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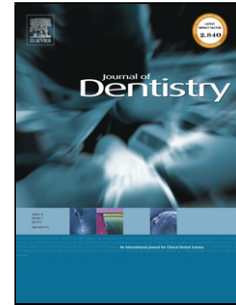
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Root caries incidence and increment in the population – a systematic review, meta-analysis and meta-regression of longitudinal studies

A short title: **Systematic review, meta-analysis and meta-regression of root caries**

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ABSTRACT

Objectives: Previous meta-analyses of root caries incidence and increment studies reported different estimates due to the limited number of studies, heterogeneity and variations in studies included. Currently, new publications and approaches to handle heterogeneity are available. This research aims to systematically review and meta-analyse root caries incidence and increment, and use meta-regression to analyse heterogeneity.

Sources: PUBMED and EMBASE databases were searched systematically.

Study selection: Longitudinal studies on root caries incidence and increment, published in English language prior to 2017, were independently checked by two authors. A pooled incidence and increment of decayed/filled root surfaces (DFS) was estimated and meta-regression analysis was performed by length of follow-up (<2 years; 2years; 3-4years and \geq 5years) and study type (observational population-based and clinical trial).

Data: Of 737 articles, 20 were included for meta-analysis. The annualised root caries incidence and increment were 18.25% [CI=13.22%-23.28%] and 0.45 [CI=0.37-0.53] root DFS respectively. Length of follow-up influenced the estimates, but not the study type. The annual root DFS incidence and increment from studies <2years were 32.95% [CI=29.13%-36.77%] and 0.64 [CI=0.38-0.89] root surfaces respectively. Studies with 5+years follow-up, the annualised root caries incidence and increment were 9.4% [CI=3.32%-15.48%] and 0.43 [CI=0.21-0.64] root surfaces respectively.

Conclusions: Length of follow-up influenced root caries estimates due to a bias towards relatively healthier older adults retained in the study. Root caries increased over time even among the healthier older adults.

Clinical significance: The increase in root caries, even among the healthier older adults, should be considered by both clinicians and healthcare planners/policy makers in their provision of services.

Key words: root caries; incidence; increment; systematic review; meta-analysis; meta-regression

INTRODUCTION

Root caries has received more attention in the last two decades due to research showing the high prevalence of root caries in populations around the world (1). With the increase in life expectancy and the increase in natural teeth retained among older adults, root caries has been predicted to become a significant public health problem (2).

Prevalence is often reported using cross-sectional data as a percentage of population with root caries at a specific time. On the other hand, incidence and increment estimates can only be reported from longitudinal data. Incidence presents the percentage of population with new root caries within a stated period of time, while the increment presents the number of new root carious lesions occurring in an individual within a stated period of time. Compared to root caries prevalence which was reported from countries around the world, incidence and increment study were mainly reported from develop countries. Root caries reported around the world is varied with root caries prevalence among population samples varying from 9.8% (3) to 71% (4), while the incidence and increment of root caries vary from 12.4% (5) to 77% (6) and 0.3 (7) to 4.4 (6) on root surfaces respectively. Some reviews conducted in the 1980s concluded that those variations were caused by a lack of consistency of reporting among the studies undertaken and the wide spectrum of population groups investigated (8).

Meta-analysis is regarded as an approach that provides a high level of evidence from a body of studies (9). Meta-analyses are ideally a subset of systematic reviews (9). A systematic review attempts to collate empirical evidence that fits eligibility criteria to answer a specific research question (9). Meta-analysis obtains a weighted average of results from various studies, and in addition to pooling effect sizes, meta-analysis can also be used to estimate disease frequencies, such as incidence and prevalence (10). However, combining studies that differ substantially in design and other factors can yield a meaningless summary result (9). In this case, the evaluation of reasons for the heterogeneity among studies can be insightful. Examination of heterogeneity is an important task in meta-analysis (9). Meta-regression is a mechanism to analyse heterogeneity in a meta-analysis; it allows the evaluation of the impact of covariates on the pooled estimate (11). Considering that root caries studies differ in design and other features, meta-analysis of root caries studies should be accompanied with a mechanism to assess heterogeneity such as meta-regression and the results should be interpreted with caution.

There are two systematic reviews with a meta-analysis of root caries incidence and increment, pooling the effect estimates of decayed and/or filled root surfaces (root DFS) (12, 13). The estimates achieved were markedly different mainly due to differences in the length of follow-up in the included studies. The first meta-analysis, which gathered evidence from available longer longitudinal studies, revealed an incidence of 8.2% annually (12) while the second meta-analysis, which gathered evidence from shorter longitudinal studies, revealed an incidence of 23.7% annually (13). The second meta-analysis claimed its estimate was better as the shorter the study, the lower the attrition of study participants.

However, even after the application of length of follow-up time criteria, the included studies were quite varied in length. The first analysis, which stated that it gathered evidence from the longer longitudinal studies, actually gathered its estimates from studies varying from three to five years in follow-up time (12). The studies used by the second analysis, which included the shorter longitudinal studies, varied from one to five years in follow-up time (13).

Furthermore, both meta-analyses included studies with observational population-based and clinical trial designs when pooling the estimate of root caries in the population. Different study designs may impact on the population root caries estimate. The sampling for a clinical trial is built around the aim of measuring the efficacy of a preventive regimen under optimal circumstances in the trial and may involve a convenience sample. Observational population-based studies may be based on a probability sample.

In the more recent meta-analysis (13), possible sources of heterogeneity were identified (including the study length but not the type of study), but have not been factored into the analysis through a meta-regression. Baseline age was presented as the only contributing factor for the heterogeneity in root caries incidence.

In addition to these methodological issues new studies are available to be included in a contemporary meta-analysis (14, 15).

Considering the shortage of studies in this field and the limitations of the previous analyses, we performed a systematic review and a quantitative meta-analysis and meta-regression of root caries incidence and increment. The research questions were:

1. What are the estimates of the root caries incidence and increment at the population level around the world?

2. Are there any differences in the estimation of the root caries incidence and increments according to the length and types of studies?
3. What are some possible sources of heterogeneity among root caries studies around the world?

MATERIALS AND METHODS

Search strategy

For the systematic review, all step-by-step procedures followed the recommendations by PRISMA (16). The authors searched PUBMED and EMBASE databases as sources for studies. PUBMED and EMBASE databases were chosen as they are major biomedical and pharmaceutical databases (13). The search terms used were root caries and increment/incidence. The search strategies are presented in Appendix 1. The inclusion criterion was all articles published in the English language prior to 2017. Articles would be included if they contained information sought in the keyword of the search and were community-based or clinical trial research. All root caries measurements were included.

Study selection

Firstly, duplicate references were removed using EndNote X7.3 software. Effort was made to track the relevant citations from reviews to make sure that there were no studies missing from the search result. Two independent investigators then screened all citations (titles and abstracts) to exclude articles which were not relevant. In case of disagreement regarding eligibility, a third reviewer's opinion was sought for further discussion and a decision was made by consensus. The full texts of included citations were downloaded. Articles that were not found electronically were requested from the authors. During the full text reading, generally, articles were included if they addressed the question and presented the data so that it could be abstracted. Articles were excluded if upon closer reading they did not address the question or we could not abstract the sought data.

Data extraction

Data were extracted from the articles using a pre-defined spread-sheet by two reviewers independently. Initially, all information such as authors, year of publication, country of the study, population being studied, the case criteria used for measurement and sample size were extracted. The synthesis also included age at baseline, follow-up period, as well as root caries incidence or increments together with its variance (standard deviation or standard error) in all kinds of root

caries measurements. The root caries estimates from clinical trial studies were taken from the control group or both from control and treatment groups if root caries estimates were found to be not statistically different between the groups ($p \geq 0.05$). The results were extracted and compiled into evidence Tables. Research that was reported in more than one article was retained only if it was reported on a different length of follow-up for the study. If research on the same length of follow-up was reported in more than one article, the one with the more complete data was retained for the meta-analysis.

Sources of heterogeneity included the population's baseline age, some study design characteristics (length of study (<2 years; 2 years; 3-4 years and ≥ 5 years), type of study (population-based study vs. clinical trial study), source of participants (random vs. volunteer), and root caries data adjustment (crude vs. adjusted/net) and clinical condition at baseline (the number of decayed and filled root surfaces, mean number of exposed root surfaces and mean number of teeth at baseline) were also recorded. For some articles that did not include this information, further searching from related study articles was done to get the information.

Methodological quality

Two independent reviewers assessed the quality of the articles using a standardised critical appraisal instruments called 'Meta-Analysis of Statistics Assessment and Review Instrument' [(MAStARI), Appendix 2] as recommended by Joanna Briggs Institute (17) and any disagreements were resolved through consensual decisions. This standard appraisal is a checklist of nine items in which the reviewer checks a 'Yes'/'No' or 'Unclear' for each item which helps to classify studies for quality by calculating the number of 'Yes' answers. Thus, for the nine items used to assess each study, a score of 0-9 was obtained for each study and the studies were then categorised as low quality (0-3), medium quality (4-6) or high quality (7-9) (18). All articles from the final search were included in the meta-analysis regardless their methodological qualities, to broaden the evidence capture. However, the results of the quality assessment are presented.

Data adjustment procedures

Methods for data adjustment followed those used by Griffin et al. (13). When possible, the crude estimate was chosen. For studies reporting caries incidence and increment for a period greater than one year, it was assumed that the root caries cases were identically distributed for each year. For some studies, the incidence and increment of all the study population could be directly extracted from the article. However, in other studies, the incidence and increment were reported for separate

groups. For these studies, the incidence and increment for the study population was estimated by taking the weighted average of the reported results for the separate groups. The associated standard error was calculated using the following formula:

$$SE \text{ in all study population in the interval study} = \sqrt{\frac{N1 * (SE \text{ group } 1)^2 + N2 * (SE \text{ group } 2)^2}{N1 + N2}}$$

To estimate the annual incidence, firstly the probability that no disease occurred during the study interval was estimated. The nth root of this value (where n represents number of years in the study) was then used to calculate the probability that no disease occurred in a given year. Finally, the annual incidence was estimated by subtracting the value from 1. To estimate the annual standard error, this formula was used:

$$\text{annual SE incidence} = \sqrt{\frac{\text{incidence} * (1 - \text{incidence})}{N}}$$

To estimate the annual increment, the increment reported for the study was divided by the years of follow-up of the study. The annual standard error was estimated by dividing the standard error reported in the study with the square root of the years of follow-up of the study.

Possible sources of heterogeneity

Several possible sources of heterogeneity were checked. They included the length of the study (<2 years; 2 years; 3-4 years and ≥ 5 years), type of study (population-based study vs. clinical trial study), source of participants (random vs. volunteer), root caries data adjustment (crude vs. adjusted/net), the age of participants at baseline and some clinical conditions at baseline oral examination (mean number of root DFS, mean number of exposed root surfaces, and mean number of teeth). This information could be taken from the incidence or increment studies included in the meta-analysis or their associated published baseline articles.

Meta-analysis and meta-regression procedures

Meta-analysis and meta-regression were conducted using Stata 13.0 software (StataCorp., College Station, TX, USA). In the case of heterogeneity (chi-square P-value<0.05 or $I^2 > 50\%$), a random-effect model was preferred. Additionally, meta-regression and sub-group analyses were performed to identify possible sources of heterogeneity between studies. Initially, univariate analysis was performed, and all related variables ($P \leq 0.20$) in the univariate analysis were included in the final

multivariable meta-regression model. Only variables with $P < 0.05$ in the final model were considered statistically significant.

RESULTS

The initial search yielded 519 articles from PUBMED and 218 articles from EMBASE. Exactly 183 articles (24.83%) were excluded due to duplication and 45 articles were excluded due to non-English language (6%). A further 470 articles were excluded after abstract reading (63.8%) based on the inclusion criteria. Details of the search flowchart are presented in Figure 1. In total, 41 articles were included for full text reading, and in the end 20 articles were included in the meta-analysis.

During the systematic review (Appendices 3 and 4), it was found that the overall quality of evidence applying the JBI-MAStARI approach was medium for all studies included in the meta-analyses. All studies included Australia, Sweden, Japan, Canada and the United States. Four studies were reported in more than one article with a different length of follow-up in the studies. The most recent study of root caries incidence in the United States across multiple centres reported incidence of root caries measured using ICDAS II (15). However, the criteria used for non-cavitated, cavitated and other root caries lesions applied in this study were reasonably similar to the criteria applied in other studies of root caries (including colour and tactile criteria), thus this study was included in the meta-analysis.

As could be seen in Appendix 3, the mean baseline age of respondents in the studies included was relatively concentrated around 60-70 years. Further, breakdown analysis by age group was not possible in this study, as not all the primary studies provided breakdown data on age groups.

Figures 2 and 3 show sub-analysis of the pooled incidence and increment according to the lengths of the follow-up in the included studies respectively. For all included studies, the annualised root caries incidence and increment were 18.25% [CI=13.22%-23.28%] and 0.45 [CI=0.37-0.53] root DFS respectively. This analysis revealed significant heterogeneity across the studies. Length of follow-up time influenced the estimates. The annual root DFS incidence and increment from studies with less than 2 years follow-up were 32.95% [CI=29.13%-36.77%] and 0.64 [CI=0.38-0.89] root surfaces respectively. In the studies with 5+ years follow-up, the cumulative annualised root caries incidence and increment were 9.4% [CI=3.32%-15.48%] and 0.43 [CI=0.21-0.64] root surfaces respectively. Figures 4 and 5 show the sub-analysis of the pooled incidence and increment

according to the study type respectively. The type of study (population-based vs. clinical trial) did not influence the estimates.

Table 1 presents the analysis of the meta-regression. During the univariate analysis, the variance of the root caries incidence estimate was explained by the length of the follow-up in the study (44.08%), baseline age (22.12%) and baseline root DFS (24.80%) respectively, while the variance of the root caries increment was explained by the length of the follow-up in the study (20.24%), root caries data adjustment (13.80%), source of participants (10.75%), baseline root DFS (2.83%) and number of exposed root surfaces (39.32%) respectively. In the multivariable analysis, all variables were not significant as the number of included studies reduced from 15 to 7 and 14 to 10 in the meta-analysis of root caries incidence and increment respectively.

DISCUSSION

This systematic review and meta-analysis demonstrated that the annual incidence and increment of the root caries were lower as the length of follow-up in a study increased. The annual root DFS incidence and increment from studies with less than 2 years follow-up were 32.95% and 0.64 root surfaces respectively while in the studies with longer than 5 years of follow-up, the cumulative annual root caries incidence and increment were 9.4% and 0.43 root surfaces respectively.

During the data extraction, it was recognised that root caries research differs in many facets. The population of interest among studies was different. Even after considering only the observational population-based and clinical trial studies, the way researchers presented root caries data varied. Root caries could be presented at the surface or tooth level as untreated root caries as well as treated or untreated root caries. Each of these measures could be presented in the root caries data adjustment process as the crude, adjusted or net incidence and increment. Some studies also chose to present root caries incidence and increment as a percentage of exposed root surfaces, expressing an attack rate corresponding to the root caries index introduced by Katz in 1980 (19). This diversity reduced the number of articles that could be pooled together if the strict inclusion criteria were applied. Furthermore, even in the population-based studies, the population of interest varied in relation to the baseline age or clinical characteristics of the study participants. Considering the diversity in root caries studies, the estimated root caries incidence and increments should be interpreted with caution.

In this analysis, we analysed the reports on root DF surfaces. When possible, the crude estimate was chosen for the analysis. Where the crude estimates were not presented, the preferred estimates were the adjusted estimates followed by the net estimates, following the recommendation made

by Griffin et al. (13). However, these differences in presenting the adjustment of root caries data (as crude, adjusted or net increments) result in a slightly different estimate of root caries (13). Beck et al. (20) developed the adjusted caries estimate by multiplying the crude increment by the complement of the number of reversals divided by baseline frequency. They argued that when baseline caries prevalence increases, the probability of examiner reversals increases and the probability of examiner increments decreases. If Beck's adjustment was set as the gold standard, the deviation from the value was lower in the measurement using crude increment compared to the net increment. Beck et al. (20) reported that compared to adjusted increment, crude root caries increment overestimated the value by 10% while the net root caries increment underestimate the value by 38%. Similarly, Slade and Caplan (21) also reported an overestimated value of root caries by 21% when measured in crude increment compared to the adjusted increment, and an underestimated root caries value by 45% using the net increment.

The length of study follow-up was a source of heterogeneity in estimated root caries incidence and increment. About 44.08% and 20.24% study variance in root caries incidence and increment respectively, were explained by the length of follow-up in the study. The shorter durations seemed to reduce the sample bias due to attrition (13), as people who drop out the study are usually the ones who tend to be ill (22) and develop more disease (22, 23). The longer studies may bias root caries results to relatively healthier elders, resembling a survivor bias. Providing the sub-analysis by length of follow-up, this study showed that root caries is still a problem even among healthier persons in studies of more than 5 years length.

Griffin et al. (13) argued that a bias could also be caused by the annualisation of root caries incidence and increment by assuming that the outcomes measured were identically distributed for each year. However, many researchers (13, 22, 24) used this assumption, as there is insufficient research about the changes in the development of root caries year by year. Future research in this field could be of value in this area.

Further variance in estimates was explained by baseline age and baseline root DFS (22.12% and 24.80% respectively) for root caries incidence, and root caries data adjustment, source of participants, baseline root DFS and number of exposed roots (13.80%, 10.75%, 2.83% and 39.32% respectively) for root caries increment respectively. When considering all the variables in the multivariable model, the number of included articles reduced from 15 to 7 and 14 to 10 in the meta-analysis of root caries incidence and increment respectively as not all the included studies reported all the variables. All variables become non-significant in the multivariable analysis. This

showed that the way researchers reported root caries studies differs, as well as showing the differences in the population of interest. Thus, there is still a need to perform root caries studies in a similar way. Future root caries research should address this issue to make the most of the advantage of pooled estimates of the disease.

This study provided a combination of systematic review, and meta-analysis to give a better understanding of root caries studies and the root caries experience. The diversity of the primary studies was a limitation. However, this study provided sub-set analyses by the length and type of the studies, as well as provided meta-regression to assess sources of heterogeneity. The use of a sub-set and meta-regression is a recommended approach to limit problem caused by a diverse source of study (11), which added a strength to this review.

Due to limited information in the baseline age, a breakdown analysis by age group was not possible. However, as the mean baseline age of the participants in the primary studies was mostly 60-70 years, this study showed that even healthy older individuals were at risk of developing root caries. Hence, population-based preventive programs can be effective in preventing root caries.

CONCLUSION

Length of follow-up time is a factor influencing estimates of root caries incidence and increment. Longer follow-up was associated with lower estimates. This appeared to reflect a healthy participant or survivor bias. Root caries increased even among the healthier older adults.

Competing interests

The author(s) declare that they have no competing interests.

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Figure 1. Flow charts of searching

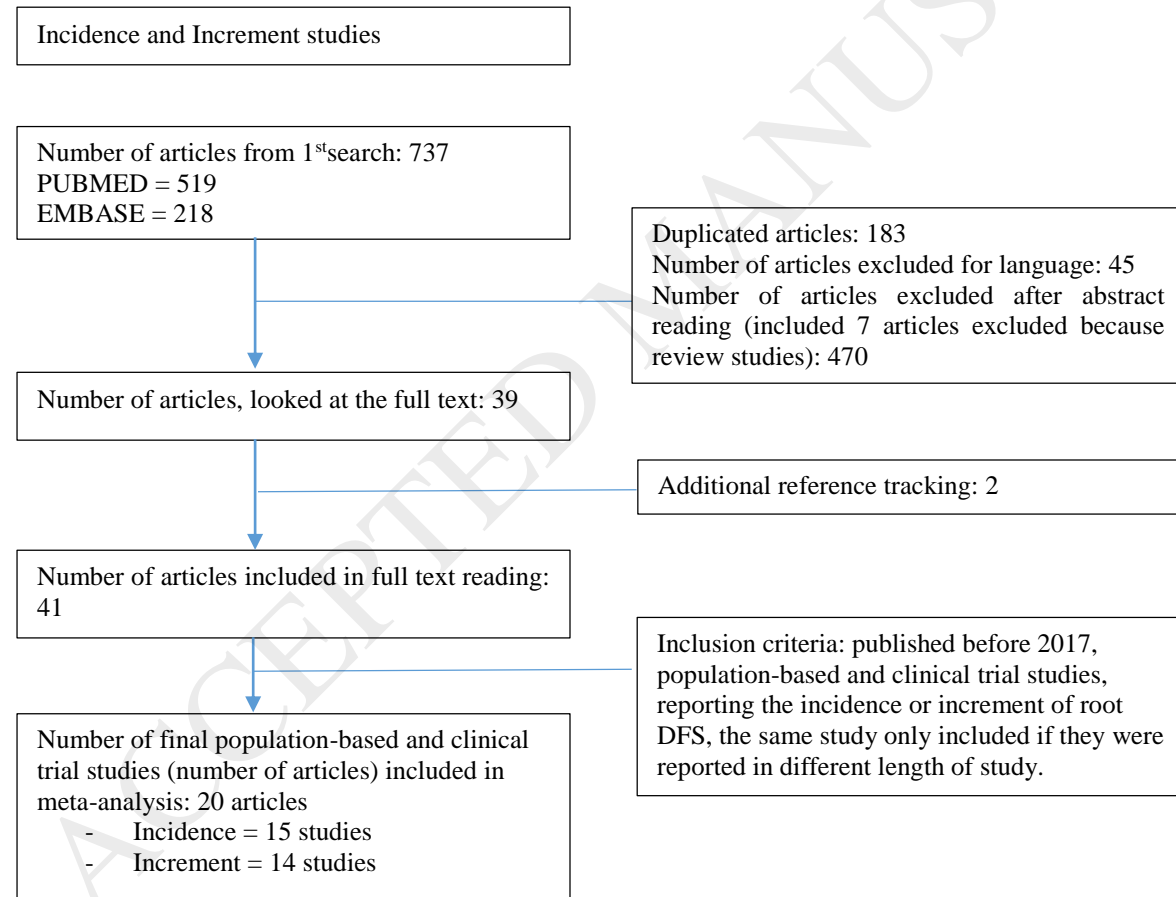


Figure 2. Annual root caries incidence and 95% confidence interval by length of study

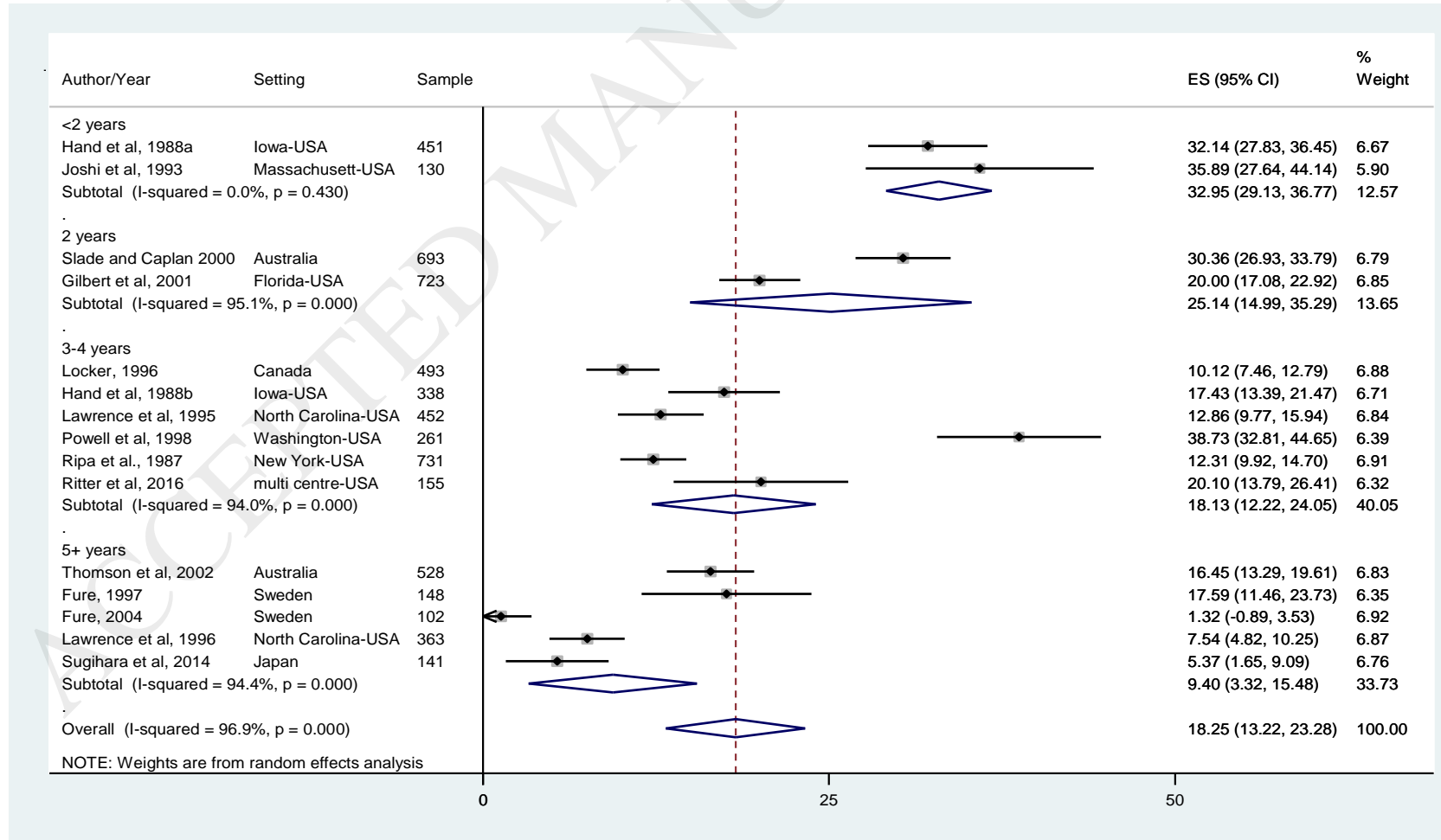


Figure 3. Annual root caries increment and 95% confidence interval by length of study

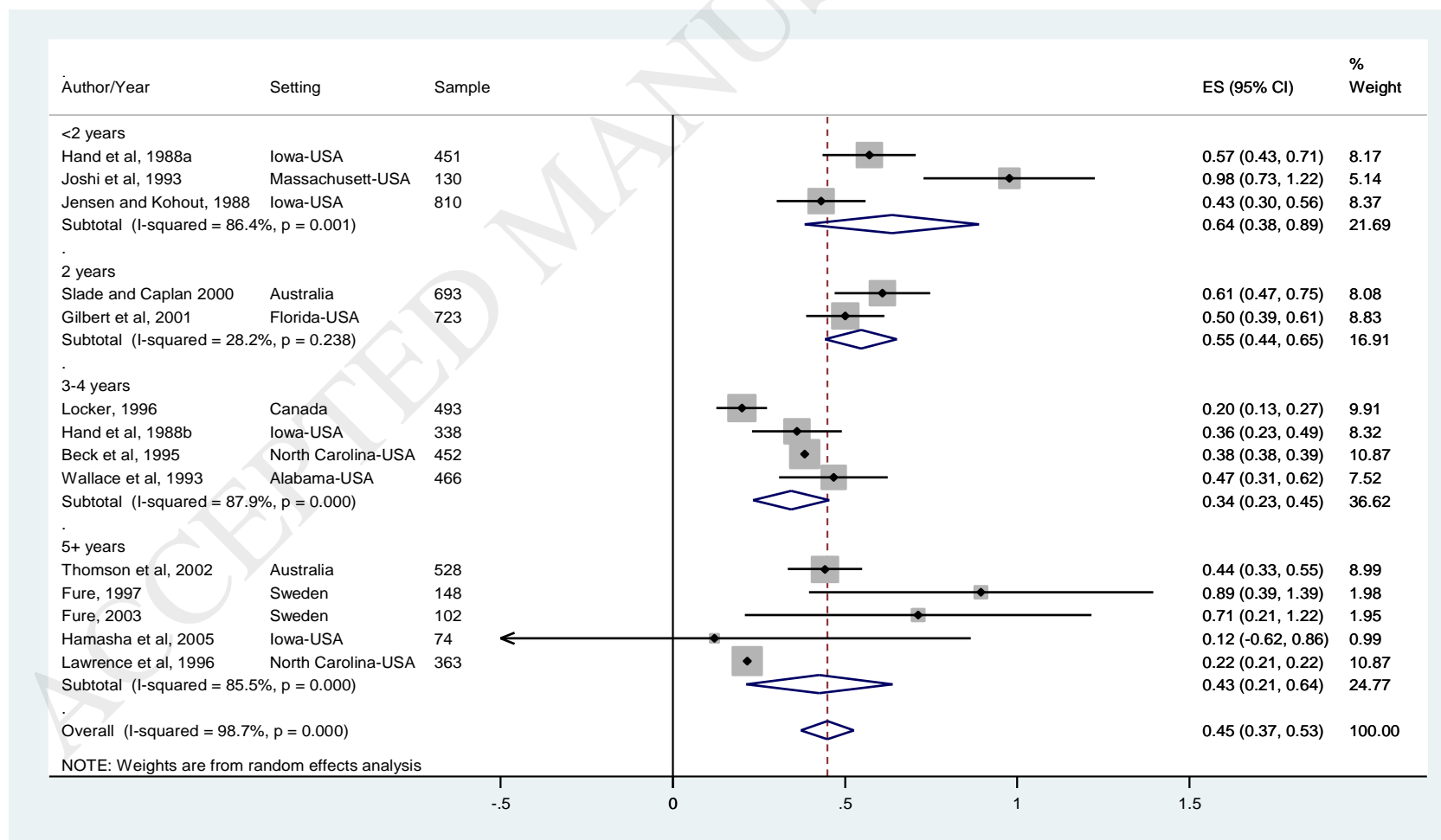


Figure 4. Annual root caries incidence and 95% confidence interval by type of study

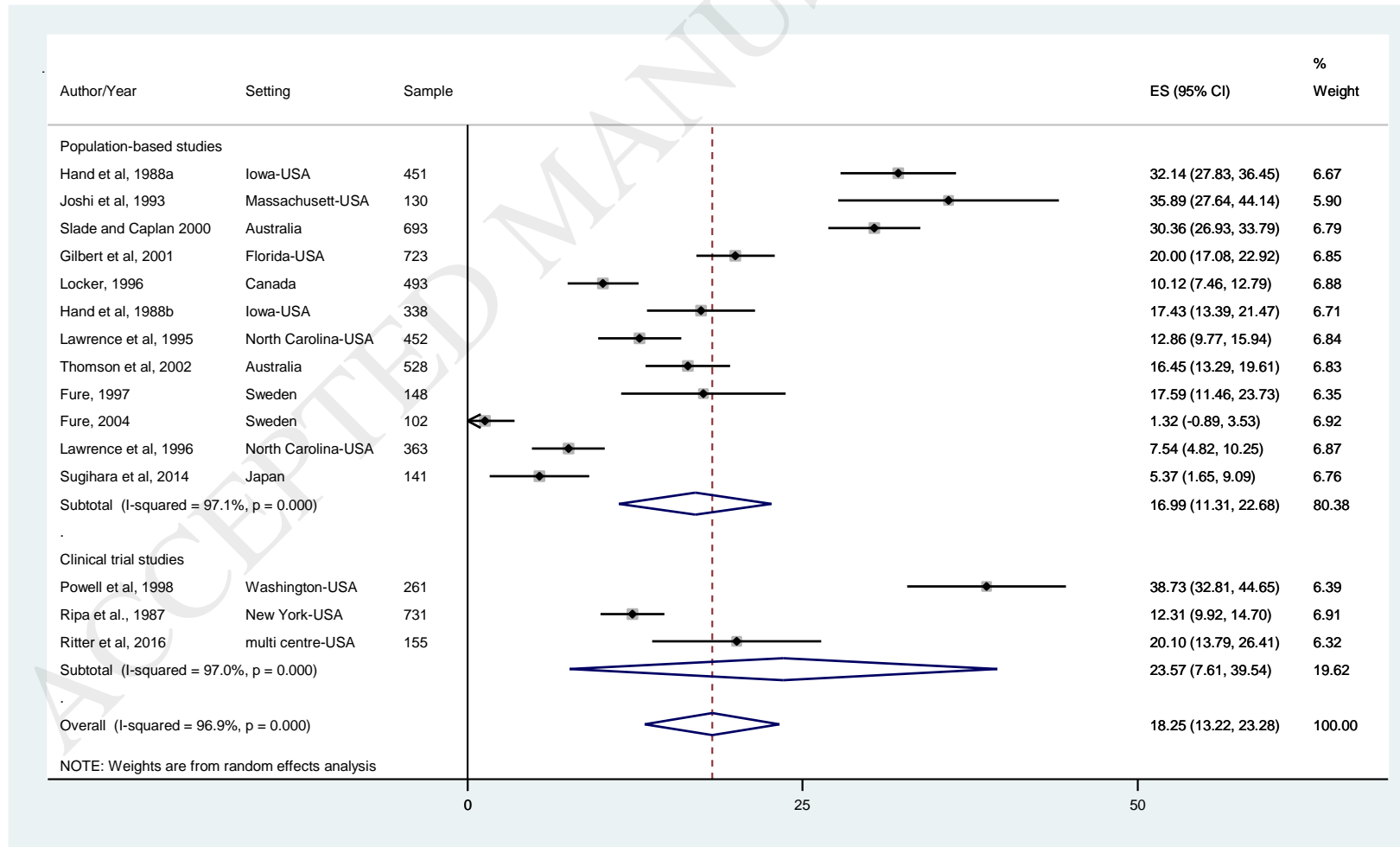


Figure 5. Annual root caries increment and 95% confidence interval by type of study

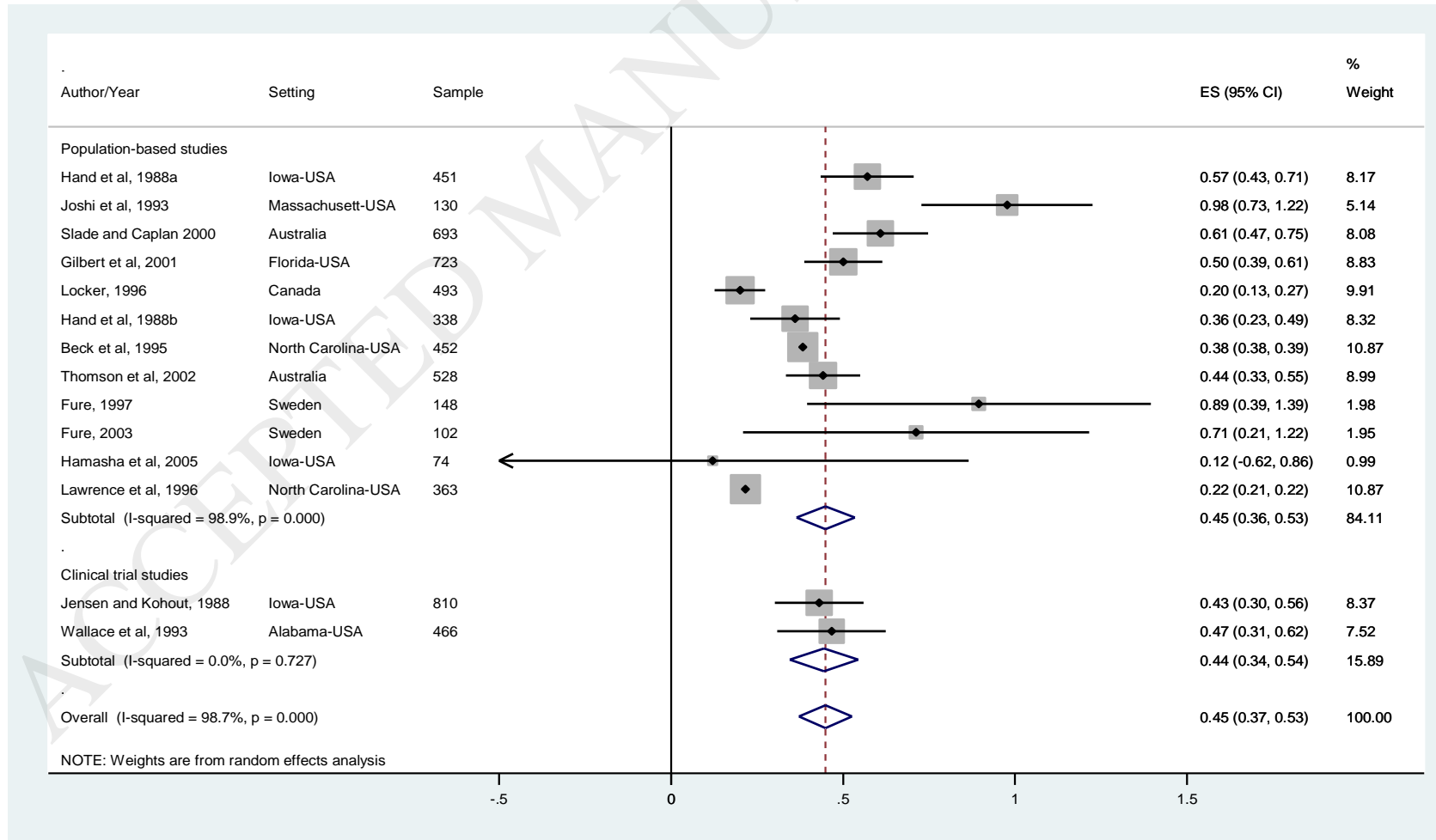


Table 1. Association between study variables and estimated incidence and increment of root DFS

Variables	Root DFS incidence %[CI]	Meta-regression			Root DFS increment Mean[CI]	Meta-regression		
		Univariate P value	Adj R- squared	Multivariate P value		Univariate P value	Adj R-squared	Multivariate P value
Number of studies included (N)		15		7		14		10
Length of the studies								
<2 years	32.95[29.13-36.77]	reference	44.08%	reference	0.64[0.38-0.89]	reference	20.24%	reference
2 years	25.14[15.00-35.29]	0.34		0.21	0.55[0.44-0.65]	0.66		0.23
3-4 years	18.13[12.22-24.05]	0.05		0.12	0.34[0.23-0.45]	0.07		0.16
5+ years	9.4[3.32-15.48]	0.007		0.10	0.43[0.21-0.64]	0.18		0.03
Type of studies								
Population-based studies	16.99[11.31-22.68]	reference	0%	-	0.45[0.36-0.53]	reference	0%	-
Clinical trial studies	23.57[7.61-39.54]	0.40		-	0.44[0.34-0.54]	0.87		-
root caries data adjustment								
Crude	17.43[11.30-23.55]	reference	0%	-	0.56[0.42-0.71]	reference	13.80%	reference
Adjusted/net	20.51[13.21-27.81]	0.66		-	0.38[0.27-0.50]	0.10		0.23
Source of participants								
Random	16.50[10.40-22.59]	reference	0%	-	0.42[0.34-0.50]	reference	10.75%	reference
Not random	22.13[11.01-33.25]	0.39		-	0.69[0.16-1.23]	0.15		0.52
Age	-	0.08	22.12%	0.73	-	0.75	0%	-
Number of teeth	-	0.36	0%	-	-	0.44	0%	-
Baseline root DFS	-	0.08	24.80%	0.12	-	0.18	2.83%	0.07
Number of exposed root surfaces	-	0.99	0%	-	-	0.04	39.32%	0.12
-squared				91.94%				79.82%