovascular conditions (arthritis, asthma, cancer, chronic lung disease, osteoporosis, Parkinson’s disease, and emotional, nervous, and psychiatric problems), and depression symptoms (≥ 4 symptoms on eight-item Centre of Epidemiological Studies Depression (CESD) scale).³⁰ Anthropometric measurements included body mass index (BMI, kg/m², categorized into underweight, normal weight, overweight and obese), and waist circumference (cm). Health behaviours included alcohol consumption (daily or almost daily, weekly to monthly, rarely to never), smoking status (never smoker, ex-smoker, current smoker), weekly physical activity (None, mild, moderate, vigorous), and dentist visits (regular, occasional, never). C-reactive protein level was used as a possible biomarker associated with cognitive decline.³¹

All covariates were measured during the baseline biennial survey in 2002/2003, except BMI, waist circumference, and C-reactive protein, which were measured only on the second biennial survey, in 2004/2005.

Statistical analyses

Cognitive function scores at baseline were categorised into quintiles (1: 4-43, 2: 44-49, 3: 50-54, 4: 55-61, and 5: 62-102). Higher cognitive scores or quintiles correspond to better cognitive function. The characteristics of the study sample were summarized according to the quintiles of the cognitive function scores. Continuous variables were

presented as mean (SD) and categorical variables were reported as frequency (%). Distributions of the outcome variables (number of teeth remaining and self-rated general oral health) were plotted against the quintile of cognitive function at baseline.

The outcome variable of the self-reported number of teeth remaining was treated as a 4-level ordinal categorical variable (20+, 10-19, 1-9, and edentulous). Accordingly, an ordinal logistic regression was used to model the impact of cognitive function score as a continuous variable on the severity of tooth loss. First, an ordinal logistic regression was carried out using the categorized number of teeth remaining as the dependent variable and cognitive function score as the only independent variable. Then we used a series of multivariable ordinal logistic regression models to assess the impact, if any, of controlling for a range of covariates that were organized by theme, such as socioeconomic status (education qualification, total net wealth, and marital status), comorbidities (cardiovascular and non-cardiovascular conditions, depression symptoms), and health behaviours (alcohol consumption, smoking status, physical exercise, body mass index, waist circumference, dentist visiting, C-reactive protein). We also dichotomized number of teeth into 20+ and less than 20, and performed the same modelling strategy on this binary outcome. A directed acyclic graph was presented in the Supplement (Fig S2) to illustrate the relation between cognitive function, oral health and all covariates, and was used in our modelling strategy.

The outcome variable of the self-rated general oral health status was grouped into a 3-level ordinal categorical variable (Excellent/very good, good, and fair/poor). We applied the same modelling strategy as for number of teeth remaining, and assessed the impact of cognitive function score on self-rated oral health.

To minimize bias caused by a small proportion of missing data in the covariate variables, multiple imputation by chained equations was used to produce 10 imputed data sets. Pooled modelling estimates and accompanying 95% CIs were generated according to Rubin's rules.³² We performed all regression models using the multiple imputed datasets, and we also performed the same models on the complete dataset as a sensitivity analysis (supplementary table S1). We assessed the proportional odds assumption for the ordinal logistic models. All tests were 2-sided, and statistical significance was set as $p < 0.05$. Statistical analyses were performed in R version 3.4.1 (<https://cran.r-project.org/>).

RESULTS

A total of 4,416 participants (average age 59.5 years, SD 8.2 years, range 50-88 years, median 58 years; 2,523 (57.3%) women; average cognitive function score 52.3, SD 10.7) were analysed in the study. Baseline characteristics of the study participants are summarized by the quintile of cognitive function score in Table 1. At baseline, higher cognitive function (higher quintile) was associated with younger participants; a higher proportion of women, daily or almost daily alcohol consumption, moderate to vigorous physical activity, and regular dentist visits; less cardiovascular or non-cardiovascular conditions; lower proportion of participants without any education qualification, CESD depression symptoms ≥ 4 ; and lowest quintile of total wealth.

Over the 12-year follow-up, the proportion of participants with 20 or more teeth remaining was significantly higher for the higher quintile of cognitive function score (quintile 5 76.2% vs quintile 1 49.1%) (Figure 1a). Self-rated general oral health status was symmetrically distributed within each quintile, while the proportion of participants reporting fair/poor oral health was significantly higher in the lower quintile of cognitive function score (quintile 5 16.8% vs quintile 1 30.0%) (Figure 1b).

The association of a lower cognitive function score with oral health outcome measures (number of teeth remaining using a 4-level ordinal measure or binary measure, self-rated oral health using a 3-level ordinal measure or binary measure) is presented in Table 2. Given that the range of cognitive function scores was 4 to 102, we reported the odds ratio with respect to a 1-standard-deviation change in cognitive function score (a change of 10.7) instead of a change of 1. When number of teeth remaining was the outcome of interest, in age- and sex-adjusted analyses, a 1-standard-deviation lower in cognitive function score was associated with a greater risk of tooth loss (Odds Ratio = 1.36, 95% CI 1.27-1.45). Adding groups of covariates to the model separately resulted in a certain degree of attenuation, particularly when socioeconomic status was taken into account (Odds Ratio reduced from 1.36 to 1.14, 95% CI 1.06-1.22). A similar effect was evident when self-rated oral health was the outcome of interest. Again, socioeconomic status was the covariate that attenuated impact the most (OR was reduced from 1.26, 95% CI 1.19-1.34 to 1.19, 95% CI 1.12-1.26). Dichotomizing the outcome variables did not change the direction nor the

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3 magnitude of the association between cognitive function score and tooth loss or self-
4 rated oral health.
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7 To gain insights into the shape of the association, we assessed the risk of tooth loss
8 across the full range of cognitive function scores by quintile in Figure 2a. There was a
9 clear stepwise association with cognitive function and the risk of tooth loss (P for
10 trend = 0.003); participants in the lowest quintile of cognitive function had a higher
11 risk of tooth loss than those in the highest quintile (OR: 1.39, 95% CI 1.12-1.74). The
12 risk of tooth loss was also higher for participants in the second quintile (OR: 1.35, 95%
13 CI 1.11-1.66), third quintile (OR: 1.22, 95% CI 0.99-1.50), and fourth quintile (OR:
14 1.16, 95% CI: 0.97-1.40). The strong **gradient association** was apparent for self-rated
15 general oral health status as shown in Figure 2b (P for trend = 0.011). Participants in
16 the lowest quintile of cognitive function scores had a higher risk of poor self-rated
17 oral health than those in the highest quintile (OR: 1.52, 95% CI 1.26-1.85). Compared
18 to people in the highest quintile of cognitive function scores, people in the lower
19 quintiles were more likely to have poorer self-rated oral health (i.e., second quintile
20 (OR: 1.29, 95% CI 1.08-1.54), third quintile (OR: 1.21, 95% CI 1.00-1.45) and fourth
21 quintile (OR: 1.19, 95% CI 1.01-1.41)).
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34 **DISCUSSION**

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36 In this 12-year prospective longitudinal cohort study, there was a significant negative
37 impact of lower levels of cognitive function on tooth loss and self-rated general oral
38 health. Lower cognitive function scores at baseline were associated with a higher risk
39 of tooth loss and poorer self-rated oral health during the 12-year follow-up. This
40 negative impact was robust, persisting despite an extensive statistical adjustment
41 process that included sociodemographic characteristics, comorbidity conditions,
42 health behaviours and biomarkers. The findings strongly suggest the importance of
43 good cognitive function for oral health in older adults.
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51 Using large cross-sectional nationally representative data, previous studies have found
52 a significant association between cognitive function and number of teeth remaining.^{12,}
53^{21, 22} Using a large longitudinal representative cohort, our study demonstrated that
54 lower cognitive function at baseline was associated with a higher number of teeth
55 remaining in the 12-year follow-up period. A few longitudinal studies have reported
56 weak or no significant association between cognitive function and oral health.^{8-10, 19,}
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²⁰ However, compared to our study, these investigations had relatively small sample sizes and shorter follow-up periods, and often used a single measure of cognitive function. Using a large nationally representative cohort dataset with a comprehensive battery of cognitive function test, our results revealed a robust association between cognitive function and tooth loss even after extensive adjustment of covariates and potential confounding factors. **It is possible that people with poor cognitive function were at higher risk of dementia, resulting in losing ability to self-care that leads to poorer oral hygiene and oral health.**¹³ Given the suggestion that cognitive function might be modifiable in older groups³³, our findings could have potential implication for health providers and policy makers.

Our study also found that higher levels of cognitive function were associated with better self-rated general oral health status. This is one of the few studies conducted in this area.^{12, 34, 35} For example, Lee et al. (2013) found that participants with normal cognitive function had better oral health-related quality of life than those participants with cognitive impairment. However, that study used cross-sectional data with a small convenience sample. Poor cognitive function is often associated with mobility problems, limited activities of daily living and self-neglect.^{36, 37} This longitudinal study has shown that baseline cognitive function was associated with self-rated oral health during the 12-year follow-up, and that poor cognitive function has a significant impact on the oral health in later life.

This study has a number of strengths including a large prospective longitudinal design with a long-term follow-up, and the study cohort is geographically and demographically representative of the ageing population in England. Therefore, the findings are generalizable. There were few missing data for a large-scale investigation, especially in relation to cognitive function. Despite these strengths, however, there are some limitations we should acknowledge. First, the available dental outcome information was limited to number of teeth remaining and self-rated oral health and was only available at the 7th biennial survey. Therefore the rate of tooth loss could not be assessed, nor the oral health impact on cognitive function could be examined. While the number of teeth remaining can be reported reliably³⁸, a more detailed clinical examination and more frequent assessment of other oral health markers, such as dental caries and periodontal conditions, would have allowed for a more detailed and comprehensive investigation of the causal and progressive association between

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3 cognitive function and oral health in this older population. Second, there could be
4 sampling bias because we included only study participants with natural teeth at
5 baseline. It is possible that participants with lower cognitive function at baseline
6 already had fewer teeth remaining or poorer oral health. Third, a substantial
7 proportion (45.9%) of participants recruited at baseline were not surveyed in the 7th
8 biennial survey, mainly because the ELSA study replenished the sample with new
9 participants from the 4th biennial survey and onwards while maintaining the similar
10 survey population size. However, the baseline cognitive function and other
11 characteristics for those without 7th survey were not different from the analytical
12 sample in the study (data not shown). Fourth, in keeping with other health behaviours,
13 diet appears to be under a degree of cognitive control³⁹ and is associated with oral
14 health.⁴⁰ However, we do not have detailed dietary data to explore the potential
15 confounding and mediating effects. Finally, although participants in the ELSA study
16 were well characterized in general, which allowed us to adjust estimates across a
17 range of covariates, there was inevitably a residual confounding issue that is intrinsic
18 to all observational studies. **This is because** some potentially important confounders
19 were either unmeasured at baseline (e.g., systemic inflammatory biomarkers such as
20 interleukin-6) or might not even be captured (e.g., dental insurance and daily tooth
21 brushing).

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37 In conclusion, **this longitudinal study in an English ageing population has**
38 **demonstrated that poor cognitive function at early stage was associated with poorer**
39 **oral health and higher risk of tooth loss in later life.** The **gradient** relationship suggests
40 that an improvement in cognitive function could potentially improve oral health and
41 reduce the risk of tooth loss in the ageing population. Practically in healthcare settings
42 therefore, the findings indicate that cognitive remediation interventions may not only
43 benefit mental wellbeing, but also help facilitate and prolong good oral health in older
44 populations.
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Author contributions: J. Kang contributed to design, analysis and interpretation, drafted the manuscript; B. Wu, D. Bunce, M. Ide, and S. Pavitt contributed to data interpretation and critically revised the manuscript; J. Wu contributed to conception and design, data acquisition, analysis and interpretation, and critically revised the manuscript. All authors gave final approval and agreed to be accountable for all aspects of the work.

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REFERENCES

1. Prince M, Bryce R, Albanese E, Wimo A, Ribeiro W, Ferri CP. The global prevalence of dementia: A systematic review and metaanalysis. *Alzheimer's and Dementia*. 2013;9:63-75.
2. Tsakos G, Watt RG, Rouxel PL, de Oliveira C, Demakakos P. Tooth loss associated with physical and cognitive decline in older adults. *J Am Geriatr Soc*. 2015;63:91-9.
3. Cerutti-Kopplin D, Feine J, Padilha DM, de Souza RF, Ahmadi M, Rompré P, et al. Tooth Loss Increases the Risk of Diminished Cognitive Function. *JDR Clinical & Translational Research*. 2016;1:10-9.
4. Kaye EK, Valencia A, Baba N, Spiro A, 3rd, Dietrich T, Garcia RI. Tooth loss and periodontal disease predict poor cognitive function in older men. *J Am Geriatr Soc*. 2010;58:713-8.
5. Batty GD, Li Q, Huxley R, Zoungas S, Taylor BA, Neal B, et al. Oral disease in relation to future risk of dementia and cognitive decline: prospective cohort study based on the Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified-Release Controlled Evaluation (ADVANCE) trial. *Eur Psychiatry*. 2013;28:49-52.
6. Takeuchi K, Ohara T, Furuta M, Takeshita T, Shibata Y, Hata J, et al. Tooth Loss and Risk of Dementia in the Community: the Hisayama Study. *J Am Geriatr Soc*. 2017;65:e95-e100.
7. Wu B, Fillenbaum GG, Plassman BL, Guo L. Association Between Oral Health and Cognitive Status: A Systematic Review. *J Am Geriatr Soc*. 2016;64:739-51.
8. Chen X, Shuman SK, Hodges JS, Gatewood LC, Xu J. Patterns of tooth loss in older adults with and without dementia: a retrospective study based on a Minnesota cohort. *J Am Geriatr Soc*. 2010;58:2300-7.
9. Chalmers JM, Carter KD, Spencer AJ. Caries incidence and increments in community-living older adults with and without dementia. *Gerodontology*. 2002;19:80-94.
10. Jones JA, Lavalley N, Alman J, Sinclair C, Garcia RI. Caries incidence in patients with dementia. *Gerodontology*. 1993;10:76-82.
11. Syrjala AM, Ylostalo P, Ruoppi P, Komulainen K, Hartikainen S, Sulkava R, et al. Dementia and oral health among subjects aged 75 years or older. *Gerodontology*. 2012;29:36-42.
12. Wu B, Plassman BL, Crout RJ, Liang J. Cognitive function and oral health among community-dwelling older adults. *J Gerontol A Biol Sci Med Sci*. 2008;63:495-500.
13. Thomson WM, Smith MB, Ferguson CA, Kerse NM, Peri K, Gribben B. Oral status, cognitive function and dependency among New Zealand nursing home residents. *Gerodontology*. 2018.
14. Naorungroj S, Slade GD, Beck JD, Mosley TH, Gottesman RF, Alonso A, et al. Cognitive decline and oral health in middle-aged adults in the ARIC study. *J Dent Res*. 2013;92:795-801.
15. Olsen I, Singhrao SK. Can oral infection be a risk factor for Alzheimer's disease? *J Oral Microbiol*. 2015;7:29143.
16. Sparks Stein P, Steffen MJ, Smith C, Jicha G, Ebersole JL, Abner E, et al. Serum antibodies to periodontal pathogens are a risk factor for Alzheimer's disease. *Alzheimers Dement*. 2012;8:196-203.
17. Singhrao SK, Harding A, Simmons T, Robinson S, Kesavalu L, Crean S. Oral inflammation, tooth loss, risk factors, and association with progression of Alzheimer's disease. *J Alzheimers Dis*. 2014;42:723-37.
18. Cekici A, Kantarci A, Hasturk H, Van Dyke TE. Inflammatory and immune pathways in the pathogenesis of periodontal disease. *Periodontol 2000*. 2014;64:57-80.
19. Ship JA, Puckett SA. Longitudinal study on oral health in subjects with Alzheimer's disease. *J Am Geriatr Soc*. 1994;42:57-63.

20. Ellefsen B, Holm-Pedersen P, Morse DE, Schroll M, Andersen BB, Waldemar G. Assessing caries increments in elderly patients with and without dementia: a one-year follow-up study. *J Am Dent Assoc.* 2009;140:1392-400.
21. Avlund K, Holm-Pedersen P, Morse DE, Viitanen M, Winblad B. Tooth loss and caries prevalence in very old Swedish people: the relationship to cognitive function and functional ability. *Gerodontology.* 2004;21:17-26.
22. Syrjala A-M, Ylöstalo P, Sulkava R, Knuuttila M. Relationship between cognitive impairment and oral health: results of the Health 2000 Health Examination Survey in Finland. *Acta Odontologica Scandinavica.* 2007;65:103-8.
23. Luo J, Wu B, Zhao Q, Guo Q, Meng H, Yu L, et al. Association between tooth loss and cognitive function among 3063 Chinese older adults: A community-based study. *PLoS ONE.* 2015;10:1-11.
24. Steptoe A, Breeze E, Banks J, Nazroo J. Cohort profile: the English longitudinal study of ageing. *Int J Epidemiol.* 2013;42:1640-8.
25. Mindell J, Biddulph JP, Hirani V, Stamatakis E, Craig R, Nunn S, et al. Cohort profile: the health survey for England. *Int J Epidemiol.* 2012;41:1585-93.
26. Knopman DS, Ryberg S. A verbal memory test with high predictive accuracy for dementia of the Alzheimer type. *Arch Neurol.* 1989;46:141-5.
27. Van der Elst W, Van Boxtel MP, Van Breukelen GJ, Jolles J. Normative data for the Animal, Profession and Letter M Naming verbal fluency tests for Dutch speaking participants and the effects of age, education, and sex. *J Int Neuropsychol Soc.* 2006;12:80-9.
28. MacDonald SW, Hultsch DF, Strauss E, Dixon RA. Age-related slowing of digit symbol substitution revisited: what do longitudinal age changes reflect? *J Gerontol B Psychol Sci Soc Sci.* 2003;58:P187-94.
29. Batty GD, Deary IJ, Zaninotto P. Association of Cognitive Function With Cause-Specific Mortality in Middle and Older Age: Follow-up of Participants in the English Longitudinal Study of Ageing. *Am J Epidemiol.* 2016;183:183-90.
30. Turvey CL, Wallace RB, Herzog R. A revised CES-D measure of depressive symptoms and a DSM-based measure of major depressive episodes in the elderly. *Int Psychogeriatr.* 1999;11:139-48.
31. Noble JM, Manly JJ, Schupf N, Tang MX, Mayeux R, Luchsinger JA. Association of C-reactive protein with cognitive impairment. *Arch Neurol.* 2010;67:87-92.
32. Rubin DB, Schenker N. Multiple imputation in health-care databases: an overview and some applications. *Statistics in medicine.* 1991;10:585-98.
33. Edwards JD, Wadley VG, Vance DE, Wood K, Roenker DL, Ball KK. The impact of speed of processing training on cognitive and everyday performance. *Aging Ment Health.* 2005;9:262-71.
34. Lee KH, Wu B, Plassman BL. Cognitive function and oral health-related quality of life in older adults. *J Am Geriatr Soc.* 2013;61:1602-7.
35. Jensen PM, Saunders RL, Thierer T, Friedman B. Factors associated with oral health-related quality of life in community-dwelling elderly persons with disabilities. *J Am Geriatr Soc.* 2008;56:711-7.
36. Zaninotto P, Batty GD, Allerhand M, Deary IJ. Cognitive function trajectories and their determinants in older people: 8 years of follow-up in the English Longitudinal Study of Ageing. *J Epidemiol Community Health.* 2018.
37. Dong X, Simon MA, Wilson RS, Mendes de Leon CF, Rajan KB, Evans DA. Decline in cognitive function and risk of elder self-neglect: finding from the Chicago Health Aging Project. *J Am Geriatr Soc.* 2010;58:2292-9.
38. Liu H, Maida CA, Spolsky VW, Shen J, Li H, Zhou X, et al. Calibration of self-reported oral health to clinically determined standards. *Community Dent Oral Epidemiol.* 2010;38:527-39.

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2
3 39. Gale CR, Deary IJ, Schoon I, Batty GD. IQ in childhood and vegetarianism in
4 adulthood: 1970 British cohort study. *BMJ*. 2007;334:245.
5 40. Hujoel P. Dietary carbohydrates and dental-systemic diseases. *J Dent Res*.
6 2009;88:490-502.
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Table 1. Baseline characteristics of study participants by Quintile of General Cognitive Function, ELSA (n = 4416), 2002-2014.

Characteristic	Quintile of Cognitive Function ^a					P-value ^b
	1 (n = 982)	2 (n = 965)	3 (n = 720)	4 (n = 944)	5 (n = 805)	
Cognition function scores, mean (SD)	38.41 (5.41)	47.80 (1.69)	52.55 (1.10)	57.69 (1.96)	68.29 (6.23)	<0.001
Age in years, mean (SD)	63.02 (8.74)	60.39 (8.03)	59.21 (7.79)	58.15 (7.49)	56.21 (7.21)	<0.001
Female sex	502 (51.1)	539 (55.9)	398 (55.3)	592 (62.7)	501 (62.2)	<0.001
Married	693 (70.6)	695 (72.0)	537 (74.6)	698 (73.9)	612 (76.0)	0.078
Education level						
Degree or equivalent	61 (6.2)	106 (11.0)	128 (17.8)	212 (22.5)	264 (32.8)	
Some qualification	474 (48.3)	552 (57.2)	416 (57.8)	565 (59.9)	463 (57.5)	<0.001
No qualification	447 (45.5)	307 (31.8)	176 (24.4)	167 (17.7)	78 (9.7)	
No of cardiovascular conditions						
0	506 (51.5)	577 (59.8)	444 (61.7)	576 (61.0)	536 (66.6)	
1	319 (32.5)	263 (27.3)	218 (30.3)	293 (31.0)	218 (27.1)	<0.001
2	115 (11.7)	89 (9.2)	43 (6.0)	62 (6.6)	41 (5.1)	
≥3	42 (4.3)	36 (3.7)	15 (2.1)	13 (1.4)	10 (1.2)	
No of non-cardiovascular conditions						
0	485 (49.4)	532 (55.1)	428 (59.4)	517 (54.8)	487 (60.5)	
1	364 (37.1)	316 (32.7)	225 (31.2)	324 (34.3)	243 (30.2)	<0.001
2	108 (11.0)	89 (9.2)	51 (7.1)	88 (9.3)	63 (7.8)	
≥3	25 (2.5)	28 (2.9)	16 (2.2)	15 (1.6)	12 (1.5)	
Smoking status						
Never smoker	382 (38.9)	391 (40.5)	312 (43.3)	392 (41.5)	326 (40.5)	
Ex-smoker	433 (44.1)	443 (45.9)	310 (43.1)	420 (44.5)	356 (44.2)	0.393
Current smoker	167 (17.0)	131 (13.6)	98 (13.6)	132 (14.0)	123 (15.3)	
Weekly or almost daily alcohol consumption	266 (27.1)	272 (28.2)	207 (28.7)	309 (28.8)	299 (37.1)	<0.001
Weekly physical exercise						
None	72 (7.3)	53 (5.5)	25 (3.5)	44 (4.7)	22 (2.7)	
Mild	148 (15.1)	100 (10.4)	61 (8.5)	70 (7.4)	58 (7.2)	<0.001
Moderate	475 (48.4)	479 (49.6)	347 (48.2)	455 (48.2)	378 (47.0)	
Vigorous	287 (29.2)	333 (34.5)	287 (39.9)	375 (39.7)	347 (43.1)	
CESD depression symptoms ≥4	181 (18.4)	136 (14.1)	85 (11.8)	102 (10.8)	77 (9.6)	
Lowest quintile of total wealth	173 (18.4)	92 (10.2)	53 (8.1)	56 (6.6)	43 (6.3)	<0.001
BMI (kg/m ²), mean (SD)	28.31 (4.69)	27.87 (4.68)	28.13 (4.77)	27.73 (5.03)	27.56 (4.93)	0.025
Waist circumference (cm), mean (SD)	97.15 (12.94)	95.29 (12.70)	95.49 (12.81)	93.84 (12.99)	93.56 (13.18)	<0.001
C-reactive protein, mean (SD)	3.58 (4.76)	3.34 (6.43)	3.45 (5.63)	3.10 (4.75)	2.99 (5.05)	0.315
Dentist visit						
Regular	365 (65.9)	417 (75.7)	294 (73.5)	423 (78.9)	391 (80.0)	
Occasional/urgent	158 (28.5)	123 (22.3)	93 (23.2)	101 (18.8)	92 (18.8)	<0.001
Never	31 (5.6)	11 (2.0)	13 (3.2)	12 (2.2)	6 (1.2)	

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Note: frequency (%) is reported unless specified; SD, standard deviation; CESD, Center for Epidemiological Studies Depression; BMI, body mass index;

a. Cognitive function scores were grouped by quintiles as follows: quintile 1 (lowest), 4-43; quintile 2, 44-49; quintile 3, 50-54; quintile 4, 55-61; quintile 5, 62-102.

b. P-value for trend for dichotomous and continuous variables; otherwise P-value for heterogeneity.

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Table 2. Odds ratios for the association between lower cognitive function scores^a and oral health status defined by tooth loss or self-rated oral health status, English Longitudinal Study of Aging (n = 4,416), 2002-2014.

Models	Oral health, odds ratio (95% CI) ^b			
	Number of teeth remaining ^c		Self-rated oral health ^d	
	4-level ordinal ^e	Binary ^f	3-level ordinal ^e	Binary ^f
Unadjusted	1.55 (1.45,1.65)	1.54 (1.44,1.65)	1.28 (1.21,1.36)	1.31 (1.22,1.41)
Age and sex	1.36 (1.27,1.45)	1.35 (1.26,1.45)	1.26 (1.19,1.34)	1.30 (1.21,1.41)
Age, sex and socioeconomic status ^g	1.14 (1.06,1.22)	1.14 (1.06,1.23)	1.19 (1.12,1.26)	1.20 (1.11,1.31)
Age, sex and comorbidities ^h	1.33 (1.24,1.42)	1.33 (1.24,1.42)	1.24 (1.17,1.32)	1.27 (1.18,1.37)
Age, sex and health behaviours ⁱ	1.27 (1.18,1.36)	1.27 (1.18,1.36)	1.20 (1.13,1.28)	1.23 (1.14,1.33)
Fully adjusted ^j	1.13 (1.05,1.21)	1.14 (1.05,1.23)	1.17 (1.10,1.24)	1.18 (1.09,1.28)

a. Per 1-standard-deviation **lower**.

b. Odds ratio estimates and 95% CIs were pooled over the ten imputed datasets.

c. Number of teeth remaining was represented by a 4-level ordinal variable (≥ 20 , 10-19, 1-9, and edentulous) or a binary variable (≥ 20 and < 20).

d. Self-rated oral health was represented by a 3-level ordinal variable (excellent/very good, good, and fair/poor); or a binary variable (excellent/very good/good and fair/poor).

e. An ordinal logistic regression model was fitted to the ordinal outcome variable.

f. A logistic regression model was fitted to the binary outcome variable.

g. Socioeconomic status was defined by participant's education qualification and total wealth.

h. Comorbidities comprised of number of cardiovascular and non-cardiovascular conditions and CESD depression score.

i. Health behaviours comprised alcohol intake, smoking status, weekly physical activity, dentist visit, C-reactive protein, body mass index and waist circumference.

j. Adjustment for all the covariates listed above.

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Fig. 1 Number of teeth remaining (a) and self-rated oral health status (b), stratified by quintile of cognitive function

Fig. 2 Odds ratios for the association between cognitive function scores and tooth loss (a) and self-rated oral health (b). Higher quintiles represent higher cognitive function scores; quintile 5 was used as the reference. Odds ratios are fully adjusted for the covariates in Table 2. Bars, 95% confidence intervals.

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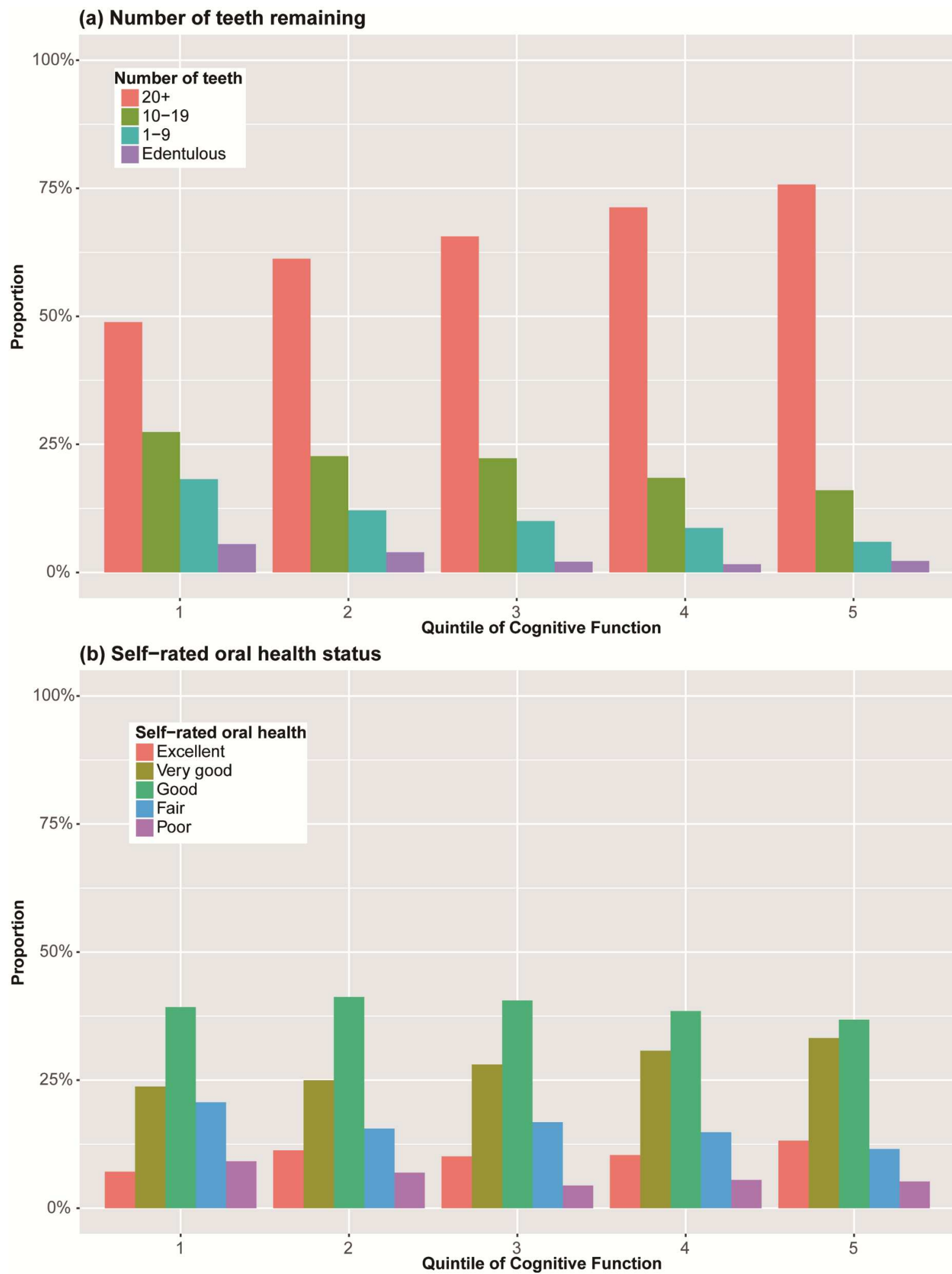


Figure 1. Distributions of number of teeth remaining (a) and self-rated oral health status (b), stratified by quintile of cognitive function

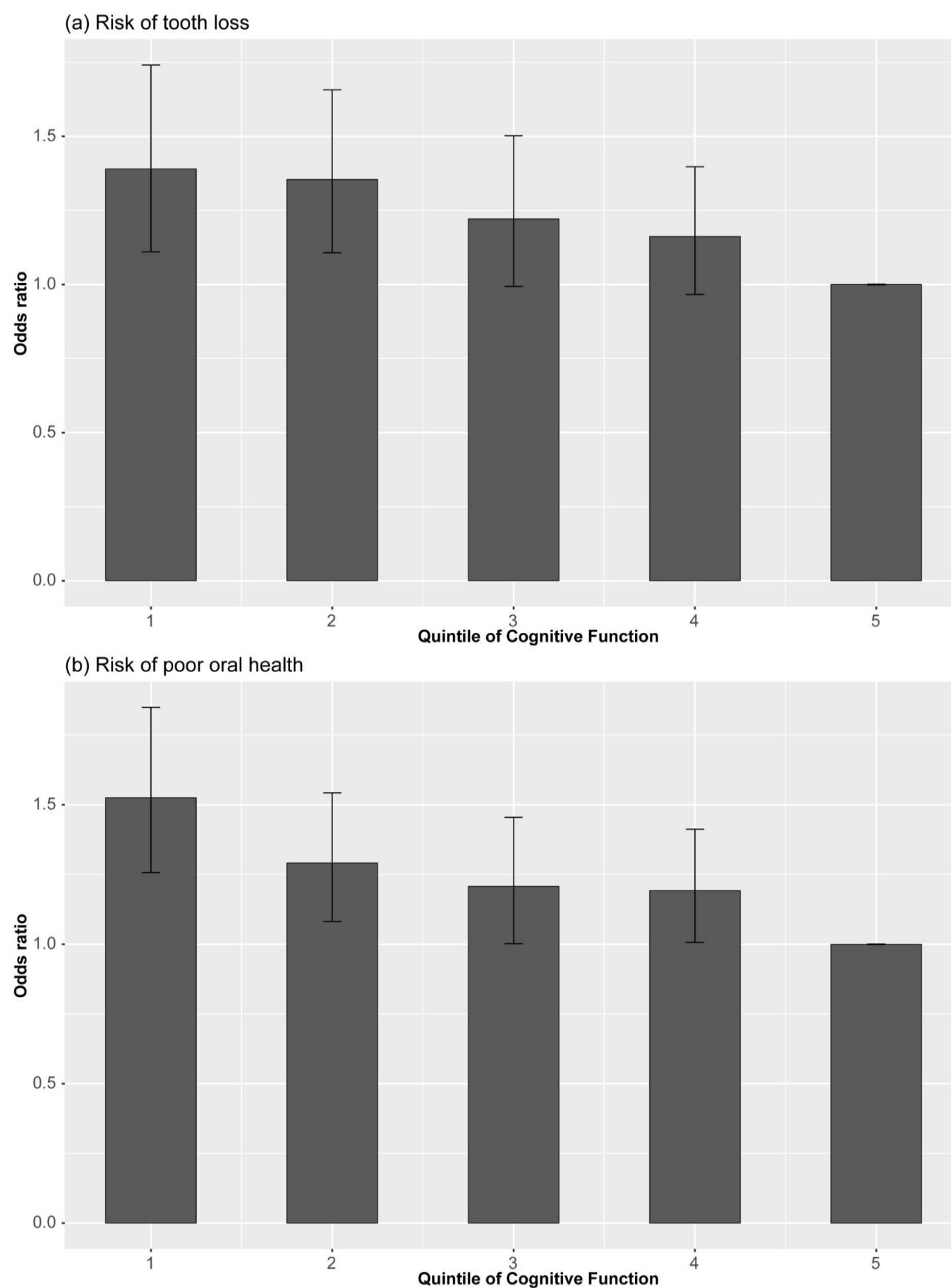


Figure 2. Odds ratios for the association between cognitive function scores and tooth loss (a) and self-rated oral health (b). Higher quintiles represent higher cognitive function scores; quintile 5 was used as the reference. Odds ratios are fully adjusted for the covariates in Table 2. Bars, 95% confidence intervals.