Reexamining the Association Between Smoking and Periodontitis in the Dunedin Study With an Enhanced Analytical Approach

Jiaxu Zeng,* Sheila M. Williams,† David J. Fletcher,‡ Claire M. Cameron,† Jonathan M. Broadbent,* Dara M. Shearer,* and W. Murray Thomson*

Background: Smoking is a major risk factor for periodontal disease. Conventional oral epidemiology approaches have found strong, consistent associations between chronic smoking and periodontal attachment loss (AL) through ages 26, 32, and 38 years, but those statistical methods disregarded the data's hierarchical structure. This study reexamines the association using hierarchical modeling to: 1) overcome the limitations of an earlier approach (trajectory analysis) to the data and 2) determine the robustness of the earlier inferences.

Methods: Periodontal examinations were conducted at ages 26, 32, and 38 years in the Dunedin Multidisciplinary Health and Development Study. The number of participants examined at those three ages were 913, 918, and 913, respectively. A generalized linear mixed model with a quasi-binomial approach was used to examine associations between chronic smoking and periodontal AL.

Results: At ages 26, 32, and 38, smokers had 3.5%, 12.8%, and 23.2% greater AL than non-smokers. Regular cannabis use was associated with greater AL after age 32, but not at age 26. Males had more AL than females. Participants with high plaque scores had consistently greater AL; those who were of persistently low socioeconomic status had higher AL at ages 32 and 38, but not at age 26. The amount of AL in anterior teeth was less than in premolars and molars. Gingival bleeding was associated with higher AL at ages 26, 32, and 38.

Conclusion: The smoking–periodontitis association is observable with hierarchical modeling, providing strong evidence that chronic smoking is a risk factor for periodontitis. *J Periodontol 2014;85:1390-1397.*

KEY WORDS

Cannabis; cohort studies; multilevel analysis; periodontal diseases; risk factors; smoking.

* Department of Oral Sciences, Sir John Walsh Research Institute, School of Dentistry, The University of Otago, Dunedin, New Zealand.
† Department of Preventive and Social Medicine, Dunedin School of Medicine, The University of Otago.
‡ Department of Mathematics and Statistics, The University of Otago.

Periodontitis is a chronic polymicrobial disease that occurs when the host response to usually commensal organisms in the plaque biofilm becomes destructive.[1] Smoking remains the most important risk factor,[2-4] with evidence suggesting that its periodontal effects occur regardless of what is smoked.[5-7] Smoking is thought to exert its effect through affecting neutrophil function, causing shifts to a more pathogenic microflora, and causing sustained peripheral vasoconstriction.[8] From a life-course perspective, the effect of chronic smoking is an example of the risk accumulation model, whereby its effects are cumulative over time.[9] Moreover, marked social gradients in the occurrence of smoking contribute to socioeconomic gradients in periodontitis,[10,11] but the extent of that contribution is currently unclear. Day-to-day self-care and plaque control are also important in the condition's occurrence.

Although previous papers have reported a strong association between smoking and periodontal disease through ages 26, 32, and 38 years in a birth cohort,[5-7] the approaches adopted for those data analyses do have limitations. A large proportion of that earlier work considered the use of hypothesis testing, logistic regression, and growth trajectory modeling to identify the risk factors.

doi: 10.1902/jop.2014.130577

One of the main concerns is that the response variable for these analyses was the prevalence, the extent, or the severity of periodontitis, yet there is considerable variation in case definitions for it in the literature. This applies no less to defining incident cases, with incident attachment loss (AL) being defined as a change in AL of ≥2, ≥4, ≥5, or even ≥6 mm, depending on the sample and the inter- and intra-examiner reliability. Such variation will inevitably lead to considerable heterogeneity in analytic outcomes. Another fundamental problem is that those methods do not account for the natural hierarchical structure of the periodontal data. Thus, while they can be used to identify person-level risk factors, the site-specific nature of the AL is unable to be taken into account.

The aim of this study is to reexamine the periodontal effects of smoking and the impact of the other putative risk factors through early to middle adulthood cross-sectionally, using a more informative approach. Multilevel modeling is recognized as the most appropriate method for analyzing data of this type, because it accounts for the hierarchical structure of the data and allows the simultaneous examination of covariates' effects on different levels, for each person, tooth, and site.[12] However, multilevel analysis carries the assumption that the random effects and measurement errors are normally distributed. This assumption is unlikely to be satisfied with AL data. To address this, a generalized linear mixed model (GLMM) with a quasi-binomial approach was used here as an extension of the traditional multilevel modeling method for data analysis.

MATERIALS AND METHODS

The Dunedin Multidisciplinary Health and Development Study is a longitudinal study of a complete birth cohort born at the Queen Mary Hospital, Dunedin, New Zealand, from April 1, 1972, to March 31, 1973.[13] Perinatal data were obtained, and the sample for the longitudinal study (N = 1,037; 52% males) was defined at age 3 years. The cohort were assessed within a month of their third birthdays and again at ages 5, 7, 9, 11, 13, 15, 18, 21, 26, 32, and 38 years (when 961 or 95% of the living cohort were assessed). More than 90% of the cohort self-identify as European.

The Otago Research Ethics Committee, Dunedin, New Zealand, granted ethics approval for each assessment phase. Study members gave written informed consent before participating. Each underwent a full day of assessments (of, for example, oral health, mental health, and cardiovascular health), which are presented as standardized modules in counterbalanced order, conducted by a different examiner kept masked to all other study data.

Clinical Assessments

Periodontal examinations were conducted at ages 26, 32, and 38 years, with only half-mouth examinations possible at age 26, but full-mouth examinations undertaken at ages 32 and 38. Third molars and implants were not included in the periodontal examinations. At age 26, dental examinations were conducted by three examiners (WMT, Dr. E. Kruger, and Dr. D.M. Boyd, University of Otago) who had been previously calibrated and who examined 85%, 10%, and 5%, respectively, of the cohort. Periodontal measurements were made in two quadrants because of time constraints (quadrants 1 and 3 for those whose study ID number was odd; quadrants 2 and 4 for those with an even ID number; the mix of odd and even ID numbers was approximately 50:50). Three sites (mesio-buccal, buccal, and disto-lingual) per tooth were examined, and gingival recession (GR) (the distance in millimeters from the cemento-enamel junction [CEJ] to the gingival margin) and probing depth (PD) (the distance from the gingival margin to the base of the pocket) were recorded, using a periodontal probe.§ Mid-buccal measurements for molars were made at the midpoint of the mesial root. All measurements were rounded down to the nearest whole millimeter. Where the gingival margin was situated >1 mm coronally to the CEJ, negative GR was recorded. Those reporting a history of cardiac valvular anomalies or rheumatic fever were excluded. At ages 32 and 38, the clinical procedures were identical, except that a full-mouth examination was now possible. Two examiners (JMB and WMT) conducted the examination at age 32, examining 53% and 47%, respectively; the second examiner was the one who had conducted the bulk of the age-26 examinations. At age 38, the examinations were conducted by three examiners (JMB, WMT, and Dr. L.A. Foster Page, University of Otago); these included the two examiners who had undertaken the age-32 examinations; they undertook 58% and 39% of the age-38 examinations, respectively, and the third completed 3%. For each individual, the AL for each site was computed by summing the GR and PD measurements.

Examiner Reliability

Replicate periodontal examinations were not possible during the assessments because of time constraints, but they were conducted on separate adult samples during the age-32 and age-38 assessments. At age 38, these gave data for 672 periodontal sites measured by the three examiners twice each, and these revealed that intra- and interexaminer reliability was high (accepting 1-mm variation in measurements as being normal measurement error[14]), with intra-examiner reliability coefficients for absolute agreement

§ PCP-2, Hu-Friedy, Chicago, IL.

of the site-level periodontal measurements pooled for the three examiners (individual examiner intra-examiner reliability coefficients in parentheses) found to be 0.95 (0.99, 0.92, 0.94) for GR; 0.73 (0.73, 0.69, 0.80) for PD; and 0.71 (0.71, 0.68, 0.79) for AL. The coefficient for the prevalence of ≥1 site with ≥4-mm AL was 0.75 (0.99, 0.74, 0.97). A 1-mm difference within and among examiners is normal measurement error in periodontal measurement. For intra-examiner reliability pooled for all three examiners, only 2.6% of measurements differed by >1 mm (2.2%, 2.5%, and 3.0% for examiners 1, 2, and 3, respectively). No measurements differed by >2 mm. Examiner 1 differed from examiner 2 by >1 mm in 5.4% of measurements and by >2 mm in only 0.8%; examiner 1 differed from examiner 3 by >1 mm in 3.2% and by >2 mm in only one (0.1%). Examiner 2 differed from examiner 3 by >1 mm in 5.0% and by >2 mm in only 0.7% of measurements. The examiner reliability was similar to that reported elsewhere.[14] Examiner reliability data for the age-32 examinations have been reported previously[15] and were acceptable. Calibration data for the age-26 assessments were not collected.

Person-Level Covariates

Smoking status. Tobacco smoking was determined at ages 15, 18, 21, 26, 32, and 38. At ages 21, 26, 32, and 38, the study asked "Have you smoked every day for 1 month or more of the previous 12 months?".

Cannabis use status. Cannabis smoking was determined by asking participants at ages 18, 21, 26, 32, and 38 how many times they had used cannabis in the previous year. They were then grouped as those who: 1) did not use cannabis (response 0); 2) used it less than weekly (0 to 51); 3) used it at least weekly (52 to 365); and 4) used it at least daily (>365). The usual method of smoking cannabis in New Zealand is not to mix it with tobacco.

Socioeconomic status (SES). SES was measured in childhood using standard New Zealand occupationally based indices,[16,17] which use a six-category classification (where, for example, a doctor scores 1 and a laborer scores 6). For adult SES measurement, participants were classified (using occupation) at ages 26, 32, and 38. The childhood SES measure used here is based on both parents and is the mean of the SES from the assessments at birth through age 15. The study used the childhood and adult SES categorizations to allocate each participant to one of the following four SES trajectories: 1) those who were in the high SES group up to the age of 15 and in adulthood (at 26, 32, and 38 years of age separately), categorized as the "high-high" group; 2) those in the low SES group at both stages, designated the "low-low" group; and the 3) "high-low" and 4) "low-high" groups, which comprised those who were downwardly and upwardly mobile, respectively.

Flossing. At ages 26, 32, and 38, participants' flossing status was assessed by a self-report question asking how often they used floss, with response options "never", "rarely", "sometimes", or "every day".

Plaque score. Six teeth (four posterior and two anterior) were examined for each participant at ages 15, 18, 26, 32, and 38. The plaque (debris) score for each participant was recorded using the simplified oral hygiene index by Greene and Vermillion[18] and was averaged over the six index teeth. The amount of plaque on teeth was rated on a four-point scale (0 = no debris or stain detectable, 1 = soft debris covering no more than the cervical one third of the tooth surface or extrinsic stains without other debris regardless of surface area covered, 2 = soft debris covering more than one third but no more than two thirds of the exposed tooth surface, and 3 = soft debris covering more than two thirds of the exposed tooth surface). Participants were assigned to one of four groups according to their plaque score: 1) very low (score 0 to 0.5); 2) low (>0.5 to 1.0); 3) moderate (>1.0 to 1.5); and 4) high (>1.5).

Tooth-Level Covariates

A tooth type variable was used to represent tooth position (mandibular anterior, maxillary anterior, mandibular premolar, maxillary premolar, mandibular molar, or maxillary molar). Bleeding on probing (BOP) was recoded as present for a tooth when any of the three sites showed bleeding within 10 seconds of being probed.

Data Analyses

Methods have been suggested previously for analyzing periodontal data using linear mixed models (random coefficient models). These take the hierarchical nature of the data into account and allow for the simultaneous estimation of the impact of the predictors at site, tooth, and person levels.[19,20] Such approaches, however, assumes normality for both the random effects and measurement errors, which may not be applicable to periodontal data. Although standard GLMMs are designed to relax the normality assumption, they are appropriate only for distributions belonging to an exponential family (such as Poisson, binomial, or gamma). The distribution of periodontal data is difficult to specify and cannot be assumed to match any of these. One way of dealing with this problem is to consider the use of a GLMM with a quasi-likelihood approach, for which the estimation process is entirely based on the mean and variance of the response variable, and hence the distribution of observations is not required to be defined. Moreover, one expects the variance of the periodontal response variable to be larger for AL

scores lying in the middle range and to be smaller for extreme cases, matching the characteristics of a binomial-type variable. Therefore, the authors adopted the quasi-binomial approach for data analysis.

Let Y_{ijk} denote the AL score for the i^{th} person, j^{th} teeth, and k^{th} site, and $E(Y_{ijk}) = \mu_{ijk}$. Because the quasi-binomial approach requires that Y_{ijk} is between 0 and 1, the response variable is transformed by defining $U_{ijk} = Y_{ijk}/y^{max}$, where y^{max} is the maximum observed AL score in the data across all available sites; hence $E(U_{ijk}) = \pi_{ijk} = \mu_{ijk}/y^{max}$. If one models π_{ijk} $(0 \le \pi_{ijk} \le 1)$, rather than μ_{ijk}, one has

$$E(U_{ijk}) = \pi_{ijk}, V(U_{ijk}) = \phi\pi_{ijk}(1 - \pi_{ijk})$$

and

$$\log(\pi_{ijk}) = \mathbf{X}'_{ijk}\boldsymbol{\beta} + \mathbf{Z}^{(3)'}_{ijk}\mathbf{b}^{(3)}_{k} + \mathbf{Z}^{(2)'}_{ijk}\mathbf{b}^{(2)}_{jk},$$

where $\mathbf{X}$ is the design matrix for the fixed effects $\boldsymbol{\beta}$, $\mathbf{Z}^{(3)}$ and $\mathbf{Z}^{(2)}$ are the design matrices for the random effects at person and tooth levels, $\boldsymbol{b}^{(3)}_{k}$ and $\boldsymbol{b}^{(2)}_{jk}$ are the corresponding random effect coefficients, and ϕ is the dispersion parameter.

Separate analysis was conducted for each age (26, 32, and 38 years). The total number of sites included in those analyses was 34,934, 72,327, and 68,553, respectively (the age-26 estimates used half-mouth examinations). The above model described the relationship between the response variable AL and the predictors. All statistical analyses were performed in R v.3.01. Models were fitted using the built-in *glmmPQL* function under library 'MASS'. The estimates of $\exp(\boldsymbol{\beta})$ at ages 26, 32, and 38 are presented separately as ratios (percentage change) with 95% confidence intervals (CIs). To demonstrate the interpretation of the ratios, a simple situation is considered where a predictor variable X_{ijk} is dichotomous, taking a value of 0 and 1; the corresponding β is expressed as

$$\log\left(\frac{\pi_{ijk}|X_{ijk}=1}{\pi_{ijk}|X_{ijk}=0}\right) = \beta.$$

Because $\pi_{ijk} = \mu_{ijk}/y^{max}$ and after exponentiation, this expression can be rewritten as

$$r = \frac{\mu_{ijk}\left|X_{ijk}=1\right.}{\mu_{ijk}\left|X_{ijk}=0\right.} = \exp(\beta).$$

This ratio is the mean of AL for $X_{ijk} = 1$ over the mean of AL for $X_{ijk} = 0$, and therefore $100(r - 1)\%$ can be interpreted as the percentage change in mean AL scores, when switching from $X_{ijk} = 1$ to $X_{ijk} = 0$.

RESULTS

A summary of the numbers included in the analysis is presented by the independent variables in Table 1. Of the 1,037 participants initially enrolled in the study, 913 were periodontally examined at age 26, and periodontal data were available for 863 (94.5%) individuals at ages 26, 32, and 38 using listwise deletion. At ages 32 and 38, respectively, 918 and 905 (98.6%) and 913 and 869 (95.1%) participants were examined and included in the analysis. Approximately equal numbers of females and males were included. The proportion of current tobacco smokers decreased with age, as did cannabis use.

Table 1.

Number (%) of Participants Periodontally Examined at Ages 26, 32, and 38 Years by Sex, Smoking, Cannabis Use, SES Trajectory Group, Flossing, and Plaque Score

Variable	Age 26	Age 32	Age 38
n	863	905	869
Sex			
Males	459 (53.2)	465 (51.4)	439 (50.5)
Females	404 (46.8)	440 (48.6)	430 (49.5)
Smoking			
Yes	328 (38.0)	297 (32.8)	216 (24.9)
No	535 (62.0)	608 (67.2)	653 (75.1)
Cannabis use			
None	428 (49.6)	568 (62.8)	646 (74.3)
Less than weekly	308 (35.7)	223 (24.6)	148 (17.1)
Weekly	93 (10.8)	97 (10.7)	75 (8.6)
Daily	34 (3.9)	17 (1.9)	0 (0)
SES trajectory			
Low-low	172 (19.9)	169 (18.7)	141 (16.2)
Low-high	64 (7.4)	90 (9.9)	100 (11.5)
High-low	331 (38.4)	274 (30.3)	213 (24.5)
High-high	296 (34.3)	372 (41.1)	415 (47.8)
Flossing			
Never	225 (26.1)	197 (21.8)	154 (17.7)
Rarely	308 (35.7)	310 (34.3)	248 (28.5)
Sometimes	274 (31.7)	342 (37.7)	381 (43.8)
Every day	56 (6.5)	56 (6.2)	86 (10.0)
Plaque score			
Very low	293 (34.0)	402 (44.4)	486 (55.9)
Low	315 (36.5)	284 (31.4)	235 (27.1)
Moderate	171 (19.8)	131 (14.5)	85 (9.8)
High	84 (9.7)	88 (9.7)	63 (7.2)

Some 3.9% of the participants smoked cannabis daily at age 26, whereas none did so at age 38. The number in each of the SES trajectory groups varied slightly at each assessment age. For example, the proportion of the participants in the "low-high" group increased between ages 26 and 38, and a reduction in the proportion was observed for the "low-low" group. The "high-high" and "high-low" groups were consistently the largest. The proportion of participants in the "never-flossing" group decreased by approximately 10% from age 26 to age 38, although the proportion using dental floss daily was consistently small. For the mean plaque scores, most participants were in the "very low" and "low" categories across the ages, with only a small proportion in the other categories.

Table 2 provides periodontal summary data by age. For calculating prevalence, a case was defined as having ≥1 site with ≥3, ≥4, ≥5, or ≥6 mm AL. The prevalence increased considerably with age, particularly with the more stringent case definitions. The extent of AL also increased, moderately between ages 26 and 32 and more substantially over the next 6 years. In addition, the standard deviations of the extent became larger with age.

Table 3 provides the estimated ratios and corresponding 95% CIs for the associations between AL and the predictors at each of ages 26, 32, and 38. At age 26, sex, smoking, plaque score, tooth type, and bleeding were the statistically significant predictors. On average, males had 4.3% greater AL than females. Similarly, smokers had 3.5% greater AL than non-smokers. For the predictors at tooth level, plaque score was strongly associated with higher AL at age 26. A high plaque score was associated with 13.2% greater AL. For tooth type, AL was greater for molars than for premolars, and anterior teeth had the least. Bleeding was associated with a 10.3% greater AL.

At age 32, the significant predictors identified at age 26 remained so, but the associations were stronger. The estimated coefficient for smoking increased from 1.035 to 1.128 between ages 26 and 32, representing an additional 9.3% greater AL for smokers over non-smokers than at age 26. The differences in AL among the tooth types were greater. For instance, maxillary molars now had an average 61.2% higher AL than the mandibular anterior teeth. Additionally, the predictors cannabis use (except for the less than weekly group) and SES became significant. Smoking cannabis weekly or daily was associated with higher AL. Those belonging to the "high-high" and the "low-high" SES transition groups had lower AL scores than those in the "low-low" group.

By age 38, all of the predictors were significant except for the variables cannabis use less than weekly, flossing sometimes, and flossing every day. The estimates for flossing suggested that using dental floss was associated with lower AL, but most of the differences were not statistically significant. Although there was no evidence to suggest that infrequent cannabis use (that is, less than weekly) was associated with greater AL, regular cannabis use was. The impacts of all covariates continued to increase with age. Tobacco smoking, plaque score, and BOP had the strongest association with greater AL. Smoking was associated with a 23.2% greater AL. For those with high plaque scores, the AL was 31.7% greater than those with low plaque scores. BOP was associated with 18.5% higher AL.

Table 2.

Summary Data on Periodontal Status at Ages 26, 32, and 38 Years

Characteristic	Age 26*	Age 32†	Age 38†
n	863	905	869
Prevalence (%): participants with ≥1 site with:			
≥3 mm AL	68.3	78.3	84.7
≥4 mm AL	17.4	29.4	43.7
≥5 mm AL	2.8	12.2	23.0
≥6 mm AL	0.7	5.9	11.9
Sites per person (mean [SD])	40.5 (2.5)	79.9 (5.8)	78.9 (7.0)
Extent (mean % [SD]) of sites with:			
≥3 mm AL	6.23 (0.09)	7.94 (0.12)	11.7 (0.17)
≥4 mm AL	0.91 (0.03)	2.00 (0.06)	4.75 (0.12)
≥5 mm AL	0.13 (0.01)	0.53 (0.03)	2.10 (0.08)
≥6 mm AL	0.03 (0.01)	0.21 (0.02)	1.10 (0.06)

* Half-mouth examinations were carried out at age 26, where maximum numbers of 14 teeth and 42 sites were examined.
† Full-mouth examinations were carried out at ages 32 and 38, where maximum numbers of 28 teeth and 84 sites were examined.

DISCUSSION

This study sets out to assess the association between smoking and periodontal disease through a life stage in the natural history of periodontitis about which little is known. The hypothesized increase in strength of important periodontal risk factors was observed, with smoking being particularly important. Intra-oral differences in periodontitis occurrence became more pronounced, with more severe AL observed in molars than in anterior teeth.

Table 3.

Parameter Estimates From the GLMM Models With a Quasi-Binomial Approach at Ages 26, 32, and 38 Years

	Age 26		Age 32		Age 38	
Predictor	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
Person-level predictors						
Sex*	1.043	1.016 to 1.071	1.074	1.042 to 1.108	1.098	1.059 to 1.139
Smoking†	1.035	1.008 to 1.064	1.128	1.090 to 1.166	1.232	1.176 to 1.289
Cannabis use						
None (Ref)						
Less than weekly	1.018	0.991 to 1.047	1.005	0.970 to 1.041	0.996	0.949 to 1.045
Weekly	1.005	0.963 to 1.049	1.063	1.010 to 1.119	1.111	1.038 to 1.190
Every day	1.023	0.958 to 1.093	1.147	1.030 to 1.278		
SES trajectory						
Low-low (Ref)						
Low-high	1.026	0.973 to 1.081	0.929	0.877 to 0.984	0.911	0.851 to 0.975
High-low	0.997	0.964 to 1.032	0.964	0.924 to 1.006	0.939	0.888 to 0.992
High-high	0.985	0.950 to 1.021	0.934	0.895 to 0.975	0.920	0.873 to 0.971
Flossing						
Never (Ref)						
Rarely	0.995	0.964 to 1.028	1.006	0.966 to 1.047	0.944	0.895 to 0.996
Sometimes	0.997	0.964 to 1.032	0.999	0.959 to 1.040	0.963	0.915 to 1.014
Every day	0.995	0.943 to 1.050	1.059	0.990 to 1.132	0.995	0.925 to 1.069
Plaque score						
Very low (Ref)						
Low	1.065	1.034 to 1.096	1.045	1.010 to 1.081	1.076	1.032 to 1.121
Moderate	1.120	1.082 to 1.160	1.088	1.041 to 1.138	1.132	1.063 to 1.205
High	1.132	1.081 to 1.186	1.233	1.168 to 1.302	1.317	1.225 to 1.417
Tooth-level predictors						
Tooth type						
Mandibular anterior (Ref)						
Mandibular premolar	1.315	1.293 to 1.337	1.373	1.354 to 1.392	1.321	1.303 to 1.340
Mandibular molar	1.383	1.361 to 1.406	1.491	1.471 to 1.512	1.488	1.467 to 1.509
Maxillary anterior	1.062	1.045 to 1.079	1.128	1.113 to 1.143	1.138	1.123 to 1.153
Maxillary premolar	1.242	1.221 to 1.264	1.394	1.374 to 1.414	1.414	1.394 to 1.434
Maxillary molar	1.396	1.373 to 1.418	1.612	1.590 to 1.633	1.662	1.640 to 1.685
BOP‡	1.103	1.090 to 1.117	1.144	1.133 to 1.155	1.185	1.172 to 1.198

Ref = reference group.
* Reference = female.
† Reference = non-smoker.
‡ Reference = no BOP.

Before discussing the findings, it is appropriate to consider the study's weaknesses and strengths. As the present authors have previously highlighted, there are concerns about the use of partial recording protocols (three rather than six sites examined per tooth, and the use of half-mouth examinations at age 26) and some minor loss of representativeness due to a higher proportion of low-SES individuals not being periodontally examined.[7] Thus, the findings should be viewed with some caution. Moreover, the authors were unable to determine whether any participant had had periodontal surgery by age 38 (which could possibly have eliminated periodontal pocketing), but the proportion having done so is likely to be very low. Resource and time constraints during the age-26 assessment meant that full-mouth periodontal examination was not possible. Thus, the prevalence and extent of AL at that age is likely to have been underestimated. However, this is not expected to have biased the estimates for the explanatory variables when modeling the AL for each site. The authors base this assertion on their earlier finding with another dataset that, although using partial recording protocols does affect prevalence estimates, it does not affect estimates for risk factors.[21] Turning to the study's strengths, the Dunedin study is the only one, to the authors' knowledge, providing information on the natural history of periodontal AL with aging through the

third and fourth decades of life in a population sample, with plentiful information on childhood antecedents.

This study uses a listwise deletion procedure to handle the missing data, thus eliminating all entries with one or more missing values for any variable. If the data are missing completely at random, listwise deletion is appropriate because it would produce unbiased estimates of the regression parameters. However, for periodontal data, missing responses are often due to teeth being missing or sites being difficult to assess. In this situation, listwise deletion may bias the results and, therefore, the authors may consider multiple imputation for future investigations.

The study findings confirm the importance of chronic smoking (whether tobacco or cannabis) as a risk factor for periodontal AL. The greater strength of the association as the cohort aged underlines the cumulative nature of its effect and provides support for the contention that its effects are best considered in the light of a risk accumulation model,[9] whereby adverse exposures accumulate incrementally through the life course, with cumulative damage to the periodontal tissues.

The amount of plaque present showed consistent gradients in its association with AL at each age, but with some minor variations in effect strength for particular plaque score categories across the ages. What is clear is that the effect of the high plaque scores (representing extensive plaque accumulation on the six index teeth) increased with age, again supporting the risk accumulation life course model and supporting earlier findings in which plaque trajectories were identified and found to be strongly associated with poor oral health.[11]

In this study, the effect of flossing was not statistically significant, although the parameter estimates were mostly less than unity. A recent Cochrane Collaboration review systematically scrutinized the extant literature on the oral health benefits (or otherwise) of flossing.[22] The authors concluded that flossing was effective in reducing the occurrence of gingivitis, but there was no sound evidence to support its effectiveness in preventing periodontitis. Moreover, the paucity of long-term follow-up studies was noted. It is clear that the definitive answer to the question of whether flossing helps to prevent periodontitis needs to come from either a very long-term randomized control trial or a longstanding prospective birth cohort study. Accordingly, it might be expected that the Dunedin Study is ideally placed to contribute to the debate. However, there are two problems with the flossing data: they are based on self-reported rather than directly observed behavior, and the response categories used (particularly "rarely" and "sometimes") were not defined adequately for participants. The "never" and "every day" responses are more clear cut, but there remains the problem of the cohort's very low prevalence of daily flossing. Those who floss daily are likely to have better oral health and health behaviors overall than those who do not,[23] but any effect is only hinted at in the present findings.

That males consistently had more AL than females at each age is not surprising, given males' poorer oral health awareness, self-care, and dental visiting practices.[24] SES differences also became more marked as the cohort aged, and this finding is consistent with those on cumulative tooth loss in the cohort.[25]

Anteroposterior gradients in AL were also noted in each jaw, with greater AL observed in molars than in premolars, and more in premolars than in incisors and canines. These differences were not surprising, but the consistently greater AL observed in maxillary anterior teeth than mandibular ones (at all three ages) was somewhat surprising, given what is known about extensive AL around the mandibular anterior teeth in a small proportion of individuals.

Whereas the work for examining the periodontal effects of smoking in the Dunedin cohort appears to be largely complete, further research should focus primarily on examining the changes in AL over time. The cross-sectional studies performed here allow comparisons among populations that happen to differ in age, but it does not provide any information on the within-individual changes over time. If these are potentially of interest, the authors have to analyze the data longitudinally. Analyzing such repeated measures will enable within-individual changes to be captured and the effects of aging to be estimated.

CONCLUSIONS

This research confirmed the strong association between chronic smoking and periodontal disease. To the best of the authors' knowledge, this is the first report of the smoking–periodontitis relationship based on a large cohort study using a hierarchical model. The study confirms the findings and conclusions that have been made in previous papers based on the same data from the Dunedin study, having reached those in a way that is preferable because it respects the hierarchical nature of the data. The replication of findings is a key principle of scientific investigation.[26] The uniqueness of the Dunedin study data (there are no other extant epidemiologic studies with longitudinal periodontal data through participants' 20s and 30s) mean that this principle requires the use of an alternative analytic approach to determine the robustness (and therefore veracity) of existing findings. In addition, the approach the authors used in this paper is more suitable than the traditional multilevel models for modeling periodontal data, and it could become a standard methodology in periodontal research.

ACKNOWLEDGMENTS

The authors thank the study members for their continuing participation in the Dunedin Study, and study founder, Dr. Phil Silva (University of Otago, retired). The age-26 dental data collection was supported by the New Zealand Dental Association Research Foundation (Auckland, New Zealand) and the University of Otago (Dunedin, New Zealand). The age-32 dental data collection was supported by Grant R01 DE-015260-01A1 from the National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, Maryland, and a program grant (03/271) from the New Zealand Health Research Council (NZ HRC, Dunedin, New Zealand). The age-38 data collection was supported by a program grant from the NZ HRC (09/086). The Dunedin Multidisciplinary Health and Development Research Unit is supported by the NZ HRC. The authors also thank Professor Richie Poulton FRSNZ (University of Otago) for his valuable comments. The authors report no conflicts of interest related to this study.

REFERENCES

1. Bartold PM, Van Dyke TE. Periodontitis: A host-mediated disruption of microbial homeostasis. Unlearning learned concepts. *Periodontol 2000* 2013; 62:203-217.
2. Gelskey SC. Cigarette smoking and periodontitis: Methodology to assess the strength of evidence in support of a causal association. *Community Dent Oral Epidemiol* 1999;27:16-24.
3. Bergström J. Periodontitis and smoking: An evidence-based appraisal. *J Evid Based Dent Pract* 2006;6:33-41.
4. Genco RJ, Borgnakke WS. Risk factors for periodontal disease. *Periodontol 2000* 2013;62:59-94.
5. Thomson WM, Broadbent JM, Welch D, Beck JD, Poulton R. Cigarette smoking and periodontal disease among 32-year-olds: A prospective study of a representative birth cohort. *J Clin Periodontol* 2007;34:828-834.
6. Thomson WM, Poulton R, Broadbent JM, et al. Cannabis smoking and periodontal disease among young adults. *JAMA* 2008;299:525-531.
7. Thomson WM, Shearer DM, Broadbent JM, Foster Page LA, Poulton R. The natural history of periodontal attachment loss during the third and fourth decades of life. *J Clin Periodontol* 2013;40:672-680.
8. Heasman L, Stacey F, Preshaw PM, McCracken GI, Hepburn S, Heasman PA. The effect of smoking on periodontal treatment response: A review of clinical evidence. *J Clin Periodontol* 2006;33:241-253.
9. Nicolau B, Thomson WM, Allison PJ, Steele JG. Life-course epidemiology: Concepts and theoretical models and its reference to oral chronic conditions. *Community Dent Oral Epidemiol* 2007;35:241-249.
10. Sabbah W, Tsakos G, Chandola T, Sheiham A, Watt RG. Social gradients in oral and general health. *J Dent Res* 2007;86:992-996.
11. Broadbent JM, Thomson WM, Boyens JV, Poulton R. Dental plaque and oral health during the first 32 years of life. *J Am Dent Assoc* 2011;142:415-426.
12. Tu Y-K, Gilthorpe MS. Key statistical and analytical issues for evaluating treatment effects in periodontal research. *Periodontol 2000* 2012;59:75-88.
13. Moffitt TE, Caspi A, Dickson N, Silva P, Stanton W. Childhood-onset versus adolescent-onset antisocial conduct problems in males: Natural history from ages 3 to 18 years. *Dev Psychopathol* 1996;8:399-424.
14. Goodson JM. Clinical measurements of periodontitis. *J Clin Periodontol* 1986;13:446-460.
15. Thomson WM, Broadbent JM, Poulton R, Beck JD. Changes in periodontal disease experience from 26 to 32 years of age in a birth cohort. *J Periodontol* 2006;77:947-954.
16. Irving JC, Elley WB. A socio-economic index for the female labour force in New Zealand. *NZ J Educ Stud* 1977;12:154-163.
17. Elley WB, Irving JC. The Elley-Irving socio-economic index: 1981 census revision. *NZ J Educ Stud* 1985; 20:115-128.
18. Greene JC, Vermillion JR. The simplified oral hygiene index. *J Am Dent Assoc* 1964;68:7-13.
19. Tu YK, Gilthorpe MS, Griffiths GS, Maddick IH, Eaton KA, Johnson NW. The application of multilevel modeling in the analysis of longitudinal periodontal data — Part I: Absolute levels of disease. *J Periodontol* 2004;75: 127-136.
20. Tu YK, Gilthorpe MS, Griffiths GS, Maddick IH, Eaton KA, Johnson NW. The application of multilevel modeling in the analysis of longitudinal periodontal data — Part II: Changes in disease levels over time. *J Periodontol* 2004;75:137-145.
21. Thomson WM, Williams SM. Partial- or full-mouth approaches to assessing the prevalence of and risk factors for periodontal disease in young adults. *J Periodontol* 2002;73:1010-1014.
22. Sambunjak D, Nickerson JW, Poklepovic T, et al. Flossing for the management of periodontal diseases and dental caries in adults. *Cochrane Database Syst Rev* 2011;Dec 7:CD008829 doi: 10.1002/14651858. CD008829.pub2.
23. Thomson WM, Sheiham A, Spencer AJ. Sociobehavioral aspects of periodontal disease. *Periodontol 2000* 2012;60:54-63.
24. Ministry of Health. *Our Oral Health: Key Findings of the 2009 New Zealand Oral Health Survey*. Wellington: Ministry of Health; 2010:183.
25. Thomson WM. Social inequality in oral health. *Community Dent Oral Epidemiol* 2012;40(Suppl. 2):28-32.
26. Moonesinghe R, Khoury MJ, Janssens AC. Most published research findings are false, but a little replication goes a long way. *PLoS Med* 2007;4:e28 10.1371/journal.pmed.0040028.

Correspondence: Dr. Jiaxu Zeng, PO Box 647, Dunedin, New Zealand. E-mail: jimmy.zeng@otago.ac.nz.

Submitted September 23, 2013; accepted for publication February 9, 2014.