Infiltration and Sealing for Managing Non-Cavitated Proximal Lesions: A Systematic Review and Meta-Analysis

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Abstract

Background: Infiltration and sealing are micro-invasive treatments for arresting proximal non-cavitated caries lesions; however, their efficacies under different conditions remain unknown. This systematic review and meta-analysis aimed to evaluate the caries-arresting effectiveness of infiltration and sealing and to further analyse their efficacies across different dentition types and caries risk levels.

Methods: Electronic databases (Cochrane Library, PubMed and Embase) were searched for published literature, and references were manually searched. Split-mouth randomized controlled trials (RCTs) to compare the effectiveness between infiltration/sealing and non-invasive treatments in proximal lesions were included. The primary outcome was obtained from radiographical readings. In total, 995 citations were identified, and 16 RCTs (21 articles) were included.

Results: For subgroup analysis, infiltration and sealing reduced the odds of lesion progression (infiltration vs non-invasive: OR = 0.20, 95% CI: 0.15 to 0.29; sealing vs placebo: OR = 0.27, 95% CI: 0.18 to 0.41). For both primary and permanent dentitions, infiltration and sealing were more effective than non-invasive treatments (primary dentition: OR = 0.30, 95% CI: 0.20 to 0.45; permanent dentition: OR = 0.19, 95% CI: 0.13 to 0.27). The overall effects of infiltration and sealing were significantly different from the control effects based on different caries risk levels (OR = 0.19, 95% CI: 0.14 to 0.27). For patients with different risk levels, there were significant differences between micro-invasive and non-invasive treatments (low risk: OR = 0.23, 95% CI: 0.07 to 0.75; low to moderate risk: OR=0.38, 95% CI: 0.18 to 0.81; moderate to high risk: OR=0.17, 95% CI: 0.17 to 0.29; and high risk: OR=0.14, 95% CI: 0.07 to 0.26). Infiltration was superior to non-invasive treatments for patients at different caries risk levels (low risk: OR = 0.07, 95% CI: 0.02 to 0.22; low to moderate risk: OR=0.38, 95% CI: 0.18 to 0.81; moderate to high risk: OR=0.19, 95% CI: 0.09 to 0.38; and high risk: OR=0.14, 95% CI: 0.07 to 0.29).

Conclusion: Infiltration and sealing were more efficacious than non-invasive treatments for halting non-cavitated proximal lesions.

Introduction

Dental caries is one of the most prevalent oral diseases worldwide [1]. In terms of the susceptibility of the tooth surface to cavitation, the proximal zones have a high risk of being carious [2]. Early proximal caries lesions are prevalent but difficult to observe. Traditionally, invasive treatment methods (drill and fill) are applied; however, these methods require the removal of marginal tissue and may weaken the strength of the residual tooth structure [3]. In recent years, non-invasive or minimally invasive treatment approaches have been developed to replace traditional restorative treatments. These treatment protocols aim to restore the sound structure in a more preventive way, reduce associated pain and costs, and regain function and aesthetics [4–7]

Non-invasive treatments manage caries lesions via mechanical removal of the biofilm, antibacterial treatments or remineralization treatments. Remineralization of the enamel lesion with fluoride and casein

phosphopeptide amorphous calcium phosphate (CPP-ACP) is promising [7–9], but it lacks validity without good compliance [7, 10]. Consequently, micro-invasive treatments are developed as alternatives, as they are less dependent upon patient compliance and are more conservative than invasive treatments.

Infiltration and sealing are frequently used as micro-invasion treatments. Recently, infiltration technology has been performed clinically for non-cavitated proximal caries [11, 12]. This technique uses low-viscosity resin to occlude the micropores of non-cavitated proximal carious lesions [12, 13]. Based on the capillary force, resin penetrates into the pores of demineralized enamel and establishes a barrier to impede acid diffusion [14, 15]. In addition, sealing has been investigated to efficiently arrest lesion progression in vivo and in vitro [16–18]. The procedure of sealing involves the application of a resin sealant, polyurethane tape or adhesives after tooth separation [19–23]. Previous systematic reviews and meta-analyses have shown that micro-invasive treatments are more effective than non-invasive treatments [3, 11, 24–27]. However, there are still uncertainty about the intervention effects for patients with different dentition types and different caries risk levels, as there were not enough cases to reach a conclusion [11]. Generally, caries management with prevention or therapeutic protocols is based on the caries risk [28]. Thus, to assist in the treatment plan, it is meaningful to justify the intervention effects based on different caries risk levels. Furthermore, the latest trials are needed to qualitatively and quantitatively obtain sufficient evidence. Therefore, in this study, we conducted a systematic review and meta-analysis to evaluate the efficacies of infiltration and sealing on proximal caries lesions and analysed their efficacies based on different dentition types and caries risk levels.

Methods

This study was conducted according to the PRISMA statement [29, 30]. The protocols of the eligibility criteria, search strategy, data extraction, risk of bias assessment in the included studies, data synthesis and statistical analysis were prepared.

Eligibility criteria

The eligibility criteria were designed in accordance with the PICOS strategy.

Population (P): Children, adolescents and adults, with proximal or approximal non-cavitated caries, presumed clinically (visually intact surface) or by radiographs.

Interventions (I): Infiltration or sealing technology.

Comparisons (C): The two micro-invasive strategies were compared against each other and against non-invasive treatments (placebo or no treatment).

Outcomes (O): Lesion progression was assessed by digital radiography via digital subtraction radiography (DSR), pairwise reading or lesion stage.

Study design (S): Split-mouth randomized controlled trials (RCTs).

Reviews and meta-analyses, in situ studies, in vitro studies, case reports, study protocols, and meeting abstracts were excluded. Articles were excluded if the patients had a mixture of caries risk levels or if they had high and low caries risk without a specific distribution. Only studies with caries risk for most people (more than 80%) were collected for further classification.

Search

Electronic databases (Cochrane Library, PubMed and Embase) were searched by Y.C. and D.C. from inception to April 6, 2020. Two authors (Y.C. and D.C.) selected the eligible studies independently, and disagreements were resolved by discussion and consultation with a third person (H.L.). Eligible studies were explored without the limitation of publication type, language, year and region. The following terms were used to search the title, abstract, keywords or MeSH terms: “tooth demineralization OR tooth decay OR caries OR lesion” and “seal OR sealant OR sealing OR infiltrate OR infiltration” and “proximal OR approximal” (Appendix 1). A manual search was an auxiliary strategy to improve the comprehensiveness of retrieving studies. Studies were imported into EndNote X9. Duplicates were excluded, and the full text of eligible retrieved studies were assessed. Data were requested from authors of the original studies if necessary.

Data extraction

Data extraction was performed and recorded by two calibrated reviewers independently and in duplicate (Y.C. and D.C.), and disputes were settled by discussion. The titles and abstracts of the studies were initially examined to eliminate irrelevant studies, and then the full text of the retrieved studies was screened to obtain the included studies. The extracted data included study details (first author and year of publication), patient information (age, sample size, sample type, drop-out rate and caries risk), study design, inventions, and outcome data (caries progression).

Assessment of risk of bias in the included studies

The risk of bias of the included studies was evaluated according to the criteria in the Cochrane Collaboration’s Risk of Bias Tool. The following items were included: selection bias, performance bias, detection bias, attrition bias, reporting bias and other biases. Trials with at least 1 item regarded as high risk were identified as having a high risk of bias. Trials with an unclear bias in 1 or more key domains were identified as having an unclear risk of bias. Trials with a low risk of bias in all aspects were identified as having a low risk of bias.

Summary measures and data synthesis

The meta-analysis was conducted using Stata 16. Effect variables were calculated as odds ratios (ORs) with 95% confidence intervals (95% CIs) for binary data in this research. Meta-regression analysis was conducted to identify the influence of follow-up years on treatment efficacy. The I^2 test with a P value was used to assess statistical heterogeneity. If I^2 was more than 50%, a random-effects model was used;

otherwise, a fixed-effects model was used. As differences between the invention methods, dentition types and caries risk levels may affect the outcome data, we individually analysed these factors using subgroup analysis.

Risk of bias across studies

Publication bias should be considered if more than 10 studies are included. Thus, the included studies were analysed with Egger's test and Begg's test.

Quality of the evidence

The overall quality of the accrued evidence was assessed with The Grading of Recommendations Assessment, Development and Evaluation (GRADE) [31, 32]. According to GRADE, the evidence was graded as high, moderate, low and very low. Assessment items were risk of bias, inconsistency, indirectness, imprecision and publication bias. In this study, the quality of the evidence was evaluated using GRADEpro (online software).

Results

Study selection

A total of 995 citations were initially identified after an electronic database search (994 articles) and a manual search (1 article). The selection process is presented as a flow diagram (Fig. 1). Ultimately, 21 articles of the 16 latest studies were included (Tables 1a-b and Table 2), of which 9 articles were related to 4 different series of studies and 1 article compared infiltration and sealing to the control group individually [19-23, 33-48].

Characteristics of the included studies

The data of the included studies are summarized in Tables 1 and 2. All the studies were split-mouth RCTs. A total of 774 patients (ranging from 4.6 to 41 years) were enrolled in 16 clinical trials. There were 1994 non-cavitated proximal lesions in the trials. A total of 5 studies were included that assessed lesions in primary dentition [23, 33, 36-39], and 11 studies assessed lesions in permanent dentition [19-22, 34, 35, 40-48]. The interventions included resin infiltration (14 articles) [33-39, 41-47] and sealant (8 articles) [19-23, 40, 41, 48]. The follow-up duration ranged from 12-84 months. In terms of caries risk levels, 2 studies reported high risk [21, 46, 47], 4 studies reported moderate to high risk [33, 34, 37, 39, 40], 1 study reported low to moderate risk [38], 2 studies reported low to high risk [36, 42], 3 studies reported mixed risk levels [23, 41, 43-45] and 4 studies did not report caries risk in the articles [19, 20, 22, 35, 48]. Four caries risk statuses were included in the subgroup analysis: low [42], low to moderate [38], moderate to high [33, 34, 37, 39, 40] and high [21, 42, 46, 47]. All trials used radiographic lesion progression as the primary outcome. Methods for evaluating lesion progression included independent reading of radiographs, pairwise reading of radiographs and DSR. For data analysis, the most sensitive outcome was recorded if

two or more evaluation methods were used in a study (outcomes obtained by DSR>pairwise reading>independent reading).

Risk of bias within studies

The risk of bias within studies was summarized in Fig. 2 and Fig. 3. All of the studies had a low risk of random sequence generation and blind outcome assessment. For allocation concealment, 9 studies had an unclear risk for insufficient information on the methods of concealment [19-23, 33, 36, 39-41, 48]. Except for 6 studies with mock treatment of unclear risk [35, 38, 41-47], the remaining 9 studies were ranked as high risk because of the lack of blinding for patients and personnel. Eight studies with drop-out rates greater than 25% were regarded as having unclear attrition bias [19-21, 23, 34, 36, 39, 44, 47]. A total of 2 studies had selective reporting of data [37, 41]. Except for 1 study with no caries risk assessment at baseline [22], 1 study with unbalanced lesion allocation [37] 1 study with unbalanced lesion severity [40], and 1 study with no reporting on Score 2 [48], the other 11 studies showed a low risk of other biases.

Meta-regression analysis

The meta-regression analysis results revealed that different research durations (ranging from 12-84 months) did not influence caries progression (P>|t|: 0.997, 95% CI: -0.020 to 0.020). Thus, we chose caries progression at the longest follow-up times for continuous RCTs, similar to previous reviews [3, 24, 26].

Efficacy of infiltration and sealing for non-cavitated proximal caries

Sixteen RCTs were enrolled to assess the efficacy of infiltration and sealing for non-cavitated proximal caries. A fixed-effects model was used for the analysis, as there was no significant heterogeneity between studies (I^2 = -25.78%, Fig. 4). The overall intervention effects of infiltration and sealing were significantly different from the intervention effects of control treatment (OR = 0.23, 95% CI: 0.17 to 0.29). We analysed the two different measures (infiltration and sealing) using subgroup analysis, and we found that both invention measures reduced the odds of lesion progression compared with the control group (infiltration vs non-invasive treatments: OR = 0.20, 95% CI: 0.15 to 0.29; sealing vs placebo: OR = 0.27, 95% CI: 0.18 to 0.41).

Sixteen RCTs were related to infiltration and sealing of primary dentition or permanent dentition. There was no significant heterogeneity of the included RCTs (I^2 = -25.78%, Fig. 5). Non-cavitated proximal lesions were reduced when measures were taken in primary dentition and permanent dentition (primary dentition: OR = 0.30, 95% CI: 0.20 to 0.45; permanent dentition: OR = 0.19, 95% CI: 0.13 to 0.27, Fig. 5).

Eight RCTs were analysed for the efficacy of infiltration and sealing at different caries risk levels (Tables 1a-b). There was no significant heterogeneity among the eight RCTs (I^2 = -12.04%, Fig. 6). The overall effects of infiltration and sealing were significantly different from the overall effects of control treatment (OR = 0.19, 95% CI: 0.14 to 0.27). For patients with different caries risk levels, there were significant differences between micro-invasive treatments and non-invasive treatments (low risk: OR = 0.23, 95% CI:

0.07 to 0.75; low to moderate risk: OR=0.38, 95% CI: 0.18 to 0.81; moderate to high risk: OR=0.17, 95% CI: 0.10 to 0.29; and high risk: OR=0.14, 95% CI: 0.07 to 0.26). Six RCTs were related to infiltration at different caries risk levels. There was no significant heterogeneity among the seven RCTs (I^2 = -12.06%, Fig. 7). Significant differences in the progression rate were found among patients who were treated with infiltration and non-invasive treatments (low risk: OR=0.07, 95% CI: 0.02 to 0.22; low to moderate risk: OR=0.38, 95% CI: 0.18 to 0.81; moderate to high risk: OR=0.19, 95% CI: 0.09 to 0.38; and high risk: OR=0.14, 95% CI: 0.07 to 0.29). Two RCTs were related to sealing across different caries risk levels. Due to insufficient patient information in terms of caries risk levels in the sealing group, no subgroup analysis was conducted.

Publication bias

Begg's test and Egger's test results indicated that the included studies had no obvious publication bias (Begg's test: Z = -0.12, $P > 0.05$; Egger's test: Z = 0.45, $P > 0.05$), as shown by the funnel plot in Fig. 8.

Quality of evidence

Based on this study, infiltration or sealing arrested progression in 287 lesions per 1000 treated lesions. Infiltration arrested progression in 286 lesions per 1000 treated lesions. Sealing arrested progression in 288 lesions per 1000 treated lesions. All evidence was graded as moderate (Appendix 2).

Discussion

Micro-invasive inventions represent promising approaches for treating proximal lesions. Based on this study, infiltration and sealing can be considered effective micro-invasive inventions for halting the progression of non-cavitated proximal caries. These results were consistent with previous studies [3, 11, 27]. Based on GRADEpro, all included studies led to a moderate quality of evidence. Therefore, the conclusion from this research is robust and reliable.

With this limited research, our study could not identify a superior micro-invasive treatment for clinical application. Nevertheless, a comparison of infiltration and sealing in terms of clinical procedure could be performed. Infiltration is considered simple and acceptable for patients [33, 38, 49]. After the application of topical anaesthesia to reduce pain and the placement of the wedge, the resin penetrated the proximal lesions, and only one visit was needed for application [27, 38, 46, 47]. Comparatively, sealing is more complex than infiltration, as it requires two visits [19–23]. In addition, the commercial product "Icon" is available for standard application in resin infiltration [27]. Thus, with regard to clinical application, infiltration seems to be more suitable. Moreover, a network meta-analysis revealed that infiltration is more likely to be effective than sealing [27]. Conversely, an in vitro study showed that sealing might be more effective in preventing enamel dissolution [50], and the remaining roughness and micro-leakage after infiltration could cause plaque accumulation and biofilm formation [50–54]. Therefore, resolving these disputes requires further trials to directly compare the efficiency, applicability and cost between infiltration and sealing [27].

Based on this research, and according to subgroup analysis, infiltration and sealing is appliable regardless of dentition types. Currently, only one study has concluded that sealing is effective at halting lesion progression both in primary dentition and permanent dentition [24]. In other meta-analyses, due to a lack of sufficient data, no robust conclusions could be drawn regarding primary teeth [11]. Even though trials for primary teeth seem to be more complicated and more difficult to ensure proper controls, investigations into the efficacy of the micro-invasive treatments for primary teeth are necessary and meaningful. Specifically, comfort and acceptability during the treatment of primary teeth are worth evaluating [33, 38]. Furthermore, follow-up times are limited to more than 24 months for primary dentition due to the exfoliation of primary teeth. For 5 studies enrolled in this research, we could conclude that micro-invasive treatments were more effective than non-invasive treatments in primary dentition for the period from 12 to 24 months. Thus, there are new insights into the treatment of non-cavitated proximal caries in primary teeth, as micro-invasive treatments not only reduce children's pain and fear but also are efficacious. More studies about primary teeth are warranted to reach a more reliable conclusion.

To improve efficiency under different clinical conditions, trials are conducted in terms of patients with different caries risk levels. Thus, conducting a caries risk assessment beforehand is vital and should be considered a prerequisite. A caries risk assessment would help in caries management and oral care plans [55, 56]. In most of the included studies, caries risk levels was evaluated based on the Cariogram or modified Cariogram. Cariogram is a frequently used multifactorial risk assessment model for individuals [57]. Generally, caries risk ranges from low to high. High caries risk means a higher chance of being infected with new caries, a higher frequency for preventive instruction as well as the application of fluoride, and a higher possibility of needing restoration [58]. Therefore, to elucidate the relationship between the caries risk levels and efficacy of micro-invasive treatments, we divided the enrolled patients into four groups and then conducted subgroup analyses. Previously, four studies concluded that caries progression was not related to the caries risk levels at baseline [33, 36, 42, 59]. However, one study concluded that in children with moderate caries risk, lesion progression was 4 times higher than that in children with low caries risk [38]. In addition, one study demonstrated that there was a moderate relationship between increasing caries risk and lesion progression [23]. In this research, it was shown that micro-invasive treatments could effectively halt caries progression regardless of caries risk levels. Nevertheless, patients with low caries risk are expected to have slower caries progression [38] and to require more preventive treatments rather than therapeutic protocols to halt caries progression [28]. Non-invasive treatments are regarded as ethical and should be considered part of the treatment plan [60]. Even though, patients may refuse non-invasive treatments and favour invasive treatments under some circumstances [61]. Thus, for patients with proximal caries lesions, micro-invasive treatments seems to be a meaningful and important choice. In addition, the results of subgroup analysis with the infiltration group showed the same tendency as the results for the overall effect. Therefore, with a limited number of studies, we concluded that micro-invasive treatments could be effective options.

This study showed some strengths that enhance its reliability. To the best of our knowledge, this study was the first to evaluate the efficiency of micro-invasive treatments based on different caries risk levels. In addition, there were more studies in this review than in previously published reviews. All studies were

RCTs and had a split-mouth design, which helps improve the validity of the trials. Furthermore, there was no statistically significant heterogeneity between the enrolled studies, and there was no obvious publication bias.

Nevertheless, this review also had some limitations that should be mentioned. First, as a consequence of limited studies, patients were divided into coarse groups, and each group presented the majority of the caries risk levels in the samples. For further research, it is necessary to determine caries risk levels for every patient and to perform a detailed and precise assessment. Second, the outcome assessment of the included studies varied among independent reading, pairwise reading, and DSR. A standardized method would be better for outcome evaluation. Otherwise, with a sufficient number of included studies, researchers could conduct subgroup analysis according to the different methods of radiographic assessment, as previously reported [26]. Finally, the risk of bias in the included studies was unclear, or they had a high risk of bias, mainly due to unclear allocation concealment (due to a lack of participant and personnel blinding) or unclear attrition bias (more than 25%). The blinding of operators is unrealistic, yet the blinding of patients is feasible through placebo treatment. In terms of attrition bias, some studies have argued that in the split-mouth design, it is doubtful whether attrition would affect the overall risk of bias [23, 26]. Thus, in this research, studies with drop-out rates less than 25% were regarded as having a low risk of bias [25, 26].

Conclusions

In summary, infiltration and sealing were more efficacious than non-invasive treatments for arresting the progression of proximal carious lesions. In both primary and permanent dentition, infiltration and sealing were effective. For the intervention effects of infiltration or sealing on different caries risk levels, a larger number of trials and more detailed trials are needed for further exploration. For future studies, investigations into the efficacy, feasibility and cost-effectiveness of infiltration versus sealing are still necessary.

Abbreviations

OR
odds ratio
RCTs
randomized controlled trials

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

All data generated or analysed during this study are included in this published article [and its supplementary information files].

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Two authors (Y.C. and D.C.) independently read and assessed the abstracts and selected the articles using the full text for this systematic review. Y.C. contributed substantially to writing the manuscript and performed meta-analysis statistics. L.H. was in charge of the medical descriptions. All authors have read and approved the final manuscript.

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Tables

Due to technical limitations, table 1,2 is only available as a download in the Supplemental Files section.

Figures

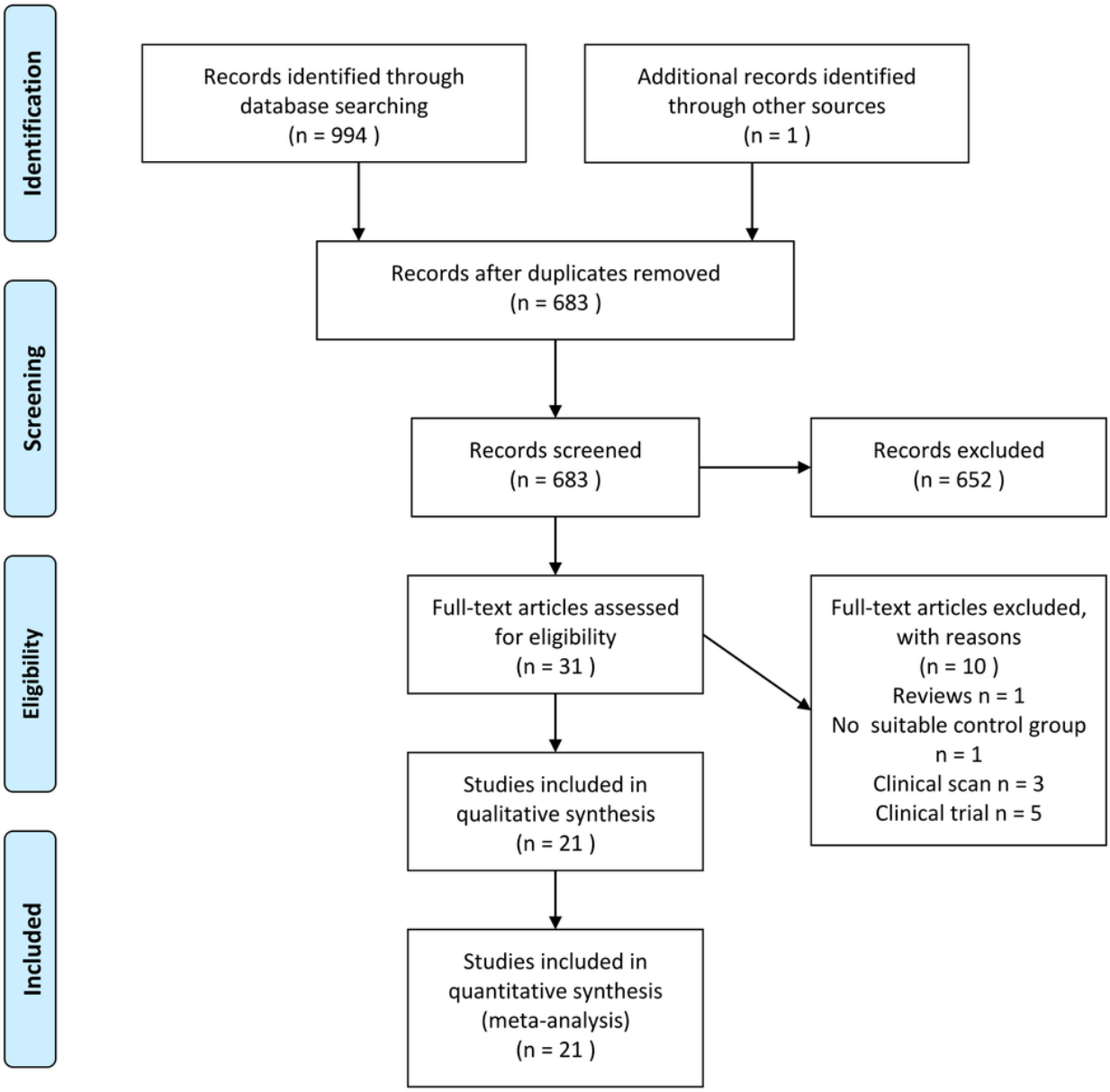

Figure 1

Flow diagram of the study selection. A total of 995 articles were included, and 21 articles were eligible for quantitative synthesis.

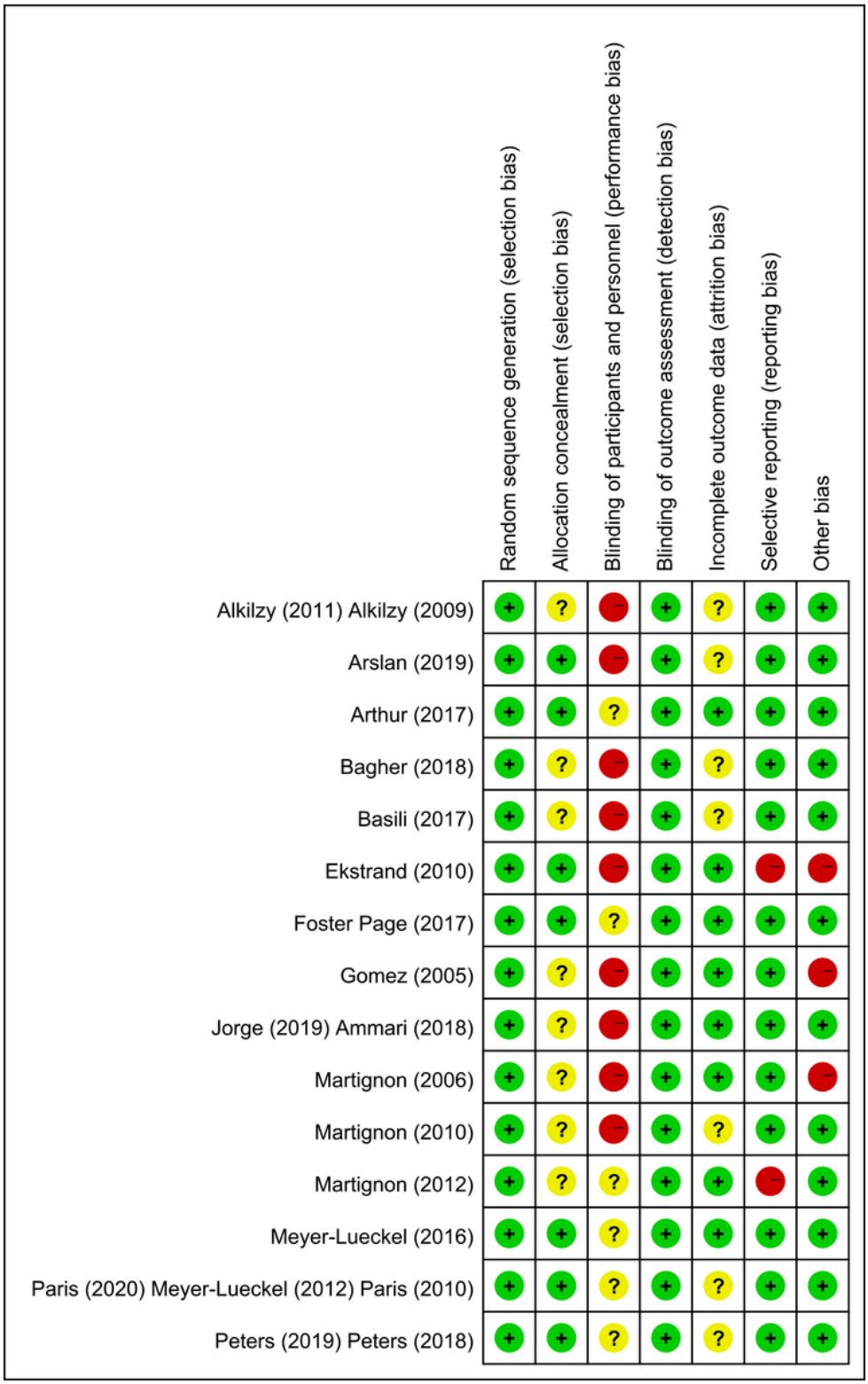

Figure 2

Risk of bias summary of the included studies. In this chart, green circles represent a low risk of bias, yellow circles represent an unclear risk of bias, and red circles represent a high risk of bias.

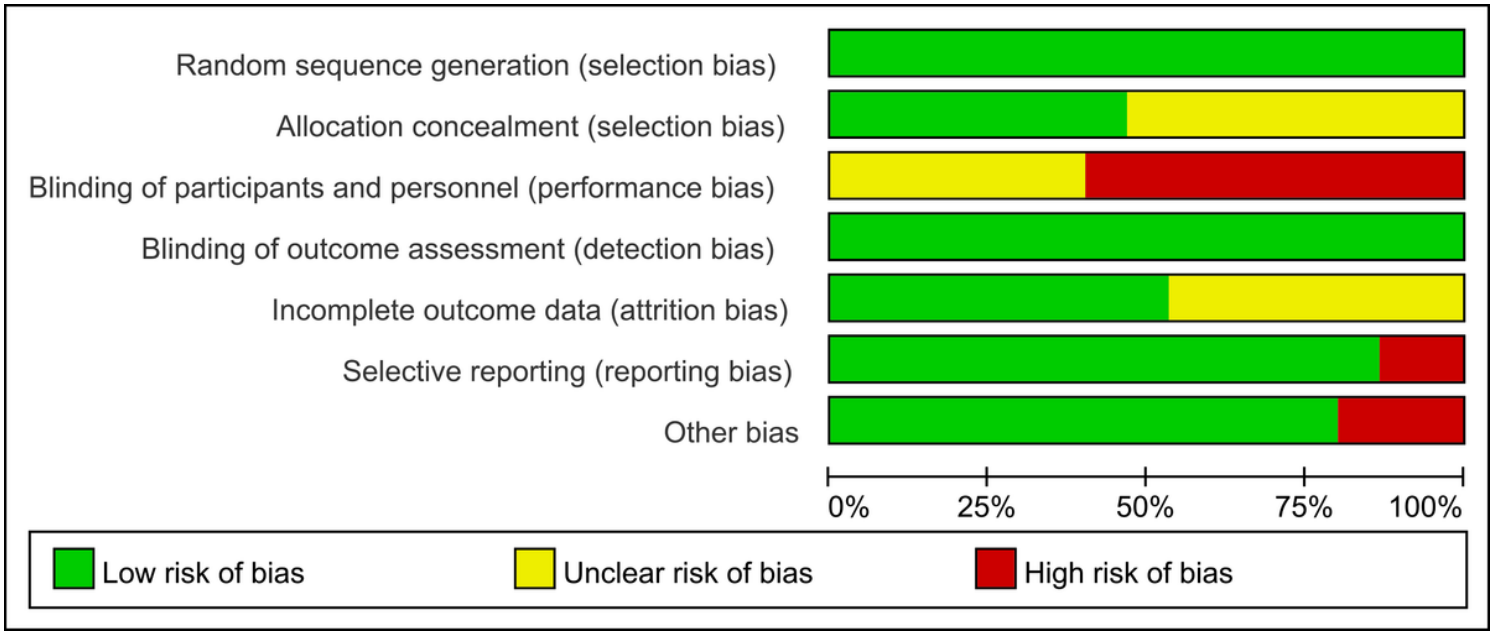

Figure 3

Risk of bias graph. In this graph, green bars represent a low risk of bias, yellow bars represent an unclear risk of bias, and red bars represent a high risk of bias.

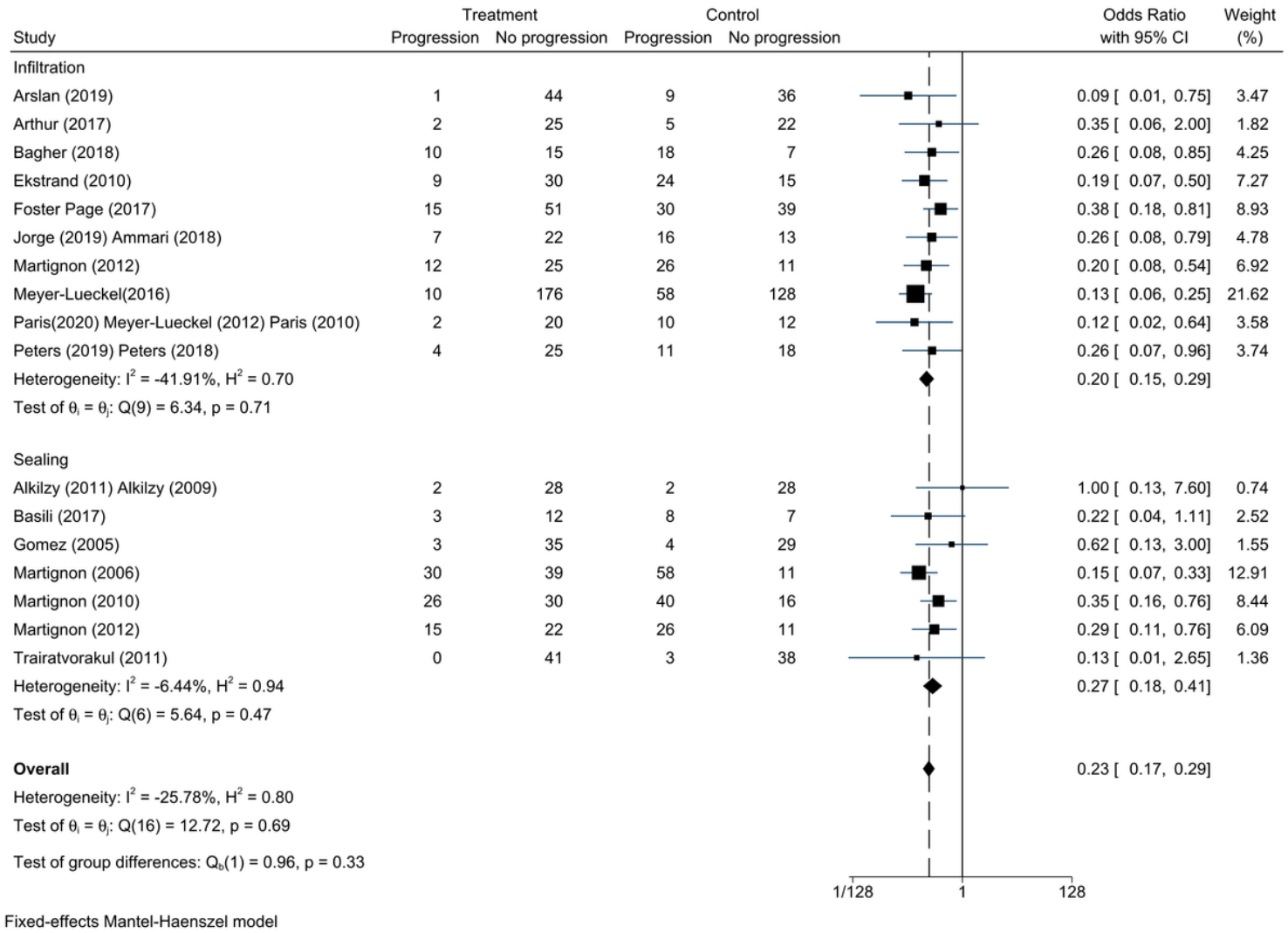

Figure 4

Comparison of the efficacy between infiltration and sealing. The overall effects of infiltration and sealing were significantly different from the control effects (OR = 0.23, 95% CI: 0.17 to 0.29). Both infiltration and sealing were more effective than non-invasive treatments (infiltration vs non-invasive treatments: OR = 0.20, 95% CI: 0.15 to 0.29; sealing vs placebo: OR = 0.27, 95% CI: 0.18 to 0.41).

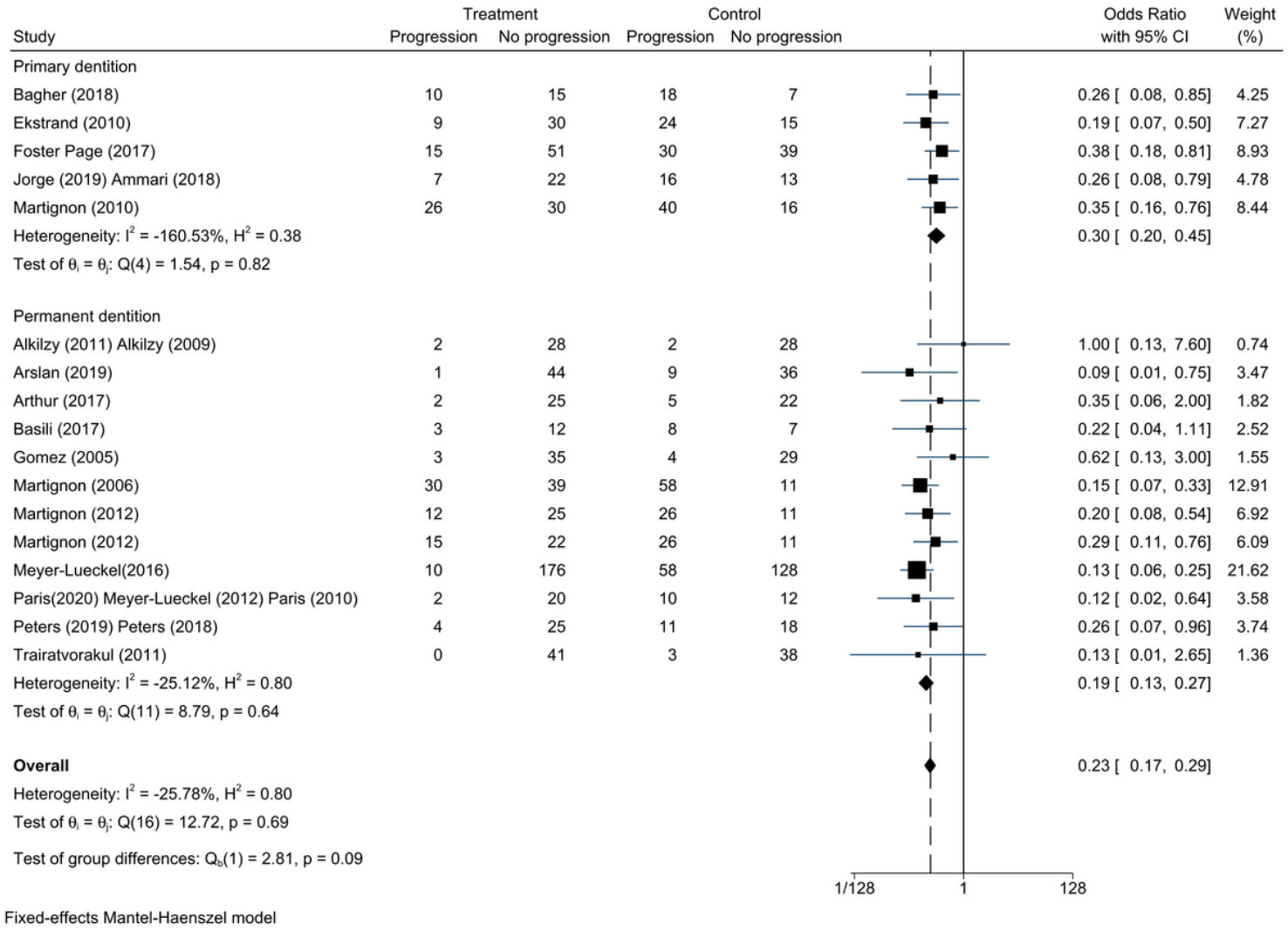

Figure 5

Comparison of the efficacy between primary dentition and permanent dentition. The overall effects of micro-invasive treatments were significantly different from control effects (OR = 0.23, 95% CI: 0.17 to 0.29). Both infiltration and sealing were more effective than non-invasive treatments in primary dentition and permanent dentition (primary dentition: OR = 0.30, 95% CI: 0.20 to 0.45; permanent dentition: OR = 0.19, 95% CI: 0.13 to 0.27).

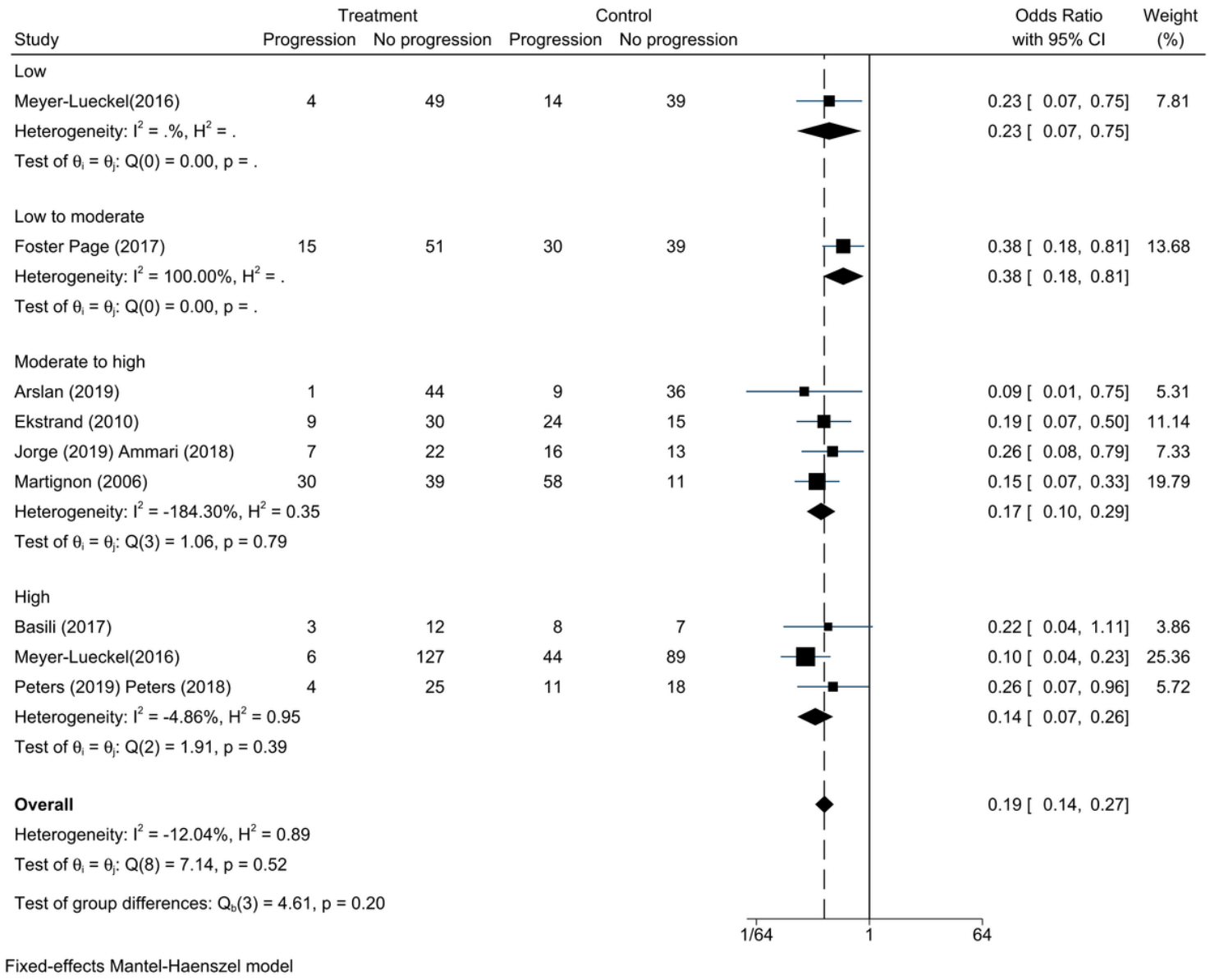

Figure 6

Comparison of the efficacy for different caries risks. For patients with different caries risk levels, there were significant differences between micro-invasive treatments and non-invasive treatments (low risk: OR = 0.23, 95% CI: 0.07 to 0.75; low to moderate risk: OR=0.38, 95% CI: 0.18 to 0.81; moderate to high risk: OR=0.17, 95% CI: 0.10 to 0.29; and high risk: OR=0.14, 95% CI: 0.07 to 0.26).

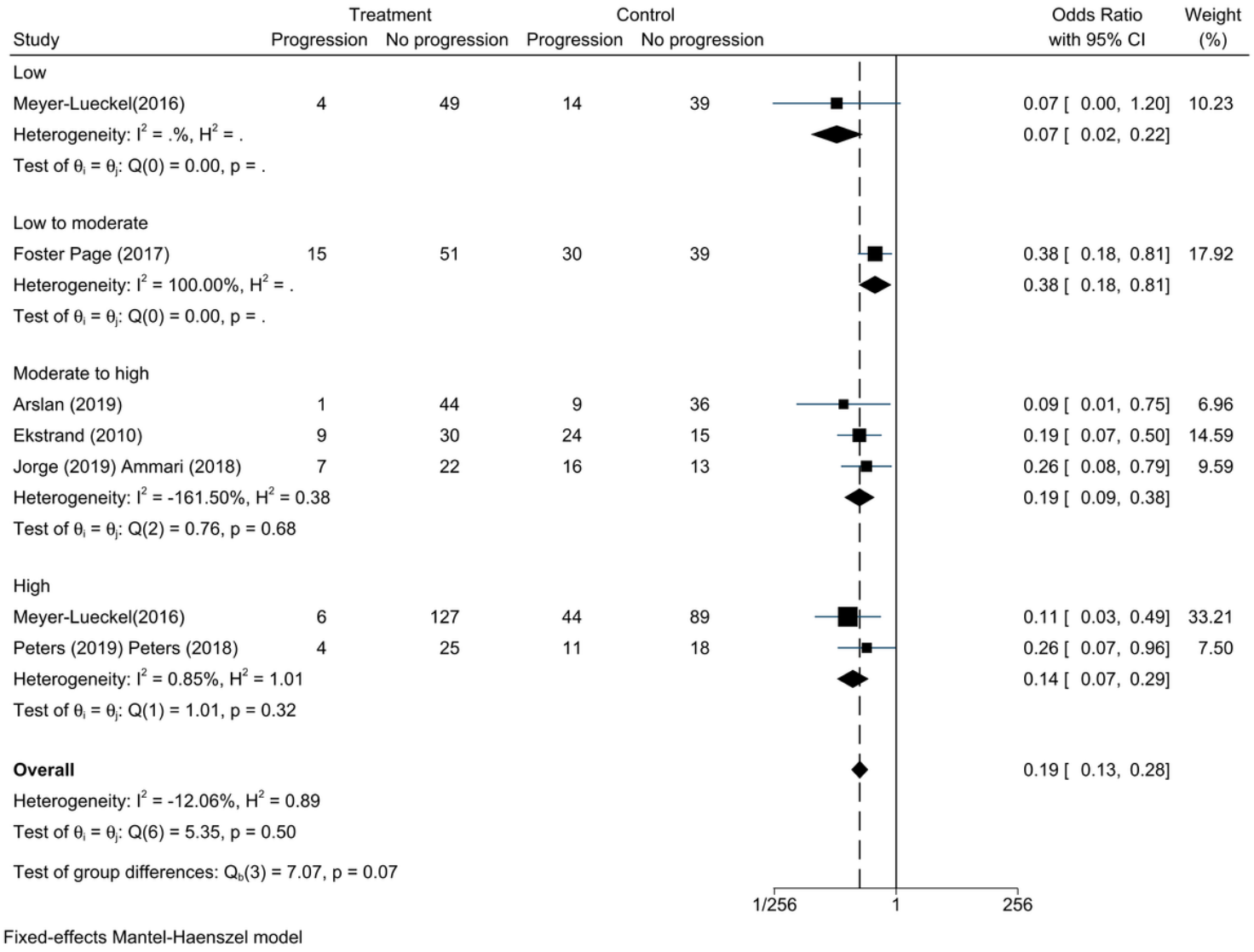

Figure 7

Comparison of the efficacy for different caries risks in infiltration. Infiltration was superior to non-invasive treatments for patients with different caries risk levels (low risk: OR = 0.07, 95% CI: 0.02 to 0.22; low to moderate risk: OR=0.38, 95% CI: 0.18 to 0.81; moderate to high risk: OR=0.19, 95% CI: 0.09 to 0.38; and high risk: OR=0.14, 95% CI: 0.07 to 0.29).

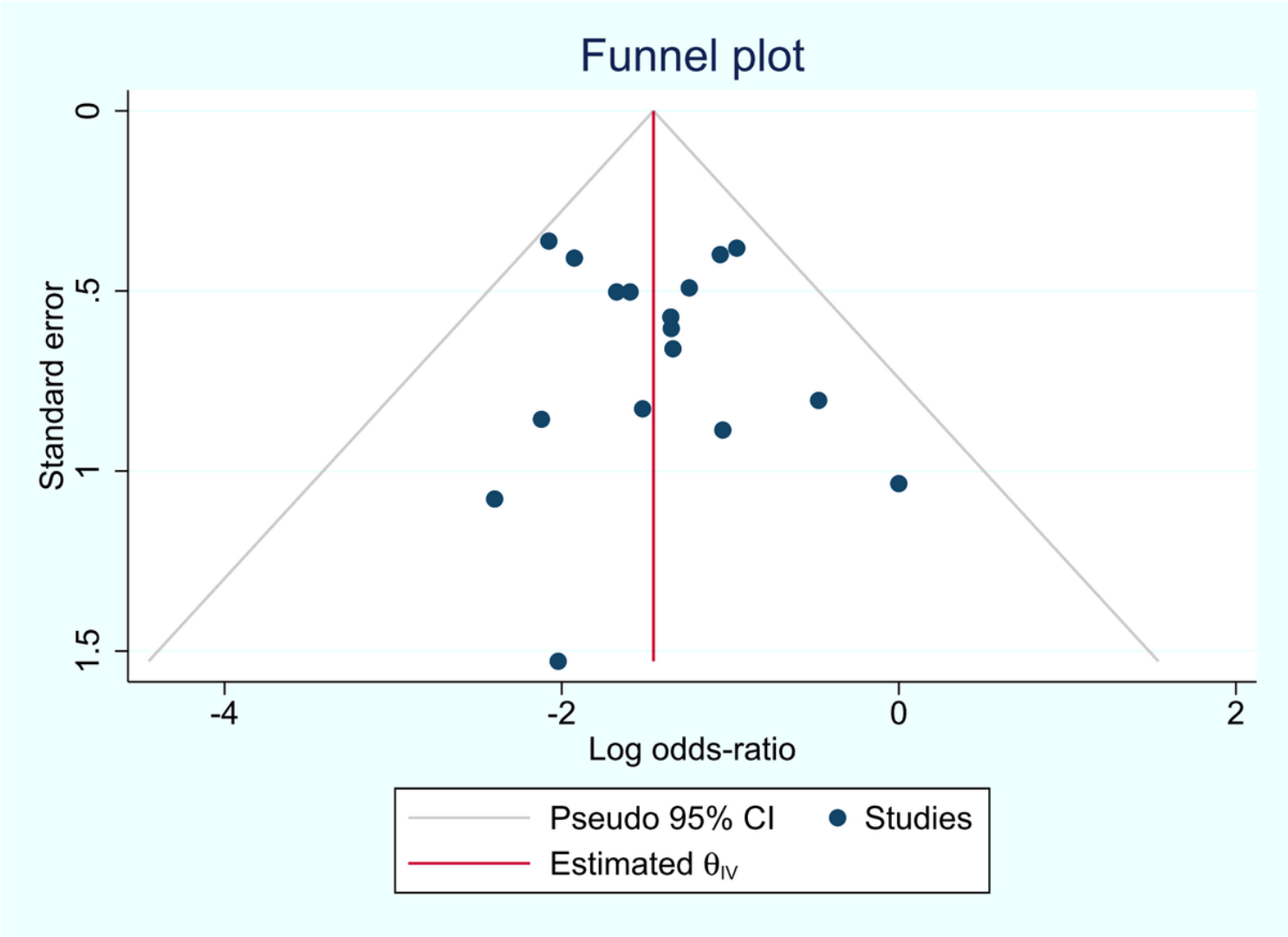

Figure 8

Funnel plot of the publication bias. The funnel plot showed that there was no obvious publication bias.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1b.xlsx
- Table2.xlsx
- Table1a.xlsx
- Appendix3.doc
- Appendix2.docx
- Appendix1.docx