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# Periodontitis and multiple markers of cardiometabolic risk in the fourth decade: a cohort study

**Dara M Shearer**[1,*], **W Murray Thomson**[1], **Claire M Cameron**[2], **Sandhya Ramrakha**[3], **Graham Wilson**[4], **Tien Yin Wong**[5,6,7], **Michael JA Williams**[8], **Rachael McLean**[2], **Reremoana Theodore**[3], and **Richie Poulton**[3]

[1]Department of Oral Sciences, Faculty of Dentistry, Dunedin, New Zealand. [2]Department of Preventive and Social Medicine, Dunedin School of Medicine, University of Otago, Dunedin, New Zealand. [3]Dunedin Multidisciplinary Health and Development Research Unit, Department of Psychology, University of Otago, Dunedin, New Zealand. [4]Department of Ophthalmology, Dunedin School of Medicine, University of Otago, Dunedin, New Zealand. [5]Singapore Eye Research Institute, Singapore National Eye Centre, Singapore, Singapore. [6]Department of Ophthalmology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore. [7]Duke-NUS Medical School, Singapore, Singapore. [8]Department of Medicine, Dunedin School of Medicine, University of Otago, Dunedin, New Zealand.

## Abstract

**Objectives:** To examine associations between periodontitis at ages 32 and 38 and a range of early cardiometabolic risk biomarkers at age 38.

**Methods:** Periodontal probing depth and bleeding on probing data collected during the age-32 and age-38 assessments in the Dunedin Multidisciplinary Health and Development Study were used to quantify periodontal inflammatory load. Retinal microvascular abnormalities, endothelial dysfunction and metabolic syndrome data were collected during the age-38 assessment. Regression models were used to examine associations between these cardiometabolic risk markers and (1) the inflammatory load at age 38 and (2) the change in inflammatory load between ages 32 and 38.

**Results:** Periodontal inflammatory load was recorded for 890 Study members at age 32, 891 at age 38, and 856 at both ages. Retinal vessel data were available for 922, endothelial dysfunction data for 909 and metabolic syndrome data for 905 at age 38. Neither the inflammatory load of periodontitis at 38 nor the changes in inflammatory load 32–38 were found to be associated with any of the three cardiometabolic risk markers.

**Conclusions:** Periodontitis was not associated with markers of cardiometabolic risk at this relatively early stage in the life course. It is possible that any influence of periodontitis on cardiometabolic health develops later in life, or periodontitis is not involved in the putative causal chain comprising systemic inflammation, cardiometabolic risk markers and subsequent cardiovascular risk.

[*]Corresponding author: dara.shearer@otago.ac.nz.

**Keywords**

Periodontitis; Cardiometabolic; Endothelial dysfunction; Peripheral arterial tonometry; Microcirculation; Retinal vascular calibre; Metabolic Syndrome

## Introduction

Evidence for associations between chronic periodontitis and atherosclerotic cardiovascular disease (ACVD) in susceptible individuals has accumulated in the past two decades[1]. The chronic inflammation of periodontitis may initiate a systemic inflammatory response which promotes or exacerbates ACVD[2]. However, evidence for a causative effect is lacking[2,3].

There has been recent interest in the early biomarkers of ACVD and cardiometabolic risk, which includes measures of retinal microvascular abnormalities, endothelial dysfunction and metabolic syndrome (MetS). These markers are associated with both clinical and subclinical ACVD across a broad range of ages[4–12].

Retinal vascular imaging is a relatively new tool in ACVD research, used to assess and quantify subtle variations and abnormalities in the retinal microvasculature[13]. In particular, venule widening has been associated with obesity, smoking and systemic inflammation[4,14,15]. Endothelial dysfunction is a pathological state of the inner lining of blood vessels (endothelium) comprising chronic inflammation and an impairment of endothelium-dependent vasodilation[16]. It is recognised as an early sign of ACVD[8–10]. MetS may be best understood as a clustering of certain cardiometabolic risk factors that often occur together and increases risk of ACVD and type 2 diabetes[11,12,17,18].

It is probable that, if the inflammatory burden of periodontitis does have an influence on ACVD risk, it would be manifest in these early biomarkers sooner than in later clinical ACVD signs. Some associations have been found between these early biomarkers and periodontitis. To date, there has been only one study of associations between periodontitis and retinal microvasculature health. In that cross-sectional study, severe periodontitis was associated with retinal venular widening in individuals with Type 2 diabetes[19]. Some researchers have reported associations between periodontitis and endothelial dysfunction[20,21], and others have reported an improvement in endothelial function following intensive periodontal treatment[21,22]. However, a 2013 study found the opposite; more severe periodontitis was associated with better endothelial function than with less severe periodontitis[23]. Associations have also been found between periodontitis and MetS[24–26], and between periodontitis and the individual components of MetS[26,27].

In view of the relatively high prevalence of both periodontal disease and ACVD, research to investigate associations between them is crucial. Elucidation of the relationship between these two conditions may contribute to the future management of ACVD, in which case the public health significance would be substantial. To date, no study has examined associations between periodontitis and multiple markers of cardiometabolic risk in a representative early middle-age cohort; early middle age is a potentially important time for intervention aimed at preventing progression to ACVD and its sequelae. The aim of this study was to investigate

(1) cross-sectional associations between periodontal inflammation at age 38, and (2) longitudinal changes in periodontal inflammation between ages 32 and 38, and those three biomarkers at age 38.

## Methods

This study used periodontal data collected during the age-32 and age-38 assessments and cardiometabolic biomarker data collected during the age-38 assessment of the Dunedin Multidisciplinary Health and Development Study (DMHDS). The DMHDS is a longitudinal epidemiological study of a birth cohort of 1,037 children born at the Queen Mary Hospital, Dunedin, New Zealand between 1 April 1972 and 31 March 1973[28]. To be eligible for inclusion, participants had to be living in the Dunedin Metropolitan area three years after their birth, of whom 91% of the 1139 eligible children participated; the 9% not included did not differ from the 91% in their sociodemographic and perinatal characteristics. The Study has a very high retention rate (over 95% of the surviving cohort assessed at both ages 32 and 38), and a wealth of physical, mental and psychosocial data has been collected. Ethics approval for the study was granted by the Otago Research Ethics Committee and participants gave informed consent.

### Periodontal assessments

As previously described [29], full-mouth periodontal examinations were conducted at ages 32 and 38. Third molars and implants were excluded from examination, and participants with a history of cardiac valvular abnormalities or rheumatic fever were not examined. Three sites (mesiobuccal, buccal, and distolingual) per tooth were examined using an NIDR probe (the Hu-Friedy PCP-2). Probing depth (PD; the distance from the gingival margin to the tip of the probe) was recorded in millimetres with measurements rounded down to the nearest whole millimeter. Gingival bleeding on probing was assessed for each tooth by observing the presence or absence of bleeding at each of the three probing sites. If bleeding was observed 10 seconds after probing at any of the three sites, then “bleeding on probing” (BOP) was recorded for that tooth. Two and three calibrated examiners were used at ages 32 and 38 respectively, and intra- and inter-examiner reliability data at each age were acceptable[30,31]. At each age, the inflammatory load was measured at the tooth level. For each tooth examined, if any of the three sites had 3+mm PD, and also had BOP at any of the three sites, the periodontal tissue of the tooth was deemed to be inflamed. A count was made of the number of inflamed teeth in order to quantify each participant’s inflamed periodontal tissue and intra-oral inflammatory load at each age, and the change in inflammatory load between ages 32 and 38 was computed.

A modified version of the simplified oral hygiene index was used to quantify plaque accumulation at age 38 whereby six index teeth were scored 0, 1, 2 or 3 according to how much of the tooth was covered with plaque[32]. The overall plaque score was the sum of the scores divided by the number of teeth scored. Study members were then categorised according to their plaque score: score 0 to 0.5 “Very low”; score >0.5 to 1.0 “Low”; score >1.0 to 1.5 “Moderate”; and score >1.5 “High”.

### Assessment of retinal vessel calibre

Digital fundus photographs were taken at the Dunedin Research Unit after 5 min of dark adaptation. The same camera (Canon NMR-45 with a 20D single-lens reflex backing; Canon, Tokyo, Japan) was used for all photographs to avoid artefactual variation from different cameras. Both the left and right eyes were photographed, and we use here data from the average for the two eyes. Retinal photographs were graded at the Singapore Eye Research Institute (National University of Singapore) using Version 3.0 of the semiautomated computer software, Singapore I Vessel Assessment (SIVA). Trained graders, blind to participants' characteristics, used SIVA to measure the retinal vessel diameters according to a standardized protocol with high inter-grader reliability[33]. Diameter (or calibre) denotes the size of the vessel lumen. Measurements were made for vessels where they passed through a region located 0.5 to 2.0 disk diameters from the optic disk margin[33]. Vessel calibres were based on the six largest arterioles and venules passing though this region and were summarised as central retinal artery equivalent (CRAE) and central retinal vein equivalent (CRVE) using the revised Knudtson-Parr-Hubbard formula[34,35].

### Endothelial function assessment

Participants had endothelial function assessed in the non-fasting state after lying supine for 10 minutes in a temperature-controlled room at 20°C. A peripheral arterial tonometry (PAT) device was placed on the index finger of each hand (Endo-PAT2000, Itamar Medical Ltd, Caesarea, Israel). PAT is a non-invasive technique that utilises a finger plethysmograph to determine digital blood volume at baseline and during reactive hyperaemia. A blood pressure cuff was placed on the right upper arm, and baseline measurements were obtained from both index fingers over two minutes. The cuff was then inflated to 200 mm Hg or 60 mm Hg above systolic blood pressure, whichever was higher, and occlusion of brachial artery flow confirmed. After 5 minutes, the cuff was deflated and recording continued for five minutes. Pulse amplitude was recorded from both fingers and analysed by an automated algorithm (Itamar Medical) that provided the average pulse amplitude for each 30-second interval over the four minutes immediately after forearm cuff deflation. PAT measured the digital pulse volume after reactive hyperaemia induced by brachial artery occlusion, and the ratio of hyperaemic to baseline pulse amplitudes was calculated as the Framingham-reactive hyperaemia index (F-RHI). The F-RHI was defined as F-RHI = ln(RHo/RHc), where RHo and RHc are the mean pulse amplitudes of the period 2 minutes after cuff deflation divided by the mean baseline amplitudes in the occluded arm and control arm, respectively[8]. For the F-RHI, lower scores indicate greater endothelial dysfunction.

### Metabolic syndrome assessment

Blood samples were collected at age 38, and glycated haemoglobin (HbA1c), triglycerides (mmol/L) and HDL cholesterol (mmol/L) were assayed. Blood pressure and waist circumference were recorded. Full details of these assays and recordings are in the online supplement. Metabolic syndrome was defined according to National Cholesterol Education Program Adult Treatment Panel III (NCEP, ATP III) criteria, whereby participants were considered to have met the criteria for MetS if they had three or more of five components: (1) glycated hemoglobin ≥5.7% (≥39 mmol/mol); (2) waist >102 cm (men), waist >88 cm

(women); (3) triglycerides ≥1.7 mmol/L; (4) HDL <1.0 mmol/L (men), <1.3 mmol/L (women); or (5) blood pressure ≥130/85 mmHg (or drug treatment for hypertension).

### Measurement of other variables

The identification of appropriate covariates was guided by the literature, and facilitated by directed acyclic graphs (DAGs; Figs S1-S3), using the DAGitty online tool[36]. A six-interval, occupationally-based measure of socioeconomic status (SES) was obtained from participants at age 38 whereby a doctor scores '1' and a labourer scores '6'[37]. Study members were then allocated to the 'High SES group' (scores 1 and 2); the 'Medium SES group' (scores 3 and 4); or the 'Low SES group' (scores 5 and 6)[29]. Study members who gave a positive response at 38 to the question "Have you smoked every day for one month or more of the previous 12 months?" were categorised as current smokers.

### Statistical analysis

Linear multiple regression models were used to examine associations between CRVE and (1) the inflammatory load at age 38 and (2) the change in inflammatory load 32–38; and between the Framingham-reactive hyperaemia index (F-RHI) and (1) the inflammatory load at age 38 and (2) the change in inflammatory load 32–38. As is standard practice, CRAE was included in the CRVE multiple regression models to control for its confounding effects[14,15]. Logistic regression models were used to examine associations between MetS and (1) the inflammatory load at age 38 and (2) the change in inflammatory load 32–38. All three analyses adjusted for the minimal adjustment set identified by the DAGs: sex, low SES, smoking, dysglycaemia and high plaque group at 38. Analyses were undertaken using SPSS version 20 (SPSS Inc. Chicago, Illinois) and Stata IC 12.0 for Windows (StataCorp 2011, Stata Statistical Software: Release 14, College Station, Tx, USA).

## Results

Periodontal examinations were carried out for 918 Study members at age 32, 900 at age 38, and 864 at both ages. Of these, 890 (96.9%) Study members had their inflammatory load recorded at age 32, 891 (99.0%) at age 38, and 856 (99.1%) at both ages. Retinal vessel data were available for 922 Study members at age 38, F-RHI data for 909, and MetS data for 905 (95.9%, 94.6% and 94.2% respectively of those assessed at age 38). Nine Study members were excluded from all analyses because of pregnancy, and three individuals with Type 1 diabetes were excluded from the MetS analysis.

There were slightly more males than females (Table 1); a quarter of the cohort were smokers, and over one in six were dysglycaemic. Half the sample was in the medium-SES group, and one-fifth in the low-SES group. Most individuals were in the low or very low plaque groups with almost one-fifth in the moderate or high groups. The mean inflammatory load (number of teeth with 1+ sites with 3+mm PD and BOP) changed little between ages 32 and 38. The inflammatory load at 32 ranged from 0.0 to 26.0 with a median of 1.0; at 38, it ranged from 0.0 to 27.0, with a median of 1.0. The change in inflammatory load between ages 32 and 38 ranged from -18.0 to 19.0, with a median of 0.0. Approximately one in three (290, 33.9%) participants experienced an increase in inflammatory load between ages 32 and

38, one in three experienced a decrease (303, 35.4%), and one in three had no change (263, 30.7%). The CRAE ranged from 105.66 to 179.47 measuring units with a median of 137.32, and the CRVE ranged from 141.07 to 245.68 measuring units with a median of 195.51. The F-RHI ranged from -0.15 to 1.92 with a median of 0.60. About one in six individuals were classified as having MetS.

Bivariate analyses of associations between the mean inflammatory load at age 38, and socioeconomic status, smoking and plaque group at 38, were carried out (Supplementary Table S1). The mean inflammatory load at age 38 was found to be higher among those who, at age 38, were of lower socioeconomic status, smokers, and or had poorer longitudinal plaque control.

## Regression models

Analysis of the CRVE linear multiple regression models found no association between the inflammatory load at age 38 and CRVE at 38 (Table 2, Model 1). For a one-point change in CRAE, CRVE was greater by a mean 0.89 measuring units. On average, men and smokers had a higher CRVE than women and non-smokers respectively. No association was found between the change in inflammatory load 32–38 and CRVE at 38 (Table 2, Model 2). In this model, for a one-point change in CRAE, CRVE was greater by a mean 0.89 measuring units. Men and smokers had a higher mean CRVE than women and non-smokers respectively.

The multiple linear regression models for F-RHI showed no association between the inflammatory load at age 38 and F-RHI at 38 (Table 2, Model 3). No association was found between the change in inflammatory load 32–38 and F-RHI at 38 (Table 2, Model 4). In both models, men had (on average) a lower F-RHI than women.

The logistic regression model showed no association between inflammatory load at age 38 and having MetS at 38 (Table 2, Model 5). Men had higher odds than women for having MetS, and people with dysglycaemia at 38 had more than seven-fold higher odds than people who did not have dysglycaemia. No association was found between the change in inflammatory load 32–38 and MetS at 38 (Table 2, Model 6). Men had higher odds than women for having MetS, and those with dysglycaemia at 38 had more than seven-fold higher odds than those who did not have dysglycaemia.

A sensitivity analysis was carried out using a 4+mm threshold for probing depth. No associations were found between this measure of periodontal inflammation and any of the cardiometabolic outcomes (Supplementary Table S2).

## Discussion

We investigated associations between periodontitis and early biomarkers of cardiometabolic risk. The inflammatory load of periodontitis was not found to be associated with retinal microvascular abnormalities, endothelial dysfunction or metabolic syndrome. We believe that this is the first comprehensive examination of the cross-sectional and longitudinal associations between periodontitis and these biomarkers at a relatively early stage in the life course. Our study provides no evidence that periodontitis was associated with

cardiometabolic risk in this age group. It is possible that any influence of periodontitis on cardiometabolic health and ACVD develops later in life. Alternatively, periodontitis is not strongly involved in the putative causal chain comprising systemic inflammation, cardiometabolic risk markers and subsequent cardiovascular risk.

It must be considered whether the finding of no evidence that periodontitis was associated with cardiometabolic risk in this age group could have been due to a particularly low prevalence of either periodontitis or the cardiometabolic markers in this cohort. The Dunedin Study prevalence of periodontitis is comparable to that of the 2009/2010 National Health and Nutrition Examination Survey (NHANES) in the United States[38]. Indeed, the prevalence in our study was slightly higher than that observed in a similar age group in the NHANES[38]. Similarly, the mean central retinal venule equivalent (CRVE) in our cohort is consistent with a range of other studies[5], as was our mean F-RHI score[8,39], and the prevalence of MetS[40].

The strengths of this study include the use of a birth cohort with a very high retention rate, together with comprehensive objective data on periodontitis at ages 32 and 38, and on cardiometabolic risk markers at age 38. The high retention means that the sample should be representative of its source population (the South Island of New Zealand). The issue of whether the findings can be generalised to other populations has been considered[41,30]. One paper provided broad support for the generalisability of the Dunedin Study findings to the total New Zealand population[41]; the other concluded that the periodontal findings from the DMHDS are likely generalisable to the New Zealand and U.S. populations[30].

Some limitations must be acknowledged. While the proportion (7.5%) who self-identify as Māori in the cohort does match the proportion of Māori in the South Island, Māori are under-represented with respect to the total New Zealand Māori population (14.9% in the 2013 Census)[29]. Periodontal recordings were made from three sites only per tooth; it is possible that this led to an underestimation of the prevalence and extent of periodontitis, and subsequently some attenuation of the strength of the associations between periodontitis and cardiometabolic biomarkers. However, the three-site protocol used in the DMHDS has been demonstrated to result in less bias than other partial recording protocols[42].

The putative pathway between periodontitis, systemic inflammation and ACVD is a biologically plausible one. The possibility of periodontal inflammation contributing to systemic inflammation (and cardiometabolic morbidity) is important both from a clinical and public health viewpoint and must be considered in the context of the very high prevalence of periodontitis in adult populations worldwide. Evidence for a causal link has been suggested by a number of randomised control trials (RCTs) reporting the benefit of periodontal treatment for systemic inflammatory markers and ACVD risk factors—although some studies were limited by small sample sizes[43–45]. However, a recent Cochrane systematic review concluded that there was insufficient evidence to determine the effect of periodontal treatment on ACVD risk in individuals with chronic periodontitis[46].

Interestingly, two consensus reports on the subject were issued within a year of each other. The Joint European Federation of Periodontology/American Academy of Periodontology Workshop concluded that “there is consistent and strong epidemiologic evidence that

periodontitis imparts increased risk for future cardiovascular disease"[47]. Meanwhile, the American Heart Association reported that, while observational studies did support an association between PD and ACVD, they do not support a causative relationship, and neither was there any evidence that periodontal interventions modify ACVD outcomes[3]. The debate is ongoing, and data from longitudinal studies such as ours contribute to an understanding of the conditions' association.

### Retinal vessel calibre

The only other study (by Boillet et al.) to examine such associations observed a cross-sectional association between severe periodontitis and wider venular calibre, but only in individuals with diabetes[19]. The latter are known to have wider retinal venules[14]. Our study differed from this one. Their sample had a mean age of 63 years; ours was much younger, at 38 years. They photographed only one eye. They were able to examine a sub-sample of 66 with diabetes; in our cohort, only six individuals had diabetes at age 38—and we did not find dysglycaemia to be associated with CRVE. Finally, the studies differed in their periodontitis case definitions; Boillet et al. classified participants as having healthy/gingivitis or moderate or severe periodontitis, whereas we used a variable that quantified inflamed periodontal tissue and the intra-oral inflammatory load. Case definitions in periodontal research are known to be somewhat arbitrary, and our use of a more nuanced approach to exposure may be viewed as an improvement.

Our finding that smoking had the greatest influence on CRVE is not surprising. Smoking is one of the most hazardous modifiable ACVD risk factors, and research has established associations between smoking and wider CRVE[14,15,45]. Much of that has involved middle-aged and older populations, and it is noteworthy that our associations between smoking and CRVE were seen at a much earlier stage in the life course. We also found that males had wider retinal venules, on average. This was consistent with findings from the Beaver Dam Eye Study[48], and the Atherosclerosis Risk in Communities (ARIC) study[15].

It is worth noting here that associations between obesity and adverse retinal microvascular changes have been found in pre-adolescent children[49], and between television screen time and adverse retinal microvascular changes in six-year-old children[50]. Given that these ACVD risk factors were associated with retinal microvascular changes at a young age (and yet we found no associations between periodontitis and retinal microvascular changes in the DMHDS cohort by age 38), it suggests that any influence periodontitis may have on CVD risk develops later in life.

### Endothelial dysfunction

Ours is the first study to examine associations between periodontitis and endothelial dysfunction using fingertip peripheral arterial tonometry (PAT). FMD has been the most widely used technique to measure endothelial function in recent years. While it is non-invasive, inexpensive and predictive of coronary artery endothelial function, its application is technique-sensitive and difficult, and protocols are not standardised[51]. By contrast, the EndoPAT device is much easier to use, is reliable, does not require extensive training, and uses automated post-test analysis[52]. The contralateral arm serves as an internal control to

correct for any systemic change in vascular tone during the test. Endothelial dysfunction measured with EndoPAT is associated with coronary microvascular endothelial dysfunction in individuals with early atherosclerosis, with cardiometabolic risk factors, and with later cardiovascular events[8,53,54].

Circumstantial evidence for a possible causal link between periodontal inflammation and endothelial dysfunction has arisen from cross-sectional studies[20,55], a review[56] and a meta-analysis[57]. In addition, a number of RCTs have provided baseline data on impaired endothelial function in participants with periodontitis, as well as reporting significant improvements in endothelial function following periodontal treatment[21,22,58–60]. Our study differs from those others in important ways. Most studies used FMD for the assessment of endothelial function[20,22,58–60] whereas we used the PAT technique. Much of the previous research was limited by small sample sizes[20,21,55,58–60], or involved participants with severe periodontitis[20,22,55,58,60]. There is considerable variation in how periodontitis experience is defined in studies; precisely how it was defined was not clear in two of those[21,59]. By contrast, we used a variable that quantified inflamed periodontal tissue and the intra-oral inflammatory load.

The inverse relation we found between male sex and PAT is consistent with other research[8]. However, our study differed from these others in that we did not find any association between periodontitis and endothelial dysfunction. Of interest, the findings of a large population-based study using FMD are the opposite of all the studies outlined above; poorer periodontal health was found to be associated with better endothelial function[23].

### Metabolic syndrome

Most of the associations found between periodontitis and MetS have been cross-sectional[24,26,61–63]. Generally, the greater the number of MetS components, the more severe the periodontitis, or the stronger the association between the two conditions. Five studies showed associations between the dysglycaemia component of MetS and periodontitis[24,26,61,62,64]; one study found no association[63]; and one reported unadjusted associations only between periodontitis and individual MetS components[65]. Nibali et al. found that those with severe periodontitis had higher serum glucose levels and leukocyte counts—and worse dyslipidaemia profiles—than those without severe periodontitis[27]. Morita et al. found that baseline periodontal status was associated with the number of MetS components four years later[25]. A temporal relationship between the two conditions was demonstrated, with periodontitis preceding conversion to one or more MetS components; periodontitis predicted hypertension and dyslipidaemia, but not obesity or hyperglycaemia. Our study differed from these others in that we could not demonstrate any association between periodontitis and MetS. That MetS was associated with dysglycaemia was not surprising, since the latter is a component of MetS. We also found sex to be associated with MetS, and these findings add to the emerging literature on sex differences in the development of MetS[66].

### Conclusions

We found no associations between periodontitis and early biomarkers of cardiometabolic risk: measures of retinal microvascular abnormalities; endothelial dysfunction; and MetS. It is possible that our cohort was too young for such associations to be found. The periodontal inflammatory burden at age 38 may not have been great enough to influence systemic inflammation and cardiometabolic risk markers. The debate about putative causal links between periodontal inflammation and cardiometabolic risk (and its sequelae ACVD and CVD outcomes) is ongoing. Objective data from longitudinal cohort studies such as the current one will make an important contribution to the continuing discussion. Following this cohort as it moves further into middle-age and beyond will contribute greatly to understanding of how (or indeed whether) oral and cardiometabolic health interrelate.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

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**Table 1.**

Sociodemographic characteristics, smoking, dysglycaemia and plaque group at 38, periodontal prevalence and periodontal inflammatory load at 32 and 38, prevalence of metabolic syndrome at 38, mean Framingham-reactive hyperaemia index at 38 and arteriolar and venular calibres at 38. Women pregnant at 38 are excluded.

| | N (%) or mean (SD) |
|---|---|
| **Sex**[1] | |
| Female | 468 (49.2%) |
| Male | 484 (50.8%) |
| **SES at 38**[2] | |
| High | 280 (29.7%) |
| Medium | 477 (50.5%) |
| Low | 187 (19.8%) |
| **Smoker at 38**[3] | |
| Yes | 252 (26.6%) |
| No | 696 (73.4%) |
| **Dysglycaemia at 38**[4] | |
| Yes | 164 (18.3%) |
| No | 730 (81.7%) |
| **Plaque group at 38**[5] | |
| High | 68 (7.6%) |
| Moderate | 93 (10.3%) |
| Low | 243 (27.0%) |
| Very low | 496 (55.1%) |
| **Prevalence of periodontitis (CDC/AAP case definition)** | |
| Moderate periodontitis at age 32[6] | 159 (17.9%) |
| Severe periodontitis at age 32[6] | 49 (5.5%) |
| Moderate periodontitis at age 38[7] | 230 (25.8%) |
| Severe periodontitis at age 38[7] | 79 (8.9%) |
| **Periodontal Inflammatory load** | |
| Mean inflammatory load at age 32 (SD)[6] | 2.9 (4.4) |
| Mean inflammatory load at age 38 (SD)[7] | 2.8 (4.6) |
| Mean change in inflammatory load 32–38 (SD)[8] | 0.0 (4.0) |
| **Arteriolar and venular calibres** | |
| Mean central retinal arteriolar equivalent (CRAE) at age 38 (SD)[9] | 137.33 (10.86) |
| Mean central retinal venule equivalent (CRVE) at age 38 (SD)[9] | 196.20 (14.83) |
| **Endothelial Function** | |
| Mean Framingham-reactive hyperaemia index at 38 (SD)[10] | 0.61 (0.38) |

| | N (%) or mean (SD) |
|---|---|
| **Metabolic syndrome**[11] | |
| Yes | 152 (16.9%) |
| No | 750 (83.1%) |

Note: not all participants responded to all items.

[1]N=952;

[2]N=944;

[3]N=948;

[4]N=894;

[5]N=900;

[6]N=890;

[7]N=891;

[8]N=856;

[9]N=922;

[10]N=909;

[11]N=905.

Dysglycaemia; glycated haemoglobin (HbA1c) ≥5.7% (≥39 mmol/mol).

Periodontal Inflammatory load is the count of the number of teeth with 1+ sites with 3+mm PD and bleeding on probing (BOP).

Metabolic syndrome (MetS) categorised according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP, ATP III) criteria (three or more of: (1) glycated hemoglobin ≥5.7% (≥39 mmol/mol); (2) waist >102 cm (men), waist >88 cm (women); (3) triglycerides ≥1.7 mmol/L; (4) HDL <1.0 mmol/L (men), <1.3 mmol/L (women); or (5) blood pressure ≥130/85 mmHg (or drug treatment for hypertension).

Three individuals with Type 1 diabetes were excluded from the MetS analysis.

**Table 2.**

Linear regression models for central retinal venule equivalent (CRVE) and Framingham Reactive Hyperaemia Index (F-RHI) at 38, and logistic regression models for metabolic syndrome at 38.

| | Central retinal venule equivalent (CRVE) at 38 | Framingham Reactive Hyperaemia Index (F-RHI) at 38 | Metabolic syndrome (MetS) at 38. |
|---|---|---|---|
| | Coefficient (95% CI) | Coefficient (95% CI) | Odds ratio (95% CI) |
| **Cross-sectional models** | **Model 1** | **Model 3** | **Model 5** |
| Inflammatory load at age 38 | 0.11 (-0.06, 0.29) | -0.00 (-0.01, 0.01) | 1.03 (0.99, 1.07) |
| CRAE at 38 | **0.89 (0.82, 0.96)** | | |
| Male | **2.50 (0.99, 4.00)** | **-0.19 (-0.25, -0.14)** | **1.63 (1.08, 2.48)** |
| Low SES at 38 | 1.29 (-0.87, 3.44) | -0.02 (-0.09, 0.06) | 1.11 (0.64, 1.91) |
| Current smoker at 38 | **2.92 (1.08, 4.77)** | -0.04 (-0.11, 0.02) | 0.98 (0.60, 1.58) |
| Dysglycaemia at 38 | 1.59 (-0.36, 3.54) | -0.04 (-0.11, 0.02) | **7.66 (5.03, 11.65)** |
| High plaque score group at 38 | -0.00 (-3.13, 3.12) | -0.09 (-0.19, 0.02) | 0.95 (0.44, 2.01) |
| **Longitudinal models** | **Model 2** | **Model 4** | **Model 6** |
| Change in inflammatory load 32–38 | -0.02 (-0.21, 0.17) | -0.00 (-0.01, 0.01) | 1.01 (0.96, 1.06) |
| CRAE at 38 | **0.89 (0.81, 0.96)** | | |
| Male | **2.61 (1.07, 4.15)** | **-0.19 (-0.25, -0.14)** | **1.55 (1.01, 2.36)** |
| Low SES at 38 | 1.57 (-0.59, 3.73) | -0.02 (-0.09, 0.06) | 1.11 (0.64, 1.92) |
| Current smoker at 38 | **3.13 (1.28, 4.97)** | -0.04 (-0.11, 0.02) | 1.05 (0.65, 1.70) |
| Dysglycaemia at 38 | 1.71 (-0.28, 3.70) | -0.04 (-0.11, 0.02) | **7.55 (4.93, 11.55)** |
| High plaque score group at 38 | 0.50 (-2.68, 3.68) | -0.09 (-0.19, 0.02) | 1.04 (0.49, 2.24) |

*Note that observations were lost when individuals had a missing observation for a variable. CI; Confidence interval. Statistically significant findings in bold type.

N = 836 for CRVE cross-sectional model, N = 808 for CRVE longitudinal model. N = 829 for F-RHI cross-sectional model, N = 802 for F-RHI longitudinal model.

N = 836 for MetS cross-sectional model, N = 808 for MetS longitudinal model.

Metabolic syndrome (MetS) categorised according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP, ATP III) criteria. Three individuals with Type 1 diabetes were excluded from the MetS analysis.

Reference categories: female (for male); high SES at 38 (for low SES at 38); not current smoker at 38 (for current smoker at 38); not dysglycaemic at 38 (for dysglycaemic at 38); low plaque score group at 38 (for high plaque score group at 38).