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Is poor oral health a risk marker for incident cardiovascular disease hospitalisation and all-cause mortality? Findings from 172 630 participants from the prospective 45 and Up Study

Grace Joshy,[1] Manish Arora,[2,3] Rosemary J Korda,[1] John Chalmers,[4] Emily Banks[1,5]

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For numbered affiliations see end of article.

Correspondence to
Dr Grace Joshy;
grace.joshy@anu.edu.au

ABSTRACT

Objective: To investigate the relationship between oral health and incident hospitalisation for ischaemic heart disease (IHD), heart failure (HF), ischaemic stroke and peripheral vascular disease (PVD) and all-cause mortality.

Design: Prospective population-based study of Australian men and women aged 45 years or older, who were recruited to the 45 and Up Study between January 2006 and April 2009; baseline questionnaire data were linked to hospitalisations and deaths up to December 2011. Study exposures include tooth loss and self-rated health of teeth and gums at baseline.

Setting: New South Wales, Australia.

Participants: Individuals aged 45–75 years, excluding those with a history of cancer/cardiovascular disease (CVD) at baseline; n=172 630.

Primary outcomes: Incident hospitalisation for IHD, HF, ischaemic stroke and PVD and all-cause mortality.

Results: During a median follow-up of 3.9 years, 3239 incident hospitalisations for IHD, 212 for HF, 283 for ischaemic stroke and 359 for PVD, and 1908 deaths, were observed. Cox proportional hazards models examined the relationship between oral health indicators and incident hospitalisation for CVD and all-cause mortality, adjusting for potential confounding factors. All-cause mortality and incident CVD hospitalisation risk increased significantly with increasing tooth loss for all outcomes except ischaemic stroke ($p_{trend}<0.05$). In those reporting no teeth versus ≥20 teeth left, risks were increased for HF (HR, 95% CI 1.97, 1.27 to 3.07), PVD (2.53, 1.81 to 3.52) and all-cause mortality (1.60, 1.37 to 1.87). The risk of IHD, PVD and all-cause mortality (but not HF or ischaemic stroke) increased significantly with worsening self-rated health of teeth and gums ($p_{trend}<0.05$). In those reporting poor versus very good health of teeth and gums, risks were increased for IHD (1.19, 1.03 to 1.38), PVD (1.66, 1.13 to 2.43) and all-cause mortality (1.76, 1.50 to 2.08).

Conclusions: Tooth loss and, to a lesser extent, self-rated health of teeth and gums, are markers for increased risk of IHD, PVD and all-cause mortality. Tooth loss is also a marker for increased risk of HF.

Strengths and limitations of this study

- This study provides empirical evidence about the magnitude of the relationship between poor oral health and cardiovascular disease (CVD), which is not necessarily causal, and its variation according to different types of CVD.
- This large cohort study investigated the relationship of self-reported oral health indicators, as markers of risk, to incident hospitalisation for various types of CVD; results indicate that tooth loss, and to a lesser extent, self-rated health of teeth and gums, are associated with increased risk of hospitalisation for ischaemic heart disease (IHD), peripheral vascular disease (PVD) and all-cause mortality.
- The ability to link to administrative records with survey data allowed virtually complete, and objective, ascertainment of hospitalisation outcomes over time; people with previous CVD could be objectively identified and excluded from the study.
- We were able to use self-reported number of natural teeth left, a valid measure in the general population, together with self-rated health of teeth and gums, as broad indicators of oral health.
- People with poor oral health are likely to be at increased risk of future CVD and may therefore benefit from referral for cardiovascular screening and early intervention, where appropriate.

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality globally, accounting for about 30% of deaths

worldwide.[1] Many effective interventions for the primary and secondary prevention of CVD rely on identifying individuals at increased risk. Despite the robustness of current risk prediction models, it is well recognised that a significant proportion of cases of CVD will occur in individuals without classic risk factors.[2]

Poor oral health (periodontal diseases and dental caries) has been shown to be associated with increased risk of atherosclerotic CVD;[3–5] however, this does not imply a causal relationship. The American Heart Association's review of observational studies in 2012,[3] which included 42 studies with self-reported/measured exposures and clinical CVD outcomes, concluded that the studies support an association between periodontal disease and atherosclerotic CVD, independent of known confounders. However, there was no evidence that periodontal interventions prevent atherosclerotic CVD, suggesting that the relationship was not causal. Periodontal diseases comprise a continuum of conditions involving inflammation of gingival tissues in response to dental plaque accumulation.[3] In adults, periodontal disease and dental caries are major causes of tooth loss; hence tooth loss and edentulism can be regarded as markers of past periodontal disease and caries.[6] Validation studies indicate that self-reports provide reasonably valid estimates for numbers of remaining teeth from clinical assessments.[7 8]

Initial hypotheses tended to focus on oral health as a potential causative factor in CVD through infection and inflammation. More recent work indicates that poor oral health may be more likely to be a 'risk marker' for CVD, that is, an indicator of underlying atherosclerosis, rather than an independent cause of CVD.[4 9–12] A risk marker for CVD is a non-causal factor associated with CVD that has the potential to serve as an indicator, or 'biomarker', of the severity of underlying pathological processes such as atherosclerosis and endothelial dysfunction.

Previous epidemiological studies have tended to focus on fatal outcomes (but not non-fatal CVD events),[4 13–15] specific individual CVD outcomes such as ischaemic heart disease (IHD)[16] and stroke,[13] or specific population groups,[17 18] resulting in a lack of clarity regarding the magnitude of the oral health–CVD relationship and its variation according to CVD subtypes. We were not able to locate any prospective population-based studies, looking at a broad spectrum of CVD outcomes, including peripheral vascular disease (PVD) and heart failure (HF).

The aim of this large cohort study was to investigate prospectively the relationship of self-reported oral health indicators, as markers of risk, to incident hospitalisation for various types of CVD, including IHD, ischaemic stroke, HF and PVD and to all-cause mortality, among men and women without a history of previous CVD at baseline.

METHODS

The Sax Institute's 45 and Up Study is a large-scale Australian cohort study of 267 153 men and women aged 45 and over, randomly sampled from the general population of New South Wales (NSW), Australia. Individuals joined the study by completing a postal questionnaire (distributed from 1 January 2006 to 31 December 2008) and giving informed consent for follow-up through repeated data collection and linkage of their data to population health databases. The study methods are described in detail elsewhere.[19]

Questionnaire data from study participants have been linked probabilistically to hospitalisations and deaths by the Centre for Health Record linkage (http://www.cherel.org.au/). The NSW Admitted Patient Data Collection (APDC) is a complete census of all public and private hospital admissions in NSW. The linked data contain details of admissions in participants from 1 July 2000 to 31 December 2011, including dates of admission and discharge; the primary reason for admission, coded using the International Classification of Diseases 10th revision—Australian Modification (ICD-10-AM);[20] up to 54 additional clinical diagnoses; and up to 50 operations or procedures, coded using the Australian Classification of Health Interventions procedure codes.[21] Dates of death were ascertained from the date of recruitment up to 31 December 2011 using linkage to the NSW Register of Births, Deaths and Marriages. Death registrations capture all deaths in NSW. Cause of death information was not available at the time of analysis.

Baseline questionnaire data include self-reported information on sociodemographic and behavioural risk factors, medical and surgical history, functional capacity and oral health. The questionnaire included a self-assessment question on oral health: 'In general, how would you rate your teeth and gums?', with the response categories being excellent, very good, good, fair and poor. The categories 'excellent' and 'very good' were combined and reported as 'very good' in this study, due to small numbers. A second question asked was 'How many of your own teeth do you have left?', with the response categories being none, 1–9 teeth left, 10–19 teeth left, ≥20 teeth left. Body mass index (BMI) was calculated from self-reported height and weight. Other baseline measures used in this study include tobacco smoking, alcohol consumption, education, region of residence, private health insurance, country of birth and physical activity sessions per week (weighted for intensity).[22]

Statistical methods

Excluding 376 (0.14%) participants with invalid age and/or date of recruitment, data from 266 777 participants from the 45 and Up Study were linked to data on hospital admissions and deaths; those with linkage errors (n=31; 0.01%) were subsequently excluded. To minimise confounding, those over 75 years of age at baseline (n=19 611; 7.4%) and those with a history of cancer at baseline (self-reported history of cancer other than melanoma and skin cancer (n=30 198; 11.3%) or hospital admission in the 6 years prior to entering the

study with diagnosis of cancers of lip, head or neck (ICD-10-AM diagnosis codes C00-C14, C30-C32) in any diagnostic field (n=389; 0.15%)) were excluded from this study. Study flow diagram is included in the online supplementary figure S1. To capture incident CVD events (ie, those occurring for the first time), those with a history of CVD at baseline (defined as self-reported CVD determined using the question 'Has a doctor EVER told you that you have… 'heart disease', 'stroke' or 'blood clot (thrombosis).'; or a hospital admission in the 6 years prior to entering the study with a major CVD diagnosis code in any diagnostic field; or a CVD-related procedure code in any procedure code field;[23] see online supplementary tables S1 and S2 for full list of codes; n=43 918; 16.5%) were also excluded. A 6-year window was used to ensure uniform probability of identification of previous diagnoses from administrative data for all participants. Following exclusion, data on 172 630 participants were available for the main analyses. Participants with missing data on number of natural teeth left (n=4933; 2.9%) and missing data on self-rated health of teeth and gums (n=6831; 4.0%) did not contribute to the corresponding analyses.

Outcomes of interest were incident hospitalisations for CVD and all-cause mortality. Primary diagnoses from hospitalisation records were grouped as IHD (ICD-10-AM I20–I25, also known as coronary heart disease, coronary artery disease and atherosclerotic heart disease); PVD (ICD-10-AM I70–I74); ischaemic stroke (ICD-10-AM I63) and HF (ICD-10-AM I50, also known as chronic HF, and is often referred to as congestive HF or congestive cardiac failure). Each outcome was defined as the first hospitalisation following recruitment into the 45 and Up Study with an outcome-specific primary diagnosis at discharge, based on ICD-10-AM three-character codes.

Although the CVD outcomes examined (IHD, PVD, HF and ischaemic stroke) are atherosclerotic in nature, other studies of risk markers (eg, erectile dysfunction) have demonstrated differing magnitudes of relationships, and hence predictive ability. Hence, it is of interest to quantify the relationship of oral health status to differing types of CVD. More specifically, peripheral arteries and certain cerebral arteries are smaller than coronary arteries and are closer in size to blood vessels in the mouth. People may therefore exhibit PVD symptoms or have cerebrovascular disease at a stage of atherosclerosis that differs from that of coronary disease. HF is often seen in more severe IHD and is often under diagnosed; if oral health status is a strong predictor of HF, this could provide clues for early diagnosis. All-cause mortality was included as an outcome since CVD is the leading cause of mortality.[1]

In the analyses of incident hospitalisations since baseline, eligible participants contributed person-years from the date of recruitment until the outcome-specific admission date, date of death or end of follow-up (31 December 2011), whichever was the earliest. Incident CVD hospitalisation rates and all-cause mortality rates since baseline and 95% CIs were calculated for the different levels of the two indicators of oral health (number of teeth left and self-rated health of teeth and gums); the rates for males and females were age standardised to the 2006 NSW population, in 5-year age-groups, using the direct method.[24] HRs were estimated using Cox regression modelling. HRs for incident CVD hospitalisation for each type of CVD (IHD I20–I25; PVD I70–I74; ischaemic stroke I63; HF I50) and all-cause mortality were estimated for the reported number of natural teeth left, using the category '≥20 teeth left' as the reference group. The HR and 95% CI are shown initially adjusted for age as a continuous variable and sex. Models are then presented additionally adjusted for covariates, known a priori to be confounders,[25–27] including tobacco smoking (current, past, never), alcohol consumption (0, 1–14 or ≥15 alcoholic drinks/week), education (<secondary school, secondary school graduation, trade/apprenticeship/certificate/diploma, university graduate), region of residence (major cities, inner regional areas, outer regional/remote areas), private health insurance (yes or no) and Australian born status (Australian born, non-Australian born), physical activity sessions per week (<7, 7–12 and ≥13, weighted for intensity) and BMI (15–19.99, 20–22.49, 22.5–24.99, 25–27.49, 27–29.99, 30–32.49, 32.5–50 kg/m^2). Missing values for covariates were included in the models as separate categories. The relationship of tooth loss (categorised as a dichotomous variable: <10 vs ≥10 teeth left) to IHD hospitalisation was examined for subgroups of age, sex, smoking, alcohol consumption, Australian born status, annual household income, educational qualification, region of residence, BMI, physical activity sessions, diabetes and private health insurance.

The proportionality assumption was verified by plotting the Schoenfeld residuals against the time variable in each model, with a stratified form or time-dependent form of the model used, where covariates displayed non-proportionality of hazards. Tests for trend were performed by modelling the exposure categories as an ordinal variable. The χ^2 test for heterogeneity was used to test for heterogeneity between subgroups. Likelihood ratio tests were used to assess statistical interaction with age. All statistical tests were two-sided, using a significance level of 5%. All analyses were carried out using SAS V.9.3 (SAS version V.9.3 (computer program). North Carolina, USA: SAS Institute, 2011).

RESULTS

The participants included 172 630 men and women aged between 45 and 75 years. Over two-third (70%) of the cohort had ≥20 teeth left and 38% reported 'very good' or 'excellent' health of their teeth and gums (table 1, see online supplementary tables S3 and S4). Oral health at baseline differed markedly according to age group, with the proportion of 65–75 year olds

Table 1 Characteristics of study population according to oral health status at baseline

	Number of natural teeth left				Self-rated health of teeth and gums				
	None	1–9	10–19	20+	Poor	Fair	Good	Very good*	Overall
N	8797	11 423	30 013	117 464	9802	30 574	62 447	62 976	172 630
Percentage of total	5	7	18	70	6	18	38	38	
Age in years (mean±SD)	64±7	63±7	60±8	56±7	59±8	59±8	58±8	57±7	58±8
Age 45–64	50	58	70	85	76	76	79	83	79
Male	37	43	49	42	48	46	43	42	43
Residing in major cities	33	38	40	46	42	42	43	46	44
Tertiary education	8	10	17	32	13	20	25	34	27
Household income ≥$70 000	9	9	19	37	12	22	29	40	30
Current smoker	15	16	12	6	25	12	7	5	8
≥15 alcoholic drinks per week	12	13	16	15	16	16	15	15	15
Highest physical activity tertile	33	32	35	36	33	32	34	39	35
Doctor-diagnosed diabetes	12	12	9	5	11	8	6	5	6
Current treatment for hypertension	29	28	23	17	23	21	20	17	19
Current treatment for hypercholesterolaemia	17	16	14	11	15	14	12	11	12
Private health insurance	43	45	59	74	35	57	70	78	68
Aspirin treated	13	12	10	7	9	9	8	7	8
Australian born	76	74	75	76	66	72	76	78	75
Overweight (BMI 25–29.99 kg/m^2)	34	35	37	37	33	36	37	38	37
Obese (BMI ≥30 kg/m^2)	26	26	25	19	26	23	22	19	21
MOS-PF score ≥75	62	62	73	84	58	72	80	87	78

Data are percentages unless otherwise stated. Percentages were calculated out of column totals (N), except for 'percentage of total' where % refers to percentage of total sample in each oral health category. There were 4933 (2.86%) participants with missing data on number of own teeth left and 6831 (3.96%) missing data on self-rated heath of teeth and gums. Overall totals include the missing cases.
*Participants who rated their health of teeth and gums as 'excellent' (n=16,495, 9.6%) and those who rated their health of teeth and gums as 'very good' (n=46,481, 26.9%) are grouped together. All of the above baseline characteristics were significantly different according to tooth loss (p<0.0001) and according to self-rated health of teeth and gums (p<0.0001); χ^2 tests were used to compare categorical variables; Kruskal–Wallis test was used to compare mean age.
BMI, body mass index; MOS-PF, Medical Outcomes Study—Physical Functioning.

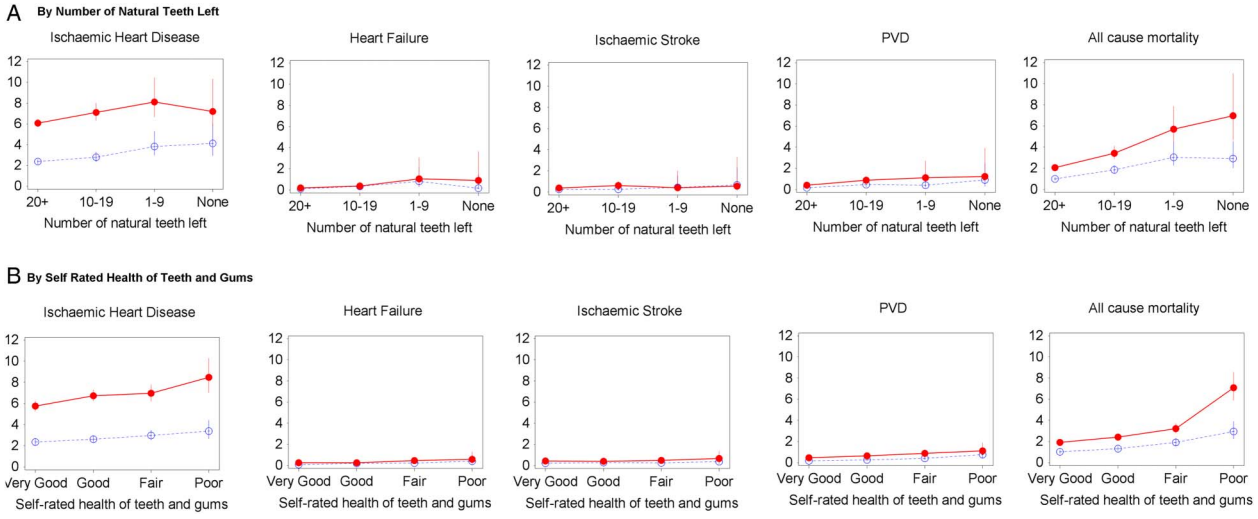

Figure 1 Age-standardised rates per 1000 person-years of all-cause mortality and incident cause-specific CVD hospitalisation since baseline, directly age-adjusted to 2006 New South Wales population. Male: ●-●-●; female: ○-○-○.

increasing with increasing tooth loss and worsening health of teeth and gums (table 1).

Overall, the prevalence of smoking, diabetes, aspirin treatment and obesity were lower among those reporting minimal/no tooth loss or very good/excellent health of teeth and gums; people with higher incomes, education, levels of private health insurance, levels of physical activity and physical functioning capacity reported better oral

health (table 1). During a median follow-up of 3.9 years (IQR 3.8–4.4 years), 3239 incident hospitalisations for IHD, 212 for HF, 283 for ischaemic stroke and 359 for PVD and 1908 deaths, were observed. The age-standardised rates of all-cause mortality and of hospitalisation for IHD were higher in men than in women; the rates were higher among those with no teeth left and those reporting 'poor' health of teeth and gums (figures 1A, B).

The adjusted HRs for IHD, HF, PVD and all-cause mortality increased with greater degree of tooth loss (figure 2; $p_{trend}<0.05$ for all comparisons, except ischaemic stroke). The HRs generally attenuated with adjustments for confounders, and they varied according to the type of outcome examined, with greater HRs for PVD and HF than for other outcomes (HRs 2.53 (1.81 to 3.52) and 1.97(1.27 to 3.07) for PVD and HF, respectively, in those with no teeth left, compared with those reporting ≥20 teeth left). The relationship of tooth loss to IHD was significantly stronger in the younger versus older age groups (likelihood ratio test $p_{interaction}=0.02$); this pattern was not observed for other outcomes ($p_{interaction}=0.05$, 0.8, 0.3 and 0.09 for HF, PVD, ischaemic stroke and all-cause mortality, respectively).

The risk of IHD, PVD and all-cause mortality also increased significantly with worsening self-rated health of teeth and gums (figure 3; $p_{trend}<0.05$ for these three outcomes). The relation of self-rated health of teeth and gums to all-cause mortality was stronger in younger versus older age groups ($p_{interaction}=0.003$); this pattern was not observed for other outcomes ($p_{interaction}=0.8$, 0.3, 0.9 and 0.8 for IHD, HF, ischaemic stroke, PVD).

When categorised as a dichotomous variable (<10 vs ≥10 teeth left), the relationship of tooth loss to IHD hospitalisation did not vary significantly according to any of the subgroup categories examined (of age group, sex, smoking, alcohol consumption, Australian born status, annual household income, educational qualification, BMI, physical activity sessions, diabetes or private health insurance) except for marginal significance ($p_{heterogeneity}=0.047$) according to region of residence

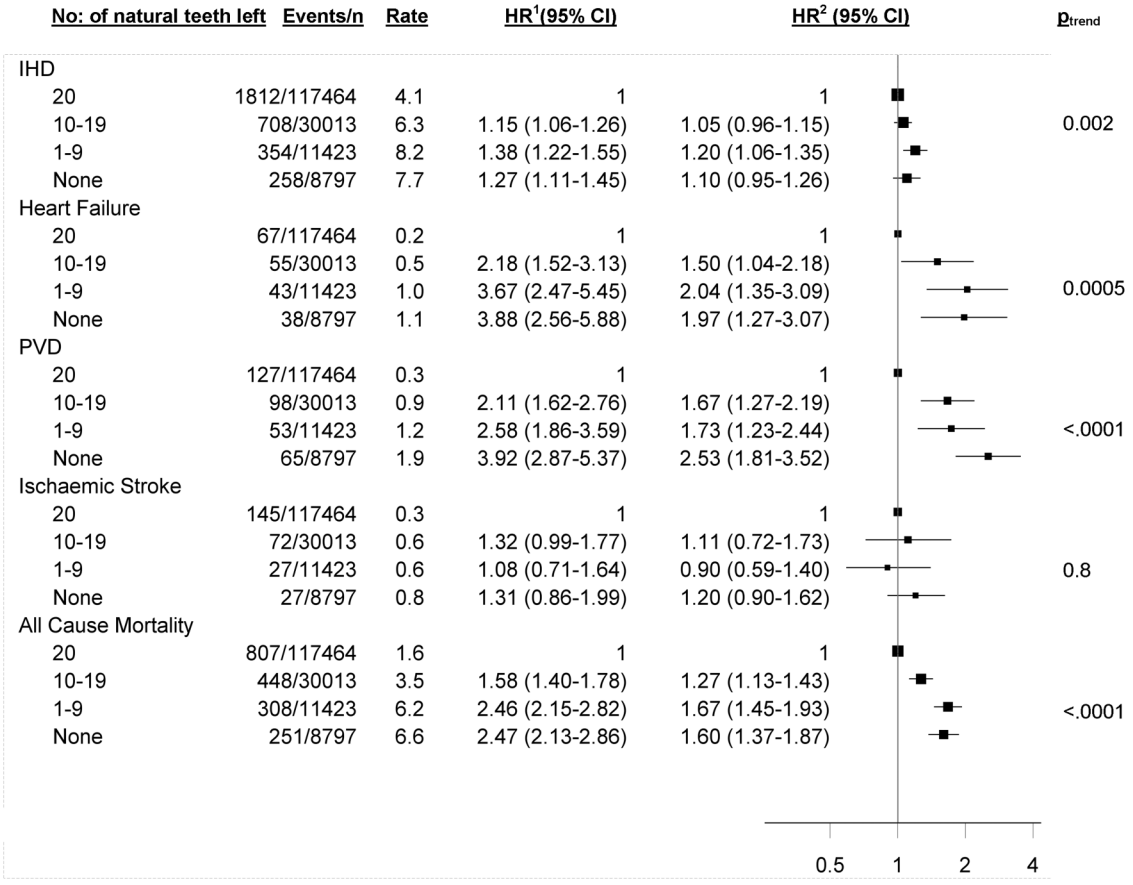

Figure 2 HR (95% CI) for incident hospitalisation for cardiovascular disease (CVD) and all-cause mortality by number of natural teeth left. Events, number of events; rate, crude rate per 1000 person years; CVD, cardiovascular disease; IHD, ischaemic heart disease; PVD, peripheral vascular disease. HR^1, adjusted for age and sex; HR^2, additionally adjusted for tobacco smoking, alcohol consumption, Australian born status, region of residence, education, health insurance, physical activity and body mass index, with missing values in covariates were coded as a separate categories (0.3%, 1.7%, 0%, 0.03%, 1.3%, 0%, 4% and 7%, respectively). There were no missing values in age or sex. HR^2s are plotted on a log scale and are represented with squares, with areas inversely proportional to the logarithm of events; 95% CIs are indicated by horizontal lines.

Self-Rated Oral Health	Events/n	Rate	HR[1](95% CI)	HR[2] (95% CI)	p_{trend}
IHD					
Very Good	994/62976	4.2	1	1	
Good	1193/62447	5.1	1.12 (1.03-1.22)	1.08 (0.99-1.17)	0.005
Fair	656/30574	5.7	1.20 (1.09-1.32)	1.13 (1.02-1.25)	
Poor	241/9802	6.6	1.35 (1.17-1.55)	1.19 (1.03-1.38)	
Heart Failure					
Very Good	47/62976	0.2		1	
Good	64/62447	0.3	1.21 (0.83-1.77)	1.00 (0.69-1.47)	
Fair	53/30574	0.5	1.91 (1.29-2.83)	1.29 (0.86-1.93)	0.1
Poor	25/9802	0.7	2.71 (1.67-4.41)	1.37 (0.82-2.27)	
PVD					
Very Good	82/62976	0.3	1	1	
Good	115/62447	0.5	1.27 (0.96-1.69)	1.11 (0.84-1.48)	
Fair	92/30574	0.8	1.95 (1.44-2.62)	1.46 (1.07-1.98)	0.003
Poor	45/9802	1.2	2.87 (1.99-4.13)	1.66 (1.13-2.43)	
Ischaemic Stroke					
Very Good	81/62976	0.3	1	1	
Good	93/62447	0.4	1.00 (0.74-1.34)	0.99 (0.74-1.34)	
Fair	62/30574	0.5	1.20 (0.85-1.69)	1.20 (0.85-1.69)	0.4
Poor	23/9802	0.6	1.17 (0.72-1.91)	1.17 (0.72-1.91)	
All Cause Mortality					
Very Good	457/62976	1.7	1	1	
Good	604/62447	2.2	1.21 (1.07-1.37)	1.08 (0.96-1.22)	
Fair	434/30574	3.3	1.68 (1.47-1.92)	1.29 (1.13-1.48)	<.0001
Poor	254/9802	6.1	2.99 (2.57-3.49)	1.76 (1.50-2.08)	

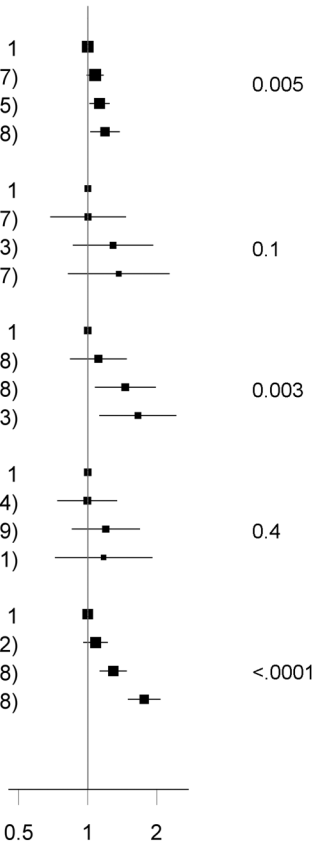

Figure 3 HR (95% CI) for incident hospitalisation for CVD and all-cause mortality by self-rated health of teeth and gums. Events, number of events; rate: crude rate per 1000 person years; CVD, cardiovascular disease; IHD, ischaemic heart disease; PVD, peripheral vascular disease. HR[1], adjusted for age and sex. HR[2], additionally adjusted for tobacco smoking, alcohol consumption, Australian born status, region of residence, education, private health insurance, physical activity and body mass index; missing values in covariates were coded as a separate category (0.3%, 1.7%, 0%, 0.03%, 1.3%, 0%, 4%, 7%, respectively). There were no missing values in age or sex. HR[2]s are plotted on a log scale and are represented with squares with areas inversely proportional to the logarithm of events; 95% CIs are indicated by horizontal lines.

(figure 4). HRs attenuated, but remained significant in sensitivity analysis using finer age categories (see online supplementary table S6).

Sensitivity analysis combining response categories of self-rated health of 'fair' and 'poor' did not make material difference to the result patterns (see online supplementary figure S2); result patterns remained similar in sensitivity analysis combining number of natural teeth left of 'none' and '1–9' (see online supplementary table S5). The increase in HRs for cerebrovascular diseases (I60–I69, G45, G46) was not statistically significant (but approached significance) in those reporting no teeth vs ≥20 teeth left (HR, 95% CI 1.24 (0.99 to 1.54)); marginal increase in HRs were observed in those reporting poor vs very good self-rated health of teeth and gums (HR, 96% CI 1.28 (1.01 to 1.63)).

Discussion

In this large population-based prospective cohort study, the risk IHD, PVD and all-cause mortality increased progressively with worsening oral health. The risk of HF increased with increasing tooth loss, but not with worsening health of teeth and gums. No significant differences were observed for ischaemic stroke. Compared with those reporting ≥20 teeth left, edentulous individuals had significantly higher relative risks (approximately twofold, ranging from 1.65 to 2.53), for HF, PVD and all-cause mortality. Compared with those reporting 'very good' health of teeth and gums, those reporting 'poor' health of teeth and gums had higher risks of 1.19 to 1.84 for IHD, PVD and all-cause mortality. The association was generally stronger and more consistent for tooth loss than for self-rated health of teeth and gums.

To the best of our knowledge, the current study, with over 170 000 participants, is larger than any previous prospective study of oral health and CVD,[13 15 16] and is the only one that looks at the association between severity of oral health problems and the risk of a range of non-fatal CVD outcomes and all-cause mortality within the same cohort. Previous epidemiologic studies varied in the oral health exposures (periodontitis (self-reported, clinical or radiographic), gingivitis, tooth loss classification, bone loss, pocket depth) and in the definition of CVD outcomes;[3 13 28–30] therefore, the

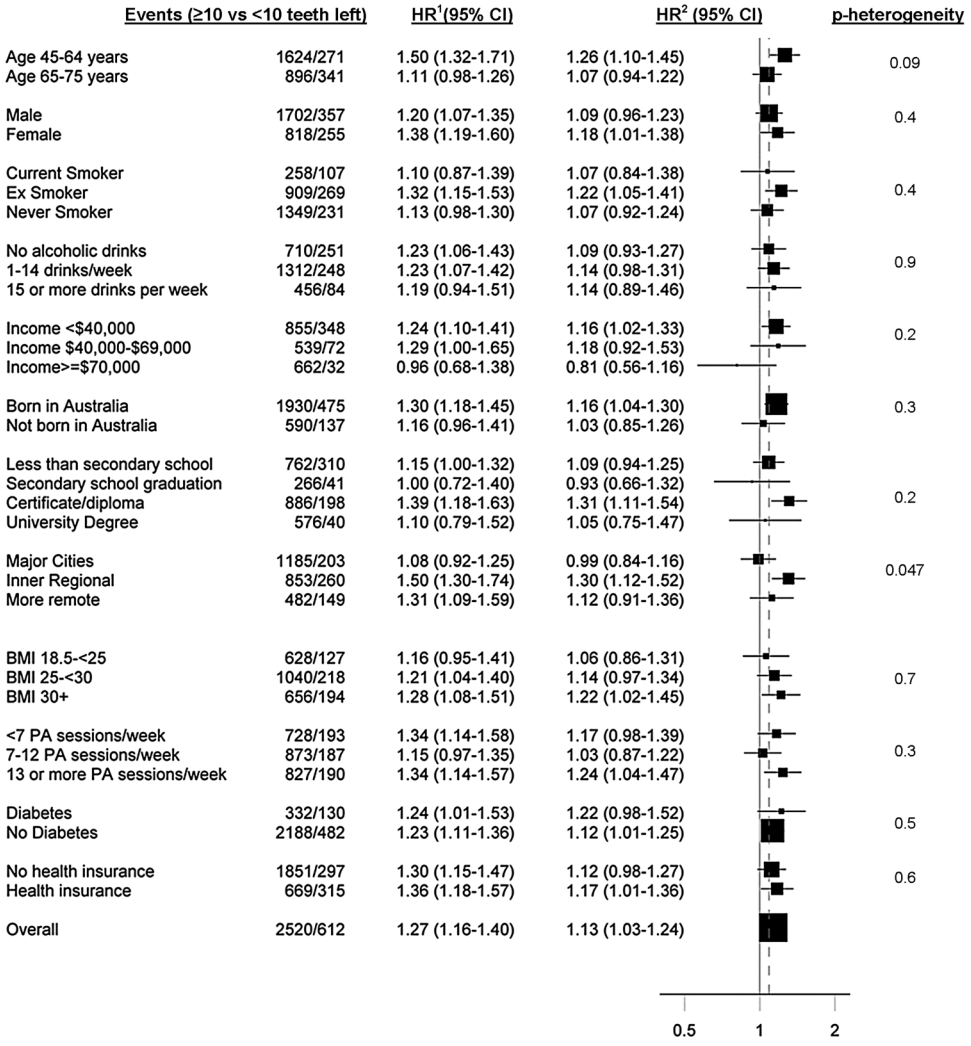

Figure 4 HR for incident hospitalisation for IHD by number of natural teeth left (≥10 vs <10 teeth left), in a range of population subgroups. Events, number of events; IHD, ischaemic heart disease; BMI, body mass index; PA, physical activity. HR^1, adjusted for age and sex. HR^2, additionally adjusted for tobacco smoking, alcohol consumption, Australian born status, region of residence, education, private health insurance, physical activity and body mass index, where appropriate. HR^2, HRs are plotted on a log scale and are represented with squares with areas inversely proportional to the variance of logarithm of HR^2s; 95% CIs are indicated by horizontal lines. The vertical dotted line represents the overall HR of incident hospitalisation for IHD.

associations have not been consistently replicated. It is difficult to draw direct comparisons with this study and other studies due to following reasons: (1) the heterogeneity of exposures used, including differences in categorisation of tooth loss and measures of periodontal disease (clinical/radiographical), (2) variations in CVD outcome definition and (3) differences in study population (inclusion of people with CVD at baseline,[16] type 2 diabetes patients only[17]). Results are generally consistent with previous studies on IHD[17 31 32] and PVD,[33] that use similar oral health indicators. A US study[31] of over 100 000 participants aged 40–75, free of CVD at baseline, reported higher risk of incident IHD (HR 1.36 (1.11 to 1.67) among men and 1.64 (1.31 to 2.05) among women with 0–10 teeth, compared with those with 25–32 teeth). Among male health professionals who reported no diagnosed coronary heart disease, cancer or diabetes at baseline, the association between tooth loss and coronary heart disease was significant among those with pre-existing periodontal disease; the association was not observed among those without pre-existing periodontal disease.[32] Early studies evaluating the association between periodontal disease and stroke reported conflicting results, primarily due to the differences in study designs and lack of power. A recent meta-analysis of cohort studies[30] found that the risk of incident ischaemic stroke was significantly increased in the presence of periodontitis (HR 1.63 (1.25 to 2.00)). Tooth loss was also a risk factor for ischaemic stroke (HR 1.39 (1.13 to 1.65)). The relationship of oral health to ischaemic stroke observed in this study should be interpreted with caution due to the relatively small number of events across exposure categories.

Our results lend strong support to previous studies on the association between poor oral health indicators and all-cause/CVD mortality.[4 13–15 17 28] The Iwate-KENCO study,[15] among men aged 40–79 years free from CVD at baseline, which used similar measures of tooth loss, reported higher risk of all-cause mortality in those with none of their natural teeth left, compared with those reporting ≥20 natural teeth left (HR 1.46 (1.12 to 1.91) when adjusted for age and 1.28 (0.97 to 1.68) when multivariate adjusted). The Scottish cohort study[4] of over 12 000 people with linked mortality showed increased risk of all-cause mortality and CVD mortality (HRs 1.30 (1.12 to 1.50) and 1.49 (1.16 to 1.92), respectively) among those with none of their natural teeth left compared with participants with natural teeth only.

Although a causal association cannot be ruled out, poor oral health is most appropriately considered as a 'risk marker' rather than a 'risk factor' for IHD, that is, it is not likely to be an independent cause of IHD. Although periodontal interventions result in a reduction in systemic inflammation and endothelial dysfunction, there is little evidence that they prevent or modify atherosclerotic vascular disease outcomes.[3] Progressively diminishing blood flow through blood vessels, the underlying cause of the CVD outcomes examined (IHD, PVD, HF and ischaemic stroke), could also result in poor blood circulation in teeth and gums. IHD is one of the main causes of HF, although it can also be caused by conditions such as high blood pressure, aortic stenosis, uncontrolled arrhythmias, mitral valve disorders and idiopathic dilated cardiomyopathy. Peripheral arteries, which are smaller than coronary arteries, are closer in size to blood vessels in the mouth and people may therefore exhibit PVD symptoms at an earlier stage of atherosclerosis. In keeping with this, tooth loss was found to be more strongly associated with PVD than other types of CVD. Oral conditions and CVD share certain risk factors, most importantly age and smoking, but also health behaviours/habits, genetic disposition, socioeconomic status, stress, obesity, diet, physical activity, access to care and diabetes mellitus.[29] Oral disease tends to be more easily diagnosed, often before the diagnosis of CVD.

As all-cause mortality is a non-specific outcome related to ill health from multiple causes, its stronger association with poor oral health indicates that poor oral health is potentially a cause or risk marker for health conditions other than CVD. Age is strongly associated with tooth loss and CVD. Oral health markers for CVD may be less relevant for the elderly, since the relationship of poor oral health with CVD tends to attenuate with age; we have limited this study to those aged 45–75 years.

Periodontal disease has been shown to have adverse effects on glycaemic control, development of type 2 diabetes and its complications.[34] Hence, since diabetes is likely to lie on the causal pathway between poor oral health and CVD for at least a proportion of individuals, we chose not to include diabetes as a covariate in the analysis models. Instead we did subgroup analysis looking at people with and without diabetes (figure 4).

In this large, population-based cohort study, we were able to look at specific CVD outcomes and all-cause mortality, adjusting for a range of potential confounding factors. The large absolute number of CVD events over a relatively short follow-up period of 3.9 years (mean 4.3 years) can be attributed to the large sample size; the observed age-standardised rates for CVD outcomes are in generally in agreement with those in the Australian population.[35] The ability to link to administrative records was a strength of the study, allowing objective ascertainment of outcomes over time and enhanced identification of people with previous CVD so that they could be excluded from the study. The validity of administrative coding for the specific CVD outcomes varies, but is generally good, with κ scores for agreement between chart review and recorded diagnoses of 0.6–0.8[36] and positive predictive values of 66–99%[37–39] for acute myocardial infarction, cerebral infarction and HF. Subgroup analyses enabled us to investigate whether the relationship of tooth loss to IHD hospitalisation and all-cause mortality varied significantly between the different subgroups, defined according to different levels of sociodemographic and health factors.

Limitations of the study include non-availability of CVD diagnoses from primary care, non-availability of dental care records and the use of self-reported survey data. This study focuses on hospitalisation for CVD and does not capture people with CVD events who were not admitted to hospital; data on cause of death were not available at the time of analysis; and over the relatively short follow-up period, a small but unknown number of participants are likely to have moved out of the area. Recent dental care is known to contribute to better self-rated health of teeth and gums,[40] but measures of visits to dentists were not available. However, this improvement in oral health is likely to be reflected in the measures used. Clinical or radiographic measures of periodontal disease were not available, but we were able to use self-reported number of teeth as a broad indicator of oral health, a highly accurate measure in the general population,[41] that has shown to be validly reported in several population groups.[7 42–45] A number of studies have shown that self-reports of tooth loss are in agreement with the results of clinical examinations.[8 46 47] For example, a prospective study comparing semiannual self-reports with biannual clinical oral examination results across a 4-year period[46] reported excellent agreement between self-reported tooth loss and clinical examination findings (κ of 0.88, concordance of 94%). Self-rated periodontal health has been validated in the Australian population, and has been used in the Australian National Survey of Adult Oral Health[48 49] as well as for periodontal disease surveillance in the USA.[50] Tooth loss may reflect conditions other than periodontal disease,[51] although it is unlikely to have a major impact on this study population aged 45–75 years. While

edentulism is an indicator of past oral disease in many individuals, complete removal of all teeth resolves the inflammation associated with periodontal disease and dental caries which supports the patterns we have observed. It must also be noted that extraction of teeth is not necessarily disease related; for example, a dentist may extract few remaining teeth to give space for a full denture. Such intricacies are not captured in our self-reported data on tooth loss. Low number of incident events for outcomes would have led to limited power in some analyses. It should be noted that although the 45 and Up cohort are broadly representative of the Australian population in this age group,[52] participants of cohort studies are likely to be healthier and have lower hospitalisation rates than the general population; further study exclusions have also been applied. However, representativeness is not necessary for valid and reliable estimates of relative risk from within-cohort comparisons.[53] Although self-reported diabetes status was available, the study did not measure glycaemic control and we are unable to distinguish between poorly controlled versus well-controlled diabetes. We are unable to look at the impact of self-neglect or poor oral hygiene, as these were not measured in the study. It is also important to note that the study results do not imply a causal association between poor oral health and CVD.

In conclusion, tooth loss, and to a lesser extent, self-rated health of teeth and gums, are associated with increased risk of hospitalisation for IHD, PVD and all-cause mortality. Tooth loss is also a marker for incident HF. Although the relationships are not particularly strong, it is possible that markers of oral health may have the potential to contribute to cardiovascular screening and prevention, by assisting in the identification of individuals at increased risk.

Author affiliations
[1]National Centre for Epidemiology and Population Health, Research School of Population Health, Australian National University, Canberra, Australian Capital Territory, Australia
[2]Faculty of Dentistry, University of Sydney, Sydney, New South Wales, Australia
[3]Department of Preventive Medicine and the Mindich Child Health and Development Institute, Icahn School of Medicine at Mount Sinai, New York, New York, USA
[4]The George Institute for Global Health, University of Sydney, Sydney, New South Wales, Australia
[5]The Sax Institute, Sydney, New South Wales, Australia

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