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SYSTEMATIC REVIEW

# Non-Invasive Methods and the Use of Infiltrating Resins for the Control of Caries Progression in Deciduous Teeth: A Systematic Review and Meta-Analysis

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**ABSTRACT**

**Objective:** To evaluate the influence of non-invasive treatment associated with the use of infiltrating resin for managing caries lesions in primary teeth. **Material and Methods:** A systematic review was performed by selecting articles from 6 online databases, using a search algorithm and eligibility criteria for data extraction and data synthesis for the papers included. Clinical trials involving primary teeth with incipient caries lesions (1/2 of the enamel or 1/3 of the outer dentin) were included, presenting full text and answering the study's guiding question. This study used the RoB 2 tool for the risk of bias assessment and GRADE for certainty of evidence. Random effects meta-analyses were implemented, and lesion progression treatment effects were estimated through relative risk (RR) and associated 95% confidence intervals. **Results:** A total of 440 studies were found. After analyzing the inclusion criteria and removal of duplicates, eight studies were analyzed for quality evidence. Five of the eight studies included in this review contributed to the meta-analysis, all with some reflections regarding the risk of bias. Overall, the results of the meta-analysis showed that non-invasive treatment, when associated with the use of infiltrating resins, significantly reduced the risk of caries progression in relation to the treatment without this addition for follow-up periods ranging from 12 months to 2 years (RR 0.51 [0.40-0.65]). **Conclusion:** There is moderate certainty of evidence that the use of infiltrating resins associated with non-invasive treatments decreases the risk of caries progression in primary teeth with incipient caries lesions (1/2 of the enamel or 1/3 of the dentin outer) when combined with non-invasive control methods alone.

**Keywords:** Dental Materials; Fluorides, Topical; Dental Caries; Tooth, Deciduous; Clinical Trial.

## Introduction

The current scenario regarding the diagnosis and treatment of caries lesions has been supported by the early detection and control of caries disease [1]. Translational research has combined basic and applied areas supporting evidence-based dentistry [2]. This has been especially important in poor regions, where resources are limited, with recent research helping identify best health practices [3]. During childhood, untreated dental caries in deciduous teeth affects around 500 million children, thus, being the most prevalent chronic disease in this age group [3,4].

Caries have a complex etiology of a multifactorial nature and dependent biofilm – sucrose [5], considered a chronic-cumulative disease shaped by social and behavioral factors [6,7]. Global reports demonstrate that the reduction in caries prevalence has been overestimated [8,9], especially in young children, whose incidence of early childhood caries has been linked to a public health problem worldwide [9-12]. The effort to control the progression of incipient proximal caries is mandatory to avoid the circle of treatment and re-treatment, known as the 'death spiral of restorations' [13].

From this point of view, preventive and minimal intervention protocols have been proposed as an option for caries control. However, methods focused on a single or few risk factors tend to fail due to the etiological complexity of caries [11-12]. Strategies such as diet control, flossing, and fluoride application are closely related to good practices in health education. However, these strategies require time, resources, and patient adherence to treatment [13]. In this context, micro-invasive approaches have been gaining prominence as they depend not on the patient's behavior [9-13]. Resin infiltration plays a prominent role and can be used up to 1/3 of the outer dentin, avoiding restorative treatment, especially on permanent teeth [11,12,14]. Nevertheless, there is still a scientific gap in primary teeth, and it is necessary to evaluate the scientific evidence provided by the most recent clinical trials to verify its broad clinical recommendation.

In a recent systematic review [15], it was found that infiltrative resins can reduce the progression of caries in permanent teeth. Still, the evidence remains to be determined as to the effectiveness of this approach in primary teeth. Data on the efficacy of infiltrative resins in primary teeth are not robust in the literature, and when they are presented in meta-analysis [16], they are clustered with data from permanent teeth, which makes their interpretation and decision-making difficult. This situation emphasizes the need to conduct the present systematic review focused only on deciduous teeth.

In this regard, the present systematic literature review aims to analyze the following leading question - What is the best strategy to control the progression of incipient caries lesions in primary teeth: non-invasive treatments (diet control, biofilm control, and fluoride control) or their use combined with resins infiltration.

## Material and Methods

### Protocol and Registration

The systematic review protocol was developed and registered on PROSPERO under protocol nº CRD 42021250816 and followed PRISMA's (Preferred Reporting Items for Systematic Reviews and Meta-Analyzes) [17] to guide to report this review and the Cochrane Handbook of Systematic Reviews for conducting systematic reviews of in vitro studies [18]. The aim of this is to guide to report of studies.

### Eligibility Criteria

This systematic review was based on the following guiding PICOS (P – incipient caries in primary teeth; I – resin infiltration; or resin infiltration plus control of diet; resin infiltration plus use of fluorides; resin

infiltration plus biofilm control (Flossing or oral hygiene); C – non-invasive treatments (diet control, biofilm control, and fluoride control); O – proximal caries progression; S –Clinical Trial) question: *What is the best strategy to control the progression of incipient caries lesions in primary teeth: non-invasive treatments (control of diet, use of fluorides and biofilm control) or their use combined with resins infiltration?* The eligible studies were identified on PubMed, Scopus, Lilacs, Open Grey, Science Direct, Web of Science, and Central Cochrane databases.

Inclusion Criteria

To properly refine the research, some inclusion criteria were defined: to have full text published, which answered the PICOS question, and clinical trials that involved incipient carious lesion (1/2 of the enamel or 1/3 of the outer dentin) in primary teeth. There were no language restrictions or period of publication.

Exclusion Criteria

Editorials, guidelines, letters, abstracts of conferences, theses, and dissertations were excluded.

Search Strategy

Keywords (MeSH and/or words) and Boolean operators were used to ensure a broader search for the subsequent analysis of the inclusion criteria. The following terms were appropriately combined and modified for each platform: "Child; Children; resin infiltrant; fluoride varnish; incipient caries; primary teeth; progression; caries development; clinical trial. The search was independently carried out by two researchers (H.C.R.A. and G.H.P.O.), and disagreements were resolved by consensus. The detailed research strategy for each platform can be consulted in the Supplementary file (Table 1).

Study Selection

In the first stage, two independent researchers performed the reading of titles and abstracts (H.C.R.A. and G.H.P.O). Duplicated studies and those that did not meet the inclusion criteria were discarded. The studies that met the inclusion criteria were selected for full reading, resulting in the selection of the articles included in this synthesis. During the searches, two other reviewers resolved disagreements (V.E.S.J. and M.V.H.).

Data Extraction

One author (H.C.R.A.) collected the information, another author (G.H.P.O.) reviewed the results, and a consensus meeting with two other authors (V.E.S.J. and M.V.H.) confirmed the data extracted. The qualitative data collected were as follows: authors, year of publication, type of study, country, sample, intervention, comparison, previous analysis of caries risk, dental surface, assessment time, outcomes, caries progression analysis method, main results, relative risk, therapeutic effect (absolute risk reduction: ARR) and preventive fraction. The preventive fraction was estimated by analyzing the occurrence of caries lesion progression in the experimental group and the control group. The formula used to obtain the calculation of the preventive fraction was PF = (Xc – Xe)/Xc, where "X" is the occurrence of caries lesion progression in each group [19].

Risk of Bias

The quality assessment of each manuscript was carried out through the Cochrane risk of bias tool (RoB 2) [18], which assesses the risk of bias taking into account the following domains: domain 1- Risk of bias arising from the randomization process; domain 2 - Risk of bias due to deviations from the intended interventions (effect of intervention assignment); domain 3 - Missing outcome data; domain 4 - Risk of bias when measuring the

outcome; domain 5 - Risk of bias in the selection of the reported result. After analyzing these five domains, each study's overall risk of bias was verified.

Certainty of Evidence

The combined quality of the studies was evaluated through the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) [20] criteria system to identify any limitations, inconsistencies, indirect evidence, inaccuracies, and other relevant considerations. Through this analysis, it is possible to classify the certainty of evidence as high, moderate, low, and very low and identify the level of importance of the evidence. Only studies considered at low risk of bias or classified as having some considerations were included in this analysis.

GRADE Working Group certainty of evidence: high certainty: very confident that the true effect lies close to that of the estimate of the effect. Moderate certainty: moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Low certainty: confidence in the effect estimate is limited: the true effect may differ substantially from the estimate of the effect. Very low certainty: very little confidence in the effect estimate: the true effect is likely to differ substantially from the effect estimate. GRADE suggests a nine-point scale to judge the importance of evidence. The upper end of the scale, 7 to 9, identifies outcomes of critical importance. Ratings of 4 to 6 represent important outcomes but are not crucial to decision-making. Ratings of 1 to 3 are items of limited significance to decision-making.

Data Synthesis and Meta-analysis

Study heterogeneity was assessed by evaluating individual study settings, inclusion and exclusion criteria, treatment methods, and data collection methods. Statistical heterogeneity was examined by visual inspection of Confidence Intervals (CIs) for estimated treatment effects on forest plots.

The chi-square test was applied to assess heterogeneity, with a p-value below the 10% level ($p < 0.1$) was considered indicative of significant heterogeneity [21]. The I2 test for homogeneity was performed to quantify the extent of heterogeneity. Studies with some considerations or low risk of general bias, analyzed by ROB2, could be considered for inclusion in the meta-analysis. Random effects meta-analyses were conducted as they were considered appropriate better to approximate the expected variations in the trial environments. Treatment effects were calculated using the relative risk (RR) for lesion progression, along with the associated 95% confidence intervals (95% CI).

We conducted the meta-analyses with RevMan (RevMan 2011 [Computer program] The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). Version 5. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011.

## Results

Research Data

A total of 440 potentially eligible articles were found in the databases selected. Following the analysis of titles and abstracts, 46 duplicated articles were identified, which were promptly excluded. For the removal of duplicates, the endnote program was used. Out of the 394 previously eligible articles, 377 did not meet the specific objective of the present systematic review, with the remaining 17 manuscripts being analyzed thoroughly. Subsequently, nine studies were discarded due to the following reasons: a) Adult patient or permanent teeth:

(n=08); b) Different control group: (n=01). Therefore, eight studies were selected to be included in this systematic review. The references included in these eight studies (n=237) were also analyzed, though no additional manuscript was integrated into the present study (Figure 1).

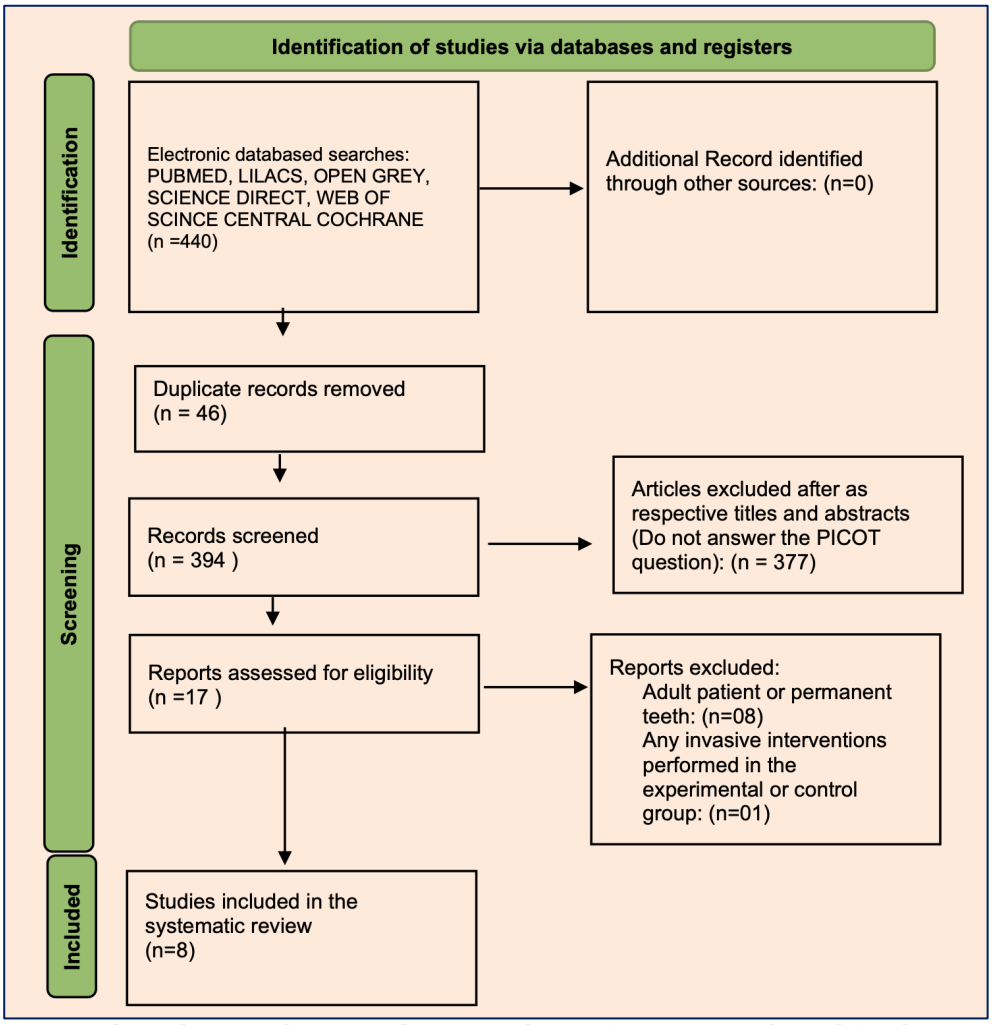


**Figure 1. Flowchart showing the research steps and selection analysis adopted for the systematic review.**

General Characteristics of The Clinical Trials Selected

Of the eight articles included in this systematic review, three were carried out in Brazil, two in Greenland, one in New Zealand, one in Poland, and one in the USA. The studies were published between 2010 and 2020. The sample of studies totaled 416 children aged between 2.5 and 9 years old. The assessment of the progression of dental caries was performed through clinical and/or radiographic examinations. The characteristics of both studies are described in Table 1.

**Table1. Individual characteristics of the studies selected for the risk of bias analysis.**

| Sample | Intervention | Comparison | Previous Analysis of Caries Risk | Surface | Assessment time | Outcomes | Caries Progression Analysis Method | Main Results | RR | Therapeutic Effect (ARR) | PF (Pc–Pe)/Pc |
|---|---|---|---|---|---|---|---|---|---|---|---|
| N=42 (23 female, 25 male), mean age 7.2 ± 0.6 years | Resin infiltration followed by fluoride varnish FV (2.26% F) application (test group) | Control only FV | Caries experience, measured by the def-s index | Proximal | 1 year | Caries lesion progression:<br><br>Visual caries assessment using ICDAS scoring system AND radiographic scores (in 78 lesions) | The lesion was considered to have progressed if the ICDAS or radiographic score increased. | After 1 year, the ICDAS scores of 31% of the test lesions, and 67% of the control lesions had progressed (p<0.01). Radiographically, 23% of the test lesions and 62% of the control lesions had progressed (p<0.01). | By radiographic (At first year)<br><br>0.32<br>[0.17-0.60] | By ICDAS Resin infiltration + FV *vs.* FV = 35.7%<br><br>By radiography Resin infiltration + FV *vs.* FV = 38.4% | By ICDAS<br>PF Resin infiltration + FV *vs.* FV (control) = 0.67<br><br>By radiograph<br>0.62 |
| N=47, aged between 5 and 8 years old, mean=6.5 years | Resin infiltration plus fluoride varnish (I+F) or sealing plus fluoride varnish (S+F) | Control only FV | Caries experience, measured by the def-s index | Occlusal | Up to 34 months after treatment (mean=22 months) | Caries lesion progression:<br><br>Visual caries assessment using ICDAS scoring system AND radiographic scores (in 139 lesions) | The lesion was considered to have progressed if the ICDAS or radiographic score increased. | Infiltration and sealing occlusal surfaces with initial caries lesions on the primary molar teeth showed high efficacy in arresting caries progression, significant for the I+F or borderline significant for the S+F compared with the F group. | By radiographic<br><br>0.41<br>[0.19-0.90] | By ICDAS: it was not possible to be calculated (data missing)<br><br>By radiographic<br><br>Resin infiltration + FV *vs.* FV = 21.28%<br><br>Sealing +FV *vs.* FV (control) = 17.03% | By ICDAS: it was not possible to be calculated (data missing)<br><br>By radiograph<br><br>PF Resin infiltration + FV *vs.* FV (control) = 0.58<br><br>PF Sealing +FV *vs.* FV (control) = 0.47 |
| In the first year - 85 patients, a mean age of 8.0 (range, 7–9)<br><br>In the second year - 69 patients, a mean age of 8.2 (range, 6–9) | Resin infiltration | Control only FV | Cariogram model | Proximal | 2 year (Radiographic -12 and 24 months) | Caries lesion progression:<br><br>Radiographic scores | The lesion was considered to have progressed if the ICDAS or radiographic score increased. | Infiltration is more efficacious than fluoride varnish for controlling carious lesions progression in proximal lesions in primary molars, and most children find the treatment acceptable | By radiographic At first year<br><br>0.45<br>[0.22-0.93]<br><br>On second years<br>0.52<br>[0.31-0.88] | By radiography Resin infiltration *vs.* FV = 1 Year<br><br>13%<br><br>2 Year<br>Resin infiltration *vs.* FV = 20.8% | By radiograph<br><br>At first year<br>PF Resin infiltration *vs.* FV = 0.55<br><br>In second year:<br>PF Resin infiltration *vs.* FV = 0.50 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| N=42 (23 female, 19 male), mean age 6.7 ± 1.3 | Resin infiltration plus oral hygiene instruction (fluoride toothpaste and flossing) | Control, oral hygiene instruction (fluoride toothpaste and flossing) | Cariogram model | Proximal | 1 year | Caries lesion progression:<br>Radiographic scores (in 84 lesions) | The lesion was considered to have progressed if the radiographic score increased. | Caries infiltration of proximal caries lesions in primary molars are significantly more efficacious than standard therapy alone (fluoride toothpaste + flossing) | By radiographic<br>0.57<br>[0.27-1.22] | By radiographic<br>Resin infiltration + oral hygiene instruction vs. control = 21.4% | By radiograph<br>PF Resin infiltration + oral hygiene instruction vs. control = 0.64 |
| N=45, mean age 6.82 ± 1.09 | Resin infiltration + FV | Control only FV | The study did not describe the method used | Proximal | 2 years | Caries lesion progression:<br>Radiographic scores (in 90 lesions) | The lesion was considered to have progressed if the radiographic score increased. | Resin infiltration as an adjunct to standard-of-care preventive measures is significantly more effective radiographically in reducing the progression of non-adjacent, incipient, proximal enamel lesions in primary molars compared with standard-of-care preventive measures alone after 24 months. | By radiographic at first year<br>0.46<br>[0.19-1.10]<br>On second year<br>0.56<br>[0.32-0.95] | By radiographic<br>Resin infiltration *vs.* FV (at first year) = 17,07%<br>Resin infiltration *vs.* FV (on second years )<br>= 32% | By radiograph<br>PF Resin infiltration *vs.* FV (at first year) = 0.53<br>PF Resin infiltration *vs.* FV (on second year) = 0.44 |
| N=50 (28 female, 22 male), mean age .27 ± 1.29 | Resin infiltration + flossing | Flossing | Cariogram model | Proximal | 2 years | Caries lesion progression:<br>Radiographic scores (in 90 lesions) | The lesion was considered to have progressed if the radiographic score increased. | The results indicate that resin infiltration was an efficacious method for controlling proximal caries lesions in primary molars. | By radiographic (In second years)<br>0.44<br>[0.21-0.90] | By radiographic<br>Resin infiltration + flossing *vs.* flossing = 31.1% | By radiograph<br>PF Resin infiltration + flossing *vs.* flossing = 0.56 |
| N=24, mean age 6 ± 1.23 years | Resin infiltration + Oral hygiene instruction + dietary recommendations | Oral hygiene instruction + dietary recommendations | Caries experience, measured by the dmft index | Proximal | 2 years | Caries lesion progression:<br>Radiographic scores (in 48 lesions) | The lesion was considered to have progressed if the radiographic score increased | Infiltrating proximal lesions decreases radiographic caries progression in primary molars after a two-year follow-up period. | By radiographic (In second years)<br>0.65<br>[0.43-0.98] | By radiographic<br>Resin infiltration + oral hygiene instruction + dietary recommendations *vs.* control = 25.1% | By radiograph<br>PF Resin infiltration + oral hygiene instruction dietary recommendations *vs.* control = 0.35 |

ARR: Absolute Risk Reduction.

Risk of Bias and Certainty of Evidence

All studies were individually assessed according to the 5 domains of the Cochrane revised risk of bias tool for randomized trials (RoB 2) [22]. Table 2 presents a summary of these domains, rated as high with some concerns and as a low risk of bias.

**Table 2. Risk of bias assessment of the studies included in the present study takes into account the five domains of the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2).**

| Studies | Domains | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | Overall |
| Sarti et al. [8] | + | ? | + | + | ? | ? |
| Jorge et al. [11] | + | ? | + | + | ? | ? |
| Ammari et al. [12] | + | ? | + | + | ? | ? |
| Bakhshandeh & Ekstrand [23] | ? | ? | + | + | ? | - |
| Turska-Szybka et al. [24] | ? | ? | + | + | ? | - |
| Ekstrand et al. [25] | + | ? | + | + | ? | ? |
| Bagher et al. [26] | + | ? | - | + | ? | - |
| Foster Page et al. [27] | + | ? | + | + | ? | ? |

+Low risk of bias; ?Some considerations; -High risk of bias.

The most critical biases found in both studies [23,24] concern selection biases related to randomization and bias in the selection of the result reported. In the study by Bakhshandeh and Ekstrand [23], randomization was performed by the pediatric dentist. However, no scientific randomization technique was considered, nor was it guaranteed that the patient did not know the intervention sequence. The study by Turska-Szybka et al. [24] only mentions the randomization employed, although the mode and process of allocation are not described. Thus, following the RoB 2 flowchart analysis for domain 1, the two studies mentioned above [23,24] were classified as requiring some considerations, while the others were considered to have a low risk of bias [8,11,12,25-27]

Regarding the analysis of biases in domain 2 (performance bias), it was found that all studies included were not evaluated for intention-to-treat, although there was no significant impact on outcomes for not doing so. After analyzing the RoB 2 flowchart for domain 2, the studies were classified as having some concerns.

Domain 3 deals with missing or lost data results. Only the study by Bagher et al. [26] was classified as a high risk of bias in this domain, as there was a significant sample loss at the end of the second year of the clinical trial, exceeding 20% of the sample. Domain 4 deals with the analysis of the risk of bias when measuring the outcome. All studies had clear outcome parameters. Therefore, they were classified as low risk of bias. Lastly, domain 5 analyzes the risk of bias related to the selectivity of reported results. No studies specified whether the data were analyzed according to a pre-established protocol prior to the survey.

Thus, after analyzing the RoB 2 flowchart and considering all domains (overall), three studies are classified as high risk of bias [23,24,26], and five studies are considered as some considerations [8,11,12,25,27]. However, despite the study by Bagher et al. [26] having been classified as having a high risk of bias, we also analyzed it from the perspective of its follow-up period of 12 and 24 months. At 24 months, there is a significant sample loss, which leads us to classify the study as a high risk of bias, according to ROB 2 guidelines. However, at 12 months, this loss is insignificant, being classified as some consideration for this interval.

The certainty and importance of evidence were also analyzed in conjunction with the GRADE system. Therefore, the existence of severe inconsistencies and risks of bias was verified, as shown in Table 3. Among the issues verified were the small sample size, the need for a clearer description in the clinical trial registration of all studies, and the significant loss of samples in one of the studies. Through this assessment, it was possible to identify the certainty of available evidence on the analyzed outcome as moderate. The importance of this outcome was rated critical, i.e., there is a clear recommendation regarding the addition of infiltrating resins in non-invasive treatments to control caries lesions in primary teeth.

**Table 3. The research steps and selection analysis were adopted for the systematic review.**
**Question**: Resin Infiltrat with or without another non-invasive method [test] compared to Caries control methods [control] for progression of caries in primary teeth [problem]
**Setting**:

| | | | Certainty assessment | | | | Nº of patients | | Effect | | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Nº of Studies | Study Design | Risk of Bias | Inconsistency | Indirectness | Imprecision | Other Considerations | Resin Infiltrant with or without another non-invasive method [ntervenção] | Caries Control Methods | Relative (95% CI) | Absolute (95% CI) | | |
| Outcome – Proximal Caries Progression | | | | | | | | | | | | |
| 6 | Randomized Trials | Serious[a,b] | Serious[c] | Not Serious[d] | Not Serious[d] | all plausible residual confounding would suggest spurious effect, while no effect was observed | 58/244 (23.8%) | 121/247 (49.0%) | RR 0.51 (0.40 to 0.65) | 240 fewer per 1.000 (from 294 fewer to 171 fewer) | ⊕⊕⊕◯ MODERATE | CRITICAL |

GRADE Working Group grades of Evidence; High Certainty: we are very confident that the true effect lies close to that of the estimate of the effect; Moderate Certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different; Low Certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect; Very Low Certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of Effect; CI: Confidence Interval; RR: Risk Ratio; [a]No intention-to-treat analysis was performed; [b]There is a lack of clear descriptions in the clinical trial registration of all studies; [c]All studies report small sample; [d]There are sample losses due to tooth exfoliation, but it does not reach critical levels in most studies. Only in the 2-year analysis by Bagher et al., Sample loss is significant.

Meta-analyses

Six studies were included in this meta-analysis [8,11,12,25-27]. Two studies [23,24] were not included in the meta-analysis because they have a high risk of bias so as not to generate a confounding variable in the meta-analysis results. As for the study by Bagher et al. [26], only data referring to the initial 12 months of the research were considered, due to the high rate of losses in the 24-month interval, as referred above. The synthesis consisted of comparisons of non-invasive methods associated or not with the use of infiltrating resins for the control of caries progression in deciduous teeth. The outcomes were obtained based on the analysis of caries lesion progression using radiograph pairs. In the follow-up period of 12 months – 2 years, there was a 51% risk of caries progression in the proximal surfaces in the control group, in which there was no use of infiltrating resins (0.51 [0.40-0.65]) (Figure 2). No statistically significant heterogeneity was detected in the studies, with the $I^2=0$ demonstrating that the studies in statistical results are homogeneous and that there was no variability.

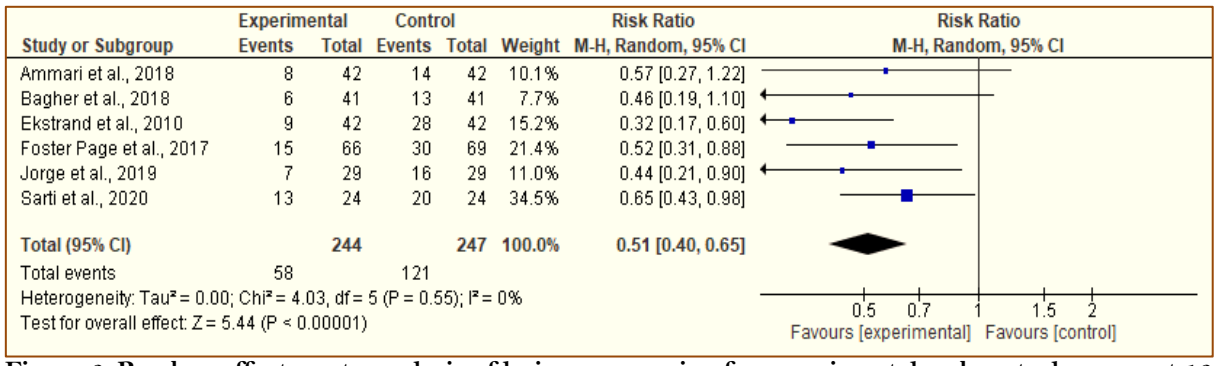


**Figure 2. Random effects meta-analysis of lesion progression for experimental and control groups at 12 months–2 years.**

## Discussion

According to the results from the present systematic review, resin infiltration associated with non-invasive approaches is effective in arresting dental caries progression in primary teeth with incipient caries lesions (1/2 of the enamel or 1/3 of outer dentin) when compared to non-invasive methods alone, in deciduous teeth. Moreover, it is important to observe that no statistical heterogeneity was observed among the studies inserted ($I^2$ =%; p=0.55), enabling to cluster the data and carry out a metanalysis of such, corroborating the findings from this revision, thus suggesting the application of resin infiltration as a preferred treatment to avoid the progression of approximal caries.

Nevertheless, this conclusion should be interpreted with caution due to the qualitative (methodological) heterogeneity between the studies, namely regarding follow-up times [12,23-25], the application of different caries detection criteria (ICDAS and radiograph) [22,25,26], as well as the adoption of several methods for an individual's caries risk assessment (Nyvad criteria and Caries Risk Analysis Instrument) [11,12,25,27]. It is worth pointing out that the sample size in some studies [8,23] can reduce the magnitude and, consequently, the assurance of the evidence presented [28].

Caries is a sucrose biofilm-dependent oral disease with a solid multifactorial influence [29]. Due to the anatomic characteristics of deciduous teeth, namely lower enamel and dentin thickness, higher permeability of these tissues, lower hardness and resistance, and greater volume of the pulp chamber, these teeth are more susceptible to dental caries, especially on proximal surfaces [30]. These are possibly the reasons which hamper the carrying out of randomized clinical trials, as a result of the rapid progression of the disease, often leading to premature teeth loss [27]. In addition, the lack of follow-up monitoring in the studies included in this review was due to the exfoliation of deciduous teeth [26]. Therefore, an intent-to-treat analysis is inappropriate as it underestimates the results. It is of vital importance that preventive strategies based on scientific evidence should be established prematurely, aiming at reducing the risk of dental caries in early childhood, as emphasized in the Bangkok Declaration [31]. It is also noteworthy that there are data on infiltrative resin for permanent teeth, and another systematic review [16], with meta-analysis, simultaneously evaluates deciduous and permanent teeth. Thus, the novelty of this review is to focus only on primary teeth.

Non-invasive treatments, namely the use of dental floss, have limited scientific findings, which prevent demonstrating the benefits of their use in preventing and reducing caries progression in deciduous teeth [28]. Nevertheless, these treatments are highly recommended as a good dental hygiene practice during childhood [32]. In treating interproximal caries, resin infiltration was developed based on the highest penetrating and infiltrating power in the body of the lesion [33] compared to regular adhesive systems [30,34]. Resin infiltration is a technique characterized by its rapid penetration, low viscosity, lower contact angle with the enamel, and

higher surface tension [35]. It is essential to point out that this technique requires greater patient cooperation, as anesthesia or the use of rotary instruments is not required, with the procedure being carried out in a single session, preserving the healthy tooth structure and paralyzing incipient caries lesions [36].

In some studies, the progression of dental caries was assessed through conventional X-rays, as the examiners did not have adequate calibration when carrying out radiograph techniques [11,23-25]. This can lead to positioning errors, misdiagnoses, and overtreatment [37]. Others used a bitewing image with silicone material to standardize the radiographic technique [12,27]. It is essential to point out that most of these studies only used radiographic parameters to assess caries lesions [11,12,23,26,27], hindering the interpretation of the results, as clinical data is essential to analyze caries progression [34].

The vast majority of the clinical trials inserted in the present review used the split-mouth design in the assessment [8,11,12,23,26,27], which is considered inappropriate due to the overlap of effects and difficulty in capturing the sample. In addition, this can limit the study's external validity [38]. Therefore, parallel-arm designs are considered the "gold standard" as they are suitable to assess the outcomes considered in the present study. Besides the sample loss due to exfoliation [11,26,27], which was significant in the work carried out by Bagher et al. [26], loss due to other reasons was also observed, namely the lack of cooperation in x-ray exams [25], besides the change of address and/or loss of contact with the parents or guardians [11,27]. Nonetheless, these did not compromise the results of the studies.

The qualitative evidence of this revision was assessed using the GRADE framework, which categorizes the evidence of the studies into four levels: high, moderate, low, and very low [39]. The studies included were classified as moderate, thus, the true effect is close to the estimate. However, all studies presented serious inconsistencies due to the small sample size [8,11,12,23,24,26,27]. The imprecision was not classified as serious, despite the significant sample loss. Nonetheless, for the purposes of the present metanalysis, only the first year analyzed in the study carried out by Bagher et al. [26] was considered, overcoming the effect of imprecision.

The present systematic review was carried out using a robust, reproducible, and detailed methodology, including the analysis of the evidence available on the use of resin infiltration in deciduous teeth through a wide range of search engines. A clear update of the data referring to the use of this material in deciduous teeth was observed, as well as the assessment of its effectiveness when combined with other prevention measures. The data of the present metanalysis consider this, establishing that resin infiltration is effective when controlling caries lesions.

However, the following limitations must be considered, namely inappropriate study design; lack of a direct comparison between resin infiltration and another micro-invasive dental material. Moreover, the effectiveness analysis was teeth-based, which minimizes the global effect and may lead to confusion due to the loss of teeth due to exfoliation or the assessment of the results using the mouth-split technique.

New studies need to be better designed and conducted in order to establish the same clinical diagnostic criteria. For example, ICDAS, as well as individualized locator instruments, need to be employed to obtain clear parameters and avoid false positives and/or negatives regarding caries progression. In particular, digital radiographs seem more suitable for this purpose due to the lower subjectivity of the software used.

## Conclusion

The use of infiltrating resin to control incipient caries lesions in primary teeth (1/2 of the enamel or 1/3 of the outer dentin), when combined with non-invasive caries prevention methods, was promising and more effective than non-invasive measures used alone for the 1-year follow-up period.

## Authors' Contributions


| | | |
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## Conflict of Interest

The authors declare no conflicts of interest.

## Data Availability

The data used to support the findings of this study can be made available upon request to the corresponding author.

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