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Citation for the published paper:

Nilsson, Helena; Sanmartin Berglund, Johan; Renvert, Stefan. (2018).

Longitudinal evaluation of periodontitis and development of cognitive decline among older adults.. Journal of clinical periodontology, vol. 45, issue 10, p. null

URL: <https://doi.org/10.1111/jcpe.12992>

Publisher: Wiley

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Longitudinal evaluation of periodontitis and development of cognitive decline among older adults.

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Running title: periodontitis and cognitive decline

Keywords: Neurocognitive disorders; epidemiology; inflammation; older adults; periodontal diseases.

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Source of funding

This study was financially supported by Region Halland Sweden and Southern Health Care Region Sweden [220291]. The Swedish National Study on Ageing and Care, SNAC (www.snac.org) is financially supported by the Ministry of Health and Social Affairs, Sweden and the participating County Councils, Municipalities and University Departments.

The authors declare that there are no conflicts of interest in this study.

Abstract

Aim: to determine whether having periodontitis is associated with cognitive decline among older adults.

Material and Methods: A prospective population study of older adults, Swedish National Study on Ageing and Care, (SNAC) provided repeated registrations of cognitive functions. Cognitive decline was defined as ≥ 3 -points deterioration from a predetermined level at baseline, using the Mini-Mental State Examination (MMSE).

Between 2001 and 2003, 715 individuals had a medical as well as a clinical and radiographic dental examination. The individuals were re-examined after 6 years. Periodontitis was defined as ≥ 4 mm bone loss at ≥ 30 % of tooth sites. Social variables were captured from questionnaires.

Results: The multivariate logistic regression analysis demonstrated a statistically significant association between prevalence of periodontitis and cognitive decline after adjustments of confounding factors of importance.

Conclusions: A history of periodontitis may be of importance for cognitive functions among older adults.

Clinical Relevance

Scientific rationale for the study: It is important to identify modifiable risk indicators for cognitive impairment and dementia. It has been proposed that diseases with an inflammatory background may have an impact on cognitive decline. Evidence of periodontitis as a putative risk indicator for the development of cognitive decline is limited.

Principal findings: This study showed that in a group of older adults in Sweden, a history of periodontal disease was an independent risk indicator for development of cognitive decline.

Practical implications: Clinicians should provide adequate periodontal care to the elderly population.

Introduction

Dementia has been defined as a clinical syndrome characterized by cognitive decline, sufficient to interfere with daily functioning (World Health Organization, 1992). The ongoing demographic transitions, leading to an increasing proportion of older adults, have a profound impact on the prevalence of dementia (Ferri et al., 2005; Prince et al., 2013). Hence, cognitive impairment and dementia are considered a major public health problem with large financial, human and social burdens (Murray et al., 2013; Wimo et al., 2017).

The most common form of dementia is Alzheimer's disease (AD) and modifiable risk factors related to AD are midlife obesity, midlife hypertension, diabetes, physical inactivity, smoking, low education and depression (Norton, Matthews, Barnes, Yaffe, & Brayne, 2014).

Life-style related factors such as alcohol consumption and a history of traumatic brain injury have also been associated to cognitive functions and dementia in elderly individuals (Li, Risacher, McAllister, & Saykin, 2016; Peters, Peters, Warner, Beckett, & Bulpitt, 2008)

Recent systematic reviews suggest that older people with dementia have multiple oral health problems (Delwel et al., 2018; Gusman et al., 2018; Leira et al., 2017; Maldonado, Laugisch, Burgin, Sculean, & Eick, 2018). However, studies on the relationship between periodontitis and cognitive decline are few but indicate an association (Gil-Montoya et al., 2014; Syrjala et al., 2012; Zenthofer et al., 2017). One possible explanation may be related to changes in daily functioning, associated with cognitive decline, affecting oral hygiene routines, resulting in higher plaque and bleeding index (Gil-Montoya, Sanchez-Lara et al., 2017; Zenthofer, Schroder, Cabrera, Rammelsberg, & Hassel, 2014). Another possible explanation to the reported association between periodontitis and cognitive decline may be related to the influence of a peripheral inflammation (Kamer et al., 2008).

Higher brain amyloid load has been reported as a central feature of Alzheimer's disease and clinical attachment loss (CAL) $\geq 3\text{mm}$ has been associated with higher brain amyloid- β (A β)

load among elderly individuals (Kamer et al., 2015). In a recent case-control study, higher plasma A β ₁₋₄₂ peptide concentrations were reported in individuals with severe periodontal disease compared to individuals with healthy periodontal status (Gil-Montoya, Barrios et al., 2017). Additionally, lipopolysaccharides from periodontal pathogens have been identified in the brain tissues of patients with Alzheimer's disease in post-mortem analysis (Poole, Singhrao, Kesavalu, Curtis, & Crean, 2013) and serum IgG levels to periodontal microbiota has been associated to risk for incident Alzheimer's disease (Noble et al., 2014).

In a retrospective case control study a modest higher risk for dementia was reported among individuals with periodontitis after adjustment for sociodemographic characteristics and comorbidities (Lee et al., 2016). In a 3-year follow-up study a two-fold higher risk for cognitive decline was reported for individuals with severe periodontitis compared to individuals without periodontitis (Iwasaki et al., 2016). To further explore a potential association between periodontitis and cognitive decline additional longitudinal studies are, however, warranted. The objective of the present study was to determine whether a diagnosis of periodontitis in individuals ≥ 60 years of age at baseline was associated with cognitive decline in a 6 year follow up study.

Material and methods

The Swedish National Study on Ageing and Care (SNAC) is a population-based, prospective and longitudinal study running at four research centres. At one of the research centres, SNAC-Blekinge, 2312 individuals were invited by mail to participate in the study. Aiming to represent the elderly population in Sweden a randomised selection was made from the Swedish civil registration database in the age cohorts, 60,66,72,78. In the age cohorts 81,84,87 (and older) all individuals in the community were invited to participate in the study.

Those who did not reply were contacted by telephone (three attempts). In total, 1402 agreed to participate and were invited by mail to take part in a medical, psychological and dental examination performed in a research clinic by professionals specially trained for the purpose. The sample of older adults in the selected age cohorts (60-96 years at baseline 2001-2003) is followed over time and all live in Karlskrona, Sweden. In the present study, individuals were assigned to the young-old age group (60,66 years), the old age group (72,28 years) and the old-old age group (81 years and older). All participants signed informed consent. The Research Ethics Committee at Lund, Sweden approved the study (LU 604-00, LU 744-00).

Definitions of variables

The cognitive outcome variable, Mini-Mental State Examination (MMSE), (Folstein, Folstein, & McHugh, 1975) was evaluated at baseline and at the six-year follow-up examinations.

Information about the level of education was collected from questionnaire and categorised according to final school grade; elementary (≤ 9 years) or higher education (> 9 years). Living conditions were grouped into living alone or living with someone. Body mass index was calculated and categorised according to World Health Organizations (WHO: s) definition (< 25 defined as underweight and normal, and pre-obese and obese ≥ 25) (World Health Organization, 2003). Known ischemic heart disease was defined as previous percutaneous coronary intervention (PCI), coronary surgery, myocardial infarction or angina pectoris. Information about smoking habits were collected from a questionnaire: "Do you smoke, regularly, occasionally, former or never"? Level of alcohol consumption was evaluated with the Alcohol Use Disorder Identification Test, AUDIT, a self-reported screening developed by the WHO in order to assess alcohol consumption and its consequences. It contains ten items, resulting in a total test score of 40 points. The test has been validated (Saunders, Aasland, Babor, de la Fuente, J R, & Grant, 1993). The cut-off for harmful drinking behaviour was set to ≥ 8 points (Conigrave, Hall, & Saunders, 1995). Information regarding traumatic brain injury was captured from questionnaires and categorised into head trauma with loss of

consciousness: yes or no. Level of depression was evaluated using the MADRS (Montgomery-Åsberg Depression Rating Scale) (Asberg, Montgomery, Perris, Schalling, & Sedvall, 1978) with the following cut-off: 0–6, absence of depression; 7–19, mild depression; 20–34 moderate depression; and 35 and above, severe depression. Outcomes from the six-year follow-up were used.

Dental examination

All individuals received a comprehensive clinical and radiographic dental examination by one of the two experienced dental hygienists. The clinical examination included registration of number of teeth present, probing pocket depth (PPD) measured at four sites at all existing teeth using periodontal probes (CP-12 probes, HU Friedy Inc.Chicago, IL, USA). The deepest probing depth for each tooth was used to calculate the proportion of teeth with a PPD value $\geq$ 5mm. Bleeding on probing was likewise examined and the proportion of teeth with bleeding at any of the four surfaces was registered. Intra-class correlation (ICC) analysis result between randomly selected cases for double assessments regarding the reproducibility of PPD values at the deepest site between the two clinicians performing the examinations was 0.76 (95 % confidence interval (CI) 0.67, 0.82; $p < 0.001$). Panoramic radiographs were taken using an orthopantomograph (Instrumentarium Dental, OP 100; Tuusula, Finland) with a standard exposure of 75kV/10 mA. The extent of alveolar bone loss was evaluated at the mesial and distal aspect of each tooth. For the purpose, a millimeter graded transparent ruler, and 2x magnification viewer and a light box source were used. The number of readable interproximal sites was used to calculate the proportion of sites with distance from the cement-enamel junction (CEJ) to the alveolar bone level exceeding 4 and 5 mm respectively. In the statistical analysis, periodontal bone-loss, $\geq$ 4mm distance from CEJ to marginal bone level on $\geq$ 30% of readable sites was used as an indicator of a history of periodontal disease. An experienced independent examiner masked to age, gender, dental and medical information performed all

the radiographic measurements. Reliability analysis were done for the double readings of the X-rays. The ICC correlation coefficient for the distance between the apex and CEJ was 0.93 (95% CI= 0,91-0,96, $p < 0.01$), based on a total of 91 observations, with a mean difference of 0,94 mm (SD $\pm 1,3$).

Cognitive Test

Mini-Mental State Examination, MMSE, one of the most widely used cognitive screening test was used. The test consists of 20 items and the total sum of the test scores is maximum 30 (worst to best) (Folstein et al., 1975). The test has been assessed with reliable change index (RCI) and a change of 2-3 is considered an actual change i.e. not caused by practice or measurement effects (Eslinger, Swan, & Carmelli, 2003; Iverson, 1998; Tombaugh, 2005). In this study individuals with MMSE-score < 25 at baseline were excluded and cognitive decline was defined as ≥ 3 -points deterioration from baseline to the six-year follow-up.

Statistical analysis

A statistical software program (IBM SPSS version 22.0, IBM Statistics, Armonk, NY, USA) was used for the analysis. Descriptive statistics were used to present the population. A Chi-square test for independence was performed to evaluate potential associations between the candidate explanatory co-variables and the dependent variable; experience of cognitive decline. The association between a history of periodontitis, defined as having periodontal bone-loss ≥ 4 mm distance from CEJ to marginal bone level on $\geq 30\%$ of readable sites and baseline characteristics was analyzed using the Chi-square-test. Low age, high education, living with someone, never smoked, no traumatic brain injury, no ischemic heart disease, AUDIT < 8 and BMI ≥ 25 were used as references in the multivariate logistic regression analysis. The impact of periodontal bone loss on the risk for cognitive decline was analyzed first univariate and thereafter the co-variables were added in blocks additionally based on

area; demographic, medical and social. Odds ratio (OR), 95% confidence interval (CI) and p-values were calculated; p-values <0.05 were regarded as statistically significant.

Results

The study population consisted of individuals who were examined both at baseline (2001-2003), and at the six-year follow-up (2007-2009). At baseline, 1402 individuals were examined. At the 6-year examination 452 of the baseline population had died, 110 (11, 6%) refused further participation, 22 individuals denied participation in the cognitive test, 14 had only completed parts of the test due to functional disabilities (visual or hearing difficulties, paresis) and 5 choose to abort before the test was fulfilled. After exclusion of individuals with MMSE-score < 25 at baseline, 715 individuals remained. In order to moderate for the potential influence of depression on the cognitive test-outcome at the six-year follow-up, additional 11 individuals with moderate and severe depression according to Svanborg (≥ 20 , MADRS) at the six-year follow-up examination were excluded. Thus, 704 individuals were available for evaluation. One-hundred fifteen individuals experienced a ≥ 3 points decline in MMSE-results during the six-year follow-up. Such a decline in cognitive function was significantly associated with high age, elementary education, living alone, experience of ischemic heart disease, BMI < 25, being edentulous, having 1-19 teeth and bone loss ≥ 4 mm at $\geq 30\%$ of readable sites (Table 1).

Data on dental status were available in 662 of the 704 selected individuals (94%). In 566 individuals, panoramic radiographs were available for analysis of alveolar bone loss in which 214 (38%) had findings of bone loss ≥ 4 mm at $\geq 30\%$ of readable sites. Bone loss ≥ 4 mm at $\geq 30\%$ of readable sites was significantly associated with cognitive decline but also with high age, lower education, male gender, current or former smoker, experience of ischemic heart disease, living alone, fewer teeth (1-19) and presence of pockets (≥ 5 mm on 30 % of teeth) (Table 2). The unadjusted odds ratio (OR) for participants with bone-loss ≥ 4 mm at $\geq 30\%$ of

readable sites compared to those without for incident cognitive decline were 2.8 (CI 1.7-4.5) and in the fully adjusted model 2.2 (CI 1.2-3.8), (Table 3). Other variables reaching statistical significance in the fully adjusted model were age, education and BMI.

Discussion

The main finding of this prospective longitudinal cohort study was that periodontitis, defined as bone loss ≥ 4 mm at $\geq 30\%$ of readable sites registered at panoramic x-rays at baseline, was an independent risk indicator for cognitive decline after 6 years.

Cognitive impairment and neurocognitive disorders have a multifactorial aetiology and in the present study adjustments were made for demographic, lifestyle and medical factors. It is well known that the impact of different risk factors most likely starts long before signs of cognitive decline are clinically evident. Therefore, in this type of study the use of alveolar-bone loss is relevant for defining a course of periodontal disease. Previous studies evaluating cognitive function and dementia in relation to oral health parameters are mainly cross-sectional. Hence, the possibility to discuss causality is limited. As cognitive decline progresses, changes in daily functioning will emerge, influencing factors such as diet and oral hygiene. Such changes may influence the risk for caries and gingivitis in these patients. In the present study, only individuals with MMSE ≥ 25 at baseline were included and therefore a possible causal relationship between a history of periodontitis and cognitive decline can be suggested. In light of the current trends, with an increasing proportion of elderly, and apparently increasing prevalence of dementia, our findings may be of importance also in a public health perspective. Current available medication exerts no clear effect on the clinical course of dementia and no curative treatments are available. Identifying and moderate modifiable risk factors is therefore critical as they may prevent or postpone the clinical onset of dementia. Few studies have evaluated the impact of periodontitis on the risk for cognitive decline longitudinally. In a recent follow-up study over 3 years, a higher risk for cognitive decline,

estimated as a decrease of ≥ 3 points in MMSE score, was demonstrated, among individuals with severe periodontitis, defined as ≥ 2 interproximal sites with clinical attachment loss of ≥ 6 mm and ≥ 1 interproximal sites with probing depth ≥ 5 mm (CDC/AAP), compared to individuals without periodontitis, after controlling for baseline health characteristics of importance (Iwasaki et al., 2016). These results are consistent with our findings. Our results are also consistent with the ones reported by Lee and coworkers (Lee et al., 2016) demonstrating that individuals with periodontitis had a higher risk of developing dementia. However, our results are in contrast to the ones reported by Arrive' and coworkers who were unable to find an association between periodontitis and dementia in a prospective follow-up study, over 15 years, in a sample of individuals aged 60-88 years, living in France (Arrive et al., 2012). A possible explanation to the conflicting results may be related to the definition of periodontitis used. In the study by Arrive' and coworkers, presence of periodontitis was evaluated using the Community Periodontal Index (CPI) (World Health Organization, 1997), which is considered as a screening tool for periodontal disease, whereas in our study periodontitis was based on actual bone loss, measured on radiographs. This underline the importance of including attachment or bone loss in the definition of periodontitis, reflecting a life-time burden of periodontal disease, when exploring a potential association to systemic diseases. A strength of our study is that a large cohort of elderly individuals were followed for a period of six years. The randomised population-based sample may also allow us to generalize the results even though the risk for selective attrition must be considered. Individuals who drop out for reasons other than death are often older and more functionally impaired. Individuals that are ill and frail may be less likely to respond and come to the research centre and in this study that is a prerequisite, as the final results rely on data from panoramic x-rays. When comparing baseline characteristics, for the group not selected or available in the final analysis, we found this group to be older, and more likely; having lower

education, living alone, having ischemic heart disease, having BMI<25 ,having less teeth (1-19) and being edentulous, more likely having bone-loss ($\geq 4\text{mm}$ distance from CEJ to marginal bone level on $\geq 30\%$ of readable sites) and pockets according to category ($\geq 5\text{mm}$ on 30% of teeth), than the selected study cohort (704). These results suggest, in addition to the exclusion of individuals with lower cognitive test outcome (MMSE <25) at baseline, that any influence of selective attrition would be that the results are underestimated. A methodological strength with the present study is that the same research team has followed the individuals during the whole study period. Other studies have added cognitive data to pre-existing oral health data (Stein, Desrosiers, Donegan, Yepes, & Kryscio, 2007; Stein, Kryscio, Desrosiers, Donegan, & Gibbs, 2010) or used self-reported data regarding oral health status (Batty et al., 2013; Gatz et al., 2006; Paganini-Hill, White, & Atchison, 2012)

Mini-Mental State Examination (MMSE) is a suitable instrument for screening for cognitive abilities in epidemiological research since it is validated and easy to administer. However, it also has some well-known limitations. The outcome relies on language skills and therefore individuals with hearing and visual disabilities had to be excluded even if they were cognitively healthy. Additionally, its ability to differentiate between subtypes of cognitive impairment and dementia has been questioned (Tombaugh & McIntyre, 1992). The study therefore needs to be repeated with other cognitive tests and with different subtypes of dementia. The underlying mechanisms explaining the association between periodontitis and cognitive deterioration are not clear and may vary between different types of dementia. Both vascular dementia and dementia of Alzheimer's type can be associated with systemic inflammation and since increasing evidence suggests that periodontitis may induce a systemic inflammatory burden, this could be a connecting pathway (Paraskevas, Huizinga, & Loos, 2008; Passoja et al., 2010). The association between experience of ischemic heart disease and periodontitis reported in the present study support this hypothesis.

The present study demonstrated that a history of periodontitis is associated with decline in cognitive functions after 6 years follow up, which may indicate that periodontitis is a risk indicator for cognitive decline. Long term intervention studies are warranted to evaluate if periodontal treatment can influence progression of cognitive decline.

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Table 1

Characteristics of the study population at baseline divided into cognitive decliners, based on deterioration of ≥ 3 p from baseline to six-year follow-up using MMSE.

	Not fulfilling criteria for cognitive decline * n (%)	Cognitive decliners, ≥ 3 p MMSE n (%)	p- value
Baseline characteristics			
Age			
60,66	308(94)	19(6)	
72,78	165(80)	42(20)	
81-96	116(68)	54(32)	<0.001
Gender			
Female	330(83)	67(17)	
Male	259(84)	48(16)	0.6
Education			
Elementary	461(82)	101(18)	
Higher	116(94)	7(6)	0.001
Living alone			
Yes	167(78)	47(22)	
No	417(87)	63(13)	0.003
Ischemic heartdisease			
Yes	88(75)	29(25)	
No	501(85)	86(15)	0.007
BMI			
Underweight and normal < 25	151(77)	44(23)	
Pre-obese and obese ≥ 25	429(86)	70(14)	0.006
Traumatic brain injury			

Yes	84(87)	13(13)	
No	501(83)	101(17)	0.4
Smoking			
Current or former	277(85)	49(15)	
Never	301 (83)	62(17)	0.46
Alcohol (Alcohol Use Disorders Intervention Scale, AUDIT ≥8)			
Yes	19(95)	1(5)	
No	546(84)	105(16)	0.18
Edentulous			
Yes	48(74)	17(26)	
No	509(85)	88(15)	0.02
Number of teeth (edentulous excluded)			
1-19	180(76)	56(24)	
20-32	329(91)	32(9)	<0.001
Pockets according to category			
0	472(86)	78(14)	
1=≥ 5mm on 30% of teeth	33(80.5)	8(19.5)	0.35
Bleeding on probing(Bop)			
0	350(87)	52(13)	
1= ≥ 30% of teeth	155(82)	34(18)	0.1
Bone-loss			
0	319(91)	33(9)	
1= ≥ 4mm distance from CEJ to marginal bone level on ≥ 30% of readable sites	166(78)	48(22)	<0.001

* Stable or minor cognitive decline (1-2p MMSE)

Table 2.

Characteristics of the study population at baseline divided into individuals having periodontal bone-loss, ≥ 4mm distance from CEJ to marginal bone level on ≥ 30% of readable sites

	Not fulfilling the criteria for periodontal bone-loss n (%)	Periodontal bone-loss n (%)	p-value
Baseline characteristics			
Age			
60,66	204(72)	78(28)	
72,78	105 (62)	65(38)	
81-96	43(38)	71(62)	<0.001
Gender			
Female	213(67)	105(33)	
Male	139(56)	109(44)	<0.01
Education			
Elementary	271(60)	183(40)	
Higher	78(75)	26(25)	<0.01
Living alone			
Yes	87 (55)	70 (45)	
No	264 (65)	143(35)	0.04
Ischemic heartdisease			
Yes	42(48)	45(52)	

No	310(65)	169(35)	<0.01
BMI			
Underweight and normal < 25	97(59)	68(41)	
Pre-obese and obese ≥ 25	254(63.5)	146(36.5)	0.3
Traumatic brain injury			
Yes	49(62)	30(38)	
No	302(62)	183(38)	0.97
Smoking			
Current or former	143(54)	123(46)	
Never	205 (70)	87(30)	<0.001
Alcohol (Alcohol Use Disorders Intervention Scale, AUDIT ≥ 8)			
Yes	9 (50)	9(50)	
No	332(84)	193(16)	0.2
Number of teeth			
1-19	96(43)	129 (57)	
20-32	256(75)	85(25)	<0.001
Pockets according to category			
0	341(66)	179(34)	
1=≥ 5mm on 30% of teeth	6(15)	34(85)	<0.001
Bleeding on probing (Bop)			
0	244 (64)	136 (36)	
1=≥ 30% of teeth	103 (57)	77(43)	0.1

Table 3. Multivariate logistic regression analysis for the outcome cognitive decline, based on deterioration $\geq 3p$ from baseline to six-year follow-up using MMSE, the odds ratio for periodontal bone-loss with additional adjustments for demographic, medical and social variables.

	Crude model n=566	Model 1 n=566	Model 2 n=558	Model 3 n=557	Model 4 n=530
Periodontal bone-loss	2.8 (1.7-4.5)	2 (1.2-3.3)	2 (1.1-3.3)	1.9 (1.1-3.2)	2.2 (1.2-3.8)
Age 72,76 81-96		3.2 (1.7-6.1) 6.2 (3.2-12.1)	2.8 (1.4-5.4) 5.8 (2.9-11.7)	2.8 (1.4-5.6) 5.5 (2.7-11.1)	2.8 (1.4-5.6) 5.3 (2.5-11.1)
Male		1.1 (0.6-1.8)	1.0 (0.6-1.7)	1.1 (0.6-1.9)	1.0 (0.5-1.8)
Living alone			1.1 (0.6-2.1)	1.1 (0.6-2.0)	1.2 (0.7-2.3)
Education, elementary			3.3	3.8	5

			(1.3-8.7)	(1.4-10.2)	(1.7-14.7)
Ischemic heart disease				1.2(0.6-2.4)	1.2 (0.6-2.3)
Body Mass Index (BMI), underweight and normal < 25				2.4(1.4-4.1)	2.1(1.2-3.7)
Traumatic brain injury					0.8 (0.4-1.9)
Smoking, current or former					1.3(0.7-2.3)
Alcohol, AUDIT≥8					0.5(0.05-4.0)

Logistic regression model, Model 1=adjustment for periodontal bone-loss, age and gender, Model 2=model 1+adjustment for living alone and education, Model 3=model 2+adjustment for ischemic heart disease and BMI, Model 4=adjustment for all variables.

Values in bold signify statistical significance $p < 0.05$. Confidence interval, CI (95%)

Supplement

Table 4

Characteristics of the study population at baseline divided into participants selected for final analysis (704) after 6 years follow-up and members of the baseline cohort not available for the final analysis (698).

	Participants	Members of the baseline cohort not available for 6 years follow-up	<i>p-value</i>
Baseline characteristics			
Age 60,66 72,78 81-96	327(82) 207(60) 170(26)	70(18) 136(40) 492(74)	<0.001
Gender Female Male	397(49) 307(52)	419(51) 279(48)	0.2
Education Elementary Higher	562(51) 123(67)	531(49) 61(33)	<0.001
Living alone Yes No	214(37) 480(66)	371(63) 252(34)	<0.001
Ischemic heartdisease Yes No	117(37) 587(54.5)	203(63) 491(45.5)	<0.001
BMI Underweight and normal < 25 Pre-obese and obese ≥ 25	195(50) 499(60)	197(50) 330(40)	0.001
Traumatic brain injury Yes No	97(54) 602(50)	84(46) 598(46)	0.4
Smoking Current or former Never	326(55) 363 51)	264(45) 348(49)	0.1
Edentulous Yes No	65(33) 596(63)	134(67) 351(37)	<0.001

Number of teeth (edentulous excluded) 1-19 20-32	236(52) 361(73)	220(48) 131(27)	<0.001
Pockets according to category 0 1=≥ 5mm on 30% of teeth	550(65) 41(47)	297(35) 47(53)	0.001
Bleeding on probing (Bop) 0 1= ≥ 30% of teeth	402(65) 189(60)	220(35) 126(40)	0.2
Bone-loss 0 1= ≥ 4mm distance from CEJ to marginal bone level on ≥ 30% of readable sites	352(73) 214(57)	128(27) 164(43)	<0.001

(The results presented for the group not available for the six years follow-up, regarding oral health variables, are based on individuals with dental examination at baseline)