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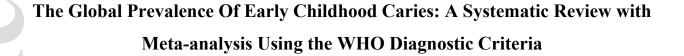
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Short running title: Early childhood caries prevalence: WHO criteria

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The Global Prevalence Of Early Childhood Caries: A Systematic Review with Metaanalysis Using the WHO Diagnostic Criteria

SUMMARY

Aim: To estimate the global prevalence of early childhood caries using the WHO criteria.

Design: Systematic review of studies published from 1960 to 2019. Data sources: PubMed, Google Scholar, SciELO and LILACS. Eligibility criteria were articles using: dmft-WHO diagnostic criteria with calibrated examiners, probability sampling, and sample sizes. Study selection: Two reviewers searched, screened and extracted information from the selected articles. All pooled analyses were based on random-effects models. Registration: Prospero-CRD42014009578.

Results: From 472 reports, 214 used WHO-criteria and 125 fitted the inclusion criteria. Sixty-four reports of 67 countries (published 1992-2019) had adequate data to be summarised in the meta-analysis. They covered 29 countries/59018 children. Global random-effects pooled-prevalence was (percentage[95% CI]) 48[43, 53]. Prevalence by continent was Africa 30[19;

45], Americas 48 [42; 54], Asia 52[43; 61], Europe 43[24; 66], and Oceania 82[73; 89]. Differences across countries explain 21.2% of the observed variance.

Conclusions: Early childhood caries is a global health problem, affecting almost half of preschool children. Limitations: Results are reported from 29/195 countries. Implications of key findings: ECC prevalence varied widely, and there was more variance attributable to between country differences rather than continent or change over time.

INTRODUCTION

Although dental caries is essentially a preventable chronic health problem¹, recent global reports show that oral health has not improved over the past 25 years² with 573 million children estimated to have untreated dental caries in primary teeth in 2015.² Early childhood caries (ECC) used to be defined as the presence of one or more decayed, missing, or filled primary teeth in children aged 71 months (5 years) or younger,³ but has recently been redefined at the Bangkok Declaration by a group of international experts, as the presence of a primary tooth with one or more carious (non-cavitated or cavitated lesions), missing (due to caries), or filled surfaces, in a child under the age of six years.⁴ The consequences of ECC includes negative impacts on growth, development, nutritional problems, and oral health-related quality of life issues, from the child and his/her family. 5 Children with dental caries experience poor school performance and poor school attendance⁶. Also, ECC poses significant social and economic consequences for the family. However, reports of the prevalence of ECC vary. Systematic and narrative reviews have focused on the prevalence of ECC in a variety of countries including India, 8 and China; 9 and geographical areas such as Southeast Asia. 10 Similarly, there are systematic reviews that focus on a particular age¹¹ or on the incidence of ECC, ¹² but do not cover all ages or prevalence. The Proceedings summary paper presented by Tinanoff et al. at the International Association of Paediatric Dentistry Conference on ECC in 2018, summarised the results of 72 studies published between 1998 and 2018 and reported a 4-year prevalence in ECC ranging from 12% to 98%. In children aged 1-, 2-, 3-, 4-, and 5-years-old these were 17%, 36%, 43%, 55%, and 63% respectively. 13 However, they included studies using methodologies with a variety of outcome measure metrics to assess and record dental caries, with the most widely used being the World Health Organization (WHO) criteria. 14,15 This is based on the presence of a tooth/teeth with a cavitated surface and whether there is evidence clinically of a history of caries; whether teeth have been filled or extracted due to dental caries. 15 In their review, Tinanoff et al., 13 also point out important methodological differences between the studies (such as variable examiner calibration and examination methods and standards). They also noted that there were a range of different diagnostic thresholds for carious lesions used. Rather than present a list of prevalences, a narrative summary, or an overall mean value, a more sophisticated and accurate way to estimate prevalence, is through evaluation of the data using meta-analyses obtained through a comprehensive systematic review of the literature. A meta-analysis can combine

studies with methodological similarities to obtain an overall point estimate of the prevalence of early childhood caries and confidence intervals around the data. However, to date, no such comprehensive data synthesis exists. Also, the latest 2019 WHO report on early childhood caries does not report the global prevalence of ECC. ¹⁶ Therefore, we aimed to conduct a systematic review of prevalence cross-sectional or cohort studies and, where possible, use meta-analyses to report the global prevalence of ECC, and describe its distribution by country, continent, and year.

MATERIAL AND METHODS

Protocol and registration

The report of this systematic review follows the MOOSE¹⁷ and PRISMA recommendations. The protocol is available on PROSPERO 2014 registration code CRD42014009578. During the execution of the review there were three minor deviations from the protocol, two of which related to the databases and timeframes searched. These changes were a result of some of the initial findings of the search strategy and close scrutiny of the chosen databases' comprehensive coverage of the area of literature required. Firstly, the BIREME database was replaced by LILACS and SCIELO, as these were considered more comprehensive and have a wider range of dates for Latin America, so the dates were also modified. Secondly, the WOS and SCOPUS reference databases were discarded as they were covered by the other databases and unlikely to yield further articles, making searching and screening them wasteful. The third deviation was a change to the risk of bias assessment tool to the Hoy *et al.* one, which was considered the one most likely to detect the areas where bias might be occurring in these studies.

Eligibility criteria

Inclusion criteria: Cross-sectional or cohort studies reporting the prevalence of ECC or caries in children under 71 months in urban or rural communities, where probability sampling was used, the diagnostic criteria was reported, and there was calibration of the examiners and the number of them stated. We excluded studies conducted on institutionalised patients.

Data sources

We searched the MEDLINE PubMed databases, Google Scholar (as a meta-search engine that searches other databases), SciELO, and LILACS (to detect non-PubMed indexed publications from developing countries and Latin America).

Search

We searched the databases for peer-reviewed articles from 1967 to January 2, 2020. Two researchers conducted and updated the searches between March 2014 up to January 2, 2020. Terms relating to caries, early childhood caries, baby bottle caries, and early caries were combined and then each search was created for each database, along with the terms children, preschoolers, and prevalence, index of decayed, filled or missing teeth (dmft) or proportion of children with caries. No language restrictions were imposed. For articles in languages other than English, French, Spanish, Portuguese, Latvian, Russian, or German, we planned to use Google translate ¹⁹ to extract the information of interest. Authors were not contacted. Details of the search terms are available in the protocol and in the supplementary material in the repository available. ²⁰ Two researchers (SU and IM) independently and in duplicate extracted each article's data. The first 50 articles were then discussed jointly, and any discrepancies were resolved by consensus.

Study selection

The titles of the articles and abstracts were screened for those meeting the inclusion criteria and those obviously not meeting the eligibility criteria were excluded. Where there was doubt, or inadequate information to make a decision, the full texts were obtained and further screened in duplicate for those that meet the inclusion criteria. We excluded studies where there was no description of the population, sample, sample size estimate, declaration of the diagnostic criteria used, number and calibration of examiners. The final doubts were resolved by consensus.

Data extraction

Data were extracted by two investigators (IM, SU) with experience in systematic reviews and one with Cochrane certification. The final form was reviewed by the second author (NI) with experience of both epidemiological and intervention reviews, including Cochrane reviews. The data items that were extracted were: reference; country and specific geographical area; data

reported from the last year of the study; type of population (urban, rural, or both); target population; source and study sample; report of sample size calculation and whether sampling was using a probability or convenience method; the diagnostic criteria used; examiner calibration; and the reported prevalence and severity of caries. Details of all items extracted from each study can be found at Uribe *et al.*²⁰

Data collection process

The extracted data items were entered by each of two researchers in a proforma created and held in Google Docs, and then exported to R statistical software21 in "csv" format for further analysis.

Risk of bias in individual studies

The risk of bias of the included articles was investigated using a modified version of the tool developed by Hoy *et al.*²² for descriptive prevalence studies. One out of the ten fields was excluded "Was the length of the shortest prevalence period for the parameter of interest appropriate?" as this was not relevant to a caries prevalence study in children. This meant that each article could score a maximum of nine points. Two authors (IM, SU) read the information explaining how to use the tool, and discussed and practiced with ten articles investigating prevalence of another topic (caries in permanent teeth). They repeated this exercise once. They then evaluated 19 articles for this systematic review, independently and in duplicate to identify areas of discrepancy, resolve them and assess inter-rater agreement (kappa = 0.877 which equates to "Almost Perfect" agreement according to Landis and Koch). Those articles that provided adequate information about seven or more items were classified as being at low risk of bias. Those between four and six were classified as moderate risk, and those with less than four as high risk. After a preliminary sensitivity analysis, we decided to consider for analysis only those studies with moderate and low risk of bias.

Reliability

Upon completion of data entry, one of the researchers (SU) re-entered 10% of the data at random and compared the results. We found less than 2% discrepancy randomly distributed from the data

initially entered so double data entry or full checking of any single field were considered unnecessary.

Summary measures

The outcome variable was caries prevalence, presented as the percentage of children with caries, within each study's sample that was recorded using the criteria of the World Health Organization¹⁵ (the outcome measure) and taken to be the number of primary teeth with cavitated dentinal caries, filled or missed teeth (dmft) > 0. The prevalence was defined as the proportion of children of the total of children with dmft > 0, and we extracted the reported overall prevalence for each study. In the cohort studies, only the last prevalence report was considered.

Synthesis of results

We performed an initial exploratory analysis of the included studies. We estimated heterogeneity using the I^2 statistic that describes the percentage of variation not due to sampling errors between studies. Higher values of I^2 show greater heterogeneity. To be included in the meta-analysis, studies had to satisfy the following criteria: (1) report the final sample size and proportion of children with caries (dmft > 0); and (2) have a low or moderate risk of bias. We used the Meta²⁴ package in the I^2 software for quantitative synthesis. Because the countries varied significantly in socioeconomic level, geography and climate amongst other factors, a random-effects model was used for the meta-analyses combining the results of all studies. We used the inverse variance method to estimate the pooled prevalence expressed as the proportion of children with caries (dmft > 0) in the total population and their 95% confidence interval. The reported prevalence in each study was around 50%, so no transformations, as logit or the double arcsine, were necessary before the random-model meta-analysis. A meta- regression was conducted to explore potential sources of heterogeneity.

Risk of bias across studies

The risk of bias across studies was estimated by assessing the difference in the studies' point prevalence estimates with respect to the pooled prevalence estimate of ECC and examining the symmetry of the funnel plot.

Additional analyses

Subgroup analysis by continent, country, and decade of publication were performed to give further insight into possible sources of heterogeneity. For those studies reporting prevalence from two or more countries, we obtained the prevalence from each country by disaggregating the reported data.

RESULTS

Study selection

The flow chart in **Figure 1** shows the detail of the search strategy findings for the number of articles.

Study characteristics

There 64 publications, reporting the prevalence from 67 countries, meeting the inclusion criteria and analysed were published between 1992 and 2019. All studies were in English (n=55), Spanish (n=4) or Portuguese (n = 5), spoken fluently by the authors, so there was no need for translation. Two studies reported prevalences for more than one country^{26,27} and one for countries on different continents.²⁸ According to the decade of publication, we analysed five studies from the 1990s, 25 from the 2000s, and 34 studies from 2010. Of the 64 publications analysed, three^{26–28} reported results from two countries, so data were entered separately for each country, giving a total of 67 prevalence estimates. The studies reported results from Africa^{26,29–33} (n = 7), Americas^{34–37,38,34–37,39–58,34–37} (n = 27), Asia^{59–83} (n = 27), Europe^{27,84–87} (n = 5) and Oceania⁸⁸ (n = 1). The studies analysed included 59,062 patients in total, with an average sample size (standard deviation) of 881(1189). The detail by continent and decade of publication is shown in **Table 1**.

Risk of bias within studies

Of the studies analyzed, half had a low risk of bias based on the tool by Doi *et al.*²² The individual studies' bias scores showed that Item 3 had the lowest percentage of compliance "Was some form of random selection used to select the sample, or, was a census undertaken?" and this was absent or poorly reported in 72% of studies, followed by Item 1 "Was the study's target population a close representation of the national population in relation to relevant variables, e.g.

age, sex, occupation?" with 53% and Item 2 "Was the sampling frame a true or close representation of the target population?" with 48% compliance. Items 6; case definition, 8; mode of data collection, and 9; the numerators and denominators were reported in all included studies. The summary of the risk of bias analysis is in **Figure 2**, and the detail is available in the open data repository.²⁰

Synthesis of results

Table 1 shows the proportion of random-effects pooled prevalence (%) [95% CI] of early childhood caries equal to 48 [43; 53] across all studies. ECC (percentage and [95%IC]) prevalences at study level ranged from 16 [15; 18] (Singapore) to 89 [87; 91] (China).

The number of studies per continent was Africa with seven, the Americas and Asia with 27 each, Europe with five, and Oceania with one. The estimated (random model) prevalence (%) by continent was: Africa 30 [19; 45], Americas 48 [42; 54], Asia 49 [40; 58], Europe 43 [24; 66] and Oceania 82 [73; 89]. Heterogeneity between studies within a continent and between continents is I^2 = 99%. The random-effects pooled prevalence of early childhood caries by continent (except for Oceania, since n = 1) is in **Figure 3**.

Risk of bias across studies

Reported prevalence versus standard error on the funnel plot in **Figure 4** showed no evidence of publication bias.

Additional analysis

We conducted a subgroup analysis by country and by the decade for year of publication (see **Table 1**), estimating, through a random-effects model, the prevalence of ECC in each country and by decade. Also, we performed a visual examination to detect whether the size of the study affected the reported prevalence, but found no visual evidence, as shown in **Figure 5**.

Prevalence by country

There were 43 countries with more than one study included (data collected from different regions). The countries reporting the highest ECC pooled prevalence within continents were

Uganda 60[56; 64] in Africa,³² Mexico 75[66; 83] in Americas,³⁶ China 89[87; 91] in Asia,⁶⁷ Lithuania 88[84; 92] in Europe,⁸⁶ and Australia 82[72; 90] in Oceania.⁸⁸

Prevalence by year of publication

The random-effects pooled prevalence (%) of early childhood caries grouped by publication year decade is as follows: in the 1990s was 55 [31; 76], for the 2000s was 45 [37; 53] and for the 2010 decade was 49 [42; 55] as shown in **Table 1**.

Meta-regression results

Meta-regression showed high heterogeneity between the different prevalence estimates. The main source of heterogeneity was the difference in prevalence between countries, which explains 32.5% of the variance in the estimate. The difference between continents explains 0.70% of the variance and the decade of publication 0%. The detail is shown in **Table 2**

DISCUSSION

Using the WHO criteria studies, early childhood caries affects 48%, almost half, of preschool children and its distribution is global, with geographical variations. Africa has a lower prevalence than the global pooled prevalence, while Asia, Oceania, and North and Central America have a prevalence above the global estimate. Europe and America are within the global estimate. However, there is a lack of certainty around the precision of the result with many countries (and regions) not represented. Differences between countries and continents suggest that there are structural differences affecting the oral health of preschool children. 89,90 This seems to be the first registered systematic review with a meta-analysis of the pooled prevalence of ECC. As with any systematic review, the accuracy of the data reported and synthesised is dependent on the comprehensiveness and accuracy of the data included. A previous narrative review by Tinanoff et al. based on 72 articles, estimated a prevalence, across countries, of between 17% in France and 98% in Australia. 13 We found similar obstacles to Tinanoff et al; little detail on calibration and a variety of diagnostic criteria, preventing comparison of many studies. Standardised surveillance systems have been recommended and this aspiration fits with the desire to move the general field of research towards common outcomes and outcome measures.⁹¹ We used the WHO criteria because the evidence suggested it was the most widely

used. 14 The WHO criteria includes only cavitated lesions, thus underestimating the prevalence of caries. 92 Although the definition of ECC published by the American Academy of Pediatric Dentistry 93 includes a non-cavitated level, only a few studies included this category. To maintain comparability, we included only those, where caries prevalence at the cavitated level was extractable. A meta-regression review by Kassebaum *et al.* shows that in 2010 untreated dental caries in primary teeth affected 9% of children (95% CI 8.7, 9.4) making it the 10th most prevalent condition. Our results support their finding that the prevalence of untreated caries has remained relatively unchanged for 20 years 2 with our findings extending this to the past three decades. Considering that caries in the primary dentition is a good predictor of caries risk in the permanent dentition, 94-96 overall our results suggest that the caries situation in the future will remain unchanged unless changes are implemented and the disease is diagnosed and treated at a lower threshold and in a way that halts the disease process, preventing progression to the stage of requiring invasive dental treatment. 97 Until the 2003 version of the WHO's main global promotion and prevention strategy, 98 the emphasis was on children aged 6 and 12 years.

Our results strongly suggest that the emphasis on promotion and prevention programs should be directed at children younger than 6 years old. The current WHO strategy for prevention of dental caries in children, focuses on schoolchildren and youth. However, the widespread presence of caries in such a young child population shown here, strongly suggests that the emphasis on promotion and prevention programs should be directed at children long before they reach school age. The current recommendation from the WHO is to let each country and area set its own health goals, and our work could help to set those goals in specific countries or geographical areas. How Also, these results can be used for estimating sample size for future national studies. A systematic review can only include the evidence available and then synthesise it. It cannot improve the quality of the available evidence but allows, among other things, the identification of aspects that could be improved in future reports.

The fact that so many studies (89/214) did not use the WHO criteria and others were excluded due to incomplete reporting of critical information, including diagnostic criteria; target population; or examiner calibration, is a wake-up call for future research. For example, most studies (86.6%) lacked sufficient information to perform a sub-group analysis by age. One way to improve this shortcoming in future studies is to indicate the number of children and

prevalence by age. While guidelines for reporting prevalence studies exist in other areas such as periodontics, ¹⁰¹ there are no such guidelines for caries prevalence studies at this time. The STROBE recommendations are a good guide for observational studies, ¹⁰² to which some recommendations, specific to caries outcomes and outcome measures should be added. ¹⁴ Future studies should report the diagnostic criteria used and when they use more than one, each prevalence should be reported, linked to the relevant diagnostic criteria. Likewise, to ensure the validity of the measurements, the calibration of the examiners and the agreement or reliability results must be reported in detail. ^{103,104} It is also essential that future studies clearly report the target population, to allow insight into how generalisable the results are to other populations. This includes reporting; the size of the target population, i.e., country-level or ethnic group, source, eligible population, and finally, the sample, indicating the assumptions for sample size estimation.

This review's overall estimate of ECC is also in line with the recent estimate. However, GBD *et al.* indicate that more economically advanced countries have more caries. Our results indicate a wide variation between countries that are generally grouped within similar economic levels. This could be explained by the fact that some of these studies are conducted in subgroups of the population. Variations in the pooled prevalence of ECC across continents and even within individual country studies suggest that the distribution of ECC is not homogeneous. Some of this variation could be explained by genetic factors, but the research available to date shows mixed results. Several studies claimed to investigate prevalence in ethnic minority populations or subgroups such as indigenous peoples of Australia and ethnically diverse groups from China, with different socioeconomic status or place of residence, i.e. rural. During data extraction of individual papers, in common with other studies we could not identify any clear definitions of rurality/urbanity, so were unable to carry out a sub-group analysis to investigate caries prevalence differences related to rurality.

Nevertheless, the variations within different countries (for example Brazil) are so wide, it could be speculated as being indicative of more structural causes, such as the distribution of dental services¹⁰⁹, socio-economic, cultural or geo-political. An alternative explanation; that the variation is driven by methodological artefacts, seems less likely to explain the large differences, especially as all studies used the WHO criteria in order to be eligible for the review, although

these could contribute. A more detailed description of geographical areas could help to interpret differences with reasons such macroeconomic, ⁸⁹ socioeconomic ¹¹⁰ and also the availability of fluoride in drinking water ¹¹¹ or toothpaste, ¹¹² interventions with evidence of effectiveness for caries prevention. ¹¹³ Future research should focus on factors contributing to the unexplained 68% variation in prevalence.

We included studies from different regions within individual countries (taking the most recent where there was more than one). ECC (percentage and [95%IC]) prevalences varied widely within some countries. This was most noticeable for some countries; for China, there were nine studies and the prevalence ranged between 35% and 89%, a difference of 54%. Similarly, large differences were noted for India with four studies and 51% variation in prevalence and Brazil; 14 studies with a 46% variation. The meta-regression analysis showed that 21% of the variation in prevalence comes from variation between countries rather than between continents or years. This could be interpreted as evidence of the global distribution of ECC, with variations within each continent. The data has some limitations because of its sparsity in some areas. For example, the estimate of 82% for Oceania likely does not represent the reality of such a large and diverse continent. Firstly, it is only a single study and secondly, although it met the review inclusion criteria, it was at high risk of bias as the study target population were a particular group of Indigenous Australian children of 4 and 6 years of the Tiwi tribe on the island of Bathurst and not representative of the national population. A study not included for lack of a probability sample indicated that the prevalence of tooth decay prevalence in Indigenous Australian children was 69% vs. 25% in non-indigenous children. 114 The Australian national oral health survey report 2012-2014 indicates that "at the beginning of school, at age 5–6 years, a little more than half of the children have had experience of caries in their primary/deciduous (baby) teeth with an average of two teeth with decay experience", 115 and the latest national oral health survey does not report prevalence in children under five. 116 In New Zealand, there was one study available but it was not included because it used school admission records without declaring the diagnostic criteria or the calibration of examiners. Although data was not included in this review, the results are worth mentioning, since they included data from 27333 children between 2 and 4 years of age where non-cavitated and cavitated lesions were considered, reporting a prevalence of 14.9% (95%CI 10.2, 20.7). 117

The unit of analysis was by study, with the most recent regional data included and we could see wide variation within country. However, with a 21% of the variance in the prevalence estimate attributable to between country, there is the possibility that this variance due to countries may be inflated for those countries where more studies have originated.

With carious lesions limited to enamel, changes in the eliciting factors and remineralisation of the lesions will arrest and reverse the disease. However, the dental profession still tend to intervene restoratively for these reversible lesions. Relying on thresholds that are so "late" in the disease process, may give data useful to observe the disease prevalence, but it means the opportunity to even possibly intervene and prevent the disease from requiring restorative-based, rather than prevention-focused, interventions, is lost. It should also be remembered that this will be an underestimate of the actual prevalence of ECC as the WHO criteria only record cavitated lesions, but the definition of ECC includes non-cavitated lesions. With almost half of children up to 71 months of age experiencing ECC, we face a huge challenge, at clinical and public health levels, and the impetus to incorporate the advances in research for the promotion and prevention of oral health, particularly in the youngest children.

CONCLUSION

Studies on the prevalence of early childhood caries (for children 6 years or younger) that used the most common outcome measure for caries, the WHO criteria, show a combined prevalence of 48% [95% CI 43, 53], with variations both between and within countries. There were no significant changes observed in the reports for the period from 1990 to 2019. There were inadequate data to allow breakdown by age and there is room for improvement in standardising data collection fields, reporting by including essential information, such as detailed prevalence by age, community type (rural/urban) and ethnicity.

BULLET POINTS

- A meta-analysis of studies from cross-sectional studies using the WHO criteria shows the prevalence of ECC to be 48% [95% CI 42, 52]
- ECC prevalence varied widely, even within country, and there was more variance attributable to between-country differences rather than by continent or by change over time, with a suggestion of structural or methodological components being responsible.

3. 5.

Out of 195 countries, prevalence data on ECC, using the WHO criteria, were available
for only 29 countries. This significant limitation must be considered in interpreting this
dataset. However, selecting out this data is balanced against the potential loss of meaning
that would result from combining studies with differing methodologies and outcome
measures.

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FIGURE LEGENDS

Figure 1. PRISMA flow diagram.

Figure 2. Risk of bias of analyzed studies (n=64 studies) using the tool by Hoy et al.²²

Figure 3. Forest plot of the pooled prevalence and 95%CIs of ECC prevalence stratified by continent and ordered by prevalence. IV = Inverse Variance Method. Box size represents the sample size.

Figure 4. Risk of bias across studies.

Figure 5. Reported prevalence per year, continent, and sample size.

Table 1. Summary of sample size and pooled prevalence of early childhood caries studies using WHO criteria.

Sample size					Prevalence	
N studies	Sum	Mean (SD)	Median	Q1-Q3‡	Pooled§	95% CI
64†	59018	881 (1190)	515	242 - 902	48	[42; 53]
7	4268	610 (304)	513	402 - 679	30	[19; 45]
27	23806	882 (1507)	283	138 - 774	48	[42; 54]
26	24155	895 (880)	595	418 - 967	52	[43; 61]
5	6709	1342 (1689)	638	505 - 1000	43	[24; 66]
1	80	80 (-)	80	-	82	[73; 89]
5	8650	1442 (1593)	988	358 - 1939	55	[31; 76]
25	14537	559 (601)	360	135 - 706	45	[37; 53]
34	35875	1024 (1397)	577	352 - 840	49	[42; 55]
	64† 7 27 26 5 1 5 25	N studies Sum 64† 59018 7 4268 27 23806 26 24155 5 6709 1 80 5 8650 25 14537	N studies Sum Mean (SD) 7 4268 610 (304) 27 23806 882 (1507) 26 24155 895 (880) 5 6709 1342 (1689) 1 80 80 (-) 5 8650 1442 (1593) 25 14537 559 (601)	N studies Sum Mean (SD) Median 64† 59018 881 (1190) 515 7 4268 610 (304) 513 27 23806 882 (1507) 283 26 24155 895 (880) 595 5 6709 1342 (1689) 638 1 80 80 (-) 80 5 8650 1442 (1593) 988 25 14537 559 (601) 360	N studies Sum Mean (SD) Median Q1-Q3‡ 64† 59018 881 (1190) 515 242 - 902 7 4268 610 (304) 513 402 - 679 27 23806 882 (1507) 283 138 - 774 26 24155 895 (880) 595 418 - 967 5 6709 1342 (1689) 638 505 - 1000 1 80 80 (-) 80 - 5 8650 1442 (1593) 988 358 - 1939 25 14537 559 (601) 360 135 - 706	N studies Sum Mean (SD) Median Q1-Q3‡ Pooled§ 64† 59018 881 (1190) 515 242 - 902 48 7 4268 610 (304) 513 402 - 679 30 27 23806 882 (1507) 283 138 - 774 48 26 24155 895 (880) 595 418 - 967 52 5 6709 1342 (1689) 638 505 - 1000 43 1 80 80 (-) 80 - 82 5 8650 1442 (1593) 988 358 - 1939 55 25 14537 559 (601) 360 135 - 706 45

[†] Of the 64 publications analysed, three reported results from two countries, so data were entered separately for each country, giving a total of 67 prevalence estimates.

[‡] First (25%) and third (75%) quartiles.

[§]Random effects model meta-analysis.

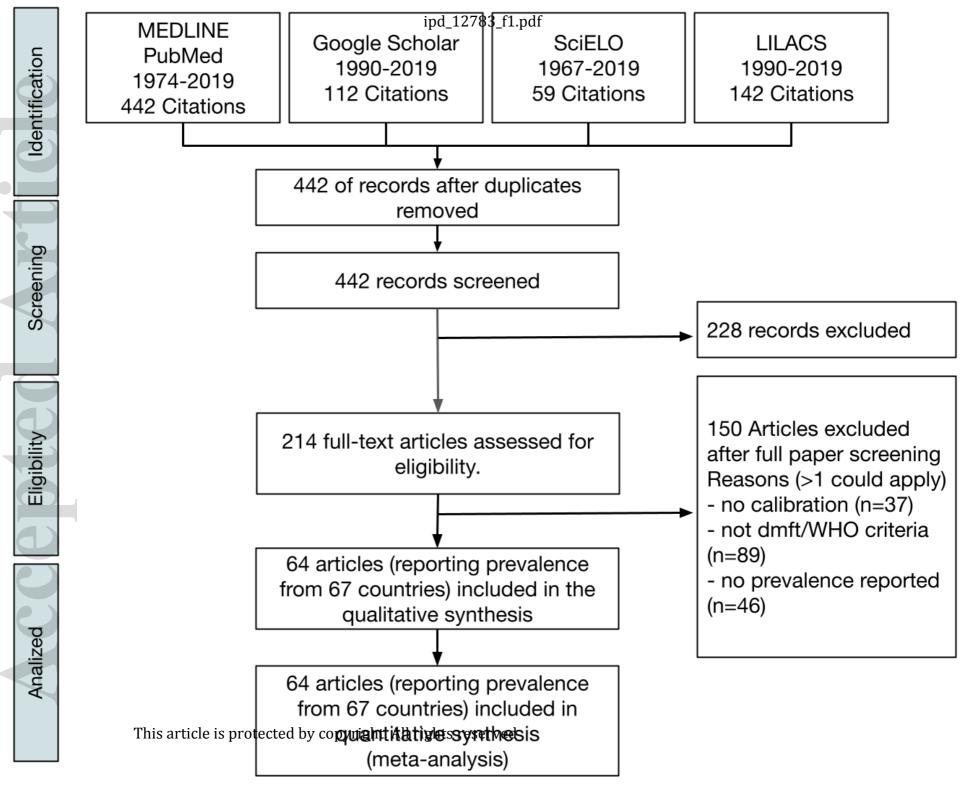
Table 2. Results of meta-regression for the prevalence of ECC.

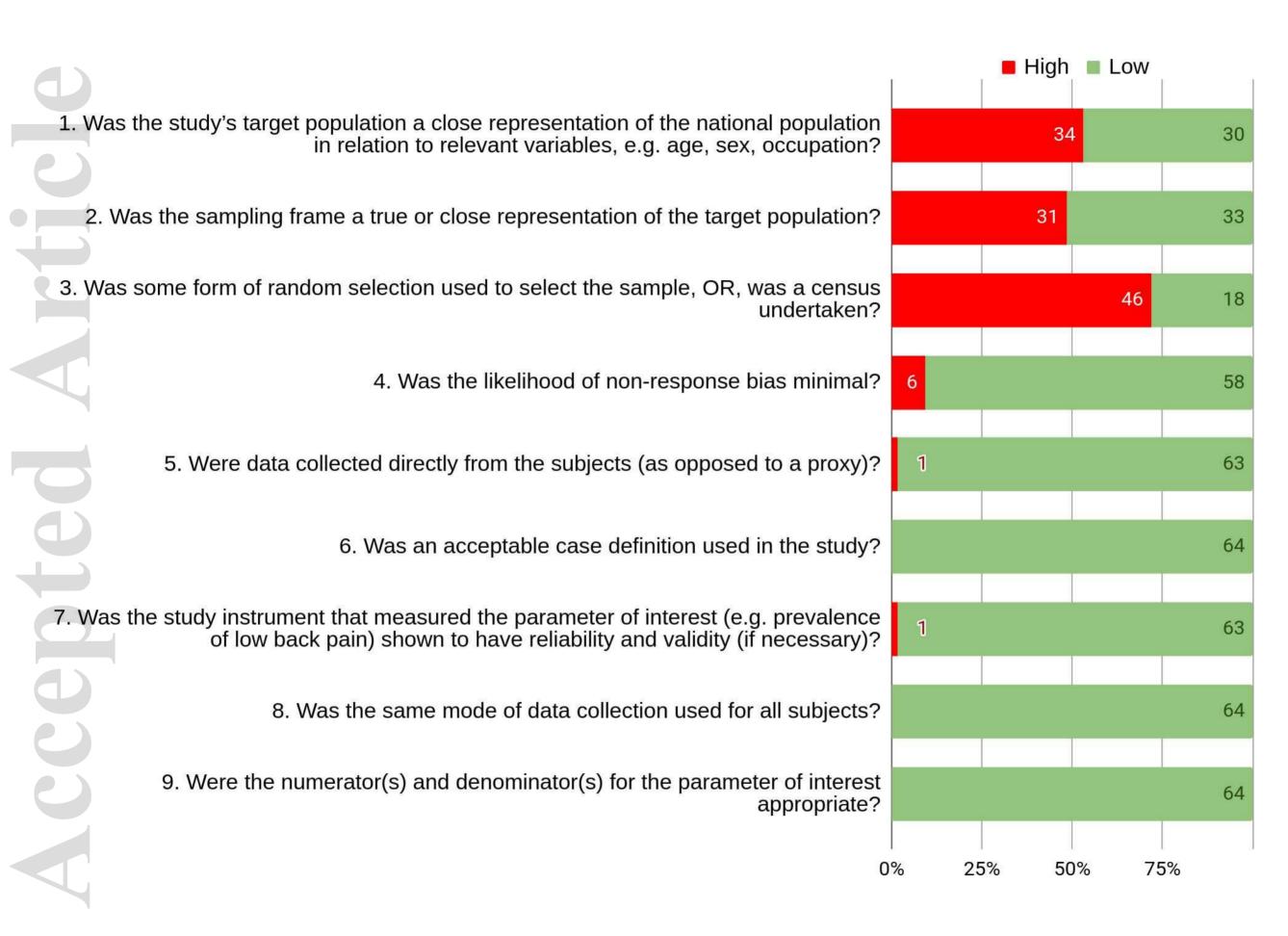
Covariate	Estimated t ²	Estimated I ² (%)	R ² Variance explained (%)
Continent	0.732	99.2	0.7
Country	0.498	98.7	32.5
Publication decade	0.786	99.3	0.0

 t^2 : estimated amount of residual heterogeneity.

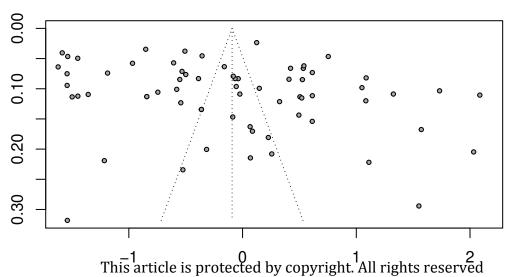
I²: residual heterogeneity / unaccounted variability.

R²: the amount of heterogeneity accounted for.





772 1.5% 1221 1.5% 513 1.5% 372 1.5% 372 1.5% 432 1.5% 586 1.5% 586 1.5% 4268 10.5% 5 < 0.01); 2 = 6 68 1.3% 2651 1.5% 1018 1.5% 602 1.5% 283 1.5% 78 1.4% 2987 1.5% 229 1.5% 128 1.5% 229 1.5% 102 1.4% 186 1.5% 338 1.5% 338 1.5% 338 1.5% 338 1.5% 408 1.5% 338 1.5% 349 350 1.5% 360 1.5% 371 1.5%	0.18 [0.16; 0.36] 0.20 [0.17; 0.36] 0.30 [0.25; 0.36] 0.30 [0.25; 0.36] 0.49 [0.44; 0.36] 0.30 [0.19; 0.36] 0.30 [0.19; 0.36] 0.37 [0.33; 0.36] 0.37 [0.33; 0.36] 0.38 [0.36; 0.36] 0.38 [0.36; 0.36] 0.41 [0.35; 0.36] 0.41 [0.35; 0.36] 0.41 [0.35; 0.36] 0.41 [0.35; 0.36] 0.42 [0.32; 0.36] 0.43 [0.44; 0.36] 0.44 [0.49; 0.36] 0.52 [0.41; 0.36] 0.54 [0.49; 0.36] 0.55 [0.46; 0.36] 0.56 [0.46; 0.36] 0.575 [0.55; 0.36] 0.68 [0.55; 0.36] 0.69 [0.55; 0.36] 0.60 [0.55; 0.36] 0.61 [0.15; 0.36] 0.62 [0.55; 0.36] 0.63 [0.52; 0.36] 0.64 [0.49; 0.36] 0.65 [0.46; 0.36] 0.66 [0.46; 0.36] 0.675 [0.66; 0.36] 0.75 [0.66; 0.36] 0.75 [0.66; 0.36] 0.48 [0.42; 0.36] 0.48 [0.42; 0.36] 0.48 [0.42; 0.36] 0.48 [0.42; 0.36]	1.24	
2651 1.5% 1018 1.5% 602 1.5% 283 1.5% 78 1.4% 2987 1.5% 728 1.5% 229 1.5% 1993 1.5% 102 1.4% 186 1.5% 338 1.5% 408 1.5% 408 1.5% 408 1.5% 408 1.5% 279 1.5% 279 1.5% 279 1.5% 332 1.5% 332 1.5% 332 1.5% 332 1.5% 34 1.4% 279 1.5% 368 1.5% 3171 1.5% 368 1.5% 378 1.4%	0.19 [0.18; 0.4] 0.23 [0.21; 0.4] 0.37 [0.33; 0.4] 0.37 [0.31; 0.4] 0.38 [0.36; 0.4] 0.38 [0.36; 0.4] 0.41 [0.35; 0.4] 0.41 [0.35; 0.4] 0.42 [0.32; 0.4] 0.48 [0.40; 0.4] 0.52 [0.41; 0.4] 0.52 [0.41; 0.4] 0.53 [0.52; 0.4] 0.54 [0.49; 0.4] 0.56 [0.46; 0.4] 0.56 [0.46; 0.4] 0.56 [0.46; 0.4] 0.575 [0.57; 0.4] 0.68 [0.66; 0.4] 0.75 [0.66; 0.4] 0.75 [0.70; 0.4]	1.21	
3171 1.5% 520 1.5% 118 1.4%	% 0.18 [0.16; 0. % 0.18 [0.15; 0.3 % 0.23 [0.16; 0.3 % 0.28 [0.25; 0.3	0.19] + 0.22] + 0.32]	
595 1.5% 977 1.5% 1116 1.5% 185 1.5% 353 1.5% 540 1.5% 789 1.5% 510 1.5% 250 1.5% 732 1.5% 833 1.5% 41.55 40.6%	0.32 [0.28; 0.36] 0.35 [0.33; 0.36] 0.36 [0.31; 0.37] 0.37 [0.34; 0.37] 0.40 [0.36; 0.37] 0.49 [0.45; 0.37] 0.60 [0.57; 0.37] 0.63 [0.57; 0.37] 0.63 [0.60; 0.37] 0.65 [0.60; 0.37] 0.65 [0.60; 0.37] 0.74 [0.70; 0.37] 0.75 [0.72; 0.37] 0.83 [0.78; 0.37] 0.85 [0.82; 0.37] 0.89 [0.87; 0.37] 0.89 [0.87; 0.37]	+ 0.37] + 0.37] - 0.38] 0.41] 0.40] 0.44] 0.53] 0.53] 0.61] 0.66] 0.66] 0.66] 0.72] 0.70] 0.78] 0.78] 0.82] 0.87]	
515 1.5% 1000 1.5% 638 1.5% 233 1.4% 6709 7.5% P < 0.01); I ² =	% 0.19 [0.16; 0.5] % 0.46 [0.43; 0.5] % 0.48 [0.44; 0.5] % 0.88 [0.84; 0.5] % 0.43 [0.24; 0. 5]	0.23] —— 0.49] 0.52] 0.92] 0.66] ——	-+
11 4 5	595 1.5% 977 1.5% 1116 1.5% 185 1.5% 353 1.5% 540 1.5% 540 1.5% 789 1.5% 250 1.5% 732 1.5% 833 1.5% 4155 40.6% (P = 0); ² = \$ 1323 1.5% 515 1.5% 515 1.5% 638 1.5% 233 1.4% 6709 7.5% < 0.01); ² = \$ 80 1.4%	595 1.5% 0.63 [0.59; 0.977 1.5% 0.63 [0.60; 0.61] [0.60; 0.63] [0.60; 0.63] [0.60; 0.65] [0.58; 0.65] [0.58; 0.65] [0.58; 0.65] [0.60; 0.74] [0.70; 0.74] [0.70; 0.789 1.5% 0.75 [0.72; 0.789 1.5% 0.79 [0.75; 0.250 1.5% 0.83 [0.78; 0.83] [0.78; 0.83] [0.78; 0.83] [0.78; 0.85] [0.82; 0.83] [0.87; 0.85] [0.82; 0.83] [0.87; 0.85] [0.82; 0.89] [0.87; 0.89] [0	595



Standard Error

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Logit Transformed Prevalence

Reported prevalence by year, sample size and continent Africa Americas Asia Europe Oceania Sample size 2000 4000 Prevalence (%) 6000 Continent Africa Americas Asia Europe Oceania This article is protected by copyright. All rights reserved 2000 2010 2020 2000 2010 2020 2000 2010 2020 2000 2010 2020 2000 2010 2020 Year