

Review Article

Is caries prevalence site-specific in cleft lip and palate patients? A systematic review and meta-analysis

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ABSTRACT

Background: Previous systematic reviews indicate that there is an increased prevalence of caries in cleft patients in comparison to their healthy control group. To date, the prevalence of caries between unilateral cleft lip and palate (UCLP) and bilateral cleft lip and palate (BCLP) has not been quantitatively evaluated. This review aims to include published studies that examined caries prevalence in patients with UCLP and BCLP to find out whether a quantitative difference exists in caries experience among them.

Materials and Methods: Medline/PubMed, Scopus, and EBSCOhost databases were searched from inception to November 2021. The protocol was registered with PROSPERO registration no. CRD2021292425. Prevalence-based studies that evaluated caries experience using the decayed–missing–filled teeth (DMFT) index in the permanent dentition or dmft in case of primary dentition in patients with UCLP or BCLP were included in the analysis with the outcome given in mean and standard deviation. Meta-analysis was performed using a random effect model through a forest plot. An adapted version of the Newcastle–Ottawa Scale for cross-sectional studies was modified to assess the quality of included studies.

Results: Three studies were included in the review. The difference in caries prevalence was statistically significant in the permanent and primary dentition which were evaluated using DMFT and dmft scores with $P = 0.01$ and $P = 0.03$, respectively. Forest plot values were obtained for permanent dentition (DMFT) and primary dentition (dmft), 0.57 (95% confidence interval [CI]: 1.03–0.11) and 0.36 (95% CI: 0.69–0.03), respectively. The result of the meta-analysis indicates that patients with BCLP have higher caries prevalence.

Conclusion: The outcome of the study indicates a higher occurrence of caries in patients with BCLP than UCLP in both permanent and primary dentition.

Key Words: Caries prevalence, cleft lip/palate, meta-analysis, site-specific, systematic review

Received: 25-May-2023
Accepted: 25-Sep-2023
Published: 26-Oct-2023

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INTRODUCTION

A common congenital abnormality that is seen in approximately 1 in 700 live births is cleft lip and palate (CLP).^[1] Cleft lip in association with the palate

is twice as common as either cleft lip or palate alone. These malformations alter the middle third of the face to varying extents. They may occur in isolation, for example in nonsyndromic patients, or can be part

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How to cite this article: Gupta A, Sethi S, Wadhwa J, Batra P, Shick EA. Is caries prevalence site-specific in cleft lip and palate patients? A systematic review and meta-analysis. Dent Res J 2023;20:111.

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of a group of abnormalities such as in syndromic cases.^[1]

The anatomical and physiological variations such as tooth malposition, nasal septum deviation, or stenosis of the nasal vestibule in the maxillary sections put patients with CLP at an increased risk of oral diseases. In addition, the probability of caries intensifies as patients with CLP are unable to maintain oral hygiene due to the inability to eliminate soft foods consumed during surgical and orthodontic treatment.^[2,3]

The most common oral health concern in patients with CLP is dental caries. Prevention and early detection are paramount for the multidisciplinary management of patients with CLP.^[4] Prevalence of dental caries and caries experience is depicted using the decayed, missing, and filled teeth (DMFT) index that numerically describes the prevalence of past and present caries and is calculated by totaling the number of decayed (D), missing due to caries (M), filled (F), and teeth (T). Caries experience in the permanent dentition is denoted by upper case letters (DMFT) and lower case letters are used to represent caries experience in the primary dentition (dmft).^[1] Zhu *et al.*^[5] discovered a greater occurrence of caries in patients with CLP than those with cleft lips with/without alveolus.^[5] It is well documented in the literature that higher plaque levels and caries rates are seen in the maxillary anterior teeth.^[2,6,7,34] This may be attributed to difficulty in brushing, lack of flexibility of the surgically corrected lip, limited access to teeth located within the cleft structure, and the patient's anxiety about brushing around the cleft area. The scarcity of guidance that caregivers receive on nutrition and oral hygiene may also lead to higher caries rates.^[2] Caregivers of children affected with CLP often consider dental care to be less important than medical and surgical care.^[8] The high expense of dental treatment and the fact that many CLP patients must travel far distances for treatment further limit their access to dental care. It has been postulated that the structure of the cleft region, surgery and surgical scar tissues, limited movement of the lips, and enamel defects interfere with the maintenance of adequate oral hygiene in patients with CLP.^[9]

Literature has found high caries prevalence due to poor oral hygiene^[10,11] in children with CLP compared to healthy children of the same age, in disparity to the outcome of studies conducted by Moura *et al.* and Parapanisiou *et al.*^[12,13] These inconsistencies have been

linked to factors such as the limited sample size and wide age range, the lack of a control group, and the inability to differentiate between the various types of cleft. Despite multiple investigations, there is scarce literature on how site-specificity in patients with CLP influences caries prevalence.^[4] Antonarakis *et al.* 2013^[4] performed a systematic review with meta-analysis to analyze the prevalence of caries in nonsyndromic patients with cleft lip and/or palate and concluded that nonsyndromic patients with CLP tend to have higher caries prevalence, both in the permanent and the deciduous dentition, in comparison with matched non-CLP controls.^[4] Worth *et al.* 2017^[1] did another meta-analysis to determine if individuals with an orofacial cleft were at a higher risk of caries. The study concluded that people with cleft lip and/or palate had greater caries prevalence, both in the primary and permanent dentition.^[1] In addition, Hasslöf and Twetman conducted a systematic analysis in 2007^[14] that included case-control studies but could not reach a conclusive decision about the association of CLP with caries prevalence.^[14]

This revised review will provide an overview of the latest research in this field and also give a complete re-appraisal of previous literature. The goal of the present article was to include published studies that examined caries prevalence in patients with unilateral CLP (UCLP) and bilateral CLP (BCLP) to find out whether there exists a quantitative difference in caries experience among them. To the best of our knowledge, no prior attempt has been made to conduct a meta-analysis to assess the difference in caries prevalence between patients with UCLP and BCLP.

MATERIALS AND METHODS

Using the established Preferred Reporting Items for Systematic Reviews and Meta-Analysis checklist,^[15] the systematic review protocol was framed [Refer to Supplementary Table 1].

Utilizing the population, intervention, comparison, and outcomes framework of systematic review, the review question was formulated that defines the population (nonsyndromic CLP patients), intervention (recording DMFT index), comparison (nonsyndromic UCLP and BCLP patients), and outcome (DMFT score).

The formulated research question was "Is caries prevalence site-specific in patients with CLP?" The review protocol was registered on PROSPERO with registration number CRD2021292425.

Eligibility criteria

Strict inclusion criteria were set to identify relevant articles from the database. The identification and filtering of articles were performed by two examiners (S. S. and A. G.). Full text of relevant articles was obtained and independently screened by both reviewers. Inclusion criteria were based on studies that described different types of clefts, only considered nonsyndromic UCLP and BCLP patients, included either permanent or primary dentition or both, and reported data in the form of DMFT/dmft score for different types of clefts in the form of mean and standard deviation (SD). Only articles published in English from inception to November 2021 were considered. Exclusion criteria were based on the elimination of studies that did not describe the type of cleft, studies that evaluated syndromic UCLP and BCLP patients, and studies that did not categorize data individually for each cleft type rather results were given in terms of cleft and noncleft groups. Studies, in which the aim did not match the aim of the review and studies with the presence of any confounding factor that interfered with the outcome were also excluded. Case reports, letters, short communications, case series, and reviews were eliminated.

Outcome assessed

Caries experience was assessed using the DMFT index in permanent dentition or dmft in the case of deciduous dentition in patients with UCLP and BCLP. The outcome was given in mean and SD.

Information sources and search

To identify relevant articles that met the specified inclusion criteria, a MEDLINE/PubMed, Scopus, and EBSCOhost search were carried out. Manual screening and selection of studies were also done through references to selected studies. The search was implemented by two examiners (J. W. and S. S.) in November 2021. MeSH (Medical Subject Headings) was paired with “AND” and “OR” to establish a database ([cleft lip palate] AND [caries prevalence]). Titles and abstracts were first screened against the inclusion and exclusion criteria. Full texts were independently obtained and evaluated for the second screening by the two researchers (S. S. and J. W.). Any discrepancies were resolved by a craniofacial research expert (P. B.). Figure 1 depicts a flowchart of the process of selection of included studies.

Data collection process and data items

Table 1 shows data extraction from the included studies that were performed by two reviewers

independently (J. W. and S. S.) under the following headings: Author and year, sample size, age group, types of clefts, results, and conclusion. A modified Newcastle–Ottawa Scale (NOS) was applied to evaluate the risk of bias.

Quality assessment of included studies

For quality assessment of cross-sectional studies for the systematic review, the Newcastle–Ottawa Scale was adapted. This scale has been adapted from the Newcastle–Ottawa Quality Assessment Scale for cohort studies.^[18] Table 2 shows a modified version of the NOS scale which was used to assess study quality. Each study with established criteria received a grade of very good, good, satisfactory, or unsatisfactory based on the number of stars provided for sufficient methodology. In our analysis, one study was rated as good and the other two were rated as satisfactory.

Synthesis of findings

The data readings of the study were also tabulated and a meta-analysis was performed using the forest plot. Statistics from three studies were analyzed. Depending on the characteristic of effect size, data from three included studies were obtained. For each included study, continuous data were obtained to calculate the random risk ratio using the Mantel–Haenszel method. The heterogeneity of the included studies was investigated by inspecting study characteristics and using the I^2 statistic in cases where sufficiently similar studies were meta-analyzed. The measuring scale in all the included studies was different, therefore, meta-analysis utilizes mean difference as effect size. The calculations included the division of the mean difference in each study by that study's SD to create an index (standardized mean difference). This index was found to be constant among studies. A funnel plot of studies with continuous data was plotted to assess publication bias for both permanent and primary dentition.

RESULTS

Study selection

The search database yielded a total of 858 articles [Figure 1]. Duplicate studies were removed and abstracts of the remaining 456 articles were screened. Of these, 21 articles underwent screening by reading full-text articles. At the end of the screening, only three articles that fulfilled the inclusion criteria were included in the present analysis. Eleven studies were excluded as data

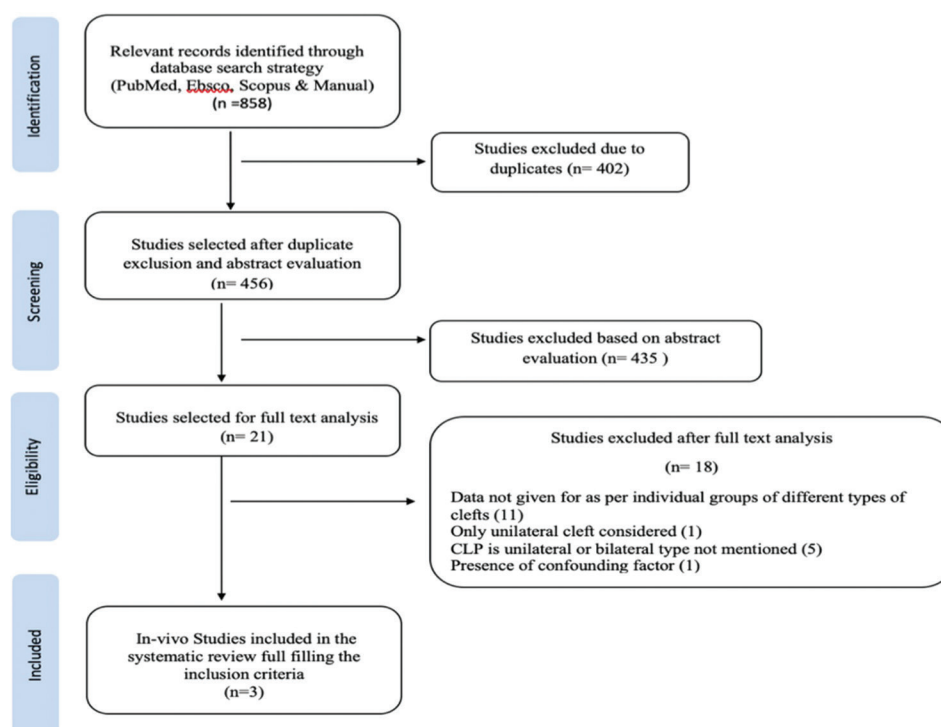


Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analysis flowchart of included studies. CLP: Cleft lip and palate.

Table 1: Data extraction was done under the following headings author and year, sample size, age group, types of clefts, results, and conclusion

Author and year	Age group	Type of clefts	Sample size	Results	Conclusion
Hazza'a <i>et al.</i> , 2011 ^[9]	4–8 years 8–12 years >12 years	UCLP and BCLP	98 controls and 98 clefts	Although there was a slight increase in the caries level in the BCLP subjects in both primary and permanent teeth, this difference was not statistically significant. However, when the total sample was considered, it was found that the caries experience in the BCLP is significantly higher than in the UCLP in both permanent (5.96±6.48 vs. 3.42±3.96) and deciduous dentition	Bilateral cleft lip and palate patients appear to be at a higher risk of caries experience and poorer in oral hygiene than those with UCLP patients
Mutarai <i>et al.</i> , 2008 ^[16]	26 months	The cleft group consisted of children with cleft lip (15.9%), cleft palate (20.3%), UCLP (43.5%), and BCLP (20.3%)	69 clefts and 69 controls	Children with oral clefts had a higher prevalence (DMFT) and severity (DMFT/tooth) of ECC compared to those without oral clefts. UCLP patients had a dmft index of 0.62±0.35 and 0.66±0.25 for BCLP patients	Children with oral clefts in southern Thailand had greater caries experience when compared with non-cleft subjects
Besseling and Dubois, 2004 ^[17]	4–6 years 11–13 years 14–16 years	Cleft lip and cleft lip and alveolus, UCLP, BCLP, and cleft palate	154	The mean number of caries-affected teeth for 4–6-year-old children was 9.95, 2.97 for 11–13-year-old children, and 4.93 for 14–16-year-old children, respectively. Children aged 4 to 6 who had a UCLP and BCLP had considerably more caries and a higher dmft index than children of the same age who just had a cleft lip or a cleft lip and alveolus	Vietnamese children with oral clefts have a high number of teeth damaged by dental caries, necessitating specific care for their oral health

BCLP: Bilateral cleft lip and palate, UCLP: Unilateral cleft lip and palate, ECC: *Early childhood caries*, DMFT: Decayed, Missing, and Filled Teeth

were not given for individual sub-types of clefts and instead, results represented only cleft and noncleft groups.^[3,6,8,10,12,19-23] Five studies with CLP patients that did not segregate results among UCLP and BCLP were also excluded.^[13,24-27] One study

considered only UCLP patients.^[28] One study had to be excluded due to the presence of a confounding factor, in which the association of caries prevalence and carbohydrate intake of patients with CLP was evaluated.^[29]

Study description

To generate a complete brief approximation of the difference in caries experience between patients with UCLP and BCLP, a random effects meta-analysis was done. Since the studies involved different populations throughout the world, random effects meta-analysis was employed to account for variance in caries prevalence outcomes. For a study to be a part of a meta-analysis, it must give an account of the sample size and mean dmft/DMFT for each group, and either the SD, standard error (SE), SE of difference, or *P* value. Meta-analysis was conducted using Revman 5.3. The analysis involved studies comparing patients with UCLP and BCLP patient groups in terms of caries prevalence for both permanent and primary dentition.

Characteristics of included studies

The data for included studies were extracted from the included studies under the following headings: author and year, sample size, age group, types of clefts, results, and conclusion. The data from the included studies were collected in the age group ranging from 4 to 16 years. It was unclear among included studies whether any surgical intervention, prior dental treatment, or any follow-up was taken

into consideration before recording DMFT. All the studies concluded that patients with BCLP were more susceptible to caries than patients with UCLP.^[9,16,17]

Synthesis of results

Figures 2a and b show forest plot illustrations of random effect meta-analysis of included studies for the primary dentition (dmft) and permanent dentition (DMFT), respectively. In the current analysis, the standard mean difference obtained for primary teeth in mixed dentition was 0.36 (95% confidence interval [CI]: 0.69–0.03) and for permanent dentition was 0.57 (95% CI: 1.03–0.11). The variation was statistically significant for caries experience in the permanent dentition evaluated using a DMFT score with a *P* = 0.01 and moderate statistical heterogeneity among included studies with (*I*²-34%, *P* < 0.05). On the other hand, the difference was also statistically significant in primary teeth with mixed dentition using dmft with a *P* = 0.03 and no statistical heterogeneity among included studies with (*I*²-0%, *P* < 0.05). The result of the meta-analysis indicates that patients with BCLP have higher caries prevalence. The funnel plot

Table 2: Assessment of study quality using a modified version of the Newcastle–Ottawa Scale created for cross-sectional studies

Author cross-sectional studies	Selection Maximum 5 stars	Comparability Maximum 2 stars	Outcome Maximum 3 stars	Quality score
Hazza <i>et al.</i> , 2011 ^[9]	★★★★	★	★★★	8-Good
Mutarai <i>et al.</i> , 2008 ^[16]	★★★	★	★★	6-Satisfactory
Besseling <i>et al.</i> , 2004 ^[17]	★★	★★	★★	6-Satisfactory

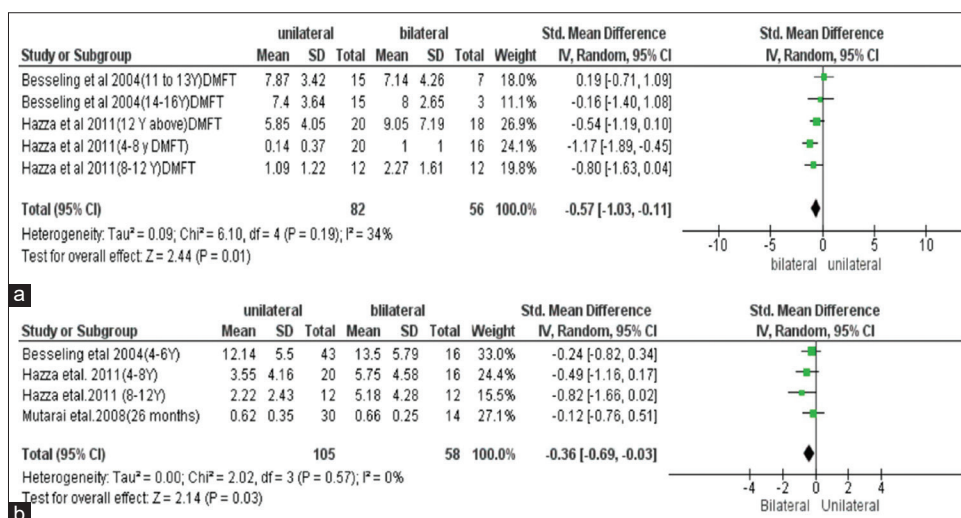


Figure 2: (a) Forest plot for permanent dentition (decayed, missing, and filled teeth [DMFT]), (b) Forest plot for deciduous dentition (DMFT). DMFT: Decayed, missing, and filled teeth, CI: Confidence interval, SD: Standard deviation.

as per Supplementary Figures 1 and 2 was visually symmetrical suggesting a lack of publication bias.

DISCUSSION

This study focused on the difference in caries prevalence among patients with UCLP and BCLP. So far, such a segregated analysis has not been performed and highlights an area of focus for health promotion and disease prevention activities for cleft patients. The findings of this meta-analysis show that patients with BCLP have higher dmft and DMFT scores than patients with UCLP. This could be associated with the massive envelopment of anatomical structures in clefts.^[30]

Past craniofacial research has already established a link between higher caries prevalence in cleft patients than noncleft.^[1,3,5,6,8,10,14,20,24,31] Similarly, our literature search revealed studies that showed that higher caries prevalence was associated with BCLP. Up until now, however, this evidence was inconclusive. Previous theories stated that the predisposition of patients with CLP to acquire caries is a consequence of poor oral health. Reasons given for this included (1) Deficiency in flexibility caused by invasive lip repair and (2) The structure of the cleft causing discomfort while brushing that poses a challenge in maintaining good oral hygiene.^[11] Furthermore, crowding, a higher frequency of supernumerary teeth, and an underdeveloped maxilla with arch space deficiency make brushing and flossing more challenging and effective cleaning of the teeth by the tongue and saliva. In past studies and in our findings, no statistically significant association between gender and caries experience has been shown.^[9,12]

Another paramount factor is food impaction commonly seen in patients with CLP, as food tends to escape through the nose and regurgitate into the oral cavity. This tends to increase the risk of caries development as substrates for cariogenic bacteria are present in the mouth more frequently and for longer periods.^[2,24] Enamel hypoplasia, which has shown to be of higher prevalence in CLP patients.^[2] Socioeconomic status is an additional factor associated with increased caries prevalence in patients with CLP. Cleft patients born into low socioeconomic status or those born in low-and middle-income countries with low access to specialized cleft care exhibit increased caries prevalence. Attention must be given to the issue of health inequities.^[29,32] Oral health IQ of the

primary caregivers may also explain higher caries rates; parents may feed their children snacks high in added sugars to console them to be empathetic in light of the CLP.^[4] Furthermore, patients with CLP tend to retort to mocking at school as a result of their dental malposition by showing less interest in their oral hygiene.^[4]

The findings of the conducted meta-analysis point toward the site-specific nature of caries prevalence in patients with CLP which draws attention to the need for routine dental checkups. Previous literature reports a higher incidence of UCLP than BCLP, however, caries prevalence is higher in BCLP due to reasons previously discussed.^[33,34] Although the overall incidence of bilateral BCLP is less, its negative impact on oral hygiene, the increased caries prevalence, and the negative effect on quality of life should not be neglected. Therefore, it is paramount to focus on future cleft care initiatives and research on-site specificity of caries prevalence in CLP patients.

Limitations

However, there were a few limitations of this study. First, the population group and type of dentition compared were heterogeneous. This could affect the outcome as the occurrence of caries maybe more in a particular type of population. Caries prevalence also is dictated by the type of dentition, for example, bottle feeding and inability to maintain proper hygiene might result in higher caries prevalence in deciduous dentition in comparison to permanent. The second limitation can be that the review is based on only three articles due to a lack of literature that provides the proper result concerning different types of clefts. This also indicates the scope for further randomized controlled trials that involve data on both UCLP and BCLP patients.

CONCLUSION

The outcome of the study indicates that there is a higher occurrence of caries in patients with BCLP than UCLP in both permanent and primary dentition. From the findings of the study, one can state that caries prevalence in patients with CLP is site-specific. Therefore, there is a need for special care and attention in CLP patients to maintain good oral hygiene and prevent the decay of teeth at a young age.

Financial support and sponsorship
Nil.

Conflicts of interest

The authors of this manuscript declare that they have no conflicts of interest, real or perceived, financial or nonfinancial in this article.

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Supplementary Table 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist table

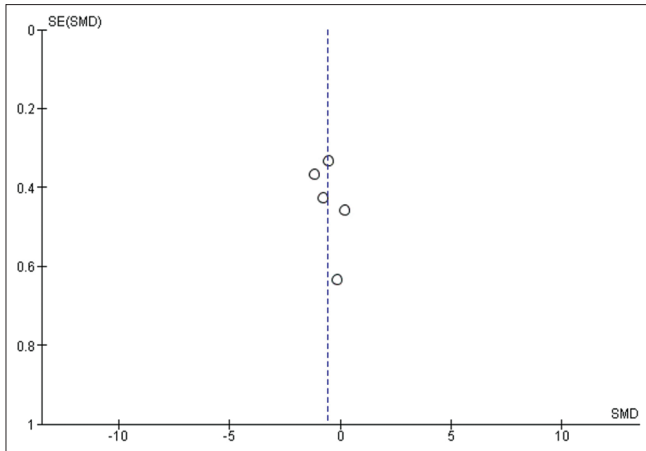
Section and topic	Item number	Checklist item	Location where item is reported
Title			
Title	1	Identify the report as a systematic review	1
Abstract			
Abstract	2	See the PRISMA 2020 for Abstracts checklist	1
Introduction			
Rationale	3	Describe the rationale for the review in the context of existing knowledge	2
Objectives	4	Provide an explicit statement of the objective (s) or question (s) the review addresses	2
Methods			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses	3
Information sources	6	Specify all databases, registers, websites, organizations, reference lists, and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted	3
Search strategy	7	Present the full search strategies for all databases, registers, and websites, including any filters and limits used	3
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process	3
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	3
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g., for all measures, time points, and analyses), and if not, the methods used to decide which results to collect	3 and Table 1
	10b	List and define all other variables for which data were sought (e.g., participant and intervention characteristics and funding sources). Describe any assumptions made about any missing or unclear information	3 and Table 1
Study risk of bias assessment	11	Specify the methods used to assess the risk of bias in the included studies, including details of the tool (s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process	5
Effect measures	12	Specify for each outcome the effect measure (s) (e.g., risk ratio and mean difference) used in the synthesis or presentation of results	5
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g., tabulating the study intervention characteristics and comparing against the planned groups for each synthesis [item #5])	5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions	5
	13c	Describe any methods used to tabulate or visually display the results of individual studies and syntheses	5
	13d	Describe any methods used to synthesize results and provide a rationale for the choice (s). If meta-analysis was performed, describe the model (s), method (s) to identify the presence and extent of statistical heterogeneity, and software package (s) used	5
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g., subgroup analysis and meta-regression)	5
	13f	Describe any sensitivity analyses conducted to assess the robustness of the synthesized results	5
Reporting bias assessment	14	Describe any methods used to assess the risk of bias due to missing results in a synthesis (arising from reporting biases)	Table 2
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome	5

Contd...

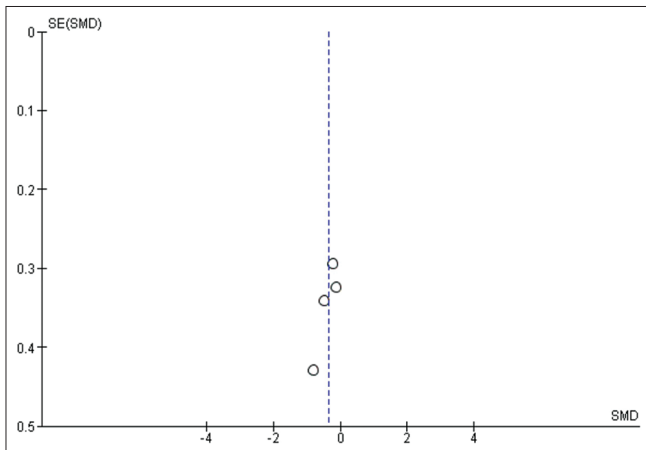
Supplementary Table 1: Contd...

Section and topic	Item number	Checklist item	Location where item is reported
Results			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram	3
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded	3, 5
Study characteristics	17	Cite each included study and present its characteristics	7
Risk of bias in studies	18	Present assessments of risk of bias for each included study	5 and Table 2
Results of individual studies	19	For all outcomes, present, for each study: (a) Summary statistics for each group (where appropriate) and (b) An effect estimate and its precision (e.g., confidence/credible interval), ideally using structured tables or plots	4 and Table 1
Results of syntheses	20a	For each synthesis, briefly summarize the characteristics and risk of bias among contributing studies	4 and Table 1
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g., confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect	5
	20c	Present results of all investigations of possible causes of heterogeneity among study results	5
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results	5
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed	5
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed	5
Discussion			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence	6
	23b	Discuss any limitations of the evidence included in the review	6
	23c	Discuss any limitations of the review processes used	6
	23d	Discuss the implications of the results for practice, policy, and future research	6
Other information			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered	2
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared	2
	24c	Describe and explain any amendments to information provided at registration or in the protocol	2
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review	6
Competing interests	26	Declare any competing interests of review authors	7
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: Template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review	NA

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, *et al.* The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. For more information, visit: <http://www.prisma-statement.org/>. NA: Not available



Supplementary Figure 1: Funnel plot for permanent dentition (decayed, missing, and filled teeth). SMD: 0.57 (95% CI: 1.03 to 0.11).



Supplementary Figure 2: Funnel plot for deciduous dentition (decayed, missing, and filled teeth). SMD: 0.36 (95% CI: 0.69 to 0.03).