

Remaining teeth, cardiovascular morbidity and death among adult Danes

Berit Lilienthal Heitmann and Michael Gamborg

Objective - To examine whether the number of remaining teeth was associated with development of cardiovascular morbidity and mortality over 5-12 years.

Method - Prospective observational study among 1474 men and 1458 women born 1922, 1932, 1942 or 1952 from The Danish MONICA follow up study (MONItoring trends in and determinants of Cardiovascular disease) in 1987-88 and 1993-94. Subjects were followed in Danish registers for fatal and non-fatal cardiovascular disease, coronary heart disease or stroke.

Results - Tooth loss was strongly associated with incidence of stroke, and to a lesser extent, incidence of cardiovascular disease and coronary heart disease, during an average 7.5 years of follow-up. Compared to those with most teeth remaining, the edentulous suffered >3-fold increased hazard (HR) of developing stroke (HR=3.25; 95% CI:1.48-7.14), whereas the risk of developing any cardiovascular disease, (CVD), was increased by 50% (HR=1.50; 95% CI:1.02-2.19). Risk for coronary heart disease (CHD) was increased by 31%, but was not significant after adjustment for education, age, smoking, diabetes, alcohol intake, systolic blood pressure and body mass index (HR=1.31; 95% CI:0.74-2.31). Associations were similar for men and women.

Conclusion - These findings may have implications for future prevention of cardiovascular disease in general, and of stroke in particular, because tooth loss may serve as a simple and early means to identify high-risk individuals.

Artiklen er oprindeligt publiceret i *Preventive Medicine* 2008; 47: 156-60.

Studies suggest a link between chronic infection, such as periodontal infection, and development of CVD (1,2). Proposed mechanisms include direct influences of periodontal bacteria (3,4), effects of toxins from microorganisms in serum (5-7), clotting factors and inflammatory markers in response to infection (6,8,9), or common genetic determinants of both periodontal disease and CVD (1). However, the evidence for an association between oral infection and atherosclerosis is weak, and based on few studies only (2). Simple ways of identifying otherwise healthy subjects, with increased risk of CVD, are of great importance for preventing CVD. If periodontal infection is linked to CVD, high-risk subjects may potentially be identified through their history of long-term exposure to infection/inflammation, by counting the loss of permanent teeth. Indeed, some studies showed that tooth loss may identify subjects at increased risk of CVD (10,5,11-16), even without presence of parodontitis marginalis (5). However, not all studies find evidence of such an association (17,18) and confounding by socio-economic status (SES) was a concern in several studies.

The aim of this study was to examine associations between number of remaining teeth during middle-age, and development of CVD, CHD, and stroke, after taking confounding from education, smoking and other variables into account.

Materials and method

In total, 4807 subjects were selected from the Central Person Register in 1982, among citizens born either 1922, 1932, 1942 or 1952, and living in the Copenhagen County (19). Of these, 226 were of non-Danish origin. The remaining 4581 Danes were invited to a health examination, of which 3608 participated. In 1987-88, a second invitation was sent to the 3608 subjects, and 2987 attended. This examination included counting of remaining teeth (20). A third examination, also including teeth counting, was performed in 1993-94, 2656/2987 attended. Response and non-response was described elsewhere (21). The study was part of the Danish MONICA project (22).

In 1987-88, 1156/2987 subjects, and in 1993-94 2656/2656 had their teeth counted. Subjects were included in this study based on their first counting of teeth (1156 from 1987-88 and 1776 from 1993-94), and followed until the end of 1999 for morbidity from CVD, CHD or stroke. The project was approved by the Ethics Committee for the Copenhagen County, and is in accordance with the Helsinki Declaration.

Measures

Using an dental mirror and light, a dentist (in 1987-88) and a trained nurse (in 1993-94) counted remaining teeth after the removal of non-fixed partial or full dentures. Bridge pillars were counted as non-missing teeth, as were roots left visible in the mouth.

Body weight was measured to nearest 0.1kg, subjects dressed in light clothes or underwear only, using a lever balance. Height was measured to nearest 1cm, subjects being without shoes. BMI was calculated as body weight/height-squared and divided into: BMI<18 kg/m², 18kg/m²<BMI<25 kg/m², 25 kg/m²<BMI<30 kg/m² and BMI>30 kg/m².

Systolic (SBP) and diastolic blood pressures (DBP) were measured with a London School of Hygiene sphygmomanometer, using one of three different cuffs. Duplicate measurements were taken on left arm after minimum 5 minutes rest in supine position. Means of duplicate measures were calculated. Pulse-pressure was calculated as the difference between SBP and DBP.

Questionnaire data

Subjects were classified into former, non- or current smokers of either 1-14, 15-24 or >25 cigarettes/day. Pack/year of cigarette use in current and former smokers, was calculated using current tobacco consumption equating one cigarette=1g, a cheroot=3g, and a cigar=5g tobacco. Alcohol intake from beer, wine and spirits was grouped into: <1, 1-6,7-13,14-27, >28 drinks/week. Also, absolute intake was recorded. Schooling was classified: <7yrs, 8-11yrs or >12yrs. SES was assessed in five categories using a validated classification of self-reported information on type of employment, vocational education and number of subordinates (23). Civil status: Married/co-habiting, divorced, widowed, or living alone was recorded, and, subjects informed whether a doctor had ever told them they suffered from diabetes (yes/no).

Endpoints

Information on fatal and non-fatal CVD, CHD or stroke was retrieved from the National Patient Registry of Hospital Discharges, the Cause of Death Register and the Central Person Register. Subjects were followed until December 31st 1999, for an average of 7.5yrs. For incidence of CVD, ICD-8 codes 390-458 and ICD-10 codes I00-I99 were used. For CHD ICD-8 codes: 410-414, and ICD-10 codes: I20-I25 were used, whereas ICD-8 codes: 430-436, and ICD-10 codes: I60-I64 were used for incidence of stroke. 308/2932 subjects had a diagnosis of CVD prior to the health exami-

nation, 66/2866 had CHD and 42/2890 had stroke. These were excluded from further study.

Statistical Analyses

To achieve the highest precision the population was, for each combination of gender and endpoint, divided into five groups with an equal number of cases, according to number of teeth. We used a Cox regression model with age as underlying time axis. Adjustment was made for whether tooth counting was performed in 1987-88 or 1993-94. First (models I), we compared the risk associated with tooth loss. In none of the analyses were interactions between gender, tooth loss, and endpoint significant, and a second analysis (models II) merged the two genders, but estimated the baseline hazard separately for men and women. A third analysis (models III) adjusted for education and smoking, and subsequent analyses included either one or both these variables. Final analyses (models IV) included all potential confounders. Analyses were performed using SAS Version 8.2 (SAS Institute Inc. Cary, NC, USA).

Results

In total, 1474 men and 1458 women participated with complete information from questionnaire and health examination. Table 1 shows their characteristics. During follow-up, 164 women and 227 men developed a first CVD. Similarly, 44 women and 116 men developed CHD, and 38 women and 86 men developed stroke.

Table 2 shows the proportion of men and women developing either CVD, CHD or stroke by quintile of remaining teeth. For the edentulous, the proportion developing CVD was >4 times higher than among those with all teeth remaining. The proportion developing CHD among the edentulous was around 6 times that of those with all teeth, as was the proportion of men who developed stroke. For edentulous women, the proportion that developed stroke was 15 times larger than among those with all teeth.

Table 3A-C presents results from the Cox regression analysis by gender. The upper parts of the tables show the risk associated with quintile of tooth number for men and women while, in the left panel, taking co-variation from age and whether counting of teeth took place in 1987-88 or 1993-94. Similarly, in the right panel all co-variables are taken into account. Crude analyses indicated that being edentulous was associated with developing CVD, CHD and stroke. In adjusted analyses, associations remained significant for stroke but became insignificant for men as well as women for both CVD and CHD. Associations were

not statistically different by gender (all $P > 0.37$), and data was merged to obtain greater power. Neither smoking nor schooling modified the associations between tooth loss

and the endpoints. (All P -values > 0.31 for interactions with schooling and all $P > 0.13$ for smoking).

Fig. 1 shows the inverse relationships between tooth

Table 1. Characteristics of 1474 men and 1458 women from the Danish MONICA Cohort examined in either 1987/88 or 1993/94.

	Men		Women		P difference
	Mean	(SD)	Mean	(SD)	
Number of teeth	21.3	(10.0)	20.8	(9.9)	0.008
BMI (kg/m ²)	26.3	(3.7)	25.1	(4.4)	<0.0001
Systolic BP (mmHg)	131	(2.0)	127	(19)	<0.0001
Current smokers (%)	48.4		53.7		0.005
More than 6 drinks/week (%)	51.6		46.3		0.005
Diagnosis of diabetes (%)	3.3		1.7		0.006
≤ schools: 7 years (%)	33.7		34.8		
8-11 years (%)	55.4		56.6		
≥ 12 years (%)	11.0		8.6		0.10
Married/cohabiting (%)	75.7		66.2		
Divorced (%)	11.8		17.1		
Widowed (%)	3.5		9.6		
Living alone (%)	9.0		7.2		0.0001

Table 2. Proportion of men and women examined in either 1987/88 or 1993/94, developing cardiovascular disease (CVD), coronary heart disease (CHD) or stroke by quintile of number of teeth.

Quintile with number of Teeth*	Development of CVD		Development of CHD		Development of Stroke	
	n	%	n	%	n	%
Men						
0	49/147	(33.3)	28/141	(19.9)	14/144	(9.7)
1-10	49/157	(31.2)	23/124	(18.5)	10/133	(7.5)
11-22	45/167	(26.9)	25/183	(13.7)	12/249	(4.8)
23-27	53/318	(16.7)	26/303	(8.6)	10/382	(2.6)
28-32	43/507	(8.5)	21/674	(3.1)	8/542	(1.5)
Women						
0	39/133	(29.3)	14/153	(9.2)	14/152	(9.2)
1-13	35/141	(24.8)	8/99	(8.1)	7/87	(8.0)
14-23	36/233	(15.5)	9/121	(7.4)	7/95	(7.4)
24-26	30/256	(11.7)	7/342	(2.0)	7/154	(4.5)
27-32	41/565	(7.3)	11/726	(1.6)	6/952	(0.6)

* Varies slightly depending on endpoint, but 1st quintile generally included 0 teeth and 5th quintile generally 26 teeth or more.

Table 3A. Risk of incident CVD by quintile of number of teeth for men and women examined in either 1987-88 or 1993-94.

Quintile§ of Number of teeth	Number of events	Crude Model (I)		Adjusted Model (IV)	
		Hazard ratio	95 % Confidence interval	Hazard ratio	95 % Confidence interval
MEN					
1st	45	1.95	[1.23 3.11]	1.51	[0.90 2.52]
2nd	47	1.96	[1.25 3.07]	1.41	[0.86 2.29]
3rd	43	1.95	[1.25 3.04]	1.66	[1.04 2.66]
4th	51	1.41	[0.93 2.13]	1.21	[0.79 1.87]
5th	41	1.0		1.0	
WOMEN					
1st	36	1.99	[1.21 3.29]	1.63	[0.91 2.93]
2nd	31	1.75	[1.06 2.90]	1.39	[0.79 2.43]
3rd	33	1.11	[0.68 1.82]	1.01	[0.59 1.71]
4th	28	1.18	[0.72 1.91]	1.26	[0.75 2.11]
5th	36	1.0		1.0	

Figures in the left panel were adjusted for age and whether number of teeth was counted in 1987-88 or 1993-94. Figures in the right panel represent the fully adjusted model.

§: 1st quintile included 0 teeth for all analyses except for associations with CVD for men where 1st quintile was 0-4 teeth. 5th quintile generally included 26 teeth or more, except for associations with stroke for the women where 5th quintile was 22-32 teeth.

Table 3B. Risk of incident CHD by quintile of number of teeth for men and women examined in either 1987-88 or 1993-94.

Quintile§ of Number of teeth	Number of events	Crude Model (I)		Adjusted Model (IV)	
		Hazard ratio	95 % Confidence interval	Hazard ratio	95 % Confidence interval
MEN					
1st	25	2.85	[1.53 5.32]	1.75	[0.88 3.46]
2nd	23	2.73	[1.45 5.13]	1.86	[0.95 3.64]
3rd	22	2.02	[1.09 3.73]	1.21	[0.63 2.34]
4th	25	1.57	[0.87 2.85]	1.24	[0.68 2.28]
5th	21	1.0		1.0	
WOMEN					
1st	12	2.29	[0.92 5.70]	0.57	[0.19 1.70]
2nd	7	2.29	[0.84 6.23]	0.92	[0.32 2.71]
3rd	9	2.00	[0.76 5.31]	1.10	[0.40 3.01]
4th	6	0.70	[0.26 1.90]	0.42	[0.15 1.21]
5th	10	1.0		1.0	

Figures in the left panel were adjusted for age and whether number of teeth was counted in 1987-88 or 1993-94. Figures in the right panel represent the fully adjusted model.

§: 1st quintile included 0 teeth for all analyses except for associations with CVD for men where 1st quintile was 0-4 teeth. 5th quintile generally included 26 teeth or more, except for associations with stroke for the women where 5th quintile was 22-32 teeth.

Table 3C. Risk of incident stroke by quintile of number of teeth for men and women examined in either 1987-88 or 1993-94.

Quintile§ of Number of teeth	Number of events	Crude Model (I)		Adjusted Model (IV)	
		Hazard ratio	95 % Confidence interval	Hazard ratio	95 % Confidence interval
MEN					
1st	13	2.22	[0.72 6.85]	2.43	[0.95 6.28]
2nd	9	1.82	[0.57 5.82]	1.91	[0.71 5.15]
3rd	11	1.22	[0.40 3.68]	1.34	[0.52 3.44]
4th	9	1.34	[0.43 3.58]	1.07	[0.42 2.76]
5th	6	1.0		1.0	
WOMEN					
1st	13	4.39	[1.38 13.9]	5.32	[1.98 14.3]
2nd	7	4.99	[1.49 16.8]	5.39	[1.77 16.4]
3rd	6	3.21	[0.91 11.3]	4.44	[1.45 13.5]
4th	6	2.00	[0.60 6.62]	3.03	[1.01 9.16]
5th	6	1.0		1.0	

Figures in the left panel were adjusted for age and whether number of teeth was counted in 1987-88 or 1993-94. Figures in the right panel represent the fully adjusted model.

§: 1st quintile included 0 teeth for all analyses except for associations with CVD for men where 1st quintile was 0-4 teeth. 5th quintile generally included 26 teeth or more, except for associations with stroke for the women where 5th quintile was 22-32 teeth.

number and hazard for CVD. The four lines represent hazards of CVD before and after adjustment for different co-variables. Associations became weaker with inclusion of more co-variates, but remained stable and significant whether none (HR=1.98; 95% CI:1.41-2.78), some (education and smoking HR=1.82; 95% CI:1.26-2.64), or all co-variates (HR= 1.50; 95% CI:1.02-2.19) were included. (95% CI's not shown but available upon request)

Fig. 2 shows the inverse relationships between tooth number and hazard for CHD. Crude analyses were significant (HR=2.68; 95% CI:1.60-4.47) but associations became weaker with inclusion of co-variates, and significance was lost after inclusion of all co-variates (HR=1.31; 95% CI:0.74-2.31) (95% CI's not shown but available upon request)

Fig. 3 shows the inverse relationships between tooth number and the hazard for stroke. Only small differences in the hazard were seen whether no co-variate (HR=3.71; 95% CI:1.88-7.31), education and smoking (HR=3.35; 95% CI:1.54-7.26), or all co-variates (HR= 3.25; 95% CI:1.48-7.14) were included (95% CI's not shown but available upon request). Around 85% of our strokes were ischemic. Subgroup analyses including ischemic strokes only, revealed

similar associations, as for all strokes; HR=2.79; 95% CI:1.27-6.14 in the fully adjusted model.

Further analyses, including confounding from SES, based on information on type of employment, vocational education and number of subordinates, or from pack-year, gave essentially similar results: e.g. CVD: HR=1.58; 95% CI:1.07-2.34, CHD: HR=1.47; 95% CI:0.82-2.65, and stroke: HR=3.59; 95% CI:1.60-8.07.

Adjustment for alcohol using absolute amount also gave similar results e.g. in the fully adjusted models HR=1.51; 95% CI:1.03-2.21 for CVD, HR=1.30; 95% CI:0.74-2.29 for CHD, and HR=3.17; 95% CI:1.44-6.96 for stroke.

Also, results were virtually similar, whether analyses were adjusted for pulse pressure, in addition to or as well as SBP: HR=1.47; 95% CI:1.00-2.16 for CVD, HR=1.29; 95% CI:0.73-2.28 for CHD, and HR=3.26; 95% CI:1.48-7.16 for stroke. Finally, results were similar after excluding diabetics (HR=1.47; 95% CI:0.99-2.18 for CVD, HR=1.58; 95% CI:0.88-2.87 for CHD, and HR=3.31; 95% CI:1.48-7.39 for stroke).

The hazard for stroke for subjects with no teeth compared to subjects with all teeth in the maxilla was HR=2.40; 95% CI:1.28-4.49. Similarly for the mandibula HR=3.57; 95%

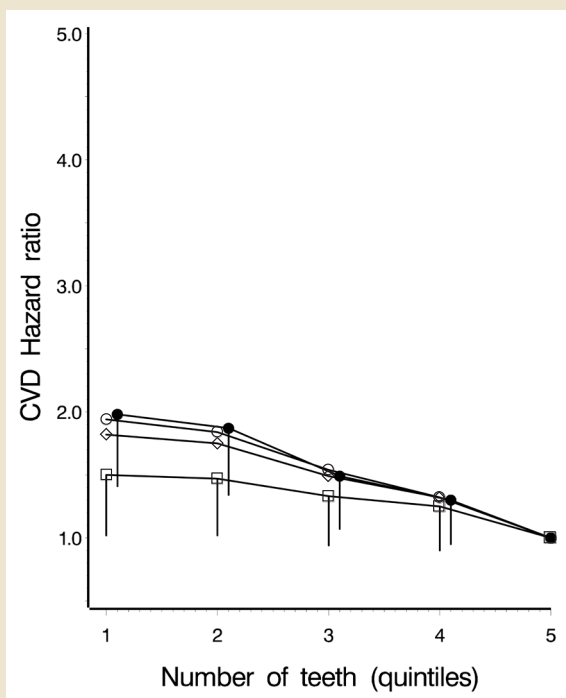


Fig 1. The relationship between quintiles of number of teeth and the hazard ratio for incident CVD, among 2624 subjects from the Danish MONICA study examined in either 1987-88 or 1993-94.

Footnotes:

The baseline hazard (5th quintile) represents the hazard for subjects with all teeth left. All models were adjusted for age, gender and whether tooth counting was performed 1987-88 or 1993-94. Model 2 was further adjusted for education. Model 3 further adjusted for smoking and model 4 for all confounders (age, gender, whether tooth counting was performed 1987-88 or 1993-94, education, smoking, civil status, alcohol intake, diabetes, systolic blood pressure and BMI). The vertical lines are the lower part of the confidence interval presented for model I and for model IV.

Models I: Closed circles, first quintile compared to fifth: HR=1.98; 95% CI: 1.41-2.78

Models II: Open circles, first quintile compared to fifth: HR=1.94; 95% CI: 1.35-2.78

Models III: Open diamonds, first quintile compared to fifth: HR=1.82; 95% CI: 1.26-2.64

Models IV: Open boxes, first quintile compared to fifth: HR=1.50; 95% CI: 1.02-2.19

§ 5th quintile: 28-32 teeth for men and 27-32 teeth for women

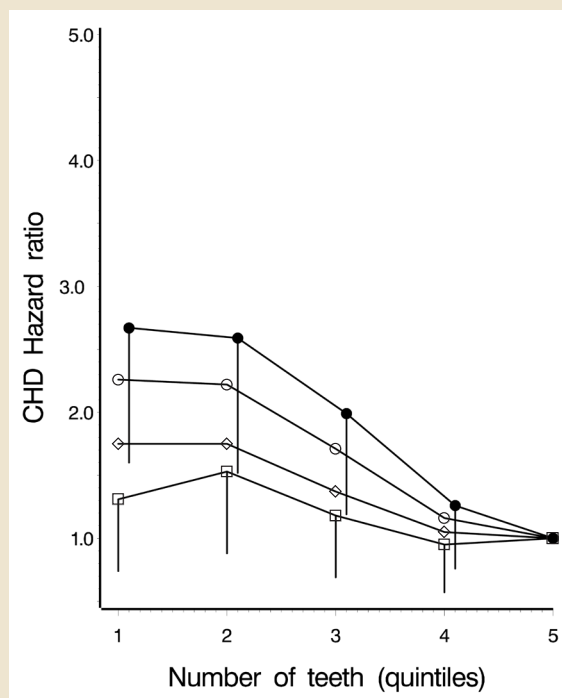


Fig 2. The relationship between quintiles of number of teeth, and the hazard ratio for incident CHD, among 2866 subjects from the Danish MONICA study examined in either 1987-88 or 1993-94.

Footnotes:

The baseline hazard (5th quintile) represents the hazard for subjects with all teeth left. All models were adjusted for age, gender and whether tooth counting was performed 1987-88 or 1993-94. Model 2 was further adjusted for education. Model 3 further adjusted for smoking and Model 4 further adjusted for both education and smoking. Model 5 was adjusted for all confounders (age, gender, whether tooth counting was performed 1987-88 or 1993-94, education, smoking, civil status, alcohol intake, diabetes, systolic blood pressure and BMI).

The vertical lines are the lower part of the confidence interval presented for model I and for model IV.

Models I: Closed circles, first quintile compared to fifth: HR=2.68; 95% CI: 1.60-4.47

Models II: Open circles, first quintile compared to fifth: HR=2.26; 95% CI: 1.32-3.88

Models III: Open diamonds, first quintile compared to fifth: HR=1.75; 95% CI: 1.00-3.04

Models IV: Open boxes, first quintile compared to fifth: HR=1.31; 95% CI: 0.74-2.31

§ 5th quintile: 27-32 teeth for men and 26-32 teeth for women

CI:1.89-6.74. Stronger associations were seen between tooth loss of the lower (HR=3.69; 95% CI:1.33-10.22) than the upper jaw (HR=0.89; 95% CI:0.34-2.38), and joint analyses

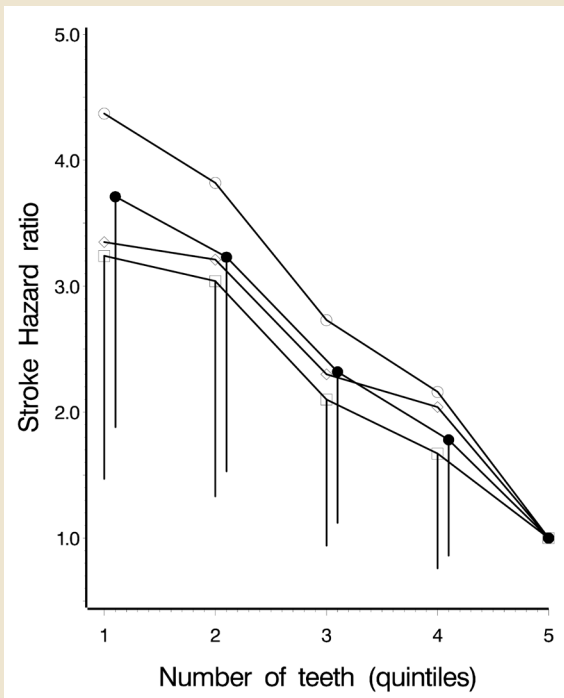


Fig 3. The relationship between quintiles of number of teeth and the hazard ratio for incident stroke among 2890 subjects from the Danish MONICA study examined in either 1987-88 or 1993-94.

Footnote:

The baseline hazard (5th quintile) represents the hazard for subjects with all§ teeth left. All models were adjusted for age, gender and whether tooth counting was performed 1987-88 or 1993-94. Model 2 was further adjusted for education. Model 3 further adjusted for both education and smoking and model 4 for all confounders (age, gender, whether tooth counting was performed 1987-88 or 1993-94, education, smoking, civil status, alcohol intake, diabetes, systolic blood pressure and BMI).

The vertical lines are the lower part of the confidence interval presented for model I and for model IV.

Models I: Closed circles, first quintile compared to fifth: HR=3.71; 95% CI: 1.88-7.31

Models II: Open circles, first quintile compared to fifth: HR=4.37; 95% CI: 2.07-9.24

Models III: Open diamonds, first quintile compared to fifth: HR=3.35; 95% CI: 1.54-7.26

Models IV: Open boxes, first quintile compared to fifth: HR=3.25; 95% CI: 1.48-7.14

§ 5th quintile: 28-32 teeth for men and 22-32 teeth for women.

Discussion

We demonstrated strong and independent associations between tooth loss in middle-age and development of CVD or CHD, and especially of incident stroke, over an average of 7.5 yrs. The edentulous suffered a more than 3-fold increased risk of developing stroke, compared to those with most teeth remaining. Associations were similar for men and women, and remained significant for stroke and CVD, after adjustment for multiple co-variates, including smoking, SES and education, all known to influence both tooth loss and stroke or CVD development. Associations also appeared similar for smokers and non-smokers, as well as for the more and less educated.

The reason for tooth loss in our study is unknown. It has been argued that the main reason behind tooth loss after age 40 years may be periodontal disease (24), and, even if this is still under debate (18), that tooth loss could be a proxy measure of periodontal disease or exposure to chronic infection. In agreement with this argument, several studies find that both periodontal disease and tooth loss relate to incidence of CVD, CHD or stroke (10,5,12-14,16). Some even find that tooth loss is associated with subsequent stroke, without presence of periodontal disease (5,16).

Tooth loss was assessed by a dentist or a trained nurse, rather than by self-report, which may explain our findings of strong associations with stroke, compared to others (5). In agreement, Cabrerea et al. (25) also reported strong associations with stroke, while using x-rays rather than self-reports to assess tooth loss. Another explanation could be our use of register based endpoints, rather than reports from the subjects or next of kin.

The stronger associations for stroke than CHD are puzzling. The anatomical relationship between the maxilla and the cavernous sinus or vascular complex, or the common lymphatic drainage, may facilitate local spreading of infectious agents, and may account for the apparent closer link to stroke than CHD. Indeed, case-studies have reported thrombophlebitis of the cavernous sinus of dental origin (26). However, the hazards for stroke were lower for maxillary- than mandibulary edentulism, arguing against this hypothesis.

We lack information on periodontal infection or inflammatory markers in relation to missing teeth, which could strengthen an argument against social class as the driving factor behind edentulism. However, the different risk of stroke and CHD argues against a common infectious or inflammatory pathway linking atherosclerosis to these endpoints, and argues for SES as a common determinant.

showed confidence intervals that were marginally overlapping, only, and non-significant in the maxilla (P=0.67).

On the other hand Cabrera et al. (25) showed that associations between tooth loss and CVD remained strong after control for various measures of SES.

Also, residual confounding from diabetes remains, as we lacked information on HbA1C or other measures related to insulin sensitivity. However, such confounding will be unlikely to explain the different results for stroke and CHD. Also, associations for stroke remained essentially similar whether adjusting for pulse- rather than blood pressure, from the more comprehensive measure of smoking (pack-year), from a more ample SES criteria, or from whether alcohol intake was included as a continuous or discrete variable. We could not adjust for salt intake, as salt intake cannot be extracted with great validity from any of the dietary methods, including the diet history method. However, we have found no support from other literature for salt intake being related to tooth loss. Salt is therefore not likely to have confounded our results substantially. Similarly, we found essentially similar results before and after adjusting for intake-frequency of fruit, vegetables, sweets or meat (data not shown). Hence, the different association for stroke and CHD remains puzzling.

It may be argued that our results are in conflict with results from interventions among survivors from CHD, suggesting that prophylactic antibiotics have negligible effects on the probability of a second CHD (27,28). However, short-term use of prophylactics may not be effective in relation to chronic infections like parodontitis marginalis, and, additionally, several of the oral bacteria, like streptococcus mutants may not be influenced by such treatment (12). Furthermore, *primary* prevention interventions among subjects free of CHD are absent from the literature.

Perspectives

Periodontal disease is common (29), and in our study of 35-65 year olds >20% had lost all teeth. Given the high risk of stroke among edentulous, the public health implications for cardiovascular health may be substantial. Our data suggest that 1/3 stroke events, and 1/12 CVD events may be attributed to those factors responsible for tooth loss. If these associations are biological rather than social phenomena, there is no reason to assume they cannot be generalized to other populations. However, caution should be taken in interpreting associations for tooth loss as associations with periodontal disease.

Conclusion

Tooth loss was strongly associated with 7.5-year incidence of stroke, and to a lesser extent incidence of CVD and

CHD. It is encouraging that a simple measure like tooth loss, whether or not reflecting a chronic oral infection, can identify subjects at risk for stroke. This knowledge may be used to enforce early cardio-protective preventative initiatives.

Dansk resumé

Resterende tænder, kardiovaskulær sygdom og død blandt ældre danskere

Formålet var at undersøge associationer mellem tandtab og udvikling over 5-12 år, af kardiovaskulær sygdom og død.

I alt deltog 1474 mænd og 1458 kvinder, født i enten 1922, 1932, 1942 og 1952 fra det danske MONICA- opfølgingsstudie (MONitoring trends in and determinants of Cardiovascular disease) i 1987-88 og 1993-94. Alle deltagere blev fulgt op i danske registre for udvikling af kardiovaskulær sygdom, herunder koronar hjertesygdom, slagtilfælde og død af disse sygdomme.

Resultaterne viste, at tandtab, over en gennemsnitlig opfølgingsperiode på 7.5 år, var stærkt korreleret med forekomst af slagtilfælde og i mindre grad associeret med forekomst af kardiovaskulær og koronar hjertesygdom.

Sammenlignet med de deltagere, der havde flest tilbageblivende tænder, havde tandløse 3 gange større risiko for at udvikle et slagtilfælde (HR3.25; 95% CI:1.48-7.14), og risikoen for at udvikle kardiovaskulær sygdom var forøget med 50%. Risikoen for koronar hjertesygdom var forøget med 31%, men var ikke-signifikant når der blev justeret for uddannelse, alder, rygning, diabetes, alkoholforbrug, systolisk blodtryk og BMI. Styrken af associationerne var ens for mænd og kvinder.

Disse fund kan have implikationer for fremtidig forebyggelse af kardiovaskulær sygdom generelt og i særdeleshed forebyggelse af slagtilfælde, da tandtab kan medvirke til at identificere grupper i befolkningen med særlig fremtidig risiko for kardiovaskulære lidelser.

References

1. JSHIPURA KJ, DOUGLASS CW, WILLETT WC. Possible explanations for the tooth loss and cardiovascular disease relationship. *Ann Periodontol* 1998; 3: 175-83.
2. MEURMAN JH, HÄMÄLÄINEN P. Oral health and morbidity – implications of oral infections on the elderly. *Review. Gerodontology* 2006; 23: 3-16
3. HARASZTHY VI, ZAMBON JJ, TREVISAN M, ZEID M, GENCO RJ. Identification of periodontal pathogens in atheromatous plaques. *J Periodontol* 2000; 71: 1554-60
4. DI NAPOLI M, PAPA F, BOCOLA V. Periodontal disease, C-reactive protein, and ischemic stroke. *Arch Intern Med* 2001; 161: 1234-5.

5. Joshipura KJ, Hung HC, Rimm EB, Willett WC, Ascherio A. Periodontal disease, tooth loss, and incidence of ischemic stroke. *Stroke* 2003; 34: 47-52.
6. Ross R. Atherosclerosis: an inflammatory disease. *N Engl J Med* 1999; 340: 115-26.
7. Lopes-Virella MF, Virella G. Immunological and microbiological factors in the pathogenesis of atherosclerosis. *Clin Immunology and Immunopathol* 1985; 37: 377-86.
8. Sammalkorpi K, Valtonen V, Kerttula Y, Nikkilä E, Taskinen MR. Changes in serum lipoprotein pattern induced by acute infections. *Metabolism* 1988; 37: 859-65.
9. Hertzberg MC, Meyer MW. Effects of oral flora on platelets: possible consequences in cardiovascular disease. *J Periodontol* 1996; 67 (10 Suppl): 1138-42.
10. Wu T, Trevisan M, Genco RJ, Dorn JP, Falkner KL, Sempos CT. Periodontal disease and risk of cerebrovascular disease: the first national health and nutrition examination survey and its follow-up study. *Arch Intern Med* 2000; 160: 2749-55.
11. Paunio K, Impivaara O, Tiekso J, Mäki J. Missing teeth and ischaemic heart disease in men aged 45-64 years. *Eur Heart J* 1993; 14 (Suppl K): 54-6.
12. Genco R, Chadda S, Grossi R, Dunford G, Taylor G, Knowler W. et al. Periodontal Disease is a predictor of cardiovascular disease in a native American population. *J Dent Res* 1997; 76: 308.
13. Hung HC, Joshipura KJ, Colditz G, Manson JE, Rimm EB, Speizer FE et al. The association between tooth loss and coronary heart disease in men and women. *J Public Health Dent* 2004; 64: 209-15.
14. Holmlund A, Holm G, Lind L. Severity of periodontal disease and number of remaining teeth are related to the prevalence of myocardial infarction and hypertension in a study based on 4,254 subjects. *J Periodontol* 2006; 77: 1173-8.
15. Mattila KJ, Nieminen MS, Valtonen VV, Rasi VP, Kesäniemi YA, Syrjälä SL et al. Association between dental health and acute myocardial infarction. *BMJ* 1989; 298: 779-81.
16. Elter JR, Offenbacher S, Toole JF, Beck JD. Relationship of periodontal disease and edentulism to stroke/TIA. *J Dent Res* 2003; 82: 998-1001.
17. Ragnarsson E, Eliasson ST, Gudnason V. Loss of teeth and coronary heart disease. *Int J Prosthodont* 2004; 17: 441-6.
18. Tuominen R, Reunanen A, Paunio M, Paunio I, Aromaa A. Oral health indicators poorly predict coronary heart disease deaths. *J Dent Res* 2003; 82: 713-8.
19. Jensen KH, Jorgensen T. Incidence of gallstones in a Danish population. *Gastroenterology* 1991; 100: 790-4.
20. Heitmann BL. Body fat in the adult Danish population aged 35-65 years: an epidemiological study. *Int J Obes* 1991; 15: 535-45.
21. Heitmann BL, Garby L. Composition (lean and fat tissue) of weight changes in adult Danes. *Am J Clin Nutr* 2002; 75: 840-7.
22. Kirchoff M, Schroll M, Kirkby M, Hansen BS, Sanders S, Sjol A et al. Screening I. Danmonica. Part of the MONICA project (Multinational Monitoring of Trends and Determinants in CVD. *CVD Epidemiol Newslett* 1983; 34: 32.
23. Møller L, Kristensen TS, Hollnagel H. Social class and cardiovascular risk factors in Danish men. *Scand J Soc Med* 1991; 19: 116-26.
24. Klock KS, Haugejorden O. Primary reasons for extraction of permanent teeth in Norway: changes from 1968 to 1988. *Community Dent. Oral Epidemiol* 1991; 19: 336-41.
25. Cabrera C, Hakeberg M, Ahlqwist M, Wedel H, Bjorkelund C, Bengtsson C et al. Can the relation between tooth loss and chronic disease be explained by socio-economic status? A 24-year follow-up from the population study of women in Gothenburg, Sweden. *Eur J Epidemiol* 2005; 20: 229-36.
26. el Fakir Y, Jiddane M, Abid A. Thrombophlebitis of the cavernous sinus of dental origin. Apropos of a case with a review of the literature. *Rev Stomatol Chir Maxillofac* 1993; 94: 55-9.
27. Groppo FC, Castro FM, Pacheco AB, Motta RH, Filho TR, Ramacciato JC et al. Antimicrobial resistance of *Staphylococcus aureus* and oral streptococci strains from high-risk endocarditis patients. *Gen Dent* 2005; 53: 410-3.
28. Etminan M, Carleton B, Delaney JA, Padwal R. Macrolide therapy for *Chlamydia pneumoniae* in the secondary prevention of coronary artery disease: a meta-analysis of randomized controlled trials. *Pharmacotherapy* 2004; 24: 338-43.
29. Hugoson A, Norderyd O, Slotte C, Thorstensson H. Oral hygiene and gingivitis in a Swedish adult population 1973, 1983, and 1993. *J Clin Periodontol* 1998; 25: 807-12.

Information about the authors:

Berit Lilienthal Heitmann, professor in nutritional epidemiology, cand. odont, ph.d., Research Unit for Dietary Studies, Danish Epidemiology Science Center, at the Institute of Preventive Medicine, Copenhagen University Hospital, Research Centre for Prevention and Health, Glostrup University Hospital, Glostrup, Denmark

Michael Gamborg, statistician, Research Unit for Dietary Studies, Institute of Preventive Medicine, Copenhagen University Hospital