The Association Between Tooth Loss and Coronary Heart Disease in Men and Women

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Abstract

Objectives: *This paper evaluates the relation of tooth loss to incidence of coronary heart disease in two large cohort studies.* ***Methods:*** *Participants included 41,407 men and 58,974 women free of any cardiovascular diseases at baseline. We recorded 1,654 incident coronary heart disease events (562 fatal events) among men during 12 years of follow-up and 544 events (158 fatal events) among women during 6 years of follow-up.* ***Results:*** *After controlling for important cardiovascular risk factors, compared to men with 25–32 teeth at baseline, men with 0–10 teeth had a significantly higher risk of coronary heart disease (relative risk [RR]=1.36; 95 percent confidence interval [CI]=1.11, 1.67). The relative risk increased to 1.79 (95% CI=1.34, 2.40) when limited to fatal events. Women with 0–10 teeth were also at increased risk of coronary heart disease compared to women with 25–32 teeth (RR=1.64; 95% CI=1.31, 2.05). The association was similar for fatal events (RR=1.65; 95% CI=1.11, 2.46). The association between number of teeth and incidence of coronary heart disease was similar between men with and without a history of periodontal disease, and there was no significant association between tooth loss during follow-up and coronary heart disease.* ***Conclusions:*** *This study showed a significant association between number of teeth at baseline and risk of coronary heart disease and the mechanisms to explain this association should be further clarified. [J Public Health Dent 2004;64(4):209-15]*

Key Words: myocardial infarction, coronary heart disease, periodontal disease, tooth loss, inflammation, infection, cardiovascular disease, diet, nutrition.

The relation between tooth loss and cardiovascular diseases is important due to the high prevalence of periodontal disease and tooth loss (1-4). Since a significant association between poor oral health and coronary heart disease was first reported in 1989 (5), investigators have analyzed data from several prospective studies to clarify the temporal relationship between periodontal disease, tooth loss, and coronary heart disease (6-11).

DeStefano et al. (6) initially reported that edentulousness was significantly associated with elevated risk of coronary heart disease, but that study lacked information on smoking status for almost two-thirds of participants. Two other studies showed that fewer teeth or edentulousness appeared to be associated with risk of cardiovascular disease after controlling for potential confounders (9). In our review of studies that evaluated both periodontal disease and tooth loss as risk factors for coronary heart disease, most studies showed similar or higher associations between tooth loss and coronary heart disease, compared to periodontal disease and coronary heart disease, suggesting that periodontal disease may not completely explain the tooth loss–coronary heart disease relationship (12).

In a cohort of male health professionals with six-year follow-up, we did not find an association between history of periodontal disease and coronary heart disease, but found an elevated risk of coronary heart disease among those with 0–10 teeth compared to those with 25–32 teeth (7). However, the relative risk (RR) was not significant (RR=1.32; 95% CI=0.98, 1.77), possibly due to limited power. Now, after an extended follow-up of 12 years, we have more statistical power due to increased number of coronary heart disease cases, and additional data on tooth loss during follow-up. Hence, we reanalyzed this male cohort and also evaluated these relationships in a female cohort.

Methods

Study Populations. *Health Professionals Follow-up Study (HPFS):* In 1986, a cohort of 51,529 male health professionals 40–75 years of age consisting of 29,683 dentists, 3,745 optometrists, 4,185 pharmacists, 2,218 osteopathic physicians, 1,600 podiatrists, and 10,098 veterinarians, completed detailed mailed questionnaires that included a comprehensive diet survey, questions on life-style practices, and a medical history including questions on remaining teeth number and history of periodontal diseases with bone loss. After 1986, biennial questionnaires were used to update information on potential risk factors and medical conditions including incident tooth loss and periodontal disease in the past two years.

Nurses' Health Study (NHS): In 1976, a total of 121,700 female registered nurses aged 30–55 years residing in 11 US states completed a mailed questionnaire that inquired about life-style practices, potential risk factors for cardiovascular disease and cancer, and medical history. The follow-up ques-

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tionnaires have been sent out every two years to update the information. The questions related to oral health were added in the 1992 questionnaire. Both cohort studies were approved by the Institute Review Board of Human Subjects, and the response to the self-reported questionnaires constituted the participants' informed consent.

Data Collection. *Outcome:* The primary endpoint, coronary heart disease (coronary heart disease), was defined as symptomatic nonfatal myocardial infarction, fatal coronary heart disease, or sudden death within one hour of onset of symptoms without plausible causes other than coronary heart disease, that occurred after the return of the 1986 questionnaires for HPFS or the 1992 questionnaires for NHS and before January 31 (men) or May 31 (women), 1998. The follow-up and confirmation of endpoints were described previously in detail (13,14). We identified potential cases from the questionnaires, then requested permission to review their medical records. Study physicians reviewed these medical records using the World Health Organization's criteria, including symptoms plus either diagnostic electrocardiographic changes or elevated cardiac enzyme levels, without knowing the self-reported risk factors, including dental status.

Fatal coronary heart disease was confirmed by hospital records, autopsy report, or death certificate. Death certificates along with medical records were used to ascertain cause of death. Fatal coronary disease was categorized as "definite" if: (1) it was confirmed by hospital record or autopsy; or (2) coronary disease was listed as the cause of death on the certificate. This was the underlying and most plausible cause, and evidence of previous coronary disease was available. We did not rely on the statement of the cause of death on the death certificate alone as providing sufficient confirmation of death due to coronary heart disease. If no medical records were available, we categorized persons in whom coronary heart disease was the underlying cause on the death certificate as "presumed coronary heart disease." Persons who experienced sudden death within one hour of onset of symptoms and had no plausible cause other than coronary disease were also categorized as coronary heart disease cases. Analyses limited to confirmed cases yielded results very similar to those obtained when all cases were included, although with less precision.

Assessment of Dental Measures: In the HPFS, participants reported history of periodontal disease with bone loss and baseline number of teeth (0, 1–10, 11–16, 17–24, and 25–32) in 1986. On subsequent biennial questionnaires, they reported the number of teeth lost (0, 1, 2, 3, 4, and 5 or more) and diagnosis of periodontal disease with bone loss in the past two years. In the NHS, participants reported the number of remaining teeth, number of teeth lost, and experience of periodontal surgery in past two years in 1992 only. Although we have no information on the validity of self-reported tooth loss in a previous two-year interval, self-reported number of teeth has been highly correlated with the actual number of teeth on clinical examination in a general population (correlation coefficient=0.97) (15). Hence, we expect that the number of remaining teeth as well as incident tooth loss during follow-up are reported reliably in these cohorts of health professionals. For the self-reported history of periodontal diseases, the questionnaire measure compared well with radiographs among a subsample of the HPFS (16,17).

Dietary Assessment: Diet was assessed in 1986 for HPFS and 1990 for NHS using an expanded semiquantitative food frequency questionnaire described in detail elsewhere (18-20). Participants reported their average frequency of consumption of a specified portion size for each food over the past year in nine categories, ranging from never or less than once per month to six or more times per day. The average daily intakes of individual fruits and vegetables were combined to compute total fruit and vegetable intake (21). Nutrients were computed by multiplying the frequency of consumption of each food unit by the nutrient content of the specified portion (22). Validity of the dietary data was assessed by comparison with multiple weighed dietary records (18,23,24).

Data Analysis: In the analyses, we excluded those who reported daily energy intake outside the plausible range (<3,360 or >17,640 kJ/d for men, and <2,510 kJ/d or >14,644 kJ/d for women) or who left 70 or more of the 131 dietary questions blank at baseline. We further excluded those who reported myocardial infarction, angina, stroke, coronary artery bypass grafting or angioplasty, or other heart diseases, or those with no information on remaining teeth number at the baseline questionnaire. There were 41,407 eligible men and 58,974 eligible women.

We identified 1,654 men with coronary heart disease (562 fatal events) from the date of return of questionnaires in 1986, and 544 women with coronary heart disease (158 fatal events) from the date of return of questionnaires in 1992, to the diagnosis of coronary heart disease, death, or Jan. 31, 1998 (men), or May 31, 1998 (women), whichever came first. Participants who reported coronary heart disease events or who died were excluded from subsequent follow-up. Thus, each participant could contribute only one endpoint and the cohort at risk included only those free of coronary heart disease.

In this study, we analyzed tooth loss in three ways: First, for the analysis of baseline number of teeth, participants with 25–32 teeth were used as the referent group to compute the relative risks (RR) of coronary heart disease for participants with 0–10, 11–16, and 17–24 teeth in both cohorts. Second, for recent tooth loss, men with tooth loss in the past two years were compared to those with no tooth loss in the past two years. Third, for cumulative tooth loss during follow-up, men reporting at least one tooth lost during follow-up were defined as exposed in subsequent follow-up and compared to men without tooth loss.

For these last two analyses, we excluded edentulous participants in 1986 because they could not lose teeth during the follow-up period. We also assumed that men with missing data for incident tooth loss did not lose teeth during the two-year period because there were fewer than 10 percent of participants on average who lost teeth within two years. Since tooth loss in the past two years was first assessed in 1988, we can only include coronary heart disease incidence from 1988 to 1998, during which time 1,342 coronary heart disease cases occurred. For the NHS, we only had data on history of tooth loss in 1990–92 to predict subsequent coronary heart disease.

In the multivariate model, we adjusted for age (five-year categories),

TABLE 1
Means or Percentages of Age-standardized* Selected Cardiovascular Risk Factors by Number of Teeth at Baseline

Risk Factors	Men†				Women†			
Number of teeth	25–32	17–24	11–16	0–10	25–32	17–24	11–16	0–10
Number of participants	34,788	4,532	904	1,183	38,032	11,883	2,925	6,134
Age (years)	52.5	58.1	61.3	63.4	56.7	59.3	60.6	61.5
Alcohol intake (g/day)	11.3	11.7	11.8	12.2	6.7	6.5	6.4	5.9
Physical activity (MET/wk)	21.8	19.5	17.9	16.9	23.1	21.3	25.7	22.5
Body mass index (kg/m2)	24.9	25.0	25.1	25.2	25.7	26.4	26.8	27.0
% current smokers	8.7	14.4	17.2	21.1	10.0	16.1	22.6	28.3
History at baseline (%)								
Hypertension	19.3	21.1	20.7	22.1	30.0	34.1	33.1	36.6
High cholesterol	10.2	9.9	7.1	8.6	43.7	44.7	43.3	42.6
DM	2.3	3.5	3.9	3.7	3.7	4.9	5.8	7.0
Family history of CHD (%)	11.7	12.0	11.7	11.1	19.6	20.6	21.8	20.7
Dentist (%)	61.2	46.3	36.9	31.8				
Menopause status (%)	NA	NA	NA	NA				
Not yet					23.8	22.4	22.1	22.4
Yes, never hormone use					24.8	29.6	32.5	33.8
Yes, past hormone use					32.7	28.0	25.1	21.6
Yes, current hormone use					15.6	16.7	16.1	16.7
Supplement use (%)								
Multivitamin	41.9	41.6	39.9	39.2	43.7	41.8	40.6	39.8
Vitamin E	19.1	17.7	17.7	14.6	18.7	17.2	15.6	15.0
Aspirin	25.8	28.6	25.6	25.3	59.0	58.9	58.4	57.2
Dietary intake (daily)‡								
Fruit & vegetable (serving)	5.7	5.2	5.1	4.9	5.8	5.5	5.3	5.1
Fiber	21.1	20.0	19.2	18.6	18.5	17.7	17.4	16.8
Potassium	3,378	3,289	3,244	3,213	2,890	2,836	2,822	2,791
Carotene	9,869	8,723	8,432	8,095	9,335	8,689	8,460	7,924
Folate	358	342	338	331	316	305	297	292
Vitamin B_6	2.23	2.15	2.13	2.10	1.92	1.88	1.85	1.84
Vitamin B_{12}	9.03	9.10	9.13	9.42	6.47	6.70	6.85	7.16

*Means and percentage for all variables except age are standardized for age.
†Men in 1986 and women in 1992.
‡Standardized for age and total energy intake.

smoking (never, former, current; and 1–14, 15–24, and ≥25 cigarettes per day), alcohol consumption (five categories), body mass index (five categories), physical activity (five categories), family history of myocardial infarction, multivitamin supplement use, vitamin E use, and history of hypertension, diabetes, and hypercholesterolemia, and profession (HPFS cohort only) and menopausal status and hormonal use (NHS cohort only). For the analyses of incident tooth loss, we also adjusted for remaining teeth number at baseline. Because these risk factors might change over time, to better control the confounding effects, these variables were updated based on the biennial questionnaires and analyzed using Cox proportional hazards models with time-dependent variables (25).

We added the dietary variables to the models to evaluate whether diet mediated the association between baseline teeth and coronary heart disease. We assessed dietary factors that have been associated with cardiovascular disease, and which were likely to be impacted by tooth loss, specifically fruits and vegetables, dietary fiber, carotene, vitamins B_6 and B_{12}, folate, potassium, and dietary patterns, as in our previous manuscript (26). We performed subgroup analyses by periodontal disease history, profession, multivitamin and aspirin use, history of diabetes and hypertension, body mass index, age, and smoking status, controlling for the same variables as above.

Results

Table 1 presents the number of participants, mean age and age-adjusted means of traditional cardiovascular disease risk factors, and dietary intakes at baseline by categories of baseline teeth number. We found that those with fewer teeth number had a more adverse cardiovascular disease risk profile in both cohorts. After adjusting for age in each cohort, participants with 0–10 teeth had lower levels of physical activity, higher percentage of current smokers, higher body mass index, higher prevalence of hyperten-

TABLE 2
Relative Risk (RR) and 95% Confidence Interval (CI) of Coronary Heart Disease (CHD) for Number of Teeth at Baseline and Incident Tooth Loss During Follow-up

	CHD Case Number	Age and Smoking Adjusted RR (95% CI)	Multivariate RR¶ (95% CI)	CHD Deaths	Multivariate RR¶ (95% CI) (Fatal CHD Case Only)
Men					
Baseline number of teeth*					
25–32	1,222	1.00	1.00	372	1.00
17–24	254	1.15 (1.00, 1.32)	1.10 (0.95, 1.26)	106	1.26 (1.01, 1.57)
11–16	71	1.41 (1.11, 1.80)	1.35 (1.06, 1.72)	25	1.19 (0.79, 1.80)
0–10	107	1.49 (1.22, 1.83)	1.36 (1.11, 1.67)	59	1.79 (1.34, 2.40)
Incident tooth loss†					
Incidence in past two years	128	0.93 (0.77, 1.12)	0.86 (0.72, 1.04)	32	0.69 (0.48, 1.01)
Cumulative incidence	258	0.99 (0.86, 1.14)	0.94 (0.82, 1.09)	90	1.03 (0.80, 1.33)
Women					
Baseline number of teeth‡					
25–32	241	1.00	1.00	66	1.00
17–24	123	1.28 (1.03, 1.60)	1.14 (0.92, 1.42)	33	1.02 (0.66, 1.55)
11–16	43	1.60 (1.15, 2.22)	1.34 (0.97, 1.87)	11	1.07 (0.56, 2.05)
0–10	137	2.13 (1.70, 2.65)	1.64 (1.31, 2.05)	48	1.65 (1.11, 2.46)

*41,407 eligible participants and 1,654 coronary heart disease cases (562 fatal events) in 1986–98.
†40,508 eligible participants and 1,342 coronary heart disease cases (417 fatal events) in 1988–98; additionally adjusting for baseline teeth number in the model.
‡58,974 eligible participants and 544 coronary heart disease cases (158 fatal events) in 1992–98.
¶The multivariate model includes: age (5-year categories), smoking (never, former, current, 1–14,15–24, and ≥25 cigarettes per day), alcohol consumption (5 categories), body mass index (5 categories), physical activity (5 categories), family history of myocardial infarction, multivitamin supplement use, vitamin E use, history of hypertension, diabetes, and hypercholesterolemia in both cohorts and professions for men only, and for women only, menopausal status and hormone use.

sion and diabetes, lower percentages of multivitamin and vitamin E supplement use, and lower intake of most beneficial nutrients than other participants. The percentages of participants with hypertension, high cholesterol level, and aspirin use appeared to be higher in the female cohort than in the male cohort.

Table 2 shows the associations between baseline number of teeth and incident tooth loss, and coronary heart disease. In both cohorts, number of teeth at baseline was significantly associated with incidence of coronary heart disease. Men with 0–10 teeth or 11–16 teeth had a significantly increased risk (RR=1.36; 95% CI=1.11, 11.67) for developing coronary heart disease compared to men with 25–32 teeth after adjusting for confounders (RR=1.36 with 95% CI=1.11, 1.67 for men with 0–10 teeth; and RR=1.35 with 95% CI=1.06, 1.72 for men with 11–16 teeth). The RR for men with 0–10 teeth increased to 1.79 (95% CI=1.34, 2.40) when limited to fatal coronary heart disease events. Incident tooth loss was not associated with coronary heart disease in either the model adjusted for only age and smoking or the multivariate-adjusted models. The RR for coronary heart disease and fatal coronary heart disease comparing women with 0–10 teeth to women with 25–32 teeth at baseline was 1.64 (95% CI of 1.31, 2.05) and 1.65 (95% CI=1.11, 2.46), respectively. Incident tooth loss during 1990–92 was not related to the subsequent coronary heart disease events.

We found no consistent differences in the associations between tooth loss and coronary heart disease across subgroups of other risk factors (Table 3). There seemed to be a similar association between tooth loss and coronary heart disease among men with or without history of periodontal disease. Compared to men with 25–32 teeth, men with 0–10 teeth had an RR of 1.46 (95% CI=1.03, 2.09) among those who reported history of periodontal disease, and an RR of 1.35 (95% CI=1.04, 1.76) among those with no history of periodontal disease at baseline. For men who never smoked, the association between tooth loss and coronary heart disease appeared to be stronger than among men who had ever smoked (RR=1.78 for never smokers and RR=1.25 for ever smokers), but such a difference was not found among women.

Controlling for several dietary variables (not shown in the table), the multivariate-adjusted RR of coronary heart disease comparing participants with 0–10 teeth to participants with 25–32 teeth (RR=1.36) was essentially unchanged after additionally adjusting for fiber (RR=1.34) and after adjusting for dietary patterns (RR=1.33) among men. Among women, the RR only decreased from 1.58 to 1.54 after adjusting for fiber and to 1.53 after adjusting for dietary patterns.

Discussion

In this study, we found that the number of teeth at baseline was significantly associated with risk of coronary heart disease. Participants with fewer teeth at baseline were more likely to develop coronary heart disease in subsequent follow-up, but we did not observe any relationships be-

TABLE 3
Stratified Multivariate* Relative Risk (RR) and 95% Confidence Interval (CI) of Coronary Heart Disease (CHD) for Baseline Number of Teeth (0–10 vs 25–32)

	Men		Women	
Stratified Variables	No. CHD Cases	RR* (95% CI)	No. CHD Cases	RR* (95% CI)
Periodontal diseases				
Yes	338	1.46 (1.03, 2.09)		
No	1,316	1.35 (1.04, 1.76)		
Dentist				
Yes	940	1.29 (0.92, 1.81)		
No	714	1.41 (1.08, 1.84)		
Multivitamin use				
Yes	640	1.35 (0.97, 1.88)	229	1.48 (1.04, 2.10)
No†	722	1.42 (1.04, 1.93)	206	1.89 (1.31, 2.71)
Aspirin use				
Yes	484	1.23 (0.84, 1.81)	323	1.79 (1.34, 2.39)
No	1,170	1.41 (1.11, 1.81)	221	1.42 (0.99, 2.03)
DM				
Yes		1430.83 (0.38, 1.84)	90	2.27 (1.32, 3.91)
No	1,511	1.44 (1.16, 1.78)	454	1.52 (1.18, 1.95)
Hypertension				
Yes	570	1.77 (1.30, 2.41)	305	1.60 (1.19, 2.16)
No	1,084	1.15 (0.83, 1.58)	239	1.70 (1.21, 2.40)
Age (years)				
≤55	518	1.22 (0.60, 2.47)	97	1.72 (0.91, 3.23)
>55	1,136	1.43 (1.15, 1.78)	447	1.64 (1.29, 2.09)
Smoking				
Ever	1,029	1.25 (0.98, 1.59)	358	1.72 (1.31, 2.26)
Never	625	1.78 (1.21, 2.61)	186	1.57 (1.05, 2.37)
Body mass index				
≤25	629	1.25 (0.89, 1.77)	236	1.66 (1.17, 2.34)
>25	1,025	1.45 (1.12, 1.87)	308	1.63 (1.21, 2.19)

*The multivariate model includes: age (5-year categories), smoking (never, former, current, 1–14, 15–24, and ≥25 cigarettes per day), alcohol consumption (5 categories), body mass index (5 categories), physical activity (5 categories), family history of myocardial infarction, multivitamin supplement use, vitamin E use, history of hypertension, diabetes, and hypercholesterolemia in both cohorts and professions for men only, and for women only, menopausal status and hormone use.

†Participants did not take multivitamin or any other supplements.

tween recent tooth loss and risk of coronary heart disease.

Diet and chronic inflammatory mediators have been considered as two major causal pathways linking oral health and cardiovascular diseases (8,27-29). The number of remaining teeth at baseline and incident tooth loss during follow-up are both indicators of oral health. Incident tooth loss among adults and older adults is likely to reflect recent and severe periodontal disease. On the other hand, number of remaining teeth at baseline tends to represent extractions in a more distant time period, which is more likely due to dental caries, and has a wider range (25–32 teeth vs 0–10 teeth) than incident tooth loss, hence may be more likely to impact diet and less likely to reflect the inflammatory pathway.

Our results suggest that participants with 0–10 teeth at baseline had significantly higher risk of coronary heart disease than participants with 25–32 teeth. This association was also seen among men who did not report prior periodontal disease. This suggested that other factors such as diet also may play a role in the association between oral health and coronary heart disease. However, we observed only minimal reductions in relative risks comparing those with 0–10 teeth to those with 25–32 teeth after further controlling several dietary variables; the reductions were slightly higher among females. It is possible that random measurements error inherent in dietary information is likely to attenuate the observed association, which would limit the ability to evaluate the importance of dietary pathways. In addition, the dietary data were not obtained with the tooth loss hypothesis in mind. Therefore, aspects such as duration of cooking, which may have an impact, were not assessed (people with tooth loss could eat the same foods with more cooking). Further studies using serum level of several nutrients might be conducted to evaluate the role of diet in linking oral health and coronary heart disease.

The finding of no association between incident tooth loss and coronary heart disease is consistent with a recent study (10,11). Howell et al. (11) reported a lower RR of fatal cardiovascular disease for men with incident tooth loss in the past year. In our study, we also found that men with tooth loss in the past two years had lower risk of fatal coronary heart disease, although the relative risk was not significant (RR=0.69; 95% CI=0.48, 1.01). This may be due to avoidance of further extraction by dentists when patients have severe systemic conditions.

Unlike our earlier findings of higher risk of coronary heart disease among participants with periodontal disease (7), we did not observe a stronger association between number of teeth and coronary heart disease among men with periodontal disease history after an extended follow-up period of 12 years. Although we found a significant association of both incident tooth loss and periodontal disease with stroke and peripheral arterial disease in the male cohort (30,31), we did not find any relationships of incident tooth loss with risk of coronary heart disease in this cohort. Analyses to examine the different induction periods of incident loss of teeth were also conducted in a similar manner as our previous studies (30,31), but no associations were observed. Whether the differences among coronary arteries, and cerebral vessels in anatomy and hemodynamics, and the contribution of thrombosis to myocardial infarction

could explain the different associations should be clarified in future studies.

Extraction of teeth to treat periodontal diseases would eliminate the infection/inflammation, and therefore should lead to a reduced risk of coronary heart disease among people with tooth loss. On the other hand, antecedent periodontal disease may have a long induction period, and could persist as an association between tooth loss and coronary heart disease. Given the relative magnitude of the effects of tooth loss and periodontal disease in the published literature (12), a lack of association between recent tooth loss and coronary heart disease and the lack of a clear dose response in our study, it seems unlikely that periodontal disease could explain the entire tooth loss – coronary heart disease association. The relationship between baseline number of teeth and coronary heart disease in our study may be due to some combination of antecedent periodontal disease, antecedent endodontic inflammation, dietary changes following tooth loss, and other unknown mechanisms. A similar association between periodontal disease, tooth loss, and carotid artery plaque was also found by Desvarieux et al. (32). They reported that tooth loss level was significantly associated with carotid artery plaque prevalence and mean percentages of periodontal sites with pocket depth ≥5 mm or attachment level ≥4 mm, but there was no clear association between periodontal disease and carotid plaque prevalence.

Tooth loss and coronary heart disease share several common risk factors, which may be partially responsible for the association between them (27,33,34). However, our findings are unlikely to be explained by common risk factors for tooth loss and coronary heart disease because we have adjusted for many of these factors. Also, the homogeneity in socioeconomic status and health-related behavior of these two cohorts would further minimize the influence of other unmeasured confounders. However, residual confounding is always a possible explanation. It is important to note that we found a significant association between number of teeth at baseline and coronary heart disease in both cohorts even among participants who never smoked after controlling for other cardiovascular risk factors. Hence, unlike some other studies in which smoking has been cited as a likely explanation for this association, our results cannot be explained by smoking.

In the subgroups stratified by other variables, differences in the magnitude of the association between number of teeth and coronary heart disease were small and their 95 percent confidence intervals overlapped substantially; hence the differences across subgroups are more likely to be chance findings.

The number of teeth at baseline was inversely associated with the risk of coronary heart disease independently of cardiovascular risk factors. Diet could potentially explain at most only a very small part of the association in these cohorts. Further work is needed in different populations to understand the mechanisms for this association, and to assess whether the association may be causal.

References

1. Douglass CW, Jette AM, Fox CH, Tennstedt SL, Joshi A, Feldman HA, et al. Oral health status of the elderly in New England. J Gerontol 1993;48:M39-46.
2. Fox CH, Jette AM, McGuire SM, Feldman HA, Douglass CW. Periodontal disease among New England elders. J Periodontol 1994;65:676-84.
3. Steele JG, Walls AW, Ayatollahi SM, Murray JJ. Major clinical findings from a dental survey of elderly people in three different English communities. Br Dent J 1996;180:17-23.
4. Marcus SE, Drury TF, Brown LJ, Zion GR. Tooth retention and tooth loss in the permanent dentition of adults: United States, 1988-1991. J Dent Res 1996;75 (Spec Iss):684-95.
5. Mattila KJ, Nieminen MS, Valtonen VV, Rasi VP, Kesaniemi YA, Syrjala SL, et al. Association between dental health and acute myocardial infarction. Br Med J 1989;298:779-81.
6. DeStefano F, Anda RF, Kahn HS, Williamson DF, Russell CM. Dental disease and risk of coronary heart disease and mortality. Br Med J 1993;306:688-91.
7. Joshipura KJ, Rimm EB, Douglass CW, Trichopoulos D, Ascherio A, Willett WC. Poor oral health and coronary heart disease. J Dent Res 1996;75:1631-6.
8. Beck J, Garcia R, Heiss G, Vokonas PS, Offenbacher S. Periodontal disease and cardiovascular disease. J Periodontol 1996;67:1123-37.
9. Morrison HI, Ellison LF, Taylor GW. Periodontal disease and risk of fatal coronary heart and cerebrovascular diseases. J Cardiovasc Risk 1999;6:7-11.
10. Hujoel PP, Drangsholt M, Spiekerman C, DeRouen TA. Periodontal disease and coronary heart disease risk. JAMA 2000;284:1406-10.
11. Howell TH, Ridker PM, Ajani UA, Hennekens CH, Christen WG. Periodontal disease and risk of subsequent cardiovascular disease in US male physicians. J Am Coll Cardiol 2001;37:445-50.
12. Joshipura KJ, Douglass CW. Oral–cardiovascular disease associations do not call for extraction of teeth. J Evidence-based Dent Pract 2002;2:221-6.
13. Grobbee DE, Rimm EB, Giovannucci E, Colditz G, Stampfer M, Willett W. Coffee, caffeine, and cardiovascular disease in men. N Engl J Med 1990;323:1026-32.
14. Wolk A, Manson JE, Stampfer MJ, Colditz GA, Hu FB, Speizer FE, et al. Long-term intake of dietary fiber and decreased risk of coronary heart disease among women. JAMA 1999;281:1998-2004.
15. Douglass CW, Berlin J, Tennstedt S. The validity of self-reported oral health status in the elderly. J Public Health Dent 1991;51:220-2.
16. Joshipura KJ, Douglass CW, Garcia RI, Valachovic R, Willett WC. Validity of a self-reported periodontal disease measure. J Public Health Dent 1996;56:205-12.
17. Joshipura KJ, Pitiphat W, Douglass CW. Validation of self-reported periodontal measures among health professionals. J Public Health Dent 2002;62:115-21.
18. Rimm EB, Giovannucci EL, Stampfer MJ, Colditz GA, Litin LB, Willett WC. Reproducibility and validity of an expanded self-administered semiquantitative food frequency questionnaire among male health professionals. Am J Epidemiol 1992;135:1114-36.
19. Feskanich D, Rimm EB, Giovannucci EL, Colditz GA, Stampfer MJ, Litin LB, et al. Reproducibility and validity of food intake measurements from a semiquantitative food frequency questionnaire. J Am Diet Assoc 1993;93:790-6.
20. Hu FB, Stampfer MJ, Manson JE, Rimm E, Colditz GA, Rosner BA, et al. Dietary fat intake and the risk of coronary heart disease in women. N Engl J Med 1997; 337:1491-9.
21. Joshipura KJ, Ascherio A, Manson JE, Stampfer MJ, Rimm EB, Speizer FE, et al. Fruit and vegetable intake in relation to risk of ischemic stroke. JAMA 1999;282: 1233-9.
22. US Department of Agriculture. Composition of foods - raw, processed, and prepared, 1963-1988. Washington, DC: US Department of Agriculture, 1989; vol 8.
23. Willett WC, Sampson L, Browne ML, Stampfer MJ, Rosner B, Hennekens CH, et al. The use of a self-administered questionnaire to assess diet four years in the past. Am J Epidemiol 1988;127:188-99.
24. Salvini S, Hunter DJ, Sampson L, Stampfer MJ, Colditz GA, Rosner B, et al. Food-based validation of a dietary questionnaire: the effects of week-to-week variation in food consumption. Int J Epidemiol 1989;18:858-67.
25. Hosmer DW, Lemeshow S. Applied survival analysis: regession modeling of time to event data. New York: Wiley, 1999.
26. Hu FB, Rimm EB, Stampfer MJ, Ascherio A, Spiegelman D, Willett WC. Prospective study of major dietary patterns and risk of coronary heart disease in men. Am J Clin Nutr 2000;72:912-21.

27. Joshipura KJ, Douglass CW, Willett WC. Possible explanations for the tooth loss and cardiovascular disease relationship. Ann Periodontol 1998;3:175-83.
28. Ritchie CS, Joshipura K, Hung HC, Douglass CW. Nutrition as a mediator in the relation between oral and systemic disease: associations between specific measures of adult oral health and nutrition outcomes. Crit Rev Oral Biol Med 2002;13:291-300.
29. Hung HC, Willett W, Ascherio A, Rosner BA, Rimm E, Joshipura KJ. Tooth loss and dietary intake. J Am Dent Assoc 2003;134: 1185-92.
30. Joshipura KJ, Hung HC, Rimm EB, Willett WC, Ascherio A. Periodontal disease, tooth loss, and incidence of ischemic stroke. Stroke 2003;34:47-52.
31. Hung HC, Willett W, Merchant A, Rosner BA, Ascherio A, Joshipura KJ. Oral health and peripheral arterial disease. Circulation 2003;107:1152-7.
32. Desvarieux M, Demmer RT, Rundek T, Boden-Albala B, Jacobs DR Jr, Papapanou PN, et al. Relationship between periodontal disease, tooth loss, and carotid artery plaque: the Oral Infections and Vascular Disease Epidemiology Study (INVEST). Stroke 2003;34:2120-5.
33. Johansson I, Tidehag P, Lundberg V, Hallmans G. Dental status, diet and cardiovascular risk factors in middle-aged people in northern Sweden. Community Dent Oral Epidemiol 1994;22:431-6.
34. Hujoel PP. Does chronic periodontitis cause coronary heart disease? A review of the literature. J Am Dent Assoc 2002; 133(Suppl):31S-6S.