World Workshop on Classification of Periodontal and Peri-implant Diseases
Attachment level progression systematic review

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Mean annual attachment, bone level and tooth loss – a systematic review

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Running title: Attachment level progression systematic review

One sentence summary: Mean annual attachment level change varies considerably both within and between populations and does not support or refute differentiation between forms of periodontal diseases based upon this outcome.

Key words: Periodontal diseases, Systematic review, Chronic periodontitis, Disease progression, Periodontal attachment loss, Epidemiology

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Abstract

Background: Rate of progression of periodontitis has been used to inform on the design of classifications of periodontal diseases. However, the evidence underpinning this topic is unclear and no systematic review has yet been conducted.

Objectives: The focussed question for this systematic review was; in adults, what is the progression of periodontitis in terms of clinical attachment loss, radiographic bone loss and tooth loss?

Data sources: Highly sensitive electronic search for published data in MEDLINE, EMBASE, LILACS and unpublished, grey literature in OpenGrey up to February 2016. Reference lists of retrieved studies for full text screening and reviews were hand searched for potentially eligible studies

Study eligibility criteria & participants: Prospective, longitudinal observational studies with follow-up of at least 12 months presenting data on the primary outcome, change in clinical attachment level, in adults (at least 18 years of age). Secondary outcomes, tooth loss and bone level change were only assessed in studies reporting the primary outcome. Studies investigating specific disease populations or only on treated periodontitis patients were excluded.

Study appraisal and synthesis methods: Risk of bias and methodology were assessed using the Newcastle Ottawa scale with two additional questions on security of outcome assessment. Studies were pooled by abstracting or estimating mean annual attachment or bone level change and annual tooth loss. Random effects meta-analysis was conducted with investigation of effect of potential modifiers were possible.

Results: 11,482 records were screened for eligibility with 33 publications of 16 original studies reporting on more than 8,600 participants finally included as eligible for the review. The studies represented populations from both developing and developed economies. Mean annual attachment loss was 0.1mm per year (95% CI 0.068, 0.132, I^2=99%) and mean annual tooth loss was 0.2 teeth per year (95% CI 0.10, 0.33 I^2=94%). Observational analysis of highest and lowest mean attachment change quintiles suggested substantial differences between groups with minimal annual change in the lowest quintile and an average deterioration of 0.45mm mean attachment loss per year in the highest group. This value increased to 0.6mm per year with periodontitis alone. There was surprisingly little effect of age or gender on attachment level change. Geographical location however was associated with more than three times higher mean annual attachment loss in Sri Lanka & China (0.20mm, 95% CI 0.15, 0.27, I^2 = 83%) vs. North America & Europe (0.056mm, 95%CI 0.025, 0.087, I^2 = 99%) P<0.001.

Limitations: Limited number of studies (N=16), high variability of design in key study components (sampling frames, included ages, data analyses) and high statistical heterogeneity that could not be explained.

Conclusions: Within the limitations of the research, the data show that mean annual attachment level change varies considerably both within and between populations. Overall, the evidence does not support or refute the differentiation between forms of periodontal diseases based upon progression of attachment level change.

Systematic review registration number: PROSPERO database: CRD42016035581

Introduction

Periodontitis is characterised by non-reversible tissue destruction resulting in progressive loss of attachment eventually leading to tooth loss [1]. Severe periodontitis is the sixth most prevalent disease of mankind [2] and is a public health problem since it is highly prevalent and causes disability, impaired quality of life and social inequality [3, 4]. The prevalence of periodontitis remains high globally although periodontal health has shown signs of improvement in representative national and regional epidemiological surveys in recent decades in countries with high income [5, 6]. However, the severest forms of periodontitis have remained constantly high affecting approximately 10% of surveyed populations [6-8].

Understanding the nature of the disease is crucial to research and to the development of more effective health promotion, disease prevention and treatment. For instance, if there are different forms of periodontitis, should management strategies be tailored to the variants? It is unclear whether periodontitis comprises a group of distinct diseases (chronic periodontitis, aggressive periodontitis) [9, 10] or a syndrome with a range of presentations [11, 12]. In attempting to address these issues, the two most common criteria used to evaluate similarities and differences over the last half century or more of periodontal disease classification have included age of onset of disease and 'rate' of progression. Rate is used here, not in the usual epidemiological sense of proportion of people affected by a condition, but instead of how quickly the disease deteriorates. Age of onset is not the topic of this review and will not be addressed further although is investigated by another review [13].

Rate of progression could be important as a distinguishing criterion of forms of periodontitis and there is general consensus in most disease definitions that the primary measure of the condition is attachment level change [14]. Rapid disease progression was a criterion for periodontosis nearly half a century ago [15]. Rate of progression became embedded in the identity of certain classifications with labels such as rapidly progressive periodontitis and aggressive periodontitis [9]. However, even with promotion of this criterion to a defining characteristic, there was widespread unease about whether it was truly distinctive [9, 10, 12, 16, 17].

Clearly, much uncertainty remains about the progression of attachment loss. Systematic reviews are designed to assemble, appraise and make sense of the totality of the evidence [18] as far as possible. No previous systematic review has investigated rate of progression of attachment loss and

therefore, the aim of this study was to critically and comprehensively evaluate the evidence for progression of periodontitis and associated determinants of progression.

Methods

Focussed question

In adults, what is the progression of periodontitis in terms of clinical attachment loss, radiographic bone loss and tooth loss? The reason for limiting the investigation to adults, i.e. persons aged 18 years and older was that we were asked to constrain the investigation in this manner to avoid overlap with a separate investigation into periodontal diseases in younger individuals for the 2017 World Workshop of Classification of Periodontal and Peri-implant Diseases [13].

Objectives:

- To investigate the evidence for progression of periodontitis, defined as change in attachment level over a period of 12 months or more – What is the evidence for different mean values of progression?
- Which risk factors are associated with different mean values of progression of periodontitis?
- Which aetiological factors are associated with different mean values of progression of periodontitis?

The protocol was registered prior to commencing the study on the PROSPERO database: CRD42016035581 (www.crd.york.ac.uk/PROSPERO). The manuscript has been prepared following the PRISMA statement for reporting of systematic reviews [19].

Population

We included studies on periodontally untreated adults aged 18 years or older. Studies including both adults and younger individuals without distinction were eligible and we planned to stratify for this criterion. We planned to stratify data into studies based on baseline status of periodontitis populations, non-periodontitis populations and mixed/unclear populations if available. Studies with participants in continuous periodontal maintenance after periodontal therapy were excluded.

Exposure

The primary outcome measure was clinical attachment level change (or variants including relative attachment level change). All probing methods (manual, controlled force etc.) were included. Change of probing depth was not considered. Secondary outcome measures were only included for studies firstly presenting attachment level change. For radiographic bone loss, all methods (film, digital, subtraction customised film holders) were eligible. Tooth loss data were included irrespective

of whether the cause of tooth loss was reported or not. Clearly, tooth loss might have been related to factors other than periodontitis.

Disease determinants, risk factors and aetiological agents.

The association of attachment level progression with disease determinants was recorded where available including gender, age, socioeconomic position, genetics, lifestyle, health behaviours, nutritional and microbiological factors. Wherever possible, the quality of measurement of the determinant/exposure was assessed (see below).

Study duration of follow-up

Any study duration of at least 12 months was included or interval of follow-up. Data were recorded for all follow-ups and selected for the longest follow-up available

Types of studies

We aimed to be inclusive of research and there are many possible approaches to designing eligibility criteria for this research question. We considered as eligible any longitudinal prospective observational study with a follow-up of at least 12 months that assessed changes in clinical attachment level (or variants including relative attachment level) in adult individuals (18 years of age or above). Secondary outcomes were assessed only for those studies firstly reporting data for clinical attachment levels and comprised radiographic bone loss, tooth loss and risk factors associated with clinical attachment loss. Intervention studies, cross-sectional studies and reviews were excluded. We decided to include any prospective longitudinal study whether population- or institution-based. We excluded studies on specific disease populations such as diabetes as the aim of the review was to establish evidence as far as possible for periodontitis in general populations. Clearly, within population studies, accurate general health status might not be known. In addition, studies exclusively reporting data for treated periodontitis patients would not represent overall population values.

Inclusion criteria

- Prospective, longitudinal studies.
- Duration of follow-up: at least 12 months.
- Adults, 18 years of age or greater. Studies that also included younger participants within a combined data set were included although we planned to stratify the data separately.
- Study reporting progression of periodontitis using attachment level assessments.

- Periodontally healthy, untreated periodontitis or participants not part of periodontitis treatment investigations. We set this broadly as we anticipated that population studies would not report detailed periodontal treatment status of participants.
- Tobacco use was not an eligibility criterion. Population studies would include both tobacco users and not and we planned to analyse the effect on periodontal health if data were available.

Exclusion criteria

- Studies investigating solely specific systemic disease populations e.g. diabetes.
- Experimental studies testing the effect of interventions on periodontitis.
- Cross-sectional or retrospective studies.
- Studies only recruiting participants for periodontitis treatment or previously treated for periodontitis.

Search strategy

A highly sensitive search was conducted. Electronic databases (MEDLINE via OVID, EMBASE via OVID, LILACS) were searched using a string of medical subject headings and free-text terms (appendix 1). OpenGrey was searched for unpublished, grey literature. The search strategy was developed with ADI, a medical librarian with extensive experience in designing searches for systematic reviews. The search strategy was first designed for the MEDLINE database and was then modified appropriately for the other databases searched. There were no language or publication date restrictions. Reference lists of all studies included for full text screening and previous reviews were searched for missing records. The search results were downloaded to a bibliographic database and duplicate records were removed.

Study selection

Titles and abstracts (if available) of the studies identified in the searches were screened by two of the review authors (NG & FM), in duplicate and independently. Subsequently, the full text of all publications appearing to meet the inclusion criteria or for which there was not sufficient information in the title and abstract to make a decision, were obtained. At this first stage, any study considered as potentially relevant by at least one of the reviewers was included for the next screening phase. Subsequently, the full-text publications were also evaluated in duplicate and independently by the same review examiners. The examiners were calibrated with the first 10 full text consecutive publications. Any disagreement on the eligibility of studies was resolved through

discussion between both reviewers until consensus was reached or through arbitration by a third reviewer (IN). All potentially relevant studies that did not meet the eligibility criteria were excluded and the reasons for exclusion noted. Publications in languages other than English, Greek, Portuguese or Spanish were sent to an interpreter with clear instructions on inclusion and exclusion criteria. Inter-examiner agreement following full-text assessment was calculated via Kappa statistics. In addition, the final list of eligible studies was circulated to all members of the review group and the workshop chairmen for evaluation of possibly missing studies.

There were several studies which accounted for more than one publication since it was common to find publications investigating the same population at different follow-up intervals and/or secondary analysis of the same data. For this reason, a decision was made to pool together all relevant publications for any given principal study. FM and NG assessed the pooled studies independently and only included those reporting data on the primary and/or secondary outcomes assessed in this review for the original study sample. Disagreement on the selection of the studies was resolved in the same manner as in previous stages.

Unclear or missing data

For studies for which a clear decision on eligibility could not be made following full text assessment or when there was missing data we contacted the corresponding authors up to twice, one month apart, to seek the information needed to aid the final decision. In the absence of response, and/or if the data could not be used the studies were excluded from the final review.

Data extraction and management

Study details were collected using a form specifically designed for data extraction for this review and which was firstly piloted in a small number of studies. Two of the review authors (NG and FM) independently extracted all relevant data from all included studies except for those publications written in any language other than English, Greek, Portuguese or Spanish. In this case, data extraction (and quality assessment) was completed by interpreters who received clear instructions on how to collect the data using the data collection form. Any disagreements were resolved through debate and consensus or through assessment of a third reviewer (IN).

The following study details were extracted.

- Type of study
- Number of centres

- Sample frame (e.g community, university)
- Age of participants
- Periodontal status
- Definition of periodontitis cases
- Duration of follow-up
- Type of attachment level measurement (e.g. PAL, CAL, RAL…)
- Method of attachment level measure (e.g. manual probe, pressure sensitive probe…)
- Frequency of CAL measurement
- Method for radiographic assessment of bone loss
- Cause of tooth loss reported in study (yes/no).
- Risk factors reported in study
- Number of participants (baseline/last follow-up)
- Outcomes
    - Mean attachment level change
    - Mean attachment level change stratified by sub-groups
    - Mean radiographic bone loss
    - Mean radiographic bone loss stratified by sub-groups
    - Mean tooth loss
    - Mean tooth loss stratified by sub-groups

Quality assessment

Risk of bias was assessed using the Newcastle-Ottawa scale, appropriately modified (Appendix 2), as it is the mostly widely used tool for epidemiologic studies.

Other domains of methodological quality comprised:

- Security of measurement of attachment level. Studies were assessed as secure if the method involved appropriate training and calibration of examiners, insecure if training was absent or inadequate or unclear if unreported
- Security of assessment of bone level change. Studies were assessed as secure if the method involved standardised positioning of the radiographs e.g. cephalostat or customised film holders, insecure if standardisation was absent or inadequate or unclear if unreported.

Data synthesis

Data were first entered into evidence tables stratified by study design. Decisions on which studies to include in a meta-analysis were made depending on the similarity of chief study characteristics

related to each research question i.e. mean progression of periodontitis and association of progression with disease determinants.

When a study provided the mean progression at a known time point, it was assumed that the progression was constant over time in order to estimate the mean progression rate, i.e. the mean progression per year. When a study only provided the relevant progression information for subgroups (e.g. gender or age groups), the mean annual progression for the study was estimated as a weighted mean, with the weights being inversely proportional to the variance if the latter could be calculated or directly proportional to the frequency otherwise. The same approach was used when estimating the mean annual progression for each of the three age subgroups, namely age < 30, 30 – 50 and > 50 years. Assuming that the data were normally distributed in each study, the lowest and highest quintiles (i.e. the 20^{th} and 80^{th} percentiles) of annual progression were calculated for each study from its mean and standard deviation.

Statistical heterogeneity of mean annual progression between relevant studies was assessed using both the chi-square test and the I^2 measures. We interpreted I^2 according to the guidance of the Cochrane Handbook:

- 0% to 40%: might not be important
- 30% to 60%: may represent moderate heterogeneity
- 50% to 90%: may represent substantial heterogeneity
- 75% to 100%: considerable heterogeneity

If meta-analysis appeared appropriate, it was used to provide an overall estimate of the mean annual progression, with its 95% confidence interval, using a random effects approach if there was evidence of statistical heterogeneity and a fixed effects approach otherwise. We anticipated statistical heterogeneity and planned to investigate the contribution of risk of bias, security of disease progression method, type of population i.e. initially healthy or periodontitis. Similar methods were planned to assess the association between mean progression and potential modifiers. However, the available data were limited for meta-analysis, allowing only few exploratory analyses. For these analyses of association, a chi-squared test of heterogeneity between the overall mean annual progression for each subgroup of the potential modifier (e.g. males and females) was performed to determine the effect of the factor (i.e. gender, geographical location or age group) on

the mean annual progression . Statistical analyses were conducted by AP, a biostatistician experienced in systematic reviews and meta-analysis. A significance level of 0.05 was used for all statistical hypothesis tests. Data were analysed using Stata (StataCorp. 2015. *Stata Statistical Software: Release 14*. College Station, TX: StataCorp LP).

Results

Search (Figure 1)

A total of 11,482 potentially eligible records were found through the sensitive searches. 11,286 publications were excluded following review of the titles and abstracts and finally the full publications of 196 records were retrieved.

Inter-examiner agreement at full-text screening was excellent (Kappa score = 0.756) [20]. Following careful assessment of the full papers 116 records were excluded. Of the remaining 80 records, 4 original studies accounting for only one publication were included in the final review while 76 publications were nested into 12 different original studies which had more than one publication (e.g. different follow-up intervals). Finally, 29 of the nested publications were also included which resulted in a total of 33 publications of 16 studies which were included for data extraction and quality assessment. The reasons for exclusion of all studies that were not included at the stage of full-text review were recorded (appendix 1).

Study characteristics (table 1)

Location

We found the following study geographical locations; two studies from Brazil [21, 22], two from China [23-28], one from Germany [29, 30], one from Indonesia [31, 32], one from Japan [33, 34], one from New Zealand [35], one from Norway and Sri Lanka [36-41] and seven from the USA [42-54]

Sample characteristics

Eight studies were epidemiological samples [21, 23-29, 33, 34, 45, 46, 49, 51, 55] one was a birth cohort [35], one was a community cohort [31, 32], two were specialist periodontal clinic or practice patients [43, 44] and the status of four were unclear [22, 36-42, 53, 54].

The age groups of included participants varied. Five studies reported data on only participants below 50 years of age [23, 24, 31, 32, 35-41, 43], three studies only 50 years of age or more [33, 34, 42], seven studies with a wide included age range [21, 22, 25-30, 44-52, 55] and one study was unclear [53, 54].

Both male and female participants were included in 11 studies [21, 23-35, 43-52, 55] women only in two studies [22, 42], men only in one study [36-41] and unclear in one study [53, 54]

Study duration/follow-up was up to five years in nine studies [21-24, 33, 34, 42-45, 47-52] 6-10 years in four studies [25-30, 35-41, 55] and more than 10 years in three studies[31, 32, 46, 53, 54].

The completeness of follow-up of the initial sample was at least 80% in two studies [23, 24, 35], 50-79% in five studies [25-34, 42, 55], below 50% in four studies [21, 36-41, 47-54] and unclear in five studies [22, 43-46].

Generally, participants of the population studies included both those with and without periodontitis as would be a normal population finding. The proportion of each within the study was not stated in most publications. Periodontitis was an inclusion criterion for two studies [43, 44] and one excluded 'severe' periodontitis [45].

Clinical attachment level was measured by manual probing in most studies. Controlled force probes were employed fully or for the probing depth component alone in four studies [31-34, 42, 45]. Bone level was assessed on dental radiographs using linear measurement in both included studies [42, 45]

Risk of bias and methodological quality (table 2)
For the Newcastle-Ottawa scale, seven publications were rated 6-7 stars, eight were rated 4-5 stars and one at 3 stars out of a maximum of 7. Security of measurement of the primary outcome, attachment level change was graded as secure for 14/16 studies and insecure for the remaining two. In relation to bone level measurement of the two studies, one was assessed as secure and the other insecure.

Mean annual attachment level change (table 3, figures 2-5)

Random effects meta-analysis of nine studies with 13 data sets showed a mean annual attachment loss of 0.10mm (95%CI 0.068, 0.132) with considerable heterogeneity (I^2 = 99%) (Figure 2). When considering interproximal sites only, mean annual attachment loss was very similar to the estimate for all sites, 0.093mm (95% CI 0.022, 0.16, I^2 = 99%) (Figure 3). The estimate for the four studies reporting data only for periodontitis was considerably higher at 0.57mm, although with very wide uncertainty (95% CI-0.38, 1.51) and high heterogeneity (I^2 = 99%) (Figure 4). The combined estimate for the two studies reporting data for post-menopausal women was 0.052mm (95%CI -0.084, 0.19, I^2 = 90%) (Figure 5). The small values of <1mm change are of course not measurable but represent the effect of calculating mean change.

Exploration of subgroups (table 3, figure 2, figures 6-7)

Geographical location was associated with statistically significantly greater mean annual attachment loss for Sri Lanka & China (0.20mm, 95% CI 0.15, 0.27, I^2 = 83%) vs. North America & Europe (0.056mm, 95%CI 0.025, 0.087, I^2 = 99%) P<0.001. There was no evidence of a difference for gender; males 0.067mm (95% CI 0.023, 0.11, I^2 = 51%), females 0.070mm (95%CI 0.064, 0.076, I^2 = 0.0%) P=0.89. Similarly, differences between age groups were not statistically significant; age<30 years 0.16mm (95% CI 0.068,0.16 I^2 = 99%), age 30-50 years 0.074mm (95% CI 0.052,0.096 I^2 = 96%) & age >50 years 0.13mm (95% CI, 0.072, 0.19 I^2 = 99%) P=0.093.

For single studies where meta-analysis was not possible, additional observations were found. Overall mean annual attachment level change was greater for those with at least one site showing CAL loss of at least 3mm compared with all participants combined (those initially 26 years old 0.05mm loss vs. 0.02mm gain, initially 32 years old 0.12mm vs. 0.03mm)[35]. Selecting the 30 participants with greatest change vs. the 30 people with the least change in a rural Chinese population found change of 0.14mm vs. 0.12mm [55].

Overall, ethnicity was associated with higher mean annual attachment loss in black (0.074mm) than white participants (0.006mm) in one study [50, 51]. For presumed periodontitis only data (sites which lost at least 3mm attachment), there was little effect of gender, ethnicity, age or education [51]. In another study, older age, being male, non-white or from a low socioeconomic background was statistically significantly associated with greater attachment loss [21]. Age, calculus, gingival index but not smoking or plaque levels were statistically significantly associated with greater mean annual attachment loss in a secondary analysis of data from Sri Lanka [40]. Elsewhere, younger age (20-29 years), being male, current smokers vs. never smoker, less than 10 years school education and existing diabetes were all statistically significantly associated with greater attachment level change [29, 30].

Distribution of highest and lowest mean annual attachment level change (table 4, figure 8)

Lowest and highest quintiles (i.e. the 20th and 80th percentiles) were calculated for each study from the mean and standard deviation assuming that the data were normally distributed in each case. Caution should be exercised when interpreting these results due to the assumption of normality and also in consideration of their high between-study variability when the quintiles were combined to provide an overall estimate. However, the data overall show much different mean annual attachment level change for the lowest quintile -0.23mm i.e. gain) vs. highest (0.45mm loss). Values were similar for interproximal sites alone; lowest quintile -0.048mm, highest quintile 0.23mm. The

respective values were higher for the studies reporting on periodontitis alone; lowest quintile 0.22mm, highest quintile 0.91mm.

Mean annual tooth loss (table 5, figure 9)

Meta-analysis of included studies showed overall mean annual tooth loss was 0.20 (95%CI 0.13, 0.26, I^2 = 91%). There was no evidence of a difference comparing the geographical groupings of North America, Europe, Japan and Oceania, mean annual tooth loss 0.21 (95%CI 0.10, 0.33 I^2 = 94%) vs. South America & Asia mean annual tooth loss 0.19 (95%CI 0.11, 0.28 I^2 = 83%) P=0.80

The data from single studies where meta-analysis was not possible showed little difference in mean annual tooth loss between males (0.17) and females (0.13) in one study[29, 30]. Small differences in mean annual tooth loss with age were also reported in a Brazilian population; age less than 30 years, 0.02 vs, age at least 50 years, 0.03[21]. Elsewhere, annual tooth loss increased with advancing age; age <30 years: 0.04 (95%CI 0.027, 0.053), 30-50 years 0.13 (95% CI 0.16, 0.15) and >50 years 0.23 (95% CI 0.21, 0.25). Similarly, annual tooth loss was more than twice the magnitude comparing severe periodontitis 0.38 (95%CI 0.34, 0.42) vs. moderate periodontitis 0.17 (95%CI 0.15, 0.19)[30]. In a rural Chinese population, comparing the 30 participants with the worst attachment loss at 10 years vs. 30 people with the least attachment loss, annual tooth loss was 0.53 vs. 0.18 [55]. In another study, comparison of those with progressing disease (more than one site with attachment loss of more than 2 mm) with non-progressing disease (all others) showed the same annual tooth loss of 0.07 [31].

Mean annual bone level change (table 6)

Only two included studies also reported on bone level. These were not comparable (general population study [45] vs. post-menopausal women [42]) and therefore meta-analysis was not performed. Annual bone level loss was low with similar values in both studies 0.04mm [45] & 0.038mm [42].

Discussion

Key findings

Overall, in a general population including both people with and without periodontitis, mean annual attachment loss was 0.1mm per year and mean annual tooth loss was 0.2 teeth per year. Observational analysis of highest and lowest mean attachment change quintiles suggests substantial differences between groups with minimal annual change in the lowest quintile and a substantial average deterioration of 0.45mm mean attachment loss per year in the highest group. This value increased to 0.6mm per year with periodontitis alone. There was surprisingly little effect of age or

gender on attachment level change. Geographical location however was associated with more than three times higher mean annual attachment loss in countries with developing economies (0.2mm) compared with developed economies (0.06mm) P<0.001.

At a first glance these low values may seem remarkable, but it has to be borne in mind, that very few sites in a subject progress beyond a 3mm threshold of attachment level change. Thus most sites have no or little progression over time, which may be within the range of periodontal measurement error. Furthermore these mean values are further influenced by the observation that the periodontal attachment level change may also decrease [29, 35, 50, 51]. To what extent remission measurements reflect biological changes or measurement error, is open to debate, but they have a big influence on these mean values.

Overall completeness and applicability of the evidence

The limited number of studies that were eligible to be included in this review might seem surprising considering the long and distinguished history of periodontal epidemiology. However, most prior studies have been either cross-sectional in design or have used relatively short follow-up periods of less than one year. We focussed the review on studies that could contribute to an investigation of attachment level change over a period of at least 12 months and this, in part, accounts for the limited number of eligible studies. We excluded retrospective studies on the basis that the design of a prospective study was more likely to be robust since it was designed *a priori* to address the research question. The same could not be said of retrospective studies. Subject-based mean attachment level change was our primary outcome and is justified in terms of its fundamental importance to epidemiology and disease classification. Nevertheless, within the included studies a total of 8,607 participants contributed to follow-up data. We found other studies which presented data in different formats such as numbers of sites (overall or per participant) with different thresholds of attachment level change. We did not include these data for two reasons; firstly, there was substantial heterogeneity in the definition of what constituted a progressing site making statistical combination in meta-analysis not possible or highly selective. Secondly, we felt that number of progressing sites would be less informative to the review aims because they depend on the number of teeth present and do not include remission. The completeness of data in this review on bone level change and tooth loss is even less as we, *a priori*, planned only to include these data if presented in studies also reporting our primary outcome, attachment level change. The reason for this approach was that to include all studies on bone and tooth loss would have required additional searches resulting in a substantially increased workload for all stages of the review. It was not

possible to embark on this within the available timescale. A further limitation was the difficulty in assessing the evidence for our second and third objectives, i.e. risk factors and aetiological factors. We analysed the data as far as they allowed, but were prevented from more investigation typically by a lack of reporting or of reporting in formats that could not combined.

Aspects of the included studies that favour applicability of the evidence are the number of large population-based surveys in both developing and developed economies, with a spread of included ages. Challenges to applicability are mainly presented by the lack of consistency as will be discussed below.

Overall quality, strength and consistency of the evidence

The Newcastle-Ottawa scale demonstrated that 11/16 studies received at least 5 stars out a possible 7 indicating reasonably low levels of risk of bias. Furthermore, only two studies showed an insecure method of measurement of attachment level [44, 46] and one an insecure method of bone level [45].

The consistency of evidence is much more problematic. Whilst the total number of included participants, 8,607, might appear to be a substantial number, the high statistical heterogeneity and the major differences in study design are troubling to the development of an overview of the data. Key differences in methodology include; sampling frames (random or convenience population-based samples, patient populations, birth cohorts, practice samples), included ages (some studies only <50 years and others only 50 years or more), men or women only studies, study duration (from 2-28 years), full-mouth and partial mouth recording and inclusion of only teeth present at both baseline and follow-up vs. all teeth at baseline whether lost at follow-up or not. Remaining teeth in a mouth may represent “healthy survivor” teeth because those extracted tend to be more periodontally affected [56]. Thus, the loss of teeth due to progression of periodontitis could result in underestimation of attachment level change [16]. Whilst some studies have shown a clear effect of this phenomenon [49], others have reported little or no differences when modelling the analysis in different ways [42].

The included studies might also represent the effect of period /cohort effects such as the differences between the two Chinese samples, which were recruited approximately a decade apart. The Gusheng population had a mean annual attachment loss (0.17mm/year) almost three times than the Cheng-de cohort (0.065mm/year). The first cohort resembles much more that of low income country such as the Sri Lanka cohort from 1978 and oral health may be influenced by malnutrition, low level

of personal hygiene, whereas attachment progression of the Cheng-de cohort is comparable to the European and US cohorts. We speculate that the Cheng-de cohort might reflect the dynamic change of Chinese economy, where for example malnutrition, hygiene, access to medical care etc. have changed. To what extent period and cohort effects influence these values, cannot be explained with the available data.

The statistical heterogeneity in particular suggests that there are important differences in outcomes between studies that could not be explained. Consequently, the overall estimates from the meta-analyses, despite representing best-available evidence, should be used with caution and likely represent a low strength of evidence.

Tooth loss data are especially challenging to interpret. Tooth loss, if not exfoliation, could be due to many reasons including but not limited to severe periodontitis. Tooth extraction will be influenced by availability of dental professionals, existing disease (including periodontitis, caries and endodontic disease), patient preferences, financial considerations related to affordability of the treatment, professional practices and cultural norms [57, 58]. This might help to explain the lack of difference in annual tooth loss comparing studies conducted in North America, Europe, Japan and Oceania (potentially higher economic development) with South America and Asia (lower economic development) although the heterogeneity within these two strata was very high. Only limited information was available in the reported studies to tease out if tooth loss was determined by periodontal status, because tooth loss was not reported according to periodontal severity or progression. In the SHIP and Gusheng cohorts, tooth loss was much more pronounced in subjects with periodontitis in comparison to healthy subjects, whereas no such relation was found in the Java cohort. In the US and Germany chronic periodontitis is closely related to tooth loss in persons aged 40 years and older [59, 60].

Additional approaches to assessing progression of periodontal diseases such as quantitative assessment of bone height and density show promise[61] and would have been included if data had been presented in the included studies. These techniques have limited relevance to population epidemiology but could be valuable in small, more controlled institution-based studies. Interestingly, radiographic assessments did not form part of the common data set recently recommended for periodontal epidemiology[62].

Potential biases in the review process

In order to minimise the risk of bias in the review process, we registered the review protocol *a priori* CRD42016035581 (www.crd.york.ac.uk/PROSPERO). Screening, eligibility decisions and data abstraction were carried out in duplicate and independently. The search was also designed to minimise bias including development of a highly sensitive electronic search strategy of multiple databases, no language restrictions, and searching for grey literature. Sources of potential biases were changes to the protocol during the review process. We included two post-hoc analyses based on the data collected. These were subgrouping by geographical location and estimation of quintiles of attachment level change. Since we have treated both as purely exploratory, the level of bias introduced would seem to be low.

Agreements and disagreements with other reviews

To our knowledge, there has been no systematic review of this topic. Progression of periodontitis has been considered in previous comprehensive narrative reviews [16, 63, 64]. These reviews report values of mean annual attachment level change ranging from 0.04-1.04mm. The findings from the current systematic review are consistent with the values although the narrative reviews included fewer studies.

Implications for practice/policy

Within the limitations of the research, the data show that mean annual attachment level change varies considerably both within and between populations. This finding has important implications both for classifying periodontal diseases and for the management of periodontal health.

In relation to classification, mean annual attachment level change was a challenging concept in the 1999 Workshop on Disease Classification[9]. However, rapid attachment level loss was considered a key characteristic of aggressive periodontitis [65] whereas chronic periodontitis showed slow to moderate progression but could demonstrate periods of rapid progression [66]. Therefore, whilst it was accepted that the use of progression thresholds was problematic to defining different types of disease, the final classification incorporated such elements. Previous workshops have also struggled with such issues and accepted the substantial variability of presentation of periodontitis, including progression of attachment level change [11, 67]. Furthermore, severity of attachment loss at initial assessment (and by implication annual attachment loss at that point) can be a poor predictor of trajectory [11, 68]. A recent review of aggressive periodontitis highlighted the variability in mean annual attachment level progression although the values cited are within those found in the present systematic review. Despite the variability one of the distinctive criteria recommended for case

definition was 'relatively high progression rate of periodontal tissues loss' [69]. The operationalisation of such a characteristic is unclear. We would also highlight that the data in the incorporated studies represent 'progression' of disease based on mean values of all sites and do not inform on the behaviour or biological mechanisms of attachment level change at individual sites. This is a significant limitation of the current research base.

The 2015 Task Force Update to the 1999 classification enlarged on this issue [10]. In relation to chronic periodontitis, they acknowledged a spectrum of annual attachment level change including a slow, continuous pattern of disease progression, bursts of periodontal destruction around certain teeth in relatively short periods (random burst pattern) and many bursts of destructive periodontal disease activity at a high frequency during certain periods (multiple burst pattern). Age of onset (detection) was recommended as the general guideline to distinguish aggressive from chronic periodontitis and not annual attachment level change although this could provide supportive evidence. Overall, the results of this new systematic review do not support or refute the continuing of differentiation between forms of periodontal diseases based upon progression of attachment level change.

Prevention of periodontitis includes both prevention of gingivitis or if already established treatment of gingivitis [1]. This review has not sought to ask whether preventive outcomes are different across people who will go on to follow 'low' or 'high' trajectories of mean annual attachment loss. Since it is not currently possible to screen for such tendencies, a universal approach to prevention is indicated rather than attempting to identify individuals at high risk [70]. However, management of periodontal health should also be conceived broadly to include healthy lifestyles promotion and risk factor reduction through the combined engagement of policy makers, health professionals and empowered individuals [1] and with an understanding of the impact of social inequalities [71].

Implications for further research

The unexplained high levels of statistical heterogeneity point to a need for future studies to investigate attachment level change. Many population-based studies collect data from six sites per tooth and from all teeth other than third molars. We recommend this as part of developing a standardised data set as proposed for reporting periodontitis prevalence [62]. Standardised statistical analysis will be equally important. Important key limitations of the existing data are the presentation chiefly of the difference in full mouth mean attachment level between baseline and final evaluations. Even though some studies report little impact on the method of analysis [42], we recommend instead data analysis based on the change in attachment level for each site at each time

point still present [29, 49, 72]. This would reduce the tendency to underestimate change from the loss of teeth due to periodontitis. Employing repeated follow-up, perhaps annually, rather than one final assessment after several years might also help to prevent this effect, although this would be impractical for large epidemiological studies.

However, since many sites will show no or minimal change, calculating a full-mouth mean value will both lose information and not adequately characterise periodontal health. A consensus on more meaningful data presentations is urgently required and could include separate estimation of change for regressing and progressing sites (above an arbitrary threshold of for instance 3 mm) as well as the proportion of sites affected or, if the data are normally distributed, mean values per centile. A per centile based analysis (on tertiles, quartiles, quintiles etc) might help to dissect the within population variation of periodontal disease as well to understand, if there is a link between periodontal health and tooth loss.

Characterising participants at baseline by diagnosis i.e. periodontitis and non-periodontitis is challenging. Firstly, gingivitis and periodontitis are increasingly viewed as part of a continuum [1] and therefore an arbitrary threshold for diagnosis might lack validity. This is highlighted by the high prevalence values of at least mild forms of periodontitis which typically affect almost half of most populations [6-8]. Similar difficulties exist with case definitions for other chronic conditions such as hypertension, diabetes etc. For these conditions, case definitions are based on natural history/treatment studies, where subjects beyond a certain threshold have different health/treatment outcomes. As an analogy for periodontitis, a starting point might be to look across cohorts to determine whether there are subjects with a certain baseline periodontal status, who go on to lose more attachment and teeth and then define them as periodontally “healthy or severe”.

In addition to periodontal data, a consensus is required for a standardised data set of potential modifiers of attachment level change including certain oral microbiomes, genetic factors, lifestyle, general health and socioeconomic measures [62].

Finally, tooth loss, as a measure of periodontitis progression requires further research. Prevention of tooth loss is arguably the chief objective of prevention and treatment of periodontitis and is implicit in definitions of oral health [73]. Although this parameter would potentially seem to be ideal in terms of being an objective measure and a true endpoint for assessing the impact of periodontal diseases [74], the many contributors to tooth loss/retention (e.g. patient preference, caries, dental

professional treatment planning) complicate the interpretation of the data currently beyond very general observations. Further modelling in both existing data sets and in future research studies might help to unravel the associations between periodontal health and tooth loss.

Conclusions

Within the many limitations of the data, it is possible to conclude that mean annual attachment level change is highly variable both within and between populations. The differences in magnitude of mean annual change are clinically important representing progression values potentially commensurate with tooth retention over a lifetime to tooth loss within three decades. Only geographical location or ethnic status, a likely proxy for socioeconomic position (and its associated risk determinants), showed evidence of a statistically significant effect on mean change. Most of the substantial statistical heterogeneity between studies could not be explained from available data. Overall, the evidence does not support or refute the differentiation between forms of periodontal diseases based upon progression of attachment level change in adults (18 years of age or greater).

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Table 1. Chief characteristics of included studies.

Location Study	Sample Age Gender Random sample Duration Number at follow-up Periodontal classification at baseline Baseline year	A.L. measurement Sites per tooth Full-mouth/partial Manual/controlled force probe Analysis accounting for tooth loss effects: Only sites present at baseline and follow-up All sites NR/unclear Other comments	Attachment level change (Values represent attachment loss, + represents attachment gain)	Tooth loss	Bone level change
Tecumseh, Michigan USA Ismail et al. 1990 Burt et al. 1990	**Sample:** Tecumseh City, Michigan, USA **Age:** unclear original epidemiological study was >4 years - for the dental studies needed to have permanent teeth. **Gender:** NR **Random sample:** Unclear **Duration:** 28 years **Number at follow-up:** 801 residents (out of around 8,000) received dental examinations, 550 had permanent teeth at baseline. Table 1 indicates: Baseline N=526: 28 years: N=165 **Periodontal classification at baseline:** NR **Baseline year:** 1959	Follow-up 28 years 4 sites per tooth, full mouth Manual probe NR	**Mean annual attachment loss** Overall: 0.04mm/yr (no variance given) **Mean attachment loss** Overall: 1.12mm SD 0.85 N=165 Per age decade: Year of birth N Mean CAL change (SD) 1945-1954 58 0.88 (0.66) mm 1935-1944 36 1.21 (1.15) mm 1925-1934 49 1.23(0.78) mm 1900-1924 33 1.34 (0.78) mm 'differences not statistically significant'	Mean tooth loss at 28 years: N Mean tooth loss, 95% CI Dentate 90 3.2, 2.2,4.2 Edentulous 28 18.1, 15.5, 20.7 Number of teeth lost after 28 years in those with at least 2mm attachment loss: Person No. teeth lost 1 10 2 0 3 14 4 0 5 0 6 0 7 0 8 9 9 18 10 3	

				11 1 12 1 13 19 14 0 15 18 16 4 17 0 18 14 19 7 20 17 21 7 22 3	
Norway & Sri Lanka Loe et al. 1978a,b Hujoel et al. 1998	**Sample:** Norway: sample from high schools and population census database Sri Lanka: Tamil tea labourers working in Sri Lanka **Age:** At baseline: 17-35+ years **Gender:** All male **Random sample:** Unclear **Duration:** up to 7 years **Number at follow-up: Norway** Baseline 565 1-2 yr 381 3 yr 292 6-7yr 245 **Number at follow-up: Sri Lanka** Baseline 480 1-2 yr 422 3 yr 370 6-7yr 228 CAL, follow-up 6, 7, 15, 19, 20, 23, 26 years **Periodontal classification at baseline:** NR **Baseline year:** Norway 1969, Sri Lanka 1970	Initially M&B, then D& L added Full-mouth Manual probe N/R	**Mean annual attachment loss (mm)** (no variance reported) **Norway** Age Period Mesial Buccal N 17-23 0.09 0.14 21 19-25 0.10 0.13 13 21-27 0.06 0.11 26 23-29 0.05 0.09 37 25-31 0.07 0.09 26 27-33 0.07 0.08 22 29-35 0.08 0.11 13 31-37+ 0.08 0.12 9 **Sri Lanka** Age period Mesial Buccal N 15-21 0.18 0.18 17 17-23 0.22 0.21 18 19-25 0.23 0.23 28 21-27 0.24 0.24 24 23-29 0.25 0.22 28 25-31 0.26 0.21 25 27-33 0.24 0.23 22 29-35 0.28 0.25 18 31-37+ 0.29 0.21 16 N=number that participated in all surveys	Mean tooth loss for subjects participating in first and last examinations N No. teeth lost Norway 24 527 6 yr rate 0.11 Sri Lanka 228 169 7 yr rate 0.72 Hujoel et al. 1998 Norway Total of 188 teeth in 98 subjects lost over 26 years. Mean number of teeth lost per subject: 0.39, SD 1.02 No. teeth lost No. participants (N total=487) 0 389 1 53 2 24 3 9 4 7 5 3 6 1 11 1	
Norway Schatzle et al. 2003	Re-analysis of Loe et al. 1978	Initially M&B, then D& L added Full-mouth	**Mean annual attachment loss (mm)** Age N Mean mm/yr SE		

		Unclear	<20 65 0.0863 0.0100 20–24 317 0.1023 0.0079 25–29 351 0.0721 0.0080 30–34 291 0.0911 0.0069 35–39 181 0.0474 0.0055 40–44 128 0.0455 0.0044 45–49 140 0.0519 0.0042 50–54 61 0.0408 0.0053 55–59 23 0.0612 0.0135		
Sri Lanka Loe et al. 1986	**Rapid progression:** (1) < 21 years, minimum of 4 mm loss of attachment on at least 2 permanent molars and incisors, one of which must be a first molar. No more than 2 teeth other than first molars and incisors should have 5 mm loss of attachment, or (2) A subject before the age of 30 must have at least 8 teeth missing due to periodontal disease or with loss of attachment of 5 mm or more. At least 3 of the diseased or missing teeth should be other than first molars or incisors. **No progression:** Subjects with loss of attachment ≤2 mm on any mesial surface at any survey **Moderate progression** All other subjects	Initially M&B, then D& L added Full-mouth N/R	**Mean annual attachment loss (mm)** Age period RP(N) MP(N) NP(N) 14-19 0.13(23) 0.05(178) 0.05(86) 20-24 0.46(7) 0.11(381) 0.05(65) 25-29 1.04(46) 0.29(403) 0.09(18) 30-34 0.73(22) 0.14(314) 0.05(5) 35-39 0.97(7) 0.09(141) 0.04(1) 40-44 0.60(4) 0.07(62) 45 0.52(6) **RP: Rapid progression:** **MP: Moderate progression:** **NP: No progression:**	Mean annual tooth loss Age period RP MP NP 14-19 0.03 0.11 0.12 20-24 0.40 0.02 0.12 25-29 1.43 0.12 0.10 30-34 1.00 0.04 0.10 35-39 2.33 0.27 0.00 40-44 2.33 0.08 45 0.71 RP: Rapid progression: MP: Moderate progression: NP: No progression:	
Sri Lanka Neely et al. 2001	Only those attending both baseline and 20 year follow-up N=154, not whole sample. Analyses of participants that completed at least 2 assessment	Initially M&B, then D& L added Full-mouth All teeth	**Mean attachment level (mm)** Mean SD N BL 1.0 1.1 154 1year 1.2 1.1 140 3year 1.3 1.3 146 7year 2.7 1.4 114		

	(N=455) with this subset showed similar findings		12 years 3.4 1.8 119 15year 3.7 1.7 145 20 year 5.0 2.0 154 Regression analysis: Statistically significant effects for age, calculus, gingival index but not for smoking or plaque		
Baltimore, USA Ship & Beck 1996	**Sample:** Volunteer participants from Baltimore Longitudinal Study of Ageing. Community-dwelling, non-smoking white, middle socioeconomic class. **Age:** 29-76 **Gender:** Male N=18, female N=12 **Random sample:** No **Duration:** Mean follow-up 10.5 years, range 8-12 years **Number at follow-up:** Number at baseline not reported. Only those followed up included in study N=95 **Periodontal classification at baseline:** NR **Baseline year:** 1978-1981	Sites per tooth: 2 sites (MB & B) Only six Ramfjord teeth Manual probe Only sites present at baseline and follow-up (author contact)	**Mean attachment level mm (SD)** Baseline: 3.49mm (0.16) 10 years: 3.14mm (0.11)	***Tooth loss at follow-up** 13 teeth in 9 subjects ***Only Ramfjord teeth examined**	
Virginia Commonwealth University, USA Gunsolley et al. 1995	**Sample:** Virginia Commonwealth University Clinical Research Center or Dental Clinic. **Age:** Age: Localised juvenile periodontitis (LJP) ≤30 years, severe periodontitis (SP) ≤35 years **Gender/ethnicity:** at baseline: Black Male Female LJP 81% 35% 65%	Sites per tooth: 4 sites; MB, B, DB, ML Full-mouth not 3rd molars Manual probe NR	**Mean change in attachment level** **Severe periodontitis** All patients 0.27 mm (SE 0.15) Treated patients: 0.35mm (SE 0.20) Untreated patients: 0.15mm (SE 0.23) **Localised juvenile periodontitis** All patients: First molars and incisors only: 0.02mm (SE0.09) Other teeth: 0.11mm (SE 0.05) Treated patients: First molars and incisors only: -0.24mm (SE 0.13)	**Mean tooth loss per subject at follow-up** **Severe periodontitis** Untreated patients: 0.65 (SE 0.42) N=20 **Localised juvenile periodontitis** Untreated patients: 0.00 (SE 0.00) N=21	

	SP 83% 51% 49% **Random sample:** No, all periodontitis **Duration:** Follow-up: Days (SE) Days **LJP** All 1146 (143) Treated 1288 (198) Untreated 1018 (208) **SP** All 1562 (175) Treated 1317 (270) Untreated 1905 (229) **Number at follow-up:** Baseline Recall **LJP** All NR 40 Treated NR 19 Untreated NR 21 **SP** All NR 48 Treated NR 28 Untreated NR 20 **Localised juvenile periodontitis (LJP):** ≤30 years with localised severe disease on 1st molar or incisor and up to 2 additional teeth **Severe periodontitis (SP):** ≤35 years generalised disease including attachment loss on ≥8 teeth, ≥3 teeth not first molars/incisors **Periodontal classification at baseline:** Periodontitis Some participants treated for periodontitis **Baseline year:** N/R ?early 1980s		Other teeth: 0.03(SE0.07) Untreated patients: First molars and incisors only: 0.24mm (SE 0.13) Other teeth: 0.18mm (SE 0.07)		
Gusheng village, China Baelum et al. 1993 Baelum et al. 1997 Wu et al. 2001 Ouyang et al. 2004 Dahlen et al. 1995	**Sample:** Gusheng village, Beijing district, China. **Age:** 20-80 years, even distribution across ages **Gender:** even sampling male/female except older age groups: 60-70+: Male: 130 (69.5%)	All surfaces All teeth Manual/controlled force probe: NR N/R	**Mean attachment loss mm, SD** Overall: 10 years: 1.67mm (0.88) **Mean attachment loss different ages at 10 years, mean, SD:** 20-29y: 1.58mm (0.72) N=77 30-39y: 1.45mm (0.73) N=93 40-29y: 1.72mm (0.81) N=86	**Mean tooth loss per subject at 10 years, SD** Age 30yrs: 1±1.7 Age 60yrs: 7.2±5.1 **Mean tooth loss per subject best/worst groups at 10years, mean per person**	

	Female: 57 (30.5%) **Random sample:** Yes overall. Sub-sample, ≥16 teeth present, age 55-69, as different as possible from rest of age group with attachment loss ≥6mm and pockets ≥4mm 'Best N=30 & 'Worst N=30' **Duration:** 10 years **Number at follow-up:** Baseline: N=587 10 years (dentate) N=398 **Periodontal classification at baseline:** NR **Baseline year:** 1984		50-59y: 1.81mm (1.18) N=67 **Mean attachment loss best/worst groups at 10years, mean, SD:** Best: 1.21mm, 0.54 Worst: 1.36mm, 0.93	Best: 1.8 Worst: 5.3	
Java, Indonesia Timmerman et al. 2000 Van der Velden et al. 2006	**Sample:** Malabar/Poerbasari tea estate, Western Java low educational level no regular dental care. **Age:** 15-25 years (mean age 20 years, SD 3.2 **Gender:** At baseline: Male 50.9%, female 49.0% **Random sample:** All subjects participated at baseline **Duration:** Follow-up 7 years, 15 years **Number at follow-up:** Baseline: N=255 7 years: N=167, data analysed for 160, 7 excluded as all sites showed attachment loss at baseline 15 years: N=128 (the other 127 subjects were older p<0.001) **Periodontal classification at baseline:** NR **Baseline year:** 1987	Approximal sites only Full-mouth Manual probe for recession, controlled force probe for probing depth Only sites present at baseline and follow-up	**Mean attachment loss per patient (SD)** Baseline: 0.33mm (SD 0.3) mm (n=255) 7 years: 0.72mm (SD 0.49) (n =155 from Timmerman et al. 2000) 15 years 1.97 (SD 1.01) mm. (n=128) **Mean annual attachment loss per patient** 0.05mm during the first 7 years of observation 0.15mm during the following 8 years	Mean number of teeth present at each follow-up: Mean no. teeth (SD) Baseline 27.5 (SD 1.01) 7 year follow up 26.9 (SD 1.55) 15 year follow up 25.9 (SD 2.41) NPDS (non-progressing subjects) N=30, 21 females 9 males, Baseline 27.5 (SD 1.1) 7 years 27.0 (SD 1.6) PDS (progressing subjects) N=130, 66 females 64 males Baseline 27.4 (SD 1.1) 7 years 26.9 (SD 1.5) Progressive disease subjects (PDS): >1 site that lost attachment >2 mm. Non-progressive disease subjects (NPDS): All other subjects	
Piedmont, USA Brown et al. 1994	**Sample:** Community, Piedmont, North Carolina	Sites per tooth: 2, (B & MB)	**Mean attachment loss** Unpublished data Beck et al. 2016	**Mean tooth loss per subject (SE) at 3 years**	

Beck et al. 1995 Beck et al. 1997 (Unpublished data Beck et al. 2016) Drake et al. 1995	**Age:** ≥65 years **Gender:** Male Female Baseline NR NR 5 years 118 174 **Random sample:** Yes, stratified (white & black (black over-sampled) **Duration:** 5 years **Number at follow-up:** Follow-up dentate (N, %): Black White Baseline 448 (55.3) 362 (44.7) 18 months 263 (53.4) 229 (46.5) 5 years 150 (51.4) 142 (48.6) **Periodontal classification at baseline:** NR **Baseline year:** 1988	Full-mouth Manual probe All sites in publication. Unpublished data only sites present at baseline and follow-up provided by authors	Only sites present at baseline and follow-up **Mean attachment change at 5 years, (SD), N** **All patients** Overall: 0.2mm (0.86) N=292 **Ethnicity** White: 0.03mm (0.59) N=142 Black: 0.37mm (1.03) N=150 **Gender** Male: 0.15mm (0.83) N=118 Female: 0.24mm (0.88) N=174 All sites **Mean attachment change at 5 years, (SD), N** **All patients** Overall: 0.04mm (0.79) N=292 **Ethnicity** White: +0.05mm (+0.66) N=142 Black: 0.12mm (0.90) N=150 **Gender** Male: +0.01mm (+0.82) N=118 Female: 0.07mm (0.77) N=174 **Sites that lost ≥3mm attachment only** **Mean attachment loss at 18 months, (SE), N** Overall: 3.43mm (0.06) N=260 **Ethnicity** White: 3.37mm (0.08) N=106 Black: 3.54mm (0.06) N=154	White: 0.9 (0.2) N=228 Black: 2.2 (0.3) N=263	

			Gender Male: 3.42mm (0.06) N=115 Female: 3.43mm (0.08) N=145 **Age** 65-69y: 3.45mm (0.11) N=93 70-74y: 3.36mm (0.05) N=87 75-79y: 3.61mm (0.16) N=46 ≥80y: 3.30mm (0.1) N=34 **Education** <12 years 3.48mm (0.06) N=164 ≥12 years 3.39mm (0.11) N=89 **Black**: 65-69y: 3.36mm (0.12) N=53 70-74y: 3.55mm (0.09) N=52 75-79y: 3.49mm (0.11) N=29 ≥80y:3.52mm (0.20) N=20 **White**: 65-69y: 3.4mm (0.15) N=40 70-74y: 3.25mm (0.06) N=35 75-79y: 3.66mm (0.24) N=17 ≥80y:3.21mm (0.12) N=14 **Mean attachment loss at 3 years** Overall: 4.45mm (no variance) White: 4.3mm (0.47) N=169 Black: 4.5mm (0.48) N=169		
Erie County, USA Machtei et al. 1999	**Sample:** Subsample of Erie County Study, USA, not exhibiting severe attachment loss at baseline (interproximal attachment loss<6mm & pocket depth <5mm in ≥1mm site). **Age:** Mean age 52.17 (27-67 years) **Gender:** Of subsample, male 183 (44%), female 232 (56%) **Random sample:** No **Duration:** 5 years	Sites per tooth: 6 Full-mouth not 3rd molars Controlled force probe NR	Mean annual change in attachment level per year 0.12mm, SE 0.08	**Mean tooth loss per subject at 5 years:** 0.4 teeth/patient (range 1 to 11 teeth lost). **Total tooth loss at 5 years** 164 teeth lost in 86 individuals.	**Mean change in bone level per year** 0.04mm, SE 0.00

	Number at follow-up: Number at follow-up: 985 subjects eligible from initial sample, 415 completed all examinations Ethnicity: 95.6% white Caucasian, 3.1% African American Smoking: 40.5% former, 44.1% never, 15.4% current **Periodontal classification at baseline:** Mixed, gingivitis and periodontitis **Baseline year:** N/R ?early 1990s				
Cheng-de China Suda et al. 2000 Pei, et al. 2015	**Sample:** Cheng-de, rural village China, total population **Age:** Inclusion age: 15-44 years **Gender:** Gender at year 2: Male: 43.9% Female: 56.1% **Random sample:** Yes **Duration:** 4 years **Number at follow-up:** Numbers at baseline: N=486 2 year follow-up: N=310 4 year follow-up: N=413 **Periodontal classification at baseline:** NR **Baseline year:** 1992	2 quadrants randomly selected 6 sites per tooth Manual probe N/R	**Mean annual attachment loss:** Overall: 0.065mm/year (no variance given) **Mean attachment level mm, SD** Baseline: 1.57mm, 1.14 N=486 Year 4: 1.83mm, 1.38 N=413	**Mean tooth loss per subject at 4 years** 0.5 teeth/person	
Buffalo, USA OsteoPerio, LaMonte 2013	**Sample:** Community Sub-sample from Women's Health Initiative Observational Study (WHI-OS), greater Buffalo metropolitan area. **Age:** Post-menopausal women, 50-79 years **Gender:** Women **Random sample:** Unclear **Duration:** Follow-up 5 years	6 sites per tooth Full-mouth not 3rd molars Manual probe for recession, controlled force probe for probing depth	**Mean change in attachment level at 60 months** All sites: +0.06mm SD 0.58mm, 95% CI 0.03, 0.10, n=995 Matched sites: +0.03mm, SD 0.57, 95% CI 0.03, 0.10, n=995 Worst site (interproximal sites only): All sites: +0.11mm SD1.89, 95%CI 0.01, 0.23	**Mean tooth loss per subject at 5 years** Mean, SD 95% CI N Overall 0.53, 1.21 0.45,0.60 1,025 Extraction for periodontal reasons 0.10, 0.66 0.06, 0.14 1,020	**Overall mean bone loss** 0.19mm, SD 0.49, 95% CI 0.22, 0.16 **Mean bone loss of patients experiencing thresholds levels of bone deterioration** Threshold N Mean (SD) ≥0.52 mm 948 0.84(0.34) ≥2.00 mm 76 3.23(1.70)

	Number at follow-up: Baseline: 1,362 Follow-up: 1,025 **Periodontal classification at baseline:** NR **Baseline year:** 1997-2001	Both all teeth and only matched sites (i.e. teeth present at baseline and follow-up) analyses. Little difference noted. Periodontal disease status based on CDC/AAP definition [75]	Matched sites: 0.02mm, SD1.77, 95% CI: -0.13, 0.09 **Smoking** Never: (n=555) Mean CAL progression +0.04mm SD 0.58 (0.01, 0.09) mm Ever: Mean CAL progression +0.08 – 0.59 (0.03, 0.14) mm P value= 0.261 **Periodontal disease status** None: (n=172): +0.09mm, SD 0.50, 95% CI 0.03, 0.15) Mild/moderate: (n=515): +0.09mm SD 0.53, 95% CI 0.05, 0.14 Severe: (n=260): 0.02mm SD 0.74, 95%CI 0.12, 0.07 **Age** <65years (n=494): 0.10mm SD 0.10, 95% CI 0.06, 0.15 ≥65years (n=531) 0.02mm, SD 0.63, 95% CI -0.03, 0.08		
West Pomerania, NE Germany SHIP Gatke et al. 2012 (Unpublished data Kocher et al. 2016)	**Sample:** SHIP study. Random population sample, West Pomerania, northeast Germany **Age:** 20-79 years **Gender:** Males: 48.0%, females: 51.9% **Random sample:** Yes **Duration:** 5 years **Number at follow-up:** N with periodontal exam Baseline: N= 3,555 5 years: N= 2,566 8 subjects excluded due to missing data, therefore 5 year data based on: N=2,558 **Periodontal classification at baseline:** NR **Baseline year:** 1997-2001	All sites Half-mouth (MB, B, DB & L) Manual probe Only sites present at baseline and follow-up	**Mean change mm, SD at 5years** **All** 0.10mm, 1.01 N=2558 **Age** 20-29: 0.20mm, 0.93 N=385* 30-39: 0.11mm, 1.01 N=581 40-49: 0.08mm, 1.00 N=575 50-59: 0.01mm, 1.01 N=558 60-69: 0.15mm, 1.03 N=348* 70-81: 0.16mm, 1.26 N=111 *P<0.05 compared with 50-59 age **Gender** Female: 0.06mm, 0.94 N=1330	**Total tooth loss at 5 years:** 2260 teeth Number of subjects: 2558 **Mean annual tooth loss at 10 years, SD:** All participants 0.15, 0.26 N=2,069 **Age** <30: 0.04, 0.12 N=313 30-50: 0.13, 0.24 N=965* >50: 0.23, 0.29 N=660* P<0.001 compared with age <30 yr, **Gender** Female: 0.13, 0.23 N=1,091 Male: 0.17, 0.29 N=978* *P=0.005 compared with female **Baseline periodontitis status [75]** No/mild: 0.06, 0.11 N=997 Moderate: 0.17, 0.26 N=725*	

			Male: 0.15mm, 1.08 N=1228* *P<0.05 compared with female **Smoking** Never 0.06mm, 0.97 N=960 Former 0.05mm, 1.02 N=855 Current 0.23mm, 1.05 N=743** ** p<0.01 compared with never **School education** <10 years 0.23mm, 1.11 N=709*** 10 years 0.09mm, 0.99 N=1338* >10 years -0.04mm, 0.90 N=511 *p,0.05, ***P<0.001 compared with >10yr **Diabetes** No: 0.09mm, 1.00 N=2438 Yes 0.39mm, 1.22 N=120** ** p<0.01 compared with No **Mean change mm, SD at 10 years** **All sites at baseline and follow-up** 0.07mm, 0.09 N=1,872 **Age** <30: 0.07mm, 0.07 N=301 30-50: 0.07mm, 0.09 N=911 >50: 0.07mm, 0.09 N=660 No statistically significant differences **Gender** Female: 0.07mm, 0.09 N=991	Severe 0.38, 0.38 N=347* *P<0.001 compared with no/mild **Diabetes** No: 0.14, 0.25 N=1,960 Yes 0.28, 0.36 N=109* *P<0.001 compared with no	

			Male: 0.08mm, 0.009 N=881* *P=0.02 compared with female **Baseline periodontitis status** [75] No/mild: 0.07mm, 0.07 N=940 Moderate/ Severe 0.07mm, 0.10 N=932* *P=0.03 compared with no/mild **Diabetes** No: 0.07mm, 0.08 N=1776 Yes 0.08mm, 0.11 N=96 No statistically significant differences		
Porto Alegre, Brazil Haas et al. 2012	**Sample:** Population sample, metropolitan area, Porto Alegre, Brazil **Age:** Age: 14–103 years (mean: 37.9, SD: 13.3) **Gender:** Males: 45.3%, females: 54.7% **Random sample**: Yes **Number at follow-up:** Baseline: N= 1,465 5 years: N= 697 (number who participated in both exams) Follow-up 5 years **Periodontal classification at baseline:** NR **Baseline year:** 2001	Al sites but data for mean attachment level interproximal only Full-mouth Manual probe Only sites present at baseline and follow-up	**Mean annual proximal attachment loss** **Data analysed for change both at worst interproximal site and all four interproximal sites combined** **No 'N' values given specifically for these data** All proximal sites: 0.10mm/yr SE 0.01 Worst proximal site: 0.31mm/yr SD 0.01 % subjects with different values No/Slight (≤0.1mm/yr): 16.1% Moderate (>0.1mm/yr - ≤0.5mm/y): 67.0% Rapid progression (>0.5mm/yr): 16.9% All Proximal Sites Mean SE P* **Age (years)** < 30 0.06 0.01 Ref 30-49 0.12 0.01 <0.001 50+ 0.12 0.02 <0.001 **Gender** Males 0.12 0.01 Ref Females 0.09 0.01 0.02 **Ethnicity** Whites 0.10 0.01 Ref	Mean tooth loss per participant at 5 years: Overall: 0.82, SE 0.07 Age<30 yr: 0.53, SE 0.08 Age≥50 yr: 1.14, SE 0.17	

			Non-Whites 0.12 0.02 0.20 **Socioeconomic status** High 0.09 0.01 Ref Medium 0.09 0.01 0.96 Low 0.13 0.01 0.003		
Sao Luis, Brazil Pereira et al. 2015	**Sample:** Postmenopausal women at Materno Infantil University Hospital, Sao Luis, Maranhao, Brazil **Age:** Age: 45-77 years **Gender:** Female **Random sample:** Unclear **Duration:** 3 years **Number at follow-up:** Baseline: 99 3 years: 33 **Periodontal classification at baseline:** NR **Baseline year:** N/R ?early 2010s	Sites per tooth: 6 sites Full-mouth not 3rd molars Manual probe N/R	**Mean attachment level (mm)** initial diagnosis normal bone with subcategories for 3 year bone condition. No variance reported N Baseline 3 years Normal 8 1.96mm 2.17mm Osteopenia 5 2.02mm 2.31mm Osteoporosis 2 1.50mm 2.80mm	N/R	
Reno, USA Harris 2003	**Sample:** Periodontist private practice – all patients referred for periodontitis **Age:** Age: Mean 50.0 years (28-70) **Gender:** Male N=18, female N=12 **Random sample:** No **Duration:** Mean follow-up 2.1 years (SD 0.9, range 1.0-4.1) **Number at follow-up:** Only those followed up included in study N=30 **Periodontal classification at baseline:** Periodontitis **Baseline year:** N/R	A.L. measurement Sites per tooth: 6 Full-mouth/partial: NR Manual probe N/R	**Mean annual change in attachment level** 0.32mm, SD 0.34 (range +0.32-1.58)	**Mean annual tooth loss per subject** 0.32 (SD 0.66, range 0 - 2.9)	

Table 2. Risk of bias (Newcastle-Ottawa Scale) and methodological quality of included studies

	Selection			Comparability	Outcome				
Study (ID)	Representativeness of exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Adequacy of follow-up of cohorts	NOS Total stars Max. 7	Security of measurement of attachment level	Security of measurement of bone level change
Cheng-de China Suda et al. 2000 Pei, et al. 2015	1*	1*	1*	1*	1*	4.	**5**	Secure	n/a
Dunedin, New Zealand Thomson et al. 2013 (30)	1*	1*	1*	1*2*	1*	2*	**7**	Secure	n/a
Gusheng village, China Baelum et al. 1997 (59) Dahlen et al. 1995 (21)	1*	1*	1*	3.	1*	2.*	**5**	Secure	n/a
Java, Indonesia Timmerman et al. 2000 (55) Van der Velden et al. 2006 (43)	2*	1*	1*	2*	1*	2.*	**7**	Secure	n/a
Niigata, Japan Hirotomi et al. 2002, 2010	1*	1*	1*	1*2*	1*	2.	**6**	Secure	n/a
Buffalo, USA OsteoPerio, LaMonte 2013 (65)	3	1*	1*	1*2*	1*	2.	**5**	Secure	Secure
Piedmont, USA Brown et al. 1994 (14) Beck et al. 1997 (8) Unpublished data	1*	1*	1*	1*2*	1*	2*	**7**	Secure	n/a
Porto Alegre, Brazil Haas et al. 2012	1*	1*.2.*	1*	n/a	1*	2*	**6**	Secure	n/a
Norway Loe et al. 1978 (58)	2*	1*	1.*	N/a	1.*	3.	**4**	Secure	n/a
West Pomerania, NE Germany SHIP Gatke et al. 2012 Kocher et al. 2016 (unpublished)	1*	1*	1*	1*2*	1*	2*	**7**	Secure	n/a
Tecumseh, Michigan USA Ismail et al. 1990	1*	1*	1*	3.	1*	3.	**4**	Secure	n.a
Virginia Commonwealth University, USA Gunsolley et al. 1995	3	1*	1*	3.	1*	4.	**3**	Secure	n/a
Single publication studies									
Reno, USA Harris 2003 (47)	3	1*	1*	2.*	1*	1*	**5**	Insecure	n/a
Erie County, USA Machtei et al. 1999 (1)	2*	1*	1*	1*2*	1*	3.	**6**	Secure	Insecure
Sao Luis, Brazil Pereira et al. 2015 (102)	3	1.*	1.*	2*	1*	3.	**4**	Secure	n/a
Baltimore, USA Ship et al. 1996 (67)	3	4.	4.	1*2*	1*	1*	**4**	Insecure	n/a

Table 3. Summary table of meta-analyses: Mean annual attachment level change

Analysis	Mean annual attachment level change (mm)	95% CI	Number of data sets	I^2 %
General population, including both full-mouth and partial-mouth recording	0.100	0.068, 0.13	13	99
Only interproximal sites	0.093	0.022, 0.16	6	99
Only periodontitis	0.57	-0.38,1.51	5	99
Post-menopausal women	0.052	-0.084, 0.19	2	89
Subgroup analyses				
Effect of geographical location				
North America & Europe	0.056	0.025, 0.087	8	99
Sri Lanka & China only	0.20	0.15, 0.26	5	82
Difference between North America/Europe and Sri Lanka & China, p<0.001				
Effect of gender				
Males only	0.067	0.023, 0.11	2	50
Females only	0.070	0.064, 0.076	2	0
Difference between males and females, p=0.893				
Effect of age				
Age <30 years	0.12	0.068, 0.16	8	99
Age 30-50 years	0.074	0.052, 0.096	5	95
Age >50 years	0.13	0.072, 0.19	4	98
Difference between age groups, p=0.093				

Table 4. Quintiles of mean annual attachment change

Study	SD (mm)	n	Mean annual attachment level change (mm)	1st quintile (mm)	2nd quintile (mm)	3rd quintile (mm)	4th quintile (mm)
Kocher et al. 2016	0.09	1892	0.07	-0.0058	0.047	0.093	0.15
Loe et al. 1978 Norway Mesial	0.077	167	0.07	0.0048	0.050	0.089	0.14
Loe et al. 1978 Norway Buccal	0.092	167	0.10	0.027	0.081	0.13	0.18
Loe et al. 1978 Sri Lanka Mesial	0.071	196	0.24	0.18	0.22	0.26	0.30
Loe et al. 1978 Sri Lanka Buccal	0.071	196	0.22	0.16	0.20	0.24	0.28
Schatzle et al. 2003	0.068	1557	0.054	-0.0036	0.037	0.071	0.11
Neely et al. 2001	0.67	114	0.24	-0.32	0.072	0.41	0.81
Ismail et al. 1990	0.066	165	0.04	-0.016	0.023	0.057	0.096
Baelum et al. 1997, Dahlen et al. 1995	0.28	323	0.17	-0.067	0.097	0.24	0.40
Thomson et al. 2003	0.033	831	-0.0034	-0.031	-0.012	0.0049	0.024
Beck et al. 1997	0.39	292	0.04	-0.28	-0.058	0.14	0.36
Suda et al. 2000 Pei et al. 2015	1.79	413	0.065	-1.44	-0.39	0.52	1.57
Machtei et al. 1991	1.63	415	0.12	-1.25	-0.29	0.53	1.49
Overall mean				**-0.23**			**0.45**
Post-menopausal women							
LaMonte 2013 Osteoperio Buffalo	0.26	995	-0.012	-0.23	-0.078	0.054	0.21
Pereira 2015	0.15	15	0.13	0.0018	0.089	0.17	0.25
Overall mean				**-0.11**			**0.23**
Interproximal sites only							
Haas et al. 2012	0.26	697	0.1	-0.12	0.033	0.17	0.32

Timmerman et al. 2000 , Van der Velden et al. 2006	0.19	155	0.056	-0.10	0.0086	0.10	0.21
Smith et al. 1995	0.29	264	0.014	-0.23	-0.059	0.088	0.26
Loe et al. 1978 Norway Mesial	0.077	167	0.07	0.0048	0.050	0.089	0.14
Loe et al. 1978 SriLanka Mesial	0.071	196	0.24	0.18	0.22	0.26	0.30
Kocher et al. 2016 (SHIP)	0.11	1872	0.07	-0.023	0.042	0.099	0.16
Overall mean				**-0.048**			**0.23**
Only periodontitis							
Brown et al. 1994	0.79	260	2.3	1.62	2.09	2.48	2.95
Harris 2003	0.34	30	0.32	0.034	0.23	0.41	0.61
Gunsolley et al. 1995 SP	0.45	20	0.066	-0.31	-0.048	0.18	0.44
Gunsolley et al. 1995 LJP	0.36	21	0.086	-0.21	-0.0044	0.18	0.39
Kocher et al. 2016 (moderate & severe disease)	0.1	932	0.07	-0.014	0.044	0.095	0.15
Overall mean				**0.22**			**0.91**

Table 5. Summary table of meta-analyses: Mean annual tooth loss

Analysis	Mean annual tooth loss	95% CI	Number of data sets	I^2 %
General population. studies	0.20	0.13, 0.26	10	91
Subgroup analyses				
North America, Europe, Japan & Oceania	0.21	0.10, 0.33	6	94
South America & Asia	0.19	0.11, 0.28	4	82
Difference between groups P=0.80				

Table 6.
Mean annual bone level change (mm). Single studies (no meta-analysis)

Study	n	SD	Mean	95% CI LL	95%CI UL
General population excluding severe periodontitis					
Machtei et al. 1999	415	.002*	.04	.04	.04
Post-menopausal women					
LaMonte et al. 2013	1025	.219	.038	.025	.051

*SE given as 0.00 taken as 0.0001

Figure 1. Flowchart of inclusion of studies.

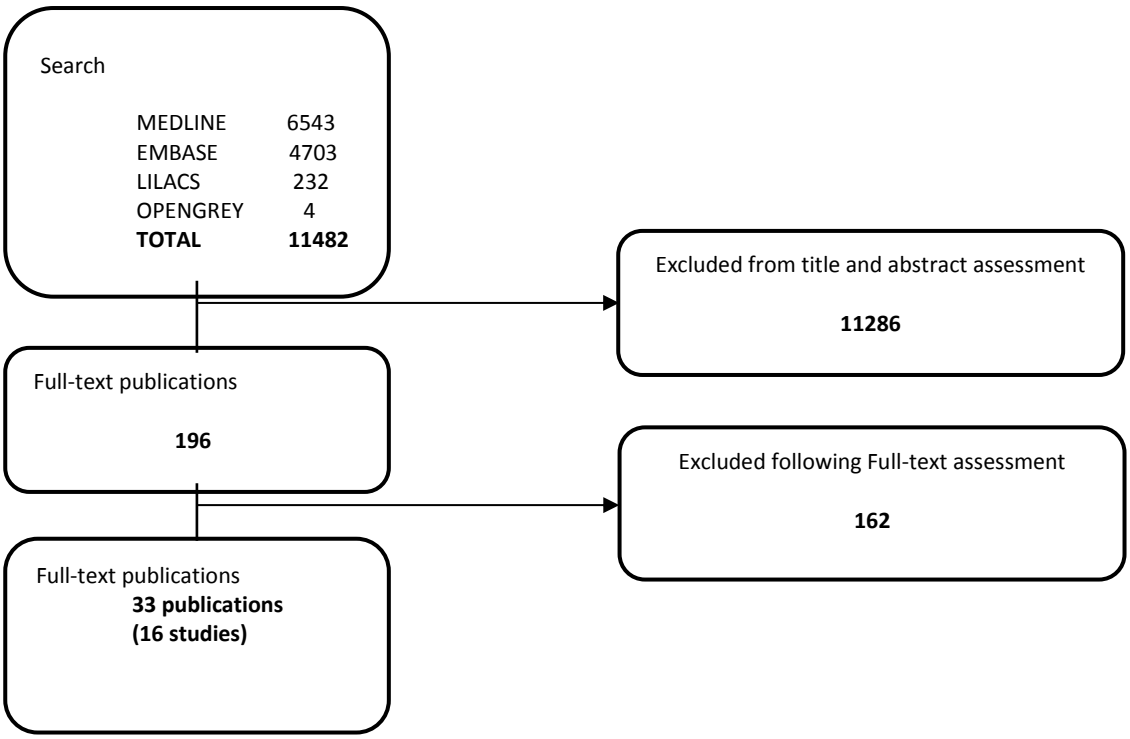


Figure 2. Random effects of meta-analysis: Mean annual attachment level change

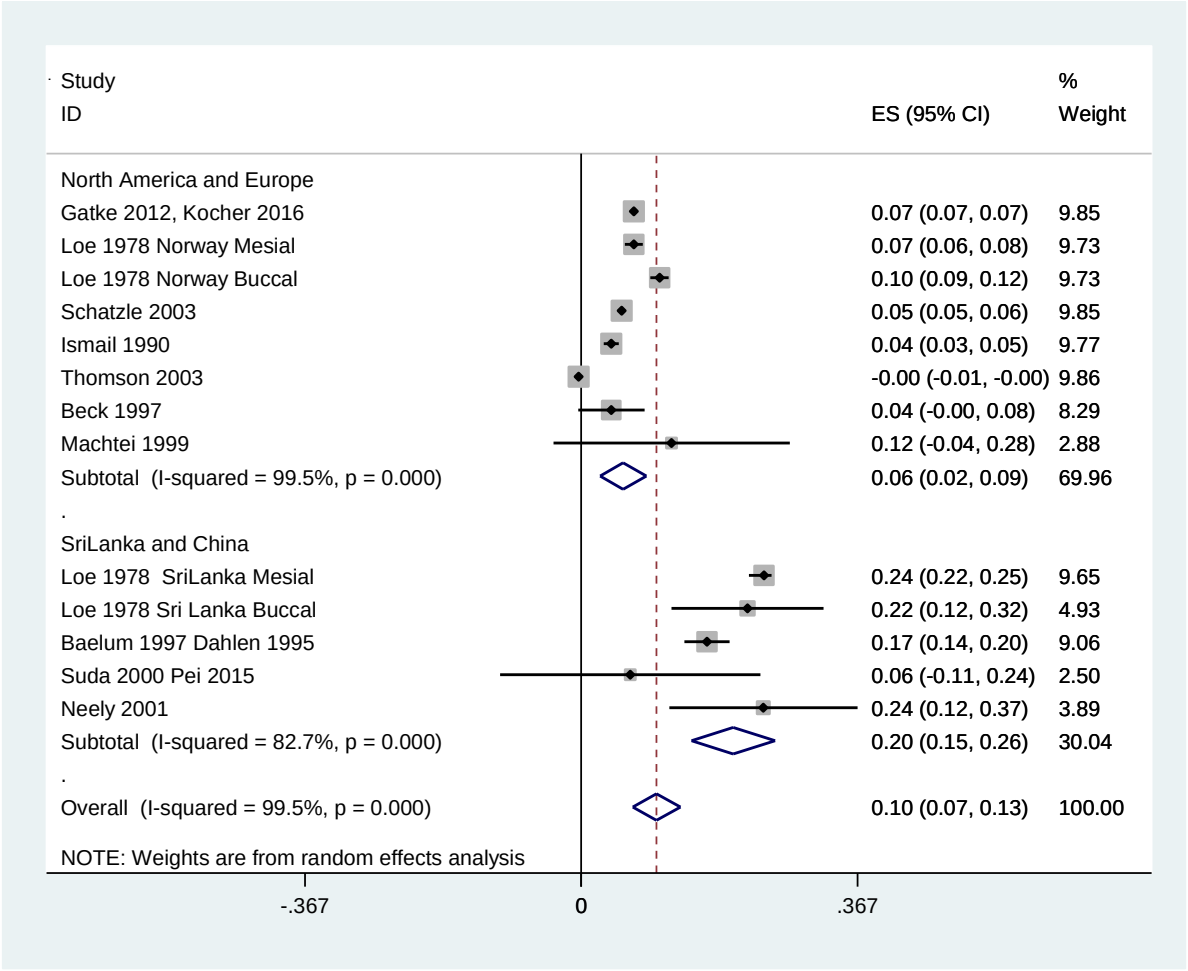


Figure 3. Random effects of meta-analysis: Mean annual attachment level change interproximal sites only

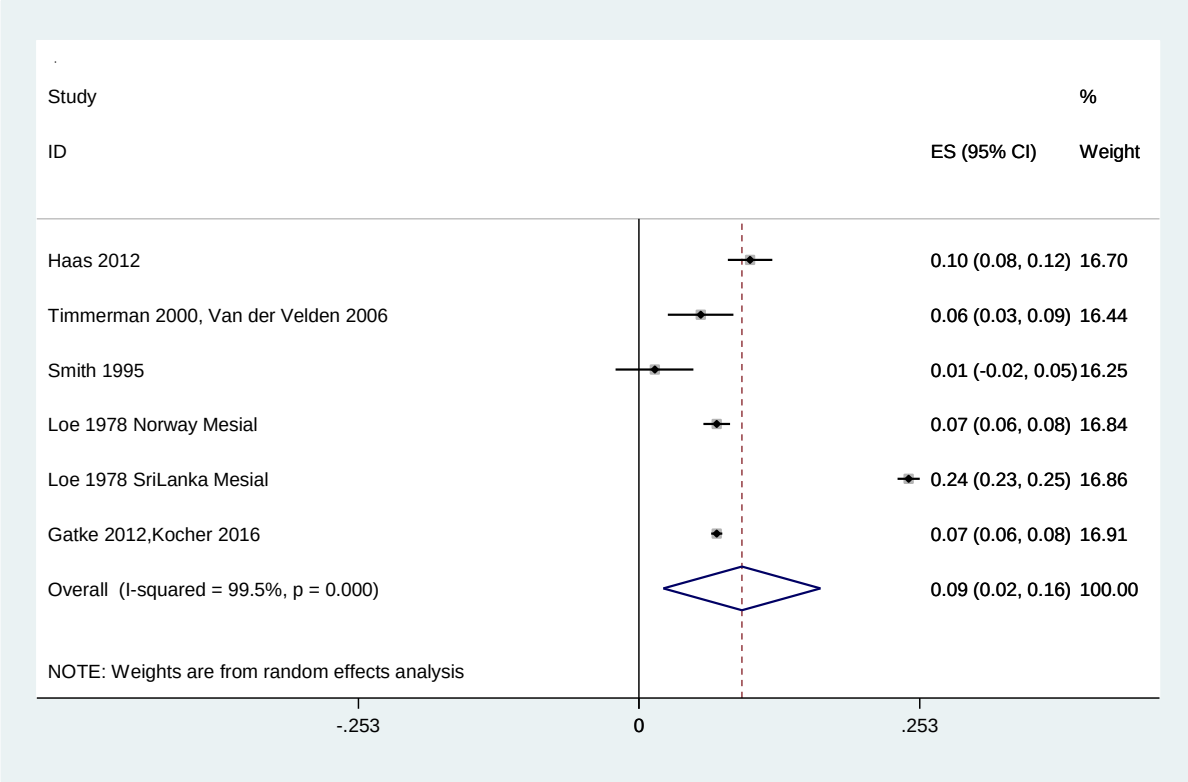


Figure 4. Random effects of meta-analysis: Mean annual attachment level change, periodontitis only.

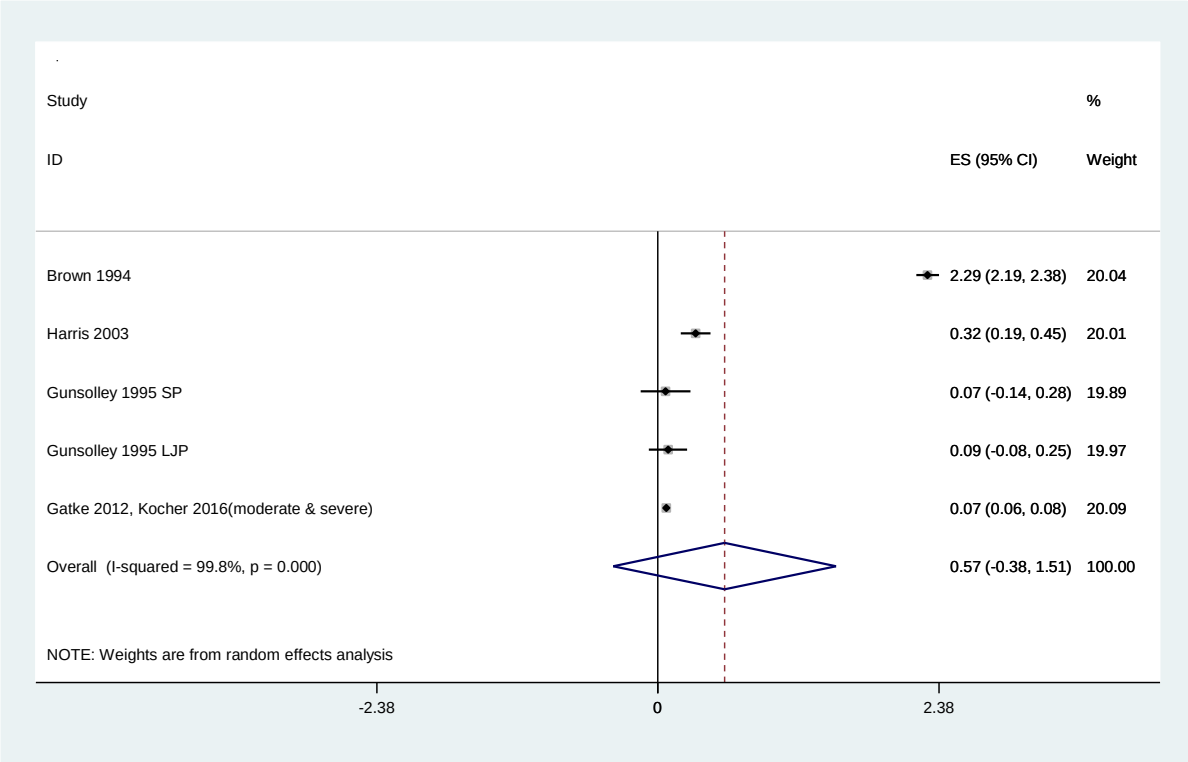


Figure 5. Random effects of meta-analysis: Mean annual attachment level change, post-menopausal women only.

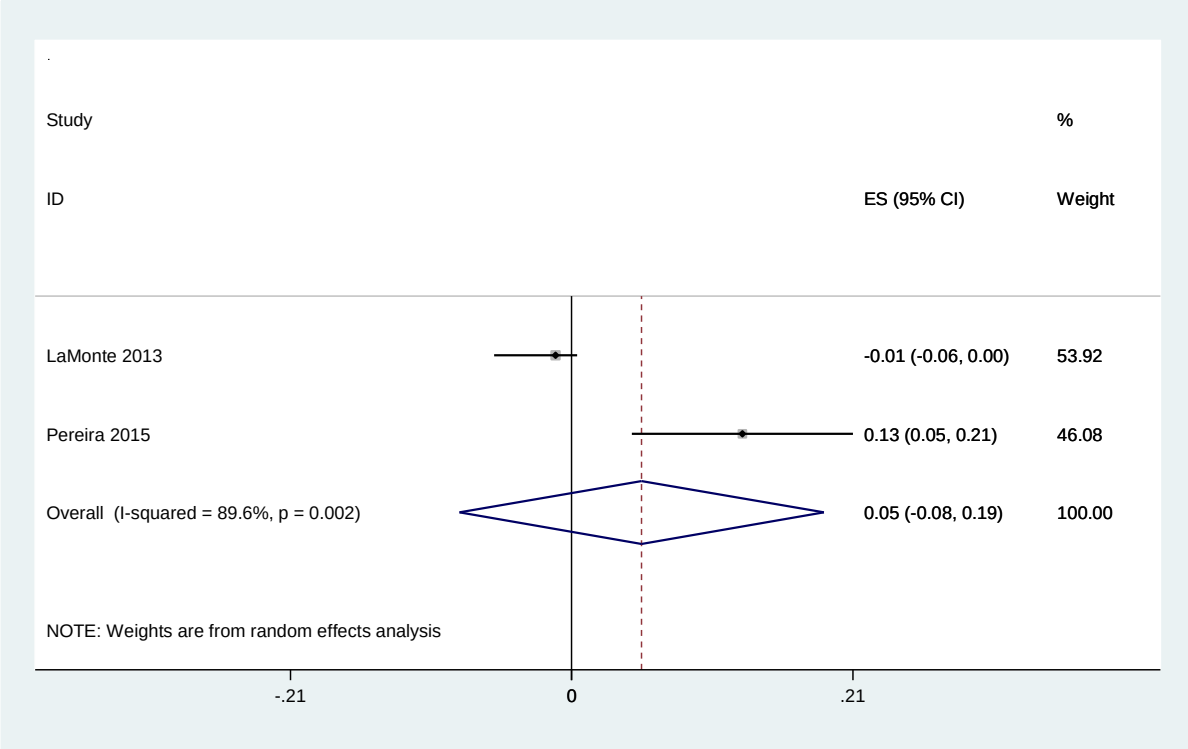


Figure 6. Random effects of meta-analysis: Mean annual attachment level change, subgroup analysis, effect of gender

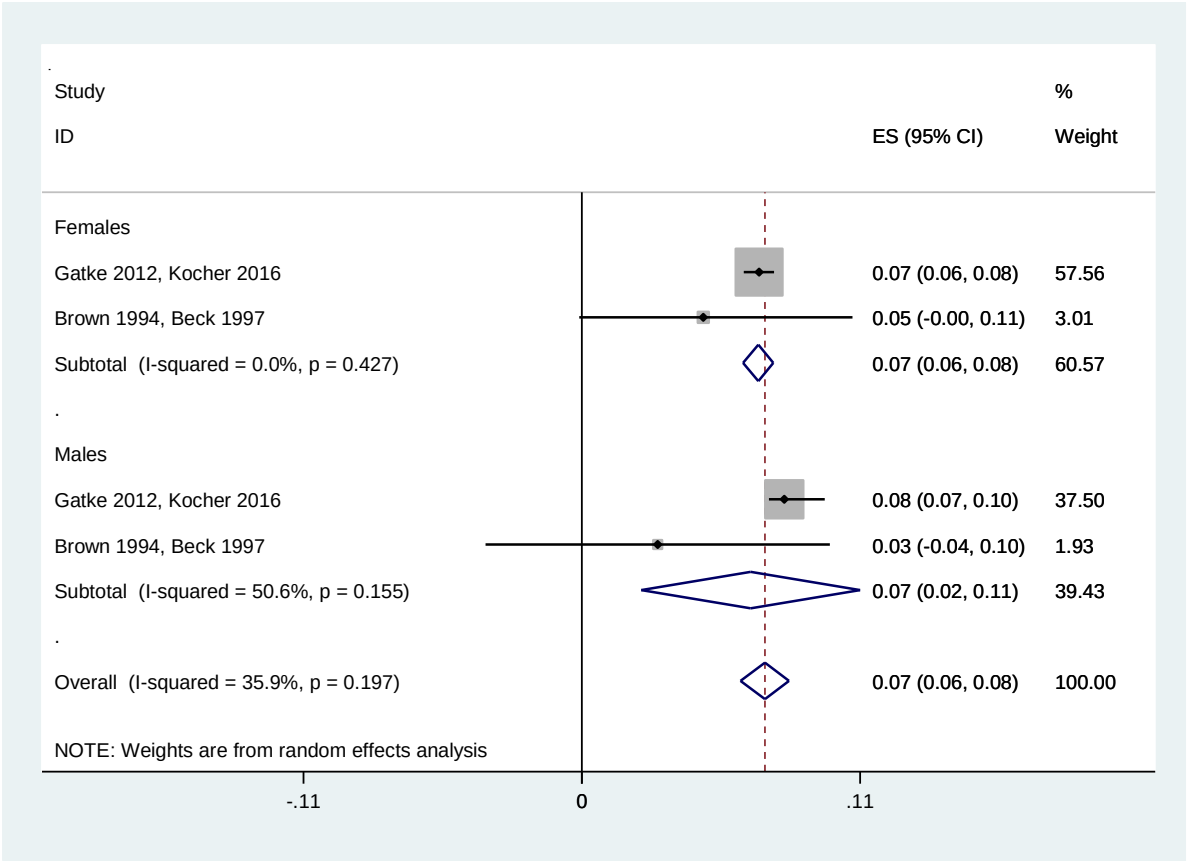


Figure 7. Random effects of meta-analysis: Mean annual attachment level change, subgroup analysis, effect of age

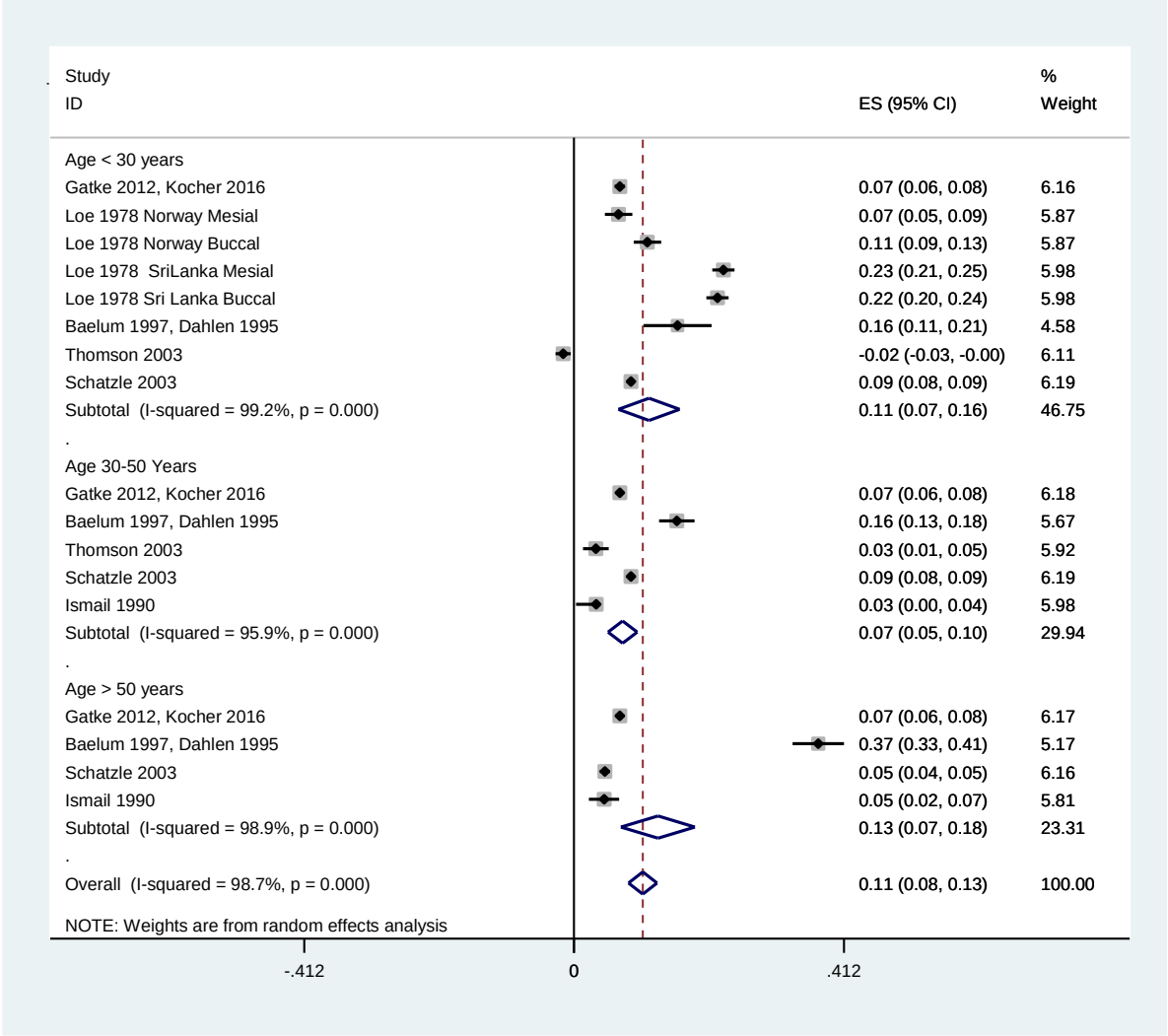


Figure 8. Distribution (with means) of highest and lowest quintiles, mean annual attachment level change (mm)

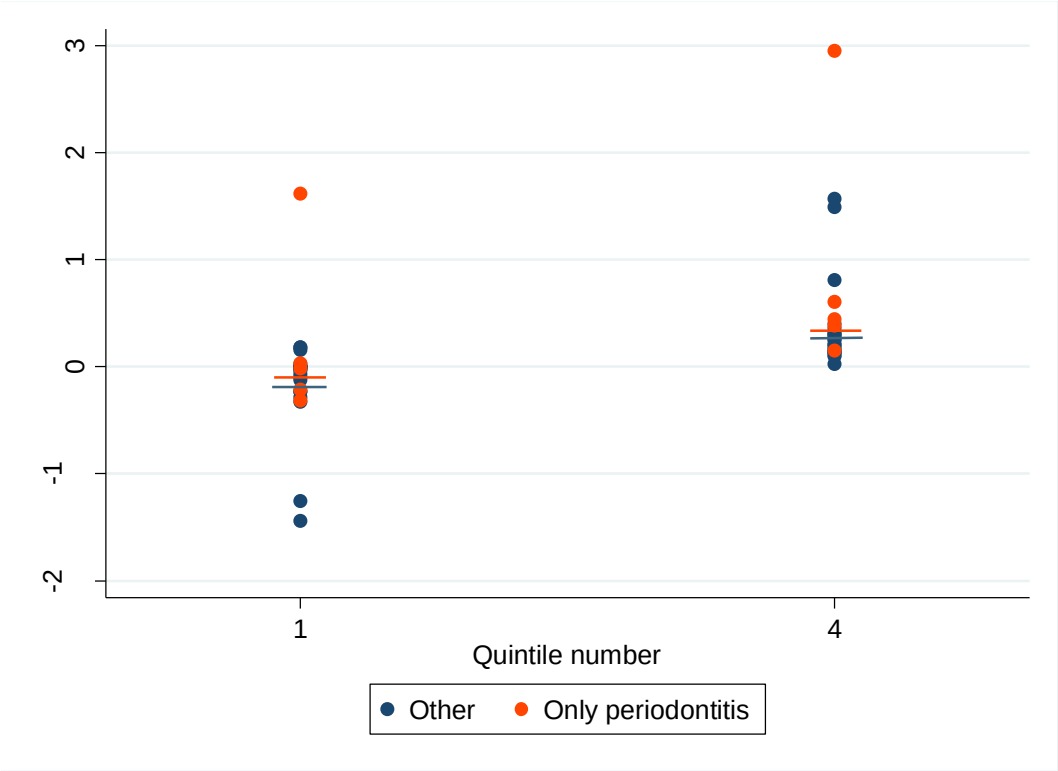
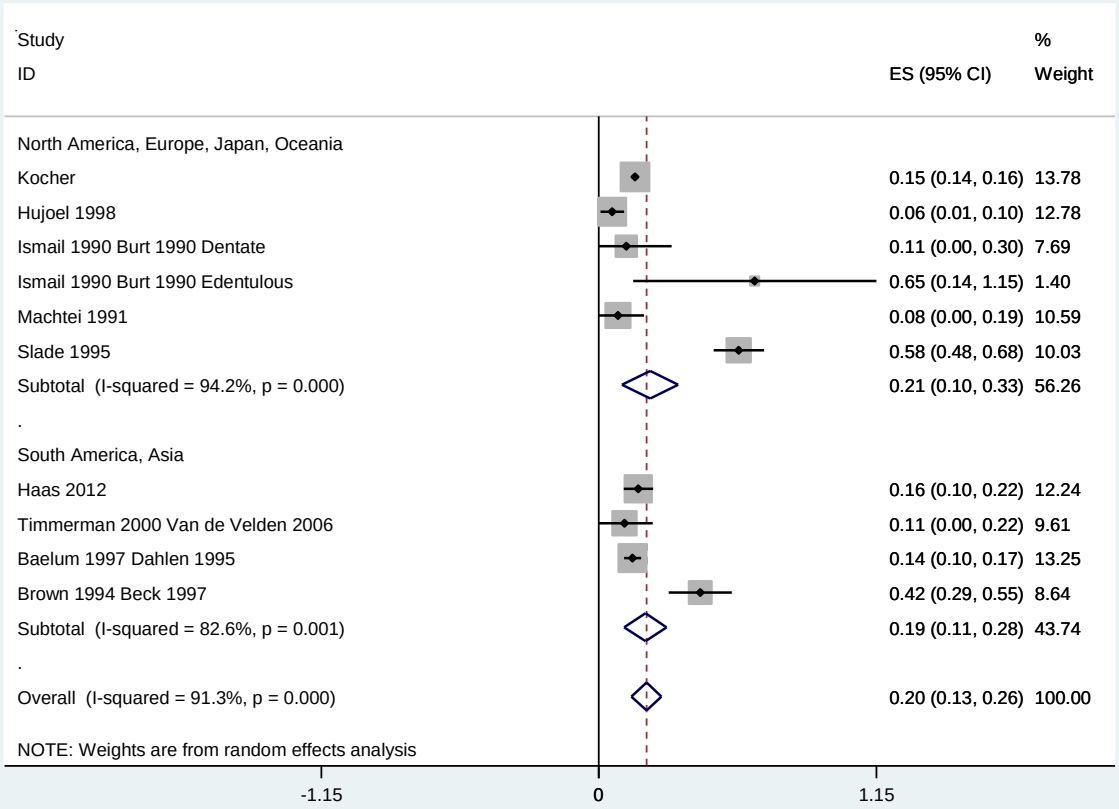


Figure 9. Random effects meta-analysis: Mean annual tooth loss.



Appendix 1. Electronic search strategies

MEDLINE –
1. exp Periodontitis/
2. Periodontal Diseases/
3. Gingival Pocket/
4. Periodontal Ligament/
5. Periodontal Attachment Loss/
6. periodont*.tw.
7. (gingiva* adj3 pocket*).tw.
8. or/1-7
9. Epidemiologic Studies/
10. Cohort Studies/
11. Follow-Up Studies/
12. Longitudinal Studies/
13. Prospective Studies/
14. (cohort adj (study or studies)).tw.
15. cohort analy*.tw.
16. (follow up adj (study or studies)).tw.
17. (observational adj (study or studies)).tw.
18. (longitudinal adj (study or studies)).tw.
19. (prospective adj (study or studies)).tw.
20. or/9-19
21. 8 and 20

EMBASE
1. exp periodontitis/
2. tooth periapical disease/
3. periodontal disease/
4. periodontal ligament/
5. periodont*.tw.
6. (gingiva* adj3 pocket*).tw.
7. or/1-6
8. cohort analysis/
9. follow up/
10. longitudinal study/
11. prospective study/
12. (cohort adj (study or studies)).tw.
13. cohort analy*.tw.
14. (follow up adj (study or studies)).tw.
15. (observational adj (study or studies)).tw.
16. (longitudinal adj (study or studies)).tw.
17. (prospective adj (study or studies)).tw.
18. (epidemiologic* adj (study or studies)).tw.
19. or/8-18
20. 7 and 19

LILACS

(Periodontitis or Aggressive Periodontitis or Chronic Periodontitis or Periapical Periodontitis or Periapical Abscess or Periapical Granuloma or Periodontal Abscess or Periodontal Abscess) and (Epidemiologic Studies or Cohort Studies or Follow-Up Studies or Longitudinal Studies or Prospective Studies) [Subject Descriptor]
or
(Periodont$ or (gingiva$ and pocket$)) and ((cohort and (study or studies)) or cohort analy$ or (follow up and (study or studies)) or (observational and (study or studies)) or (longitudinal and (study or studies)) or (prospective and (study or studies))) [Words]

OpenGrey

(Periodont* OR (gingiva* AND pocket*)) AND ((cohort AND (study OR studies)) OR "cohort analy*" OR ("follow up" AND (study OR studies)) OR (observational AND (study OR studies)) OR (longitudinal AND (study OR studies)) OR (prospective AND (study OR studies)) OR (epidemiologic* AND (study or studies)))

Appendix 2

Risk of bias and methodological quality assessment

Modified Newcastle-Ottawa Scale and additional questions

1) Representativeness of the exposed cohort (award maximum of one star)

1. Truly representative of the average adult in the community (e.g. random sample or birth cohort)* 2. Somewhat representative of the average adult in the community* 3. Selected group of adults e.g. clinic patients or volunteers 4. No description of the derivation of the cohort

2) **Ascertainment of exposure (award maximum of one star)**

1. Secure record* 2. Structured interview* 3. written self-report 4. Not reported

3) **Demonstration that outcome of interest was not present at start of study (award maximum of one star)**

1. Yes***** 2. No

4) **Comparability of cohorts on the basis of the design or analysis (award maximum of two stars)**

1. Study controls for tobacco use***** 2. Study controls for other key factors ; age, gender, SES, general health status***** 3. Not reported

5) **Assessment of outcome (award maximum of one star). Repeat for each outcome**

1§. Independent blind assessment***** 2. Record linkage***** 3. Self-report 4. Not reported

6) **Adequacy of follow-up of cohorts (award maximum of one star)**

1. Complete follow-up, all accounted for***** 2. Losses to follow-up unlikely to introduce bias - small number lost (<20%, or description provided of those lost)***** 3. High losses >20% and no description of those lost. 4. Not reported

Additional quality assessment

7) **Security of measurement of attachment level**

1. Secure (examiner training and calibration) 2. Insecure if not trained/calibrated, 3. Unclear: not reported

8) **Security of measurement of bone level change**

1. Secure: standardised positioning of radiographs e.g. cephalostat/customised film holder 2,. Insecure: not standardised 3. Unclear: not reported

Appendix 3. Excluded full-text studies

Study ID	Reason for exclusion*
Airila-Mansson et al. 2005	Subjects less than 18 years old
Anagnou-Vareldzidou 1982	No mean CAL data
Azmanova 1977	Unable to find Bulgarian translator
Banach 1982	Subjects less than 18 years old
Bautista 2005	Letter to the editor
Becker et al 1981	No CAL data
Bergstrom, & Henrikson 1970	Treatment provided - radiographic assessment only
Blakey et al. 2006	PPD only, does not measure CAL
Brown et al. 1996	Subjects less than 18 years old
Buckley & Crowley 1984	No CAL data
Cadot et al. 1991	No CAL data
Chinju et al. 1986	Cross sectional
Clerehugh et al. 1995	Subjects less than 18 years old
Costa et al. 2007	Subjects less than 18 years old
Craig et al. 2003	2 month duration
Cullinan et al. 2001	No CAL data
Cullinan et al. 2008	No CAL data
Dahlen et al. 2014	Less than 18 years old
Dowsett et al. 2001	Cross sectional
Ebersole et al. 1995	Sites with CAL over 3 mm were referred for treatment
Famili et al. 2005	Cross sectional
Farina et al. 2007	Retrospective
Feist et al. 1984	No CAL data
Feldman et al. 1986	No CAL data
Feldman et al. 1984	No CAL data
Fourel 1985	No CAL data
Gilthorpe et al. 2001	Treated population
Goodson 1984	Review
Griffiths et al. 2001	Treated, no CAL data
Gruber 1991	Adolescents
Hach et al. 2015	Cross sectional
Haffajee, et al. 1988	Surgical treatment
Haffajee et al. 1991	Less than 12 months follow-up
Halazonetis et al. 1989	No CAL data
Hamlet et al. 2008	No CAL data
Harb et al. 2012	No CAL data
Harrel & Nunn 2001	Retrospective
Haubek et al. 2009	Subjects less than 18 years old
Hohlfeld & Bernimoulin 1986	Cross sectional
Hujoel 2008	Editorial

Infante-Rivard & Payette 1980	No CAL progression data
Jain et al. 1981	Cross sectional - Does not measure CAL
Jenkins et al. 1988	Treated 3 months prior to study
Kanhai et al. 2014	No CAL progression data
Kowashi et al. 1983	Cross sectional
Kowashi et al. 1984	Cross sectional
Kumar et al. 2006	No CAL data
Kunimatsu et al. 1985	Cross sectional
Lamster et al. 1991	Treatment provided
Lang, N. P et al. 2009	No CAL data
Levy et al. 2003	Cross sectional
Lightner et al. 1971	Controlled clinical trial
Lilienthal et al. 1965	Cross sectional
Linden et al. 1996	No CAL progression data
Lopes et al. 2008	No CAL measured, uses index
Machtei et al. 1993	Less than 12 months follow-up
Machtei et al. 1993b	Less than 12 months follow-up
Machtei et al. 1994	Less than 12 months follow-up
Machtei et al. 1997	Less than 12 months follow-up
Machtei et al. 1997b	Less than 12 months follow-up
Machtei et al. 2000	Less than 12 months follow-up
Mdala et al. 2014	Treated population
Merte & Nikolaus 1990	No CAL data
Mouton et al. 1987	No CAL data and treated population
Muller 1987	Review
Muller et al. 1997	No CAL data
Nahoum & Tennenbaum 1974	Treatment provided
Nakashima et al. 1996	Sites with CAL loss were treated
Norderyd et al. 1999	No CAL data
Novaes Junior et al. 1996	Treated population
Offenbacher et al. 1986	Treated population
Oliveira Costa et al. 2007	Subjects less than 18 years old
Orwoll et al. 2009	Cross sectional
Paolantonio et al. 1985	Review
Papas et al. 1989	Review and no CAL
Papillard 1968	Cross sectional
Paulander et al. 2004	No CAL data
Paulander et al. 2004	No CAL measured
Petersson et al. 2006	No CAL data
Phipps et al. 2007	Treated population
Ramfjord et al. 1968	Review

Reddy et al. 2000	Treatment provided if attachment loss over 2 mm - rescue criteria
Rengo et al. 1989	Cross sectional
Russell 1964	Review
Schulze-Spate et al. 2015	No CAL progression data
Schwartz et al. 2012	Treated population
Siskos et al. 1984	Cross sectional
Skaar et al. 1992	Treated population
Slade et al. 1997	No CAL
Stashenko et al. 2011	Treatment provided if attachment loss over 2 mm - rescue criteria
Suomi, 1969	Cross sectional
Suomi et al. 1969	Treatment provided
Tezal et al. 2005	Mean CAL data
Tobi et al. 1997	Letter to the editor
Tran et al. 2001	Mean CAL not reported
Tu et al. 2004	Treated population
Ura et al. 1984	Cross sectional
Vathesatogkit et al. 2012	No CAL data, periodontal index
Warren et al. 2002	No CAL progression data
Wennstrom et al. 1987	Treated population
Zappa et al. 1995	Less than 12 months
Zhan et al. 2014	Review

*not including nested studies not used from original studies included in the review