Accepted: 16 July 2017

DOI: 10.1111/jcpe.12782

EPIDEMIOLOGY (COHORT STUDY OR CASE-CONTROL STUDY)

WILEY Journal of Clinical Periodontology

Natural history of periodontitis: Disease progression and tooth loss over 40 years

Christoph A. Ramseier[1] | Age Anerud[2] | Mary Dulac[2] | Martina Lulic[2] | Mary P. Cullinan[3] | Gregory J. Seymour[3] | Malcolm J. Faddy[4] | Walter Bürgin[1] | Marc Schätzle[5] | Niklaus P. Lang[1,2,5]

[1]University of Bern, Bern, Switzerland

[2]The University of Honk Kong, Hong Kong, China

[3]The University of Queensland, Brisbane, QLD, Australia

[4]Queensland University of Technology, Brisbane, QLD, Australia

[5]University of Zurich, Zurich, Switzerland

Correspondence
Prof. Dr. Niklaus P. Lang, University of Bern, Bern, Switzerland.
Email: nplang@switzerland.net

Funding information
Clinical Research Foundation (CRF); Swiss Dental Association (SSO)

Abstract

Objectives: To assess long-term attachment and periodontitis-related tooth loss (PTL) in untreated periodontal disease over 40 years.

Material and Methods: Data originated from the natural history of periodontitis study in Sri Lankan tea labourers first examined in 1970. In 2010, 75 subjects (15.6%) of the original cohort were re-examined.

Results: PTL over 40 years varied between 0 and 28 teeth (mean 13.1). Four subjects presented with no PTL, while 12 were edentulous. Logistic regression revealed attachment loss as a statistically significant covariate for PTL ($p < .004$). Markov chain analysis showed that smoking and calculus were associated with disease initiation and that calculus, plaque, and gingivitis were associated with loss of attachment and progression to advanced disease. Mean attachment loss <1.81 mm at the age of 30 yielded highest sensitivity and specificity (0.71) to allocate subjects into a cohort with a dentition of at least 20 teeth at 60 years of age.

Conclusions: These results highlight the importance of treating early periodontitis along with smoking cessation, in those under 30 years of age. They further show that calculus removal, plaque control, and the control of gingivitis are essential in preventing disease progression, further loss of attachment and ultimately tooth loss.

KEYWORDS

clinical attachment loss, longitudinal, natural history, periodontal disease progression, prediction, tooth loss

1 | INTRODUCTION

Studies on the natural history of periodontitis performed in Sri Lankan tea plantation workers between 1970 and 1985 provided basic information on oral conditions unaffected by any dental monitoring, prophylaxis, or therapy and in the absence of any professionally recommended or supervised oral hygiene practices over a period of 15 years (Löe, Anerud, Boysen, & Morrison, 1986; Löe, Anerud, Boysen, & Smith, 1978a,b,c). A subsequent examination of this distinct cohort in 1990 confirmed the ongoing progression of periodontitis and the influence of tobacco consumption or betel nut chewing on attachment loss and periodontitis-related tooth loss (PTL) over 20 years (Neely, Holford, Loe, Anerud, & Boysen, 2001, 2005).

While clinical data from these studies generally suggested an overall increase in both prevalence and severity of the disease with advancing age, different disease progression rates within the subjects were identified. Consequently, three subgroups of subjects were identified with various periodontal disease progression rates: (1) *rapid*

progression in approximately 8% of the subjects, (2) *moderate* progression in approximately 81% of the subjects, and (3) *minimal* progression in approximately 11% of the subjects. Over a period of 15 years, the annual rates of clinical attachment loss in these three subgroups were up to 1.0, 0.5, and 0.1 mm, respectively (Löe et al., 1986).

Hypothetically, studies following subjects over a number of decades may give better insight into undisturbed disease progression, particularly between subjects showing different disease susceptibility. In this context, the untreated Sri Lankan tea labourers provided a unique opportunity to further study periodontal disease progression in humans unaffected by professional or individual oral care. Hence, the goals of this analysis were (1) to assess the natural history of periodontitis by evaluating both attachment loss and PTL from the cohort examined in 1970 (Löe et al., 1986), in 1990 (Preus et al., 1995), and again in 2010 giving a total observation period of 40 years, and (2) to use the whole data set to identify factors influencing the initiation and progression of chronic periodontitis over 40 years.

Clinical Relevance

Scientific rationale of the study: The Sri Lankan cohort is documented to have had no access to oral hygiene practices for a period of 40 years. However, no predictive values exist for the clinical parameters regarding attachment and periodontitis-related tooth loss.

Principal findings: In the absence of oral hygiene and treatment, smoking and calculus were associated with disease initiation, while calculus, plaque, and gingivitis were associated with disease progression. Mean attachment loss <1.81 mm at the age of 30 yielded highest sensitivity and specificity (0.71) to allocate subjects into a cohort with a dentition of at least 20 teeth at 60 years of age.

Practical implications: Smoking cessation and calculus removal before the age of 30 years are important in preventing attachment loss so as to ensure a dentition with ≥20 teeth at 60 years of age. Calculus removal, plaque control, and the control of gingivitis are essential in preventing further disease progression, loss of attachment and ultimately tooth loss.

2 | MATERIALS & METHODS

2.1 | Ethical aspects

This study protocol was submitted to and approved by the Dental School of the University of Peradeniya, Sri Lanka and the Institutional Review Board of the University of Hong Kong SAR (UW12-118). In 2010, the subjects were informed in their native language (Tamil) by a medical doctor about the details of the study. They then gave consent by finger printing due to illiteracy.

2.2 | Participants

In 1970, a cohort consisting of 480 male tea labourers between 14 and 30 years of age was recruited at the Dunsinane, Harrow and Sheen Tea Estates, Pundaloya, Sri Lanka. The tea plantation labourers were generally healthy and had continuous access to any needed medical care. However, the subjects had never received any oral health care nor had they been exposed to any oral health promotion programs. In case of emergencies, the physician of the Estates removed a tooth without rendering further treatment. Over the entire study period of 40 years, tooth brushing was unknown to them.

This longitudinal Sri Lankan cohort was previously examined in 1970, 1971, 1973, 1977, 1982, 1985, and 1990 (Löe et al., 1978a,b,c, 1986; Neely et al., 2001, 2005; Preus et al., 1995). For this study, attempts were made to identify all subjects from the original cohort established in 1970.

2.3 | Clinical examinations

The clinical examinations took place in an outdoor facility of the Medical Clinic of the Dunsinane Tea Estate on common chairs and under field conditions. Neither compressed air nor saliva ejectors were available. Illumination was provided by applying individual front head lamps. At their examination, the subjects answered questions on smoking, betel nut chewing, and other oral habits.

Missing teeth were recorded in all subjects similar to previous assessments (Löe et al., 1978a). Clinical periodontal and dental indices were recorded for mesial, distal, facial, and oral surfaces of all teeth (four sites per tooth), except third molars.

The following clinical data were recorded using a calibrated periodontal probe (UNC15; Hu-Friedy, Chicago, IL, USA): Plaque Index (PI) (Silness & Löe, 1964), Calculus Index (CI) (Löe, 1967), Gingival Index (GI) (Löe & Silness, 1963) as well as gingival recession, and periodontal probing depth (PPD) to the nearest millimetre (Glavind & Loe, 1967; Löe, Anerud, & Boysen, 1992). Subjects were also interviewed about betel nut consumption and tobacco use. A visual inspection was performed to assess the presence of dental caries. In case of occasional root remnants, gingival recession was estimated by comparing the gingival margin with the cemento-enamel junction on adjacent teeth.

Periodontitis-related tooth loss was defined as teeth lost as a result of attachment loss. As dental caries was not observed in any of the preceding examinations, teeth were not lost due to dental caries. However, extreme hard tissue abrasions were rarely found that could have led to open pulpal lesions and hence, subsequent extractions. According to the medical staff of the Estates, traumatic tooth loss was extremely rare and not likely to have affected PTL.

For the examination in 2010, both intra- and inter-examiner reproducibility were assessed in a subgroup of 14 randomly selected subjects who were examined twice.

2.4 | Calibration of examiners

Calibration exercises for all examiners were conducted with 14 randomly selected subjects for both inter- and intra-examiner variability.

Agreement analysis of both gingival recession and PPD measurements performed by C.A.R. and M.L. revealed mean intra-class correlation coefficients of 0.63 for inter- and 0.80 for intra-examiner agreement. Assessment of the reproducibility of PI-, GI-, CI-, and RI-scores performed by N.P.L. and M.D. revealed Cohen's Kappa scores of .67, .66, .63, and .78, respectively.

2.5 | Statistical analysis

The Statistical Package SAS® Version 9.4 (SAS Institute Inc., Cary, NC, USA) was used. Descriptive statistics were performed to identify means, standard deviations, ranges, and odds ratios. The Shapiro–Wilk test was used to test for normal distribution of collected clinical data. A simple generalization of the chain binomial model (Longini, 2005) was used to describe the longitudinal data on numbers of teeth at sequential examinations after the first one in 1970, where the conditional distribution of the number of teeth at examination *i* given the number of teeth at examination *i* - 1 was assumed to be binomial for *i* = 2, 3, …, 8 with an extra dispersion parameter included to allow for possibly correlated outcomes from adjacent teeth. Logistic regression analysis was used to assess the influence of a number of predictors (covariates) observed at the earlier of each pair of successive examinations, including mean PI, mean CI, mean GI, mean loss of attachment, smoking, and betel nut chewing. An additional factor (with seven components) was included to allow for any variation between examinations not accounted for by the above covariates, and possible selection bias due to contiguous data (i.e., from subjects attending a sequence of successive examinations) being necessary for the model fitting.

Receiver Operating Characteristics (ROC) were plotted for various thresholds of age and numbers of teeth using the SAS ROC-cutoff macro (Harris, 2010). As the World Health Organization (WHO) had suggested that 20 teeth represented satisfactory oral function, the analysis concentrated on 20 teeth at the age of 60.

To identify factors influencing the initiation and progression of chronic periodontitis, ante-dependence Markov Chain modelling of data from 425 individuals with contiguous examinations was also used (Faddy, Cullinan, Palmer, Westerman, & Seymour, 2000; Schätzle et al., 2009). Disease was classified according to the definitions in the *consensus* paper at the 5th European Workshop of Periodontology (Tonetti & Claffey, 2005) and modelled in terms of age, betel nut chewing, smoking status, and PI, GI, and CI. The data on each individual at each examination were thus summarized into three periodontal disease states, denoted level 0 (up to one proximal site with attachment loss ≥3 mm), level 1 (proximal attachment loss of ≥3 mm in ≥2 non-adjacent teeth), and level 2 (proximal attachment loss of ≥5 mm in ≥30% of teeth present) (Tonetti & Claffey, 2005). Disease was assumed to progress during the period of the study through these states of increasing severity, with some regression (healing) to states of less severity also possible. Of the total number of transitions observed, only 12 (or 0.9%) were regressions from state 2, and most likely due to loss of teeth between successive examinations, so it was decided to treat state 2 as a "sink" state from which no natural regression back to state 1 or 0 was possible. The 2-state (periodontal disease levels 0 and 1) Markov chain model used in Faddy et al. (2000) and Schätzle et al. (2009) where only states 0 and 1 were observed among the (Australian and Norwegian, respectively) participants was extended to a 3-state Markov chain to accommodate transitions to periodontal disease level 2 seen in these Sri Lankan data. This model for longitudinal discrete data observed over a sequence of examinations is characterized by transition "rates" similar to mortality rates in survival analysis (i.e., transitions from state *i* = 0 or 1 correspond to "mortality" in that state, with "re-birth" in adjacent state *j* = 0, 1 or 2 ≠ *i*): one rate for transitions, or progression of disease, from state 0 to state 1; another for transitions, or regression of disease, from state 1 back to state 0; and a third for additional transitions, or progression of disease, from state 1 to "sink" state 2. These rates were made log-linearly dependent on the covariates (as described above in connexion with the logistic regression analysis of numbers of teeth) except of course loss of attachment as this is what is being modelled by the Markov chain. MATLAB (The MathWorks, Natick, MA, USA) software was used for this part of the analysis.

All covariate coefficients were estimated by maximum likelihood with a stepwise procedure used for inclusion of significant effects (both main and interactive) and exclusion of non-significant effects, using a 5% level of significance throughout. From the logistic regression analysis of numbers of teeth and the Markov chain modelling of the three periodontal disease states, relative risks (or odds ratios) of factors associated with tooth loss and progression or regression of disease could be estimated (with 95% confidence limits).

This study conforms to the STROBE guidelines.

3 | RESULTS

Out of 480 male subjects examined in 1970, a total of 75 (15.6%) were available for re-examination in 2010.

3.1 | General health and habits

According to the Medical officer and the administration of the Estates, the subjects' diet improved over the period of 40 years, and the salaries of the subjects increased continuously. Yet, the older generation analysed in this study did not communicate with the outside world, and the majority remained illiterate.

All subjects either smoked or chewed betel nut. For the purpose of this analysis, therefore, the categories "some smoking, no betel nut chewing", "always smoking, no betel nut chewing", "no smoking, betel nut chewing", and "always smoking, betel nut chewing" were formed.

Further, subject interviews in 2010 confirmed the persistent lack of professional preventive oral health care or cleaning devices other than the occasional use of bare fingers and ashes.

3.2 | Subjects' demographic data

Table 1 presents the demographic data of all subjects throughout the entire 40 years of observation and of three disease progression

TABLE 1 Demographic data of all subjects, and according to disease progression subgroups (Löe et al., 1986) at baseline (1970) and at subsequent visits over 40 years

Survey No.(Year)	1 (1970)	2 (1971)	3 (1973)	4 (1977)	5 (1982)	6 (1985)	7 (1990)	8 (2010)
All subjects								
N	480	425	370	228	159	161	154	75
%	100.0	88.5	77.1	47.5	33.1	33.5	32.1	15.6
Mean Age	20.8	21.9	23.7	27.1	34.0	35.1	42.0	61.4
Min-Max	14–31	15–32	17–34	22–37	27–42	30–45	35–50	55–70
No progression								
N	54	42	23	6	0	1	0	0
%	11.3	9.9	6.2	2.6	0	0.6	0	0
Age	17.5	18.6	20.8	23.7		32.0		
Min-Max	14–24	15–25	18–25	22–26		32–32		
Moderate progression								
N	388	350	314	205	146	146	141	69
%	80.8	82.4	84.9	89.9	91.8	90.7	91.6	92.0
Age	22.8	23.8	25.6	29.6	34.7	37.5	42.6	62.2
Min-Max	14–31	15–32	17–34	22–37	27–42	30–45	35–50	55–70
Rapid progression								
N	38	33	33	17	13	14	13	6
%	7.9	7.8	8.9	7.5	8.2	8.7	8.4	8.0
Age	22.2	23.2	24.8	28.1	33.3	35.9	41.3	60.5
Min-Max	15–29	16–30	18–32	22–36	27–41	30–44	35–49	55–65

TABLE 2 Estimated relative risks (95% confidence limits) of tooth loss associated with a unit increase in mean attachment loss for various values of interacting covariates at age 30 years

Smoking/betel nut chewing	Mean calculus index	Number of teeth	Relative risk (95% C.I.)
Some smoking, no betel nut chewing	1	20	1.94 (1.76, 2.13)
	1	28	2.16 (1.90, 2.45)
	2	20	1.59 (1.51, 1.69)
	2	28	1.78 (1.63, 1.93)
Always smoking, no betel nut chewing	1	20	1.73 (1.49, 2.02)
	1	28	1.93 (1.64, 2.28)
	2	20	1.43 (1.26, 1.62)
	2	28	1.59 (1.40, 1.81)
No smoking, betel nut chewing	1	20	1.94 (1.75, 2.16)
	1	28	2.17 (1.90, 2.47)
	2	20	1.60 (1.46, 1.76)
	2	28	1.78 (1.60, 1.99)
Always smoking, betel nut chewing	1	20	1.37 (1.11, 1.69)
	1	28	1.52 (1.23, 1.90)
	2	20	1.13 (0.92, 1.37)
	2	28	1.25 (1.03, 1.53)

subgroups as defined in 1986 (Löe et al., 1986). The study covered an age range of 15–70 years (means 1970: 22.1 years; 2010: 61.4 years).

3.3 | Periodontitis-related tooth loss

Periodontitis-related tooth loss over the entire 40-year period varied among those subjects present at the last examination (n = 75) between 0 and 28 teeth with a mean of 13.1 teeth per subject. Four subjects presented with no PTL, while 12 subjects were edentulous at the 40-year re-examination.

The logistic regression analysis of numbers of teeth over the course of the study showed that higher mean loss of attachment was associated with a greater risk of tooth loss by the next examination, through significant (p < .004) interactions with smoking/betel nut chewing, age, mean CI, and number of teeth initially present. Table 2 shows estimates of the relative risk (with 95% confidence limits) of tooth loss associated with a unit increase in mean loss of attachment, for various values of the interacting covariates. So that, for example, among those who smoked sometimes, did not chew betel nuts, were aged 30 with 20 teeth and presented with a mean CI of 1, a subject with mean loss of attachment one unit higher than another subject would be 94% more likely to lose teeth between examinations. Comparing across categories, there is greater relative risk of tooth loss from higher age, lower mean CI, and more teeth to start with; always smoking and betel nut chewing combined is associated with an appreciable reduction in relative risk of tooth loss, but smaller differences are apparent between the other categories of smoking and betel nut chewing. Neither mean PI nor mean GI showed any significant (p > .30) effects on tooth loss either as main effects or as interactions.

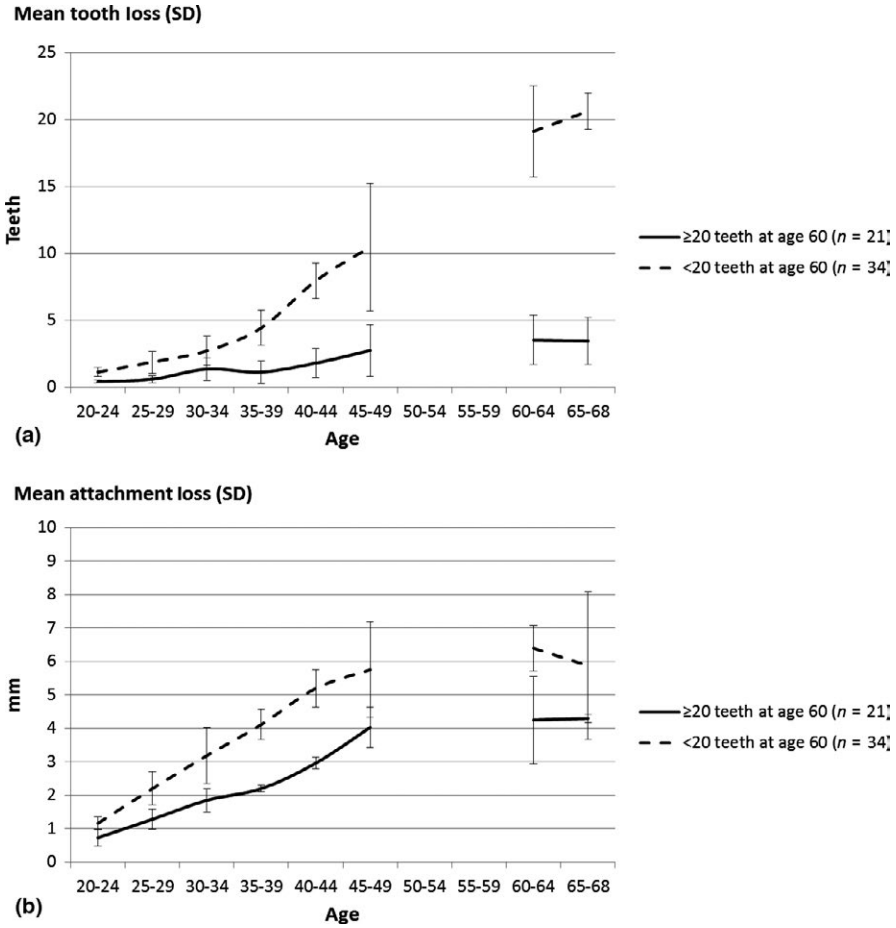

FIGURE 1 Mean tooth loss (a) and attachment loss (b) from clinical examinations 1970 through 1990 and 2010 of n = 21 subjects presenting with ≥20 teeth at 60 years of age and n = 34 subjects with <20 teeth at the age of 60 years. *SD*: standard deviations

It was evident that after 1977, the *non-progressive* subgroup was no longer present (Table 1). Therefore, further analysis was limited to the original subgroups of subjects with rapidly and moderately progressing disease. The 12 edentulous subjects were not included in further analysis. Consequently, 55 (73.3%) out of 75 subjects with available data at the age of 60 were re-grouped into a first cohort that, at age 60, presented with at least 20 teeth (n = 21, 38.2%) and a second cohort that, at age 60, had less than 20 teeth but were not edentulous (n = 34, 61.8%). Mean PTL from both cohorts is presented in Figure 1a.

3.4 | Periodontal attachment loss

Figure 1b presents the mean attachment loss during 40 years of observation in the two aforementioned cohorts. It is evident that the cohort of subjects presenting with <20 teeth at age 60 displayed significantly greater attachment loss at all observation periods. Figure 1b further shows that in both cohorts, the attachment loss was more pronounced in the first 20 years compared with the latter 20 years.

Periodontal attachment loss at age 30 years enabled the estimation of PTL at age 60 years. A cut-off at 1.81 mm attachment loss at age 30 years was able to discriminate between those with a dentition of 20 or more teeth compared with those with less than 20 teeth at age 60 with a sensitivity and specificity of 0.71 (Figure 2). Moreover, when considering attachment loss of <1.81 mm at the age of 30 years, the positive predictive value for a dentition of at least 20 teeth at age 60 was 80% (p < .001, 95% C.I.: 0.61–0.92).

3.5 | Indices for plaque, gingivitis, and calculus

No statistically significant differences were found between the two cohorts regarding the mean values of PI, GI, and CI (Figure 3a,b,c).

3.6 | Tobacco smoking and betel nut chewing

According to the oral survey in 2010, either tobacco or betel nut was consumed by all the subjects. Twelve subjects (16.0%) were only smokers, and 27 (36.0%) only chewed betel nut. No association of smoking with the number of teeth at >60 years was found.

3.7 | Factors influencing the initiation and progression of chronic periodontitis

The 425 individuals who were present at contiguous examinations starting at baseline were included in this analysis. Over the study period, their ages ranged from 14 to 69 years. The average times between examinations were 11.5 months (surveys 1–2), 24 months (surveys 2–3), 40 months (surveys 3–4), 63.5 months (surveys 4–5), 29.5 months (surveys 5–6), 60 months (surveys 6–7), and 244 months (surveys 7–8). The proportions of these 425 participants betel nut

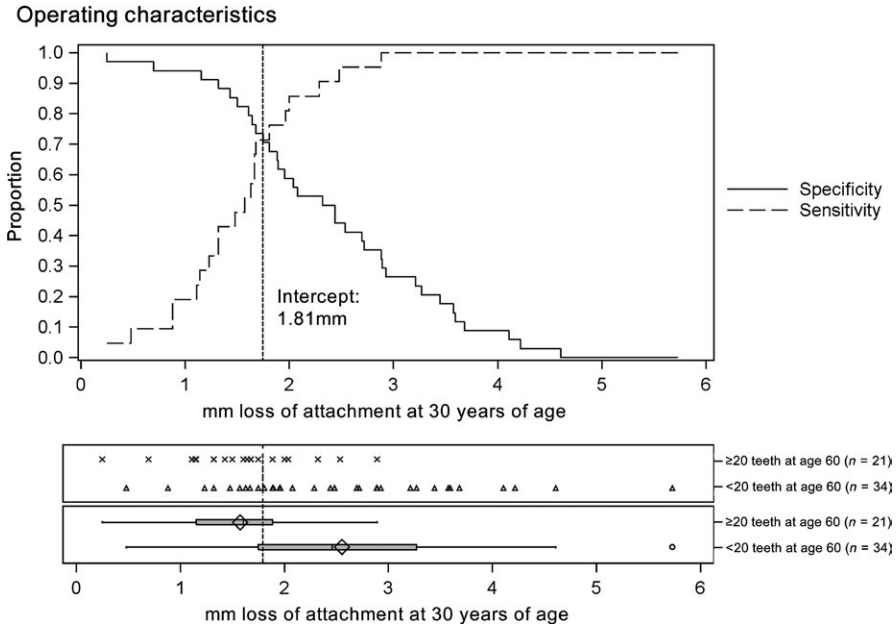

FIGURE 2 Operating characteristics reveal a cut-off at 1.81 mm attachment loss at 30 years of age reflecting the highest values of both sensitivity and specificity (0.71) for the presence of ≥20 teeth at the age of 60 years

chewing ranged from 40% at baseline to over 60%, and the proportions smoking ranged from 45% at baseline to over 80%. Their mean PI ranged from 1.14 to 2.63; mean GI ranged from 0.54 to 2.45, and mean CI ranged from 0.08 to 2.86.

Table 3 shows the estimated relative risks (with 95% confidence limits) for disease progression and regression associated with each of the significant covariates. There were no significant effects of betel nut chewing on disease progression or regression ($p > .50$), but all the other covariates had significant effects on one or more transitions ($p < .004$). Smoking and higher CI both significantly increased disease progression from level 0 to level 1, while higher age significantly reduced disease regression from level 1 back to level 0. Higher calculus, plaque, and gingival indices all significantly increased disease progression from level 1 to level 2 with the latter two indices combining interactively. There were no significant other changes in disease progression from level 0 to level 1 throughout the study ($p > .45$), but disease regression from level 1 back to level 0 was significantly reduced after the second survey ($p < .001$). There were also some significant changes in disease progression from level 1 to level 2 ($p < .001$), with a reduction between surveys 2 and 6 evident. Other apparent changes were not significant ($p > .07$).

Estimates of the proportions of subjects experiencing some disease progression in a 12-month period during the course of the study are shown in Table 4. It can be seen that 58% of smokers with a mean CI of 2 progressed from level 0 to level 1 compared with 16% of smokers with a mean CI of 1. Similarly, 40% of non-smokers with a mean CI of 2 progressed from level 0 to level 1 were compared with 10% of non-smokers with a mean CI of 1 (Table 4a).

The proportion of individuals with disease progression from level 1 to level 2 in a 12-month period between the 2nd and 6th examinations is shown in Table 4b. Here, it can be seen that 3.0% of smokers and 2.4% of non-smokers with a mean GI of 1.5 and mean plaque and calculus indices of 2.0 showed disease progression from level 1 to level 2 compared with 0.7% of smokers and 0.5% of non-smokers with a lower mean CI of 1 (Table 4b). Based on the relative risks shown in Table 3, it can be further estimated that approximately eight (or 2.82^2 from Table 3) times as many individuals (or 24% of smokers and 19% of non-smokers) with higher mean plaque and gingival indices of 2.5 and 2.0, respectively, showed disease progression, further highlighting the role of plaque and gingivitis, but not smoking, in progression from level 1 to level 2.

Furthermore, the proportion of individuals with disease regression from level 1 back to level 0 in a 12-month period decreased with increasing age. At age 20, some 9% of individuals experienced disease regression whereas only 3% at age 30 years and 1% at age 40 years experienced disease regression.

4 | DISCUSSION

The results of the present analysis showed that after 40 years in the absence of oral care, PTL significantly increased with age in all subjects. Over the 40 years, a mean of 13.1 teeth per subject was lost due to progressing periodontitis. Only 5.3% of the subjects examined in 2010 did not experience tooth loss. One-sixth of the subjects were edentulous after 40 years. PTL substantially increased during the second 20 years of observation compared with the first 20-year period.

These findings differ slightly from the results presented in another project on the natural history of untreated periodontal disease performed on the island of Java, albeit a study of shorter duration (24 years). In that study, tooth loss could not be attributed to periodontitis progression alone as the main reason for tooth loss over the 24 years was dental caries. In only 8.2% of the subjects, tooth loss could be attributed to periodontitis progression (van der Velden et al., 2015). In the present study, tooth loss was almost exclusively

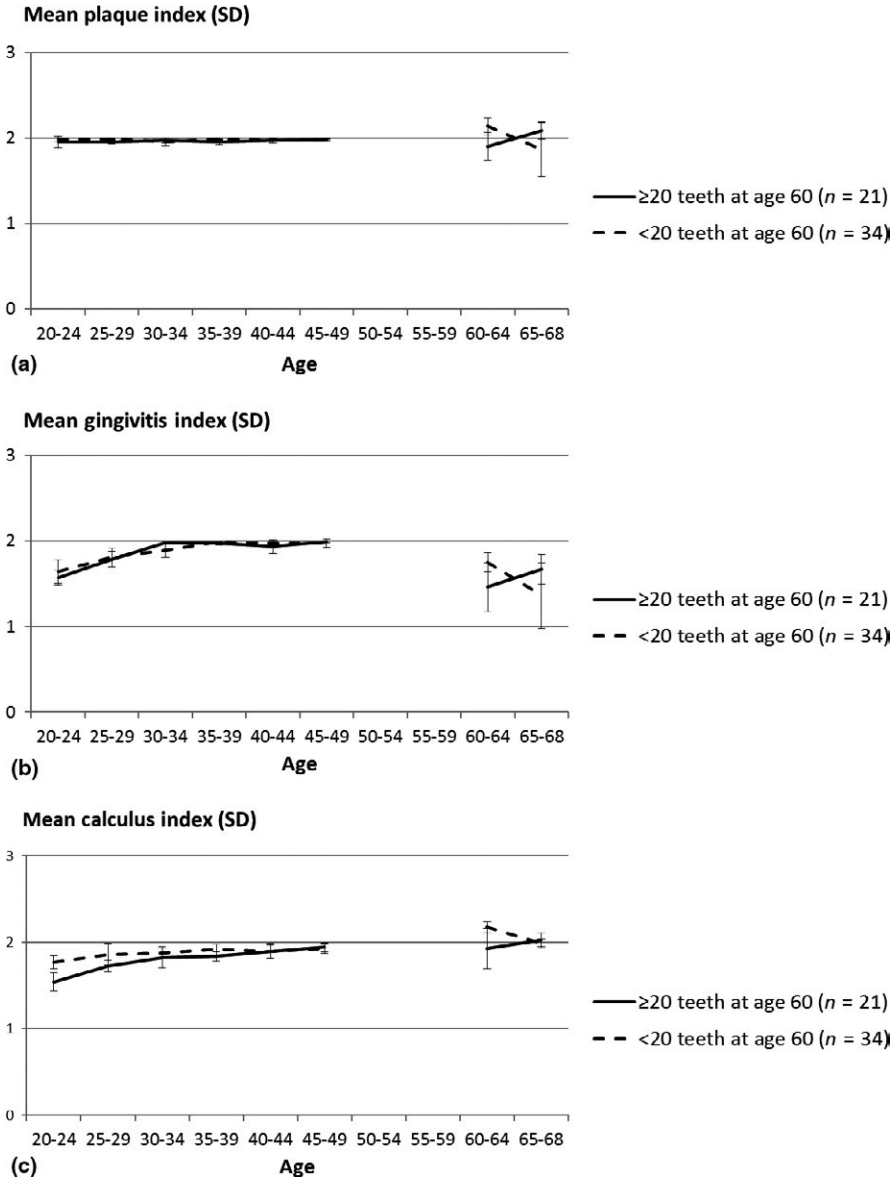

FIGURE 3 Mean Plaque Index (a), Gingivitis Index (b), and Calculus Index (c) from clinical examinations 1970 through 1990 and 2010 of *n* = 21 subjects presenting with ≥20 teeth at 60 years of age and *n* = 34 subjects with <20 teeth at the age of 60 years. *SD*: standard deviations

TABLE 3 Estimated relative risks (95% confidence limits) for disease progression and regression associated with age, smoking, and mean calculus, gingival and plaque indices

	Disease progression level 0–1	Disease regression level 1–0	Disease progression level 1–2
Age (each additional year)	1.00 (0.96, 1.04)	0.90 (0.83, 0.98)[a]	1.01 (0.98, 1.04)
Smoking (any)	1.63 (1.14, 2.34)[a]	0.80 (0.40, 1.57)	1.24 (0.79, 1.97)
Mean calculus index (unit increase)	3.40 (1.87, 6.19)[a]	0.45 (0.14, 1.48)	4.71 (1.55, 14.3)[a]
Interaction: mean gingival index ×mean plaque index (unit increase)	1.26 (0.93, 1.70)	0.99 (0.48, 2.05)	2.82 (1.49, 5.36)[a]

[a]Statistically significant.

associated with the progression of periodontal attachment loss. The reasons for this substantial discrepancy between the two populations may be found in the habit of chewing sugar containing sticks (candide orange peel) during the day in the Java population. In the present study, loss of attachment had the most influence on PTL. Of the other predictors, age, CI, tobacco consumption, and betel nut chewing influenced

TABLE 4 (a) Example estimates of the proportions of individuals experiencing some disease progression from level 0 to level 1 in a 12-month period, in terms of smoking and mean calculus index. (b) Example estimates of the proportions of individuals experiencing some disease progression from level 1 to level 2 in a 12-month period (between the 2nd and 6th examinations) in terms of smoking and mean calculus index (for mean gingival and plaque indices 1.5 and 2.0, respectively)

	Mean calculus index = 1.0	Mean calculus index = 2.0
(a)		
Some smoking	16%	58%
No smoking	10%	40%
(b)		
Some smoking	0.7%	3.0%
No smoking	0.5%	2.4%

PTL through interactions with loss of attachment, while PI and GI did not show any significant associations with PTL over 40 years.

Neely et al. (2001, 2005) documented the influence of tobacco consumption on attachment loss and PTL in the first 20-year observation period. The present analysis of data over a 40 year period has shown that smoking primarily affects attachment loss which subsequently affects PTL. However, all subjects either smoked or chewed betel nut and no detailed dose or frequency related data were available for a more detailed analysis. Nevertheless, the results of the present study confirm the previous observation on Norwegian academics that smoking is significantly associated with initial disease progression, that is, from level 0 to level 1 (Schätzle et al., 2009). Further, it has previously been shown that, in an urban Australian population, smoking does not significantly enhance disease progression to an advanced state but rather inhibits healing (disease regression) (Faddy et al., 2000). In the present study, advanced disease was considered as a "sink" with any disease regression from level 2 back to level 1, that is, from advanced disease to moderate disease being unlikely in the absence of any oral hygiene and would probably be due to tooth loss rather than healing. Because of this, the effect of smoking on disease regression from level 2 back to level 1 was not investigated. Nevertheless, the finding that smoking does not affect progression of disease from level 1 to level 2 is in keeping with Faddy et al. (2000). Notwithstanding, it is clear that the effect of smoking on disease progression and regression is complex and further longitudinal studies are required.

An obvious shortcoming in the present study was the high attrition rate of the subjects. In 1970, 480 subjects were recruited, and in 1990, 154 subjects remained resulting in an attrition rate of 67.9% in the first 20 years. In the second 20 years, the attrition rate was substantially lower (16.5%) resulting in a total attrition rate over 40 years of 84.4% with 75 subject remaining (15.6% of the original cohort).

It was evident that after 40 years, the slowly progressing cohort (originally 11%) was not present. Moreover, only six subjects of the rapidly progressing group were still available in 2010, and five out of the six were edentulous. As the original disease progression subgroups were not positively associated with PTL, two new cohorts were formed to assess the differences between subjects of variable disease susceptibility. The maintenance of a shortened dental arch up to the first molar occlusion would be an individually optimal goal for the maintenance of functionality in older adults (Fontijn-Tekamp et al., 2000). Interestingly, the World Health Organization (WHO) claimed a shortened dental arch (20 teeth to premolar occlusion) is sufficient for satisfactory oral function (Nguyen, Witter, Bronkhorst, Pham, & Creugers, 2011). Thus, in the present analysis, a cut-off of 1.81 mm mean attachment loss at age 30 predicted the presence of 20 or more teeth at age 60 years. This threshold, at age 30 years, therefore appears to represent a valuable and feasible parameter to predict functionality of the dentition 30 years later in the absence of any dental care or prophylaxis. Obviously, preventive measures may dramatically alter this predictability depending on the intensity and frequency of such measures. Therefore, the implementation of early therapy including preventive measures may be indicated best in individuals exceeding a mean attachment loss of 1.81 mm at the age of 30. A mean attachment loss of greater than 1.81 mm would suggest that the individual had several periodontitis sites with greater than 2 mm loss of attachment.

In the present study, longitudinal analysis showed that while loss of attachment was significantly associated with tooth loss, smoking and higher CI significantly increased initial disease progression. At the same time, disease regression decreased with increasing age as shown previously (Faddy et al., 2000), and CI, PI, and GI were all significantly associated with loss of attachment and progression to advanced disease.

Compared with other populations worldwide, it has to be recognized that this Sri Lankan cohort represents a population in a rather unique environment. When recruited in 1970, it originally consisted of 480 male tea labourers between 15 and 30 years of age working at the tea Estates in the central highlands of Sri Lanka, approximately 50 km from Kandy. They were healthy with a male life expectancy of 71.2 years, and according to the Medical officer of the Estates, their nutritional condition was clinically fair. The food which was partially provided by the Estate administration consisted mainly of rice and vegetables, fish, or meat curry consumed at noon and before bedtime. During their working hours, the labourers drank tea. The consumption of cigarettes and betel nut was a widespread habit. Nevertheless, dental caries was very rare in the 2010 examination.

The workers in these tea Estates had never been exposed to any preventive programs or treatment of periodontal diseases, and tooth brushing was unknown to them. In this cohort, clinically recognizable plaque (PI = 2) covered almost all surfaces of all teeth in all subjects and in all surveys revealing no statistically significant changes in oral hygiene habits between 15 (1970) and 70 years of age (2010).

No preventive or therapeutic measures were carried out in any of the scoring sessions between 1970 and 2010. As reported previously (Löe et al., 1986), the original purpose of this longitudinal investigation was to study the natural and undisturbed history of periodontal disease. Although questionable from an ethical point of view, the earlier investigators made attempts to avoid disruption of any habits and did

not instruct the subjects in home care practices. Even though global efforts were undertaken to improve oral health in third world countries, no measures were implemented in the Sri Lankan tea Estates to improve oral conditions. Comparable studies assessing periodontal disease progression over a period of 10–15 years in the past used a similar model of untreated subjects in China (Baelum, Luan, Chen, & Fejerskov, 1997) or Indonesia (Timmerman et al., 1998, 2000, 2002; Van der Velden et al., 2006). Beginning in 2008, however, oral health preventive programs were implemented in pre-school and grade school classes teaching the children of the Sri Lankan tea Estates the use of toothbrushes with fluoridated toothpastes. Nevertheless, such preventive programs for the children did not at all affect the older generation of male workers examined regularly during 40 years. Therefore, it was decided to treat all available subjects of the 2010 examination with non-surgical periodontal therapy in 2012, hereby contributing to the improvement of oral health in this unique cohort previously deprived of any professionally recommended or supervised oral hygiene practices.

In conclusion, within the limitations of the present study, the results have shown that smoking and calculus are associated with initial disease progression and that calculus, plaque, and gingivitis are associated with loss of attachment and progression to advanced disease. Further, mean attachment loss <1.81 mm at the age of 30 appears to predict a dentition of at least 20 teeth at 60 years of age. These results highlight the importance of treating early periodontitis along with smoking cessation, in those under 30 years of age, so as to prevent attachment loss, and increase the likelihood of having a dentition with ≥20 teeth at age 60 years. They further indicate that calculus removal, plaque control, and the control of gingivitis are essential in preventing disease progression, further loss of attachment and ultimately tooth loss.

ACKNOWLEDGEMENTS

This work was supported by the Clinical Research Foundation (CRF) for the Promotion of Oral Health, Brienz, Switzerland and a research grant from the Swiss Dental Association (SSO) to Dr. Christoph A. Ramseier (No. 250-10). The coordination of the study by Dr. A. Ramanathan, former medical officer of the tea Estates, Colombo, Sri Lanka is highly appreciated. Moreover, the assistance of Dr. Sarah Steiner and the dental students from the University of Peradeniya is acknowledged. The authors were fully independent in preparing the protocol, conducting the research, interpreting the results, and preparing the manuscript.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

REFERENCES

Baelum, V., Luan, W. M., Chen, X., & Fejerskov, O. (1997). A 10-year study of the progression of destructive periodontal disease in adult and elderly Chinese. *Journal of Periodontology*, *68*, 1033–1042. https://doi.org/10.1902/jop.1997.68.11.1033

Faddy, M. J., Cullinan, M. P., Palmer, J. E., Westerman, B., & Seymour, G. J. (2000). Ante-dependence modeling in a longitudinal study of periodontal disease: The effect of age, gender, and smoking status. *Journal of Periodontology*, *71*, 454–459. https://doi.org/10.1902/jop.2000.71.3.454

Fontijn-Tekamp, F. A., Slagter, A. P., Van Der Bilt, A., Van, T. H. M. A., Witter, D. J., Kalk, W., & Jansen, J. A. (2000). Biting and chewing in overdentures, full dentures, and natural dentitions. *Journal of Dental Research*, *79*, 1519–1524.

Glavind, L., & Loe, H. (1967). Errors in the clinical assessment of periodontal destruction. *Journal of Periodontal Research*, *2*, 180–184.

Harris, K. (2010). ROC Hard? No, ROC Made Easy. In: Proceedings of the SAS Global Forum 2010 Conference. Cary, NC: SAS Institute Inc.

Löe, H. (1967). The gingival index, the plaque index and the retention index systems. *Journal of Periodontology*, *38*(Suppl), 610–616.

Löe, H., Anerud, A., & Boysen, H. (1992). The natural history of periodontal disease in man: Prevalence, severity, and extent of gingival recession. *Journal of Periodontology*, *63*, 489–495.

Löe, H., Anerud, A., Boysen, H., & Morrison, E. (1986). Natural history of periodontal disease in man. Rapid, moderate and no loss of attachment in Sri Lankan laborers 14 to 46 years of age. *Journal of Clinical Periodontology*, *13*, 431–445.

Löe, H., Anerud, A., Boysen, H., & Smith, M. (1978a). The natural history of periodontal disease in man. The rate of periodontal destruction before 40 years of age. *Journal of Periodontology*, *49*, 607–620. https://doi.org/10.1902/jop.1978.49.12.607

Löe, H., Anerud, A., Boysen, H., & Smith, M. (1978b). The natural history of periodontal disease in man. Study design and baseline data. *Journal of Periodontal Research*, *13*, 550–562.

Löe, H., Anerud, A., Boysen, H., & Smith, M. (1978c). The natural history of periodontal disease in man. Tooth mortality rates before 40 years of age. *Journal of Periodontal Research*, *13*, 563–572.

Löe, H., & Silness, J. (1963). Periodontal disease in pregnancy. I Prevalence and severity. *Acta Odontologica Scandinavica*, *21*, 533–551.

Longini, I. M. (2005). Chain binomial model. *Encyclopaedia of Biostatistics*, https://doi.org/10.1002/0470011815.b2a07008

Neely, A. L., Holford, T. R., Loe, H., Anerud, A., & Boysen, H. (2001). The natural history of periodontal disease in man. Risk factors for progression of attachment loss in individuals receiving no oral health care. *Journal of Periodontology*, *72*, 1006–1015. https://doi.org/10.1902/jop.2001.72.8.1006

Neely, A. L., Holford, T. R., Loe, H., Anerud, A., & Boysen, H. (2005). The natural history of periodontal disease in humans: Risk factors for tooth loss in caries-free subjects receiving no oral health care. *Journal of Clinical Periodontology*, *32*, 984–993. https://doi.org/10.1111/j.1600-051X.2005.00797.x

Nguyen, T. C., Witter, D. J., Bronkhorst, E. M., Pham, L. H., & Creugers, N. H. (2011). Dental functional status in a southern vietnamese adult population-a combined quantitative and qualitative classification system analysis. *International Journal of Prosthodontics*, *24*, 30–37.

Preus, H. R., Anerud, A., Boysen, H., Dunford, R. G., Zambon, J. J., & Löe, H. (1995). The natural history of periodontal disease. The correlation of selected microbiological parameters with disease severity in Sri Lankan tea workers. *Journal of Clinical Periodontology*, *22*, 674–678.

Schätzle, M., Faddy, M. J., Cullinan, M. P., Seymour, G. J., Lang, N. P., Burgin, W., … Löe, H. (2009). The clinical course of chronic periodontitis: V. Predictive factors in periodontal disease. *Journal of Clinical Periodontology*, *36*, 365–371. https://doi.org/10.1111/j.1600-051X.2009.01391.x

Silness, J., & Löe, H. (1964). Periodontal disease in pregnancy. Ii. Correlation between oral hygiene and periodontal condtion. *Acta Odontologica Scandinavica*, *22*, 121–135.

Timmerman, M. F., Van der Weijden, G. A., Abbas, F., Arief, E. M., Armand, S., Winkel, E. G., … Van der Velden, U. (2000). Untreated periodontal disease in Indonesian adolescents. Longitudinal clinical data and prospective clinical and microbiological risk assessment. *Journal of Clinical Periodontology*, *27*, 932–942.

Timmerman, M. F., Van der Weijden, G. A., Armand, S., Abbas, F., Winkel, E. G., Van Winkelhoff, A. J., & Van der Velden, U. (1998). Untreated periodontal disease in Indonesian adolescents. Clinical and microbiological baseline data. *Journal of Clinical Periodontology*, *25*, 215–224.

Timmerman, M. F., Van der Weijden, G. A., Hart, A. A., Abbas, F., Winkel, E. G., & Van der Velden, U. (2002). How do data from deepest pocket per quadrant relate to full-mouth scores? Progression of untreated periodontal disease in young Indonesians. *Journal of Clinical Periodontology*, *29*, 219–223.

Tonetti, M. S., & Claffey, N. (2005). Advances in the progression of periodontitis and proposal of definitions of a periodontitis case and disease progression for use in risk factor research. Group C consensus report of the 5th European Workshop in Periodontology. *Journal of Clinical Periodontology*, *32*(Suppl 6), 210–213.

Van der Velden, U., Abbas, F., Armand, S., Loos, B. G., Timmerman, M. F., Van der Weijden, G. A., … Winkel, E. G. (2006). Java project on periodontal diseases. The natural development of periodontitis: Risk factors, risk predictors and risk determinants. *Journal of Clinical Periodontology*, *33*, 540–548. https://doi.org/10.1111/j.1600-051X.2006.00953.x

van der Velden, U., Amaliya, A., Loos, B. G., Timmerman, M. F., van der Weijden, F. A., Winkel, E. G., & Abbas, F. (2015). Java project on periodontal diseases: Causes of tooth loss in a cohort of untreated individuals. *Journal of Clinical Periodontology*, *42*, 824–831. https://doi.org/10.1111/jcpe.12446

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

How to cite this article: Ramseier CA, Anerud A, Dulac M, et al. Natural history of periodontitis: Disease progression and tooth loss over 40 years. *J Clin Periodontol*. 2017;00:1–10. https://doi.org/10.1111/jcpe.12782