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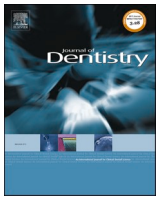

Review article

# Does the application protocol influence the masking effect of resin infiltration on MIH opacities? Systematic review and meta-analysis

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ABSTRACT

*Objective:* To compile the available evidence on the effectiveness of resin infiltration in masking demarcated opacities in permanent incisors with MIH and whether modifications to the treatment protocol impact the outcome.
*Data sources and study selection:* This review followed PRISMA2020 and was registered in PROSPERO (CRD42023414048). Searches were performed in MedLine, LILACS, BBO, Cochrane, Web of Science, Scopus, Embase, OpenGrey, and Google Scholar, by two independent reviewers. JBI and RoB2 were used to evaluate risk of bias. R software was used to perform meta-analyses.
*Results:* Eight uncontrolled, two non-randomized, and two RCTs evaluated 369 teeth in 6–31year-old participants. Six studies followed the standard resin infiltration protocol, while the others reported modifications. The meta-analysis estimated an overall proportion of total masking of 37 % (CI: 18–55). Modified protocols tended to achieve higher success rates (40 %; CI: 9–72) compared to standard protocols (30 %; CI: 17–44), though this difference was not statistically significant. The overall reduction in ΔE was 3.08 (CI: 0.74–5.42), with 1.54 (CI: 0.68–2.40) for standard protocols and 3.84 (CI: 0.80–6.89) for modified ones. Seven studies had moderate risk of bias, and three had high risk. The certainty of evidence was low due to heterogeneity ($I^2 > 80$ %) and imprecision concerns.
*Conclusion:* Resin infiltration is effective in reducing the color difference between MIH opacity and normal enamel. The achievement of total masking was not significantly different between the standard and modified protocols. Heterogeneity and lack of controlled studies limit the certainty of evidence.
*Clinical significance:* This review reinforces the effectiveness of resin infiltration in reducing the color difference between MIH opacity and normal enamel. Modifications in the protocol improved the infiltration but were not enough to be significantly superior. This review contributes to the understanding of peculiarities related to the microinvasive esthetic treatment of MIH.

## 1. Introduction

Molar-incisor hypomineralization (MIH) is a condition characterized by hypomineralization of the enamel that affects one or more first permanent molars and may also include permanent incisors [1]. According to Lopes et al. (2021) [2], the global prevalence of MIH is estimated to be 13.5 %, and affected incisors are observed in 36.6 % of cases. The affected teeth show clearly demarcated enamel opacities that range in color from white to yellow or brownish. Hypomineralized enamel is less hard and porous, which can lead to enamel breakdown and cavities, particularly in molars. Incisors are less likely to experience structural loss due to the lower masticatory forces [1,3].

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The appearance of MIH affected incisors has functional and aesthetic implications for patients, negatively impacting their well-being, self-perception and quality of life [4–6]. Patients frequently experience negative repercussions at an early age [7], with aesthetic treatment of MIH having been demonstrated to enhance the social and emotional well-being of children and adults [8–10]. Available options for aesthetic treatment, i.e., to mask, remove, or cover the affected enamel [3,11], include dental bleaching, microabrasion, restorative treatment, and resin infiltration using the ICON system (DMG, Hamburg, Germany) [12]. Resin infiltration was first presented as a minimally invasive treatment for white spot lesions opacities in 2009 [13]. The range of treatment options might be explained by the variation in the clinical presentation of hypomineralized defects.

The enamel opacity observed in MIH defects is an optical phenomenon resulting from a difference in the refractive index (RI) between the sound and affected areas of enamel. Sound enamel has an RI of 1.62, whereas the porous structure in affected enamel has an RI of 1.33 when filled with saliva or water, and 1.0 when air is present. The resin infiltration concept takes advantage of this nature. In infiltrating the porous structures with the low viscosity resin ICON Infiltrant (DMG, Hamburg, Germany), that has a RI (1.52) similar to that of sound enamel, the opacity of the defect changes to a color similar to the surrounding enamel, thus masking the defect. Once the light refraction within the enamel has returned to a state that is almost normal, the whitish appearance becomes imperceptible to the naked eye [13–15].

While initial caries and fluorosis lesions have been effectively masked with resin infiltration, demarcated opacities, such as those related to MIH, have proven more challenging, rendering it difficult to predict the success of the treatment [15–17]. Due to the histological and biochemical structure of MIH lesions, which differ from those of caries lesions and fluorosis [17,18], it has been acknowledged that the treatment protocol for resin infiltration could be adapted to specifically address demarcated opacities related to MIH [19].

A number of recent systematic reviews [12,20–22] have investigated the efficacy of resin infiltration in treating MIH opacities, concluding that it is an effective aesthetic intervention. However, the potential impact of modifications to the treatment protocol on the success of the treatment has yet to be investigated. Furthermore, these reviews either did not include the latest publications [12,20], included studies that did not show separately the outcomes of other types of opacities and those of MIH [12,20–22], included studies that did not assess the outcome of opacity masking [20,21] or focused on color stability including other DDE than MIH and caries [22]. The aim of the present study is thus to compile the available evidence on the effectiveness of resin infiltration in masking demarcated opacities in permanent incisors with MIH and to delineate whether modifications to the treatment protocol impact the success of the treatment.

## 2. Materials and methods

### 2.1. Protocol and registration

This systematic review was conducted and reported according to the PRISMA 2020 statement [23]. The protocol was registered in the PROSPERO database under the number CRD42023414048.

### 2.2. Eligibility criteria

The search strategy and inclusion criteria were defined based on the elements of the PICO question: “Is resin infiltration (Intervention) effective in masking (Outcome) molar-incisor hypomineralization opacities in incisors (Population) compared with or not compared with any other treatment (Comparison)?”. This review included controlled and uncontrolled clinical trials and quasi-experimental studies. Observational studies (case-control, cross-sectional and cohort), *in vitro* or *ex-vivo* studies, case reports and case series, review articles, opinion articles and letters were not eligible.

### 2.3. Information sources and search strategy

In April 2023, two researchers (NAP and RCJ) performed detailed search strategies following the syntax rules of each database. Alerts were set until August 2024. The following electronic databases were searched: MedLine/PubMed; Latin American and Caribbean Health Sciences (LILACS) and Brazilian Library in Dentistry (BBO)/ Virtual Health Library (VHL); Cochrane Library/Wiley; Web of Science/Clarivate; Scopus and Embase/Elsevier. Search strategies were developed using MeSH/Emtree terms, synonyms, and free terms, as well as Boolean operators OR/AND. No search restrictions were applied. Additionally, the reference lists of selected studies as well as OpenGrey and Google Scholar were searched to identify potentially eligible papers that were missed by the main database search. In the Google Scholar search, the first 100 hits were screened. Table S1 (Supplemental Material) displays the search strategy used and adaptations for each database.

### 2.4. Study selection

Electronic records identified in the search were imported into EndNote Web software (Thomson Reuters, New York, NY, USA), and duplicates were removed. Titles and abstracts were screened against the inclusion criteria by two reviewers (NAP and RCJ) to identify potentially relevant articles. Full texts of these articles were then assessed independently by both reviewers based on the inclusion criteria with final inclusion of a study having been decided by both reviewers in consensus. Disagreements were resolved through consultation and discussion with a third reviewer (VMS). Articles published in languages other than English and Portuguese were translated using Google Translate [24] and/or DeepL Translate [25].

### 2.5. Data collection

Two reviewers (NAP and RCJ) independently performed data extraction from the included studies using Microsoft Excel (Microsoft Corporation, USA) [26] collecting the following information: author, year, country of publication, study design, participant characteristics (number of participants, gender, and age), MIH severity and diagnostic criteria, inclusion and exclusion criteria, interventions (resin infiltration and comparison treatment protocol), number of treated teeth, dropouts, outcomes, assessment methods, follow-ups, adverse effects, as well as declaration of interest and funding. The corresponding authors were contacted by e-mail if data necessary for the analysis were missing. Two reminders were sent within one week if no response was received.

### 2.6. Risk of bias

The researchers (NAP and RCJ) independently performed a risk of bias assessment of the included studies. Disagreements were resolved by discussion with a third researcher (VMS). The Joanna Briggs Institute (JBI) instrument for quasi-experimental studies [27] was used for uncontrolled and non-randomized controlled studies. The Cochrane risk-of-bias tool version 2 (RoB 2) was used for randomized controlled studies [28].

### 2.7. Synthesis methods and effect measures

The studies were grouped for a narrative synthesis of results based on the treatment protocol for resin infiltration. The groups were defined as follows: standard protocol (1x etching for 2 min; 3 min for first resin infiltration) and modified protocols, which included increased acid etching (up to 3x etching for 2 min; 3 min for first resin infiltration), microabrasion followed by the standard protocol, and increased acid etching and resin infiltration application time (3x etching for 2 min; $>3$

min for first resin infiltration). In instances where multiple follow-ups were conducted, the data obtained from the final follow-up was used.

R statistical software version 4.3.3 was used to perform the meta-analyses. Studies that reported the mean ΔE values (total color difference assessed by the CIELAB system) between the opacity and the surrounding sound enamel before and after treatment were pooled in a meta-analysis, using a random-effects model, to calculate overall and subgroups effect size (mean difference in ΔE values pre- and post-treatment) in relation to the treatment protocol. A proportional meta-analysis, using a random-effects model, pooled the studies that reported the rate of successful masking. Data were summarized as dichotomous into total or partial/no masking. Statistical heterogeneity among studies was evaluated using the $I^2$ test. Values greater than 50 % indicated a possibility of a substantial heterogeneity. Funnel plots were not built because the meta-analyses included fewer than 10 studies.

### 2.8. Certainty assessment

The certainty of the evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool (GRADEpro GDT: GRADEpro Guideline Development Tool [Software]. McMaster University, 2015, developed by Evidence Prime, Inc. Available from gradepro.org.Risk of bias, inconsistency, indirectness, imprecision, and suspected publication bias were considered in the analysis [29]. Both quantitative and qualitative data sets were used to conduct the narrative GRADE assessment.

## 3. Results

### 3.1. Study selection

The study selection is outlined in the PRISMA flowchart (Fig. 1). Out of the 1674 papers retrieved from the databases in April 2023, 576 duplicates were removed. Based on the inclusion criteria, 1083 studies were excluded after reviewing the titles and abstracts. Finally, the full texts of 15 studies were evaluated [8–10,16,19,30–39]. Five studies were excluded because they did not separately demonstrate the effect of the resin infiltrant in masking the MIH opacities [9,10,19,32,36], and two studies were excluded for not including MIH opacities [35,37]. Additionally, eight studies were identified through other methods [40–47], but four were excluded for not including demarcated opacities due to MIH [40–43]. Twelve studies were included in the systematic review [8,16,30,31,33,34,38,39,44–47].

### 3.2. Study characteristics

Tables 1 presents a summary of the main characteristics of the studies included in the systematic review. Table 2 presents the infiltration protocols, assessment methods and outcomes of the studies. Regarding the study design, eight studies were uncontrolled [16,30,31,33,34,38,39,46], two were non-randomized controlled clinical trials [44,45], and two were randomized controlled clinical trials [8,47].

The participants of all studies were aged between 6 and 31 years old. The number of participants ranged from 12 to 40. No restrictions regarding gender or sex were imposed by any of the studies. The number of treated teeth ranged from 9 to 61. The reviewed studies primarily focused on permanent incisors with white-creamy MIH opacities [8,16,33,34,39,45–47]. Only one study [47] included yellow-brownish opacities in different treatment groups. Furthermore, four studies [16,31,33,38] included caries lesions and/or other DDE, such as fluorosis or demarcated opacities due to trauma.

Six studies [16,30,38,44–46] followed the standard protocol for proximal caries lesions. In five studies [8,31,33,34,47], the acid etching step was increased up to three applications. Moreover, one study [8] reported an increased application time for the infiltrant. Only one study [39], that performed microabrasion prior to resin infiltration, did not detail the resin infiltration protocol, but we assumed that the standard application was used.

Eight studies [16,30,34,38,39,44,45,47] used quantitative methods, while three [31,33,46] used qualitative methods to assess the masking effect. One study [8] used both quantitative and qualitative methods. Among the quantitative methods, six studies [8,16,30,34,38,44] used

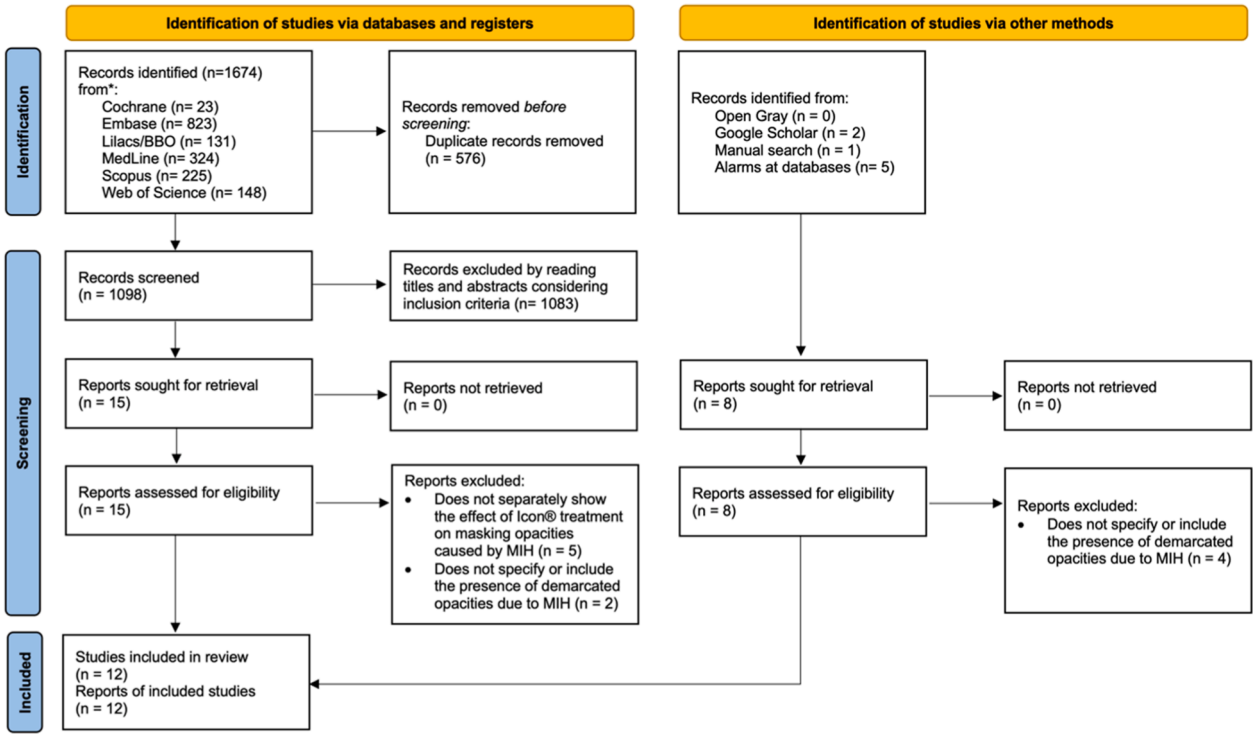


**Fig. 1.** PRISMA Flow chart describing the study selection process.

**Table 1**
Synthesis of the main characteristics of the studies included in the systematic review.

| Author (Year) Country | Study design | Number of teeth | Groups (number of treated teeth) | MIH severity and/or noteworthy clinical presentation (diagnostic criteria) | Number of participants (male, female) age range (mean age ± SD) | Inclusion criteria | Exclusion criteria | Adverse effects | Dropouts |
|---|---|---|---|---|---|---|---|---|---|
| Alghawe et al. (2024) Syria | Randomized controlled trial | 30 permanent incisors with MIH | Resin infiltration after multiple or single etching W/C multiple etching ($n$ = 8); single etching ($n$ = 8) Y/B multiple etching ($n$ = 7); single etching ($n$ = 7) | White/ creamy and yellow/ brown opacities (EAPD) | 15 (NI) 6 - 16 years (10.68 ± NI) | Children with at least one permanent incisor with MIH opacity (6–16 years). | Dental fluorosis, amelogenesis imperfecta, tetracycline staining or generalized enamel hypoplasia; undergoing orthodontic treatment; demarcated opacities not related to MIH. | Not reported | **5 teeth:** 1 W/C single, 1 Y/B single, and 3 Y/B multiple etching Inability to manually outline the opacity's infiltration |
| Altan & Yilmaz (2023) Turkey | Non-randomized controlled trial | 116 permanent central incisors with MIH | Group I ($n$ = 58): Resin infiltration Group II ($n$ = 58): Healthy, untreated control | NI | 37 (16 male, 21 female) 8 - 14 years (9.70 ± 2.08) | Labial surface of at least one permanent central incisor with MIH. | Dental caries, filling, dental anomaly on anterior teeth, periodontal disease, undergoing orthodontic treatment, and cognitive and/or behavioral conditions. | Not reported | **3 patients:** 12 teeth (test = 6; control = 6) Missed the follow-up |
| Athayde et al. (2022) Brazil | Randomized controlled trial | 59 permanent incisors with MIH | Control group ($n$ = 29): Placebo Test group ($n$ = 30): Resin infiltration | White/ creamy opacities (EAPD) | Control group: 20 (9 male, 11 female) 8 - 16 years (10.1 ± NI) Test group: 20 (8 male, 11 female) 8 - 18 years (11.2 ± NI) | Intact MIH white-creamy opacity in at least one permanent incisor, that caused esthetic discomfort. | Other DDE and previous restorative, infiltration, microabrasion and/or whitening treatment; yellow-brownish opacities and post-eruptive enamel breakdown. | No major side effects. **Bitter taste:** control = 6; test = 5 **Immediate postoperative pain/ discomfort:** control = 2; test = 3 Symptoms disappeared within hours. | **1 patient:** Test group Missed the follow-up |
| Bhandari et al. (2018) USA | Uncontrolled trial | 22 lesions on permanent incisors with MIH | Resin infiltration ($n$ = 22) | White opacities (EAPD) | NI (NI) 7 - 16 years (NI) | Grade I (mild) MIH opacities, without enamel breakdown, and sensitivity to external stimuli occasionally present. | Mental disabilities and/ or systemic diseases, active caries lesion, previously restored tooth, loss of enamel structure, clinical symptoms of irreversible pulpitis, previous bleaching. | Not reported | NI |
| Brescia et al. (2022) Italy | Retrospective study | 114 permanent incisors with DDE | NI | White opacities (Mathu-Muju and Wright classification) | 33 patients with DDE (18 male, 15 female) NI (10.4 ± 11.6) -Moderate or low-grade MIH = 24 -Moderate or low-grade Fluorosis = | Patients with anterior teeth affected by mild or moderate MIH; mild or moderate fluorosis; or post-traumatic hypomineralization infiltrated with Icon® from January to July 2020. | Previous conservative treatments; cavitated enamel defects; enamel defects with post-eruptive etiology; severe MIH; severe fluorosis. | Not reported | No loss |

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**Table 1** (*continued*)

| Author (Year) Country | Study design | Number of teeth | Groups (number of treated teeth) | MIH severity and/or noteworthy clinical presentation (diagnostic criteria) | Number of participants (male, female) age range (mean age ± SD) | Inclusion criteria | Exclusion criteria | Adverse effects | Dropouts |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | 5<br>-Trauma = 4 | | | | |
| Elbaz & Mahfouz (2017) Egypt | Non-randomized controlled trial | 40 permanent upper incisors with MIH | Group I ($n$ = 20): Resin infiltration<br>Group II ($n$ = 20): Fluoro-protector (control) | White opacities (EAPD) | 20 (NI)<br>9 –14 years (NI) | Children with bilateral maxillary permanent central incisors with MIH | NI | Not reported | NI |
| Giannetti et al. (2018) Italy | Uncontrolled trial | 38 teeth with white defects of enamel<br>MIH: $n$ = 9 | Resin infiltration ($n$ = 9) | White opacities (NI) | 17 (7 male, 10 female)<br>8 - 26 years (14.7 ± NI) | White defects of enamel in the dental aesthetic area | NI | Not reported | No loss |
| Gu et al. (2021) China | Uncontrolled trial | 36 permanent upper incisors with MIH | Resin infiltration ($n$ = 36) | White/chalky opacities (EAPD) | 12 (5 male, 7 female)<br>12 - 31 years (NI) | Maxillary anterior teeth with mild MIH, with no significant collapse in the chalky opacity area, smooth surface and hard texture. | Tooth discoloration due to caries, fluorosis, or tetracycline; previous resin infiltration or bleaching; psychiatric or other systemic diseases. | No adverse reactions such as sensitivity and discomfort were observed. | NI |
| Kim et al. (2011) South Korea | Uncontrolled trial | 38 teeth with white spot:<br>Incisors with MIH: $n$ = 20<br>Maxillary anterior teeth with POD: $n$ = 18 | Resin infiltration ($n$ = 20) | White opacities (EAPD) | 12 children with MIH (NI)<br>NI (12.5 ± NI)<br>9 children with POD (NI)<br>NI (15.1 ± NI) | Maxillary anterior teeth with white spot enamel lesions. For the teeth with DDE, only MIH opacities were selected. | NI | There was no harm or adverse effect to participants. | No loss |
| Ozgur et al. (2023) Turkey | Uncontrolled trial | **Initially:** 100 permanent anterior teeth<br>**At the follow-up:** 84 permanent anterior teeth:<br>MIH: $n$ = 61<br>White spot lesions: $n$ = 23 | Resin infiltration ($n$ = 61) | NI (EAPD) | 33 initially (NI)<br>7 - 18 years (NI)<br>29 at follow-up (10 male, 19 female)<br>7 - 15 years (10.52 ± 2.11) | Non-cavitated color change due to demineralization or hypomineralization of the enamel, affecting at least one permanent anterior tooth (7–18 years). | NI | Not reported | **4 patients:** 16 teeth<br>Not informed if the dropouts belonged to the MIH group<br>Missed the follow-up |
| Sanfelice et al. (2024) Brazil | Uncontrolled trial | 30 permanent incisors with MIH | Resin infiltration ($n$ = 30) | White/ creamy opacities (Ghanim et al., 2019 MIH Index) | 12 (7 male, 5 female)<br>6 - 15 years (NI) | Children having at least one permanent incisor affected with creamy/ white MIH opacity. | Children presenting teeth with hypersensitivity, composite restorations, and previously treated with fluoride mouth rinses, gels, foams, and/or varnishes. | Not reported | No loss |
| Warner et al. (2022) UK | Uncontrolled trial | 29 permanent central | Resin infiltration ($n$ = 6) Microabrasion | White/ creamy (EAPD) | 23 (8 male, 15 female)<br>7 - 15 years (10 ± NI) | Children enrolled in a previous study with at least one fully erupted | NI | Not reported | No loss |

(*continued on next page*)

**Table 1** (*continued*)

| Author (Year) Country | Study design | Number of teeth | Groups (number of treated teeth) | MIH severity and/or noteworthy clinical presentation (diagnostic criteria) | Number of participants (male, female) age range (mean age ± SD) | Inclusion criteria | Exclusion criteria | Adverse effects | Dropouts |
|---|---|---|---|---|---|---|---|---|---|
| | | incisors with MIH | + Resin infiltration (*n* = 23) | | | maxillary permanent central incisor with W/C opacity and good quality pre- and 6-month post-treatment clinical images. | | | |

MIH: Molar Incisor Hypomineralization; DDE: developmental defects of the enamel; POD: Post-orthodontic decalcification; W/C: White/creamy; Y/B: Yellow/brown; EAPD: European Academy of Paediatric Dentistry; NI: not informed; CIELAB: Commission Internationale d'Eclairage (International Commission on Illumination) L*a*b* (L* for lightness and a* and b* for the green-red and blue-yellow color coordinates); FDI: Fédération Dentaire Internationale (World Dental Federation).

the CIELAB color space analysis. Four studies [34,39,44,47] compared the opacity area before and after infiltration. Other studies have used different methods of analysis: digital analysis of the luminosity differences [45]; evaluation of the color matching based on the Vitapan Classical value scale [47]; and measurement of the opacity brightness through pixel intensity [39]. Regarding the qualitative methods used to assess masking, two studies [31,46] used the FDI color match, while two other studies [8,33] used pairwise reading of clinical images.

None of the included studies informed whether the protocol was published. Only five studies [8,38,44,46,47] provided the registration number of the clinical trial. Five studies [8,16,39,44,46] reported receiving funding or sponsorship, while three [30,31,47] reported not having any.

### 3.3. Synthesis and individual results

The majority of studies evaluated outcomes over a period of between one and six months [8,30,34,38,39,44,45,47], while two studies evaluated up to one week [16,46] and two studies extended this timeframe to beyond six months [31,33].

In six studies, the effects observed immediately after treatment were found to remain stable over the subsequent one-month period [8,45], six months [30,34,38,44], or 24 months [31]. In two studies, the color match exhibited a significant increase after one week in comparison with the immediate result [16,38,46]. Additionally, Giannetti et al. (2018) [33] observed a tendency for an improvement in the masking effect over time.

Only one study [16] reported no patient loss, while three studies [8,44,47] reported patient dropouts, ranging from 5 % to 16,6 %. Three studies [30,34,45] did not provide information on patient loss. In the other four studies [31,33,39,46], the authors did not inform, but it was possible to retrieve the information that there was no patient loss from the article.

### 3.4. Standard protocol

The standard protocol was employed in six studies, with a two-minute etching and a three-minute application time for the infiltrant [16,30,38,44–46]. In all studies, an improvement in the clinical appearance of the opacities was reported following resin infiltration [16,30,38,45,46]. Different methodologies were used to assess the effect of the treatment. One study [45] observed a significant reduction in the luminosity scores of the buccal surface of the tooth, as evidenced by digital photographs taken before (204.99 ± 13.85) and after the treatment (194.38 ± 5.0).

In one study [30], the ΔE, calculated between the initial and final (6 months later) total color of the opacities, was 13.2 (± 6.8), indicating a significant color change. Two studies [16,38] observed a decrease in color difference between the opacity area and the surrounding sound enamel by calculating ΔE values before and after treatment. Ozgur et al. (2023) [38] observed a significant decrease in the mean ΔE from 8.30 to 6.39 (1 week after treatment) and to 6.76 (6 months after treatment).

A final $\Delta E \leq 3.7$, indicative of total masking, was achieved in 25 % of the teeth, while partial masking and no masking effect were observed in 35 and 40 %, respectively, by Kim et al. (2011) [16]. One study [46] revealed an enhancement in color matching between the opacity and the sound enamel after resin infiltration, according to the FDI criteria. An excellent color match was achieved in 18 % of the subjects, while 74 % exhibited a good or sufficient color match and 8 % were considered as unsatisfactory color match. Considering the total of treated teeth, 26.7 % showed excellent color match, 56.7 % good or sufficient, and 13.3 % unsatisfactory (data obtained from authors). In one study [44], no significant change in the luminosity of the opacities was observed through spectrophotometer evaluation immediately after treatment. However, it was significantly reduced at one, three and six months, compared to the initial values. A significant reduction in the opacity area was detected by comparing initial and final cross-polarization photographs from 4.9 ± 3.0 $mm^2$ at baseline to 4.7 ± 3.0 $mm^2$.

### 3.5. Increased acid etching time

Four studies tested a modified protocol by increasing the etching time to up to three applications of two minutes each [31,33,34,47]. In the study by Gu et al. (2021) [34], the mean reduction in opacity area was 86 % following resin infiltration. Moreover, the ΔE (difference color between the opacity and the surrounding sound enamel) reduced significantly from 7.06 ± 1.39 at baseline to 1.72 ± 0.41 after resin infiltration [34]. According to the FDI criteria, resin infiltration after increased acid etching time resulted in 66.7 % of the subjects exhibiting an excellent color match, 29.1 % exhibiting a good or sufficient color match, and 4.2 % an insufficient color match [31]. In a study that included nine MIH opacities, one (11.1 %) showed complete resolution of the defect, and eight (88.9 %) showed partial masking [33]. Multiple etching cycles resulted in a greater reduction in the opacity area with a significant difference for the white-creamy opacities. However, the spectrophotometer analysis of color matching, using the Vitapan Classical value scale, revealed no statistically significant correlation between the color match and the number of etching times [47].

### 3.6. Increased acid etching and resin infiltration application time

A single randomized controlled trial [8] increased both the acid etching time (three cycles of two minutes each) and the application time for the infiltrant from three (standard protocol) to 30 min. Resin infiltration was compared to a placebo treatment. In the test group, ΔE reduced from 6.45 (± 3.53) to 4.22 (± 2.96) one month after treatment.

**Table 2**
Summary of outcomes.

| Author (Year) | Groups (number of treated teeth)* | Resin infiltration protocol* | Follow-ups | Masking effect measures (outcome) | Masking results* |
|---|---|---|---|---|---|
| Alghawe et al. (2024) | W/C multiple etching ($n = 8$); single etching ($n = 8$) Y/B multiple etching ($n = 7$); single etching ($n = 7$) | **Standard** **Modified:** 3 etching cycles | T0: Before T1: Immediate T3: 3 months | Percentage of opacity area infiltrated measured in digital photographs. | **W/C single:** 31.5 % (SD: 34.8 %) **W/C multiple:** 88.9 % (SD: 20.9 %) **Y/B single:** 68.3 % (SD: 44.0 %) **Y/B multiple:** 86.4 % (SD: 27.1 %) $p < 0.5$ between W/C single and W/C multiple groups. |
| | | | | Color assessment (spectrophotometer): color matching between opacities and surrounding sound enamel based on the Vitapan Classical scale | **W/C T1:** single = 7.69; multiple = 9.31$^{S}$ **W/C T3:** single = 7.81; multiple = 9.19 $^{S}$ **Y/B T1:** single = 9.43; multiple = 5.57 $^{NS}$ **Y/B T3:** single = 9.14; multiple = 5.86 $^{NS}$ **Single T1:** W/C = 4.56; Y/*B* = 11.93 $^{S}$ **Single T3:** W/C = 4.63; Y/*B* = 11.86 $^{S}$ **Multiple T1:** W/C = 6.00; Y/*B* = 10.29 $^{S}$ **Multiple T3:** W/C = 5.56; Y/*B* = 10.79 $^{S}$ $^{S}$ (p value > 0.05); $^{NS}$ (p value > 0.05) Multiple etching provided significant better outcome for W/C opacities. |
| Altan & Yilmaz (2023) | Group I ($n = 58$): Resin infiltration Group II ($n = 58$): Healthy, untreated control | **Standard** | Before Immediate 1 month 3 months 6 months | Opacity area (digital photographs): The lesion area was measured in $mm^2$, at different time points | **Group I:** Before: 4.9 ± 3 $mm^2$ Immediate: 4.6 ± 3 $mm^2$ 6 months: 4.7 ± 3 $mm^2$ ($p < 0.05$) between before and immediately, 1, 3, and 6 months after treatment. The opacity area was reduced after treatment, albeit to a small extend. |
| | | | | Color assessment (spectrophotometer): color average of whole tooth surface; L* values have been evaluated; ΔE was assessed as the difference between time points for the same area. | **ΔE (before-immediate):** group I: 10.0 ± 7.0; group II: 5.4 ± 5.8 **ΔE (before-6 months):** group I: 11.5 ± 9.0; group II: 4.5 ± 5.6 L* values (not reported in paper) were significantly lower after treatment in the test group, but not in the control group, indicating an improvement of the aesthetics. No statistical difference between ΔE within groups, indicating color stability. |
| | | | | Laser fluorescence (DIAGNOdent Pen): fluorescence average of whole tooth surface compared between groups. | **Before:** group I: 22.0 ± 15.0; group II: 2.6 ± 0.6 **Immediate:** group I: 13.0 ± 10.0; group II: 2.6 ± 0.6 **6 months:** group I: 13.4 ± 9.9; group II: 2.8 ± 0.5 The difference between groups was significant at all time points ($p < 0.05$). |
| Athayde et al. (2022) | Control group ($n = 29$): Placebo Test group ($n = 30$): Resin infiltration | **Modified:** 3 etching cycles (rubbing the tip of the applicator). Resin infiltrant application for 30 min. | Before Immediate 1 month | Color assessment (digital photographs): ΔE between the opacity and the surrounding sound enamel at different time points. | **ΔE (before):** test group: 6.5 ± 3.5; control group: 6.0 ± 2.6 **ΔE (Immediate):** test group: 4.1 ± 3.1; control group: 7.4 ± 3.5 **ΔE (1 month):** test group: 4.2 ± 3.0; control group: 6.1 ± 2.5 $p < 0.05$ between groups immediately and 1 month after treatment. ΔE decreased significantly in the test group, but not in the control group. |
| | | | | Qualitative masking assessment (pair-wise reading of digital photographs): total, partial, or no masking. | **Totally masked:** 57 % (examiner 1); 46 % (examiner 2) **Partially masked:** 32 % (examiner 1); 50 % (examiner 2) **Not masked:** 11 % (examiner 1); 4 % (examiner 2) $p < 0.001$ compared to control group where only one opacity was judged as partially masked. |
| Bhandari et al. (2018) | Resin infiltration ($n = 22$) | **Standard** | T1: Before T2: Immediate T3: 6 months | Color assessment (digital photographs): ΔL, Δa, Δb and ΔE were assessed as the difference between time points for the same area. | **ΔL Difference T1-T2:** −4.8 ± 1.9 **ΔL Difference T1-T3:** −7.9 ± 7.4 **ΔE Difference T1-T2:** 8.8 ± 5.9 **ΔE Difference T1-T3:** 13.2 ± 6.8 ΔL and ΔE decreased, indicating an immediate aesthetic improvement. These changes further increased over the 6 months follow up. |
| Brescia et al. (2022) | Resin infiltration ($n = 24$ patients) | **Modified:** 3 etching cycles | T0: Before T1: 1 year T2: 2 years | Qualitative masking assessment (digital photographs): color matching between opacities and surrounding sound enamel according to FDI criteria. | FDI value decreased from 4.0 (T0) to 1.5 (T1) and remained almost constant at T2 (1.46), indicating a significant aesthetic improvement. **T2:** "clinically excellent" = 66.67 % "clinically good" = 20.83 % |

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**Table 2** (*continued*)

| Author (Year) | Groups (number of treated teeth)* | Resin infiltration protocol* | Follow-ups | Masking effect measures (outcome) | Masking results* |
|---|---|---|---|---|---|
| | | | | | "clinically sufficient" = 8.3 %<br>"clinically unsatisfactory" = 4.2 % |
| ElBaz & Mahfouz (2017) | Group I ($n$ = 20): Resin infiltration<br>Group II ($n$ = 20): Fluoro-protector (control) | **Standard** | P0 & R0 - Before<br>P1 & R1 - Immediate<br>P2 & R2 - 1 week<br>P3 & R3 - 1 month | Color assessment (digital photographs):<br>ΔE between the opacity and the surrounding sound enamel at different time points. | ΔE significantly decreased from baseline (204.99 ± 13.85) to after immediate treatment (194.63 ± 4.2), 1 week (194.83 ± 4.7) and 1 month (194.38 ± 5.0) after treatment ($p$ < 0.05). |
| | | | | Gray level results (periapical digital radiographs):<br>changes in radio-density (pixel) were converted into gray levels at different times. | Significant improvement in radio-density from baseline (83.98 ± 0.9) to after immediate treatment (110.83 ± 0.35), 1 week (110.65 ± 1.54), and 1 month (110.13 ± 0.93) after treatment ($p$ < 0.05). |
| Giannetti et al. (2018) | Resin infiltration ($n$ = 9) | **Modified:**<br>Up to 3 etching cycles | Before<br>T1: Immediate<br>T2: 1 month<br>T3: 12 months | Qualitative masking assessment (pair-wise reading of digital photographs): total, partial, or no attenuation of the opacity. | **T1:** partially attenuated ($n$ = 7); no attenuation ($n$ = 2)<br>**T2:** 1 tooth became totally attenuated<br>**T3:** 2 more teeth were partially attenuated<br>**Total:** partial attenuation ($n$ = 8), total attenuation ($n$ = 1). |
| Gu et al. (2021) | Resin infiltration ($n$ = 36) | **Modified:**<br>Up to 2 etching cycles<br>(not exceeding 6 min in total) | T0: Before<br>T1: 1 week<br>T2: 6 months | Color assessment (spectrophotometer):<br>ΔE between the opacity and the surrounding sound enamel at different time points. | ΔE T0 (7.63 ± 1.39); ΔE T1 (2.08 ± 0.63); ΔE T2 (1.72 ± 0.41)<br>T0 x T1 and T0 x T2: $p$ < 0.001, indicating significant improvement.<br>T1 x T2: $p$ > 0.05, indicating stability. |
| | | | | Opacity area (digital photographs):<br>calculation of the opacity and infiltration area at different time points. | Lesion area: T0 (37.71 ± 5.42); T1 (6.84 ± 2,17); and T2 (5.35 ± 2.09)<br>T0 x T1 and T0 x T2: $p$ < 0.001<br>T1 x T2: $p$ > 0.05<br>Success rate: T1 (82.86 ± 12.51) and T2 (86.02 ± 10.63) ($p$ > 0.05). |
| Kim et al. (2011) | Resin infiltration ($n$ = 20) | **Standard** | T1: Before<br>T2: Immediate<br>T3: 1 week | Qualitative masking assessment (digital photographs):<br>ΔE between the opacity and the surrounding sound enamel at different time points.<br>Masking was ranked based on ΔE values thresholds in total, partial, or no masking. | Masking: complete (25 %; $n$ = 5); partial (35 %; $n$ = 7); no (40 %; $n$ = 8).<br>ΔE decreased significantly after infiltration (between T1 and T2, T1 and T3 and T2 and T3 = $p$ < 0.05). |
| Ozgur et al. (2023) | Resin infiltration ($n$ = 61 at follow-up) | **Standard** | T0: Baseline<br>T1: Immediate<br>T2: 1 week<br>T3: 6 months | Color assessment (spectrophotometer):<br>ΔE between the opacity and the surrounding sound enamel at different time points. | **T0:** $\Delta E = 8.30 \pm 4.05$<br>**T1:** $\Delta E = 5.77$<br>**T2:** $\Delta E = 6.39$<br>**T3:** $\Delta E = 6.76 \pm 2.66$<br>The ΔE values decreased significantly from T0 to T1, T2, and T3 ($p$ < 0.01). |
| Sanfelice et al. (2024) | Resin infiltration ($n$ = 12 patients) | **Standard** | T1: Before<br>T2: Immediate<br>T3: 1 week | Qualitative masking assessment (digital photographs):<br>pairwise reading using FDI color match criteria and translucency criteria evaluation scale. | **T1:** clinically unsatisfactory (100 %; $n$ = 12)<br>**T2:** clinically unsatisfactory (8 %; $n$ = 1)<br>clinically sufficient/satisfactory (42 %; $n$ = 5)<br>clinically good (42 %; $n$ = 5)<br>clinically excellent/very good (8 %; $n$ = 1)<br>**T3:** clinically unsatisfactory (8 %; $n$ = 1)<br>clinically sufficient/satisfactory (8 %; $n$ = 1)<br>clinically good (66 %; $n$ = 8)<br>clinically excellent/very good (18 %; $n$ = 2)<br>T1 and T2 ($p$ = 0.0005); T1 and T3 ($p$ = 0.0005); T2 and T3 ($p$ = 0.0019) |
| Warner et al. (2022) | Resin infiltration ($n$ = 6)<br>Microabrasion + Resin infiltration ($n$ = 23) | **NI**<br>Microabrasion step prior to resin infiltration | Before<br>6 months | Opacity area (digital photographs):<br>the whole labial surface and the lesion areas were measured in $mm^2$, before and after treatment. | **Mean opacity surface area:**<br>Before: 14.3 mm2 (SD 7.5; range = 3.9–38.3 mm2)<br>6 months: 9.4 mm2 (SD 9.0; range = 0–39 mm2)<br>($p$ < 0.001)<br>**Proportion of the tooth surface covered by visible opacity:**<br>Before: 22.5 % (SD 10.5; range = 6.8 %–53.2 %)<br>6 months: 14.7 % (SD 12.7; range = 0 %–49.4 %)<br>($p$ < 0.000) |
| | | | | Greyscale pixel value (digital photographs):<br>measurement of the opacity brightness using pixel intensity in relation to adjacent surrounding normal enamel. | **Mean maximum greyscale pixel value:**<br>Before: 53,065.9 (SD 4740.0; range = 43,813.0–65,535.0)<br>6 months: 49,039.7 (SD 3795.9; range = 42,093–54,323)<br>($p$ < 0.001)<br>**Mean minimum greyscale pixel value:**<br>Before: 39,565 (SD 4361; range = 29,317–47,862) |

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**Table 2** (*continued*)

| Author (Year) | Groups (number of treated teeth)* | Resin infiltration protocol* | Follow-ups | Masking effect measures (outcome) | Masking results* |
|---|---|---|---|---|---|
| | | | | | 6 months: 40,416 (SD 4534; range = 32,228–50,060) ($p = 0.534$) |

* Only key data relevant to this review are summarized. Furthermore, if multiple follow up time points were assessed only the values for directly after treatment and the latest follow up are shown. W/C: White/creamy; Y/B: Yellow/brown; L*a*b* (L* for lightness and a* and b* for the green-red and blue-yellow color coordinates); ΔL: lightness difference; Δa: green-red color difference; Δb: blue-yellow difference; ΔE: total color difference; FDI: Fédération Dentaire Internationale (World Dental Federation); NI: not informed.

No reduction in the mean ΔE was observed in the control group, which was 5.98 (± 2.57) at baseline and 6.06 (± 2.52) after treatment. Two examiners agreed on 42.9 % total masking, 46.4 % partial masking, and 10.7 % no masking after resin infiltration (data obtained from the authors).

### 3.7. Resin infiltration combined with previous microabrasion

In one study [39], 23 teeth were infiltrated after previous microabrasion, and six teeth were treated with resin infiltration alone. However, the results are not presented separately. Therefore, we considered all 29 teeth as having received the combined treatment. A significant reduction in the opacity area was seen after treatment from 14.3 (± 7.5) $mm^2$ to 9.4 (± 9.0) $mm^2$. Also, the proportion of the tooth surface affected by the opacity reduced significantly from 22.5 % (± 10.5) to 14.7 % (±12.7).

### 3.8. Meta-analysis results

Fig. 2 shows the proportional meta-analysis pooling the studies that presented the rate of total masking as outcome. Three studies that reported their results as total, partial or no masking were recombined into "total masking" or "partial/no masking" [8,16,33]. Two studies used the FDI scale, presenting their results as clinically excellent, clinically good, clinically sufficient, or clinically unsatisfactory [31,46]. Clinically excellent results were considered as "total masking" and clinically good, sufficient or unsatisfactory results were combined into "partial/no masking". Data from Brescia et al. [31] were reported per patient rather than per tooth. Despite our efforts to obtain tooth-level data from the authors, we did not receive a response. Consequently, the patient-level data were included in the meta-analysis based on several assumptions. First, we assumed there was no significant variation in the number of treated teeth per patient, given that an average of 3.5 (2.9–4.0) teeth were treated per patient. This suggests that success rates would be comparable at both the tooth and patient levels. Second, we considered the use of patient-level data to be a conservative approach, as it reduces the study's weight in the meta-analysis, thus rather favoring the conclusion that the treatment was less successful. The overall mean proportional of total masking was 37 % (CI: 18 –55). The modified treatment protocol, based on increased etching or increased etching and application time tended to show higher success rate (40 %; CI: 9 –72) comparing to the standard protocol (30 %; CI: 17 –44), although the difference was not statistically significant. A high heterogeneity among studies was observed ($I^2 = 77.2$ %).

Fig. 3 shows the meta-analysis pooling the studies showing the mean difference of the ΔE between the opacity and the surrounding sound enamel pre- and post-treatment. The overall reduction in the ΔE was 3.08 (CI: 0.74 –5.42). A reduction of 1.54 (0.68 –2.40) was observed with the standard application protocol, comparing to 3.84 (CI: 0.80 –6.89) when a modified protocol was used, with no statistical difference although the confidence interval of the ΔE value in the standard protocol was below the overall mean. Heterogeneity between the studies was high ($I^2 = 98$ %).

### 3.9. Risk of bias in studies

Quality assessment of the randomized clinical trials and the uncontrolled and non-randomized controlled clinical trials are presented in Tables 3 and 4, respectively. None of the ten studies [16,30,31,33,34,38,39,44–46] met all nine checklist criteria. Seven studies [16,31,34,38,44–46] were considered to have moderate risk of bias, and three studies [30,33,39] were considered to have high risk of bias. Table S2 (Supplemental Material) presents the reasons why each of the studies achieved or not achieved the JBI criteria.

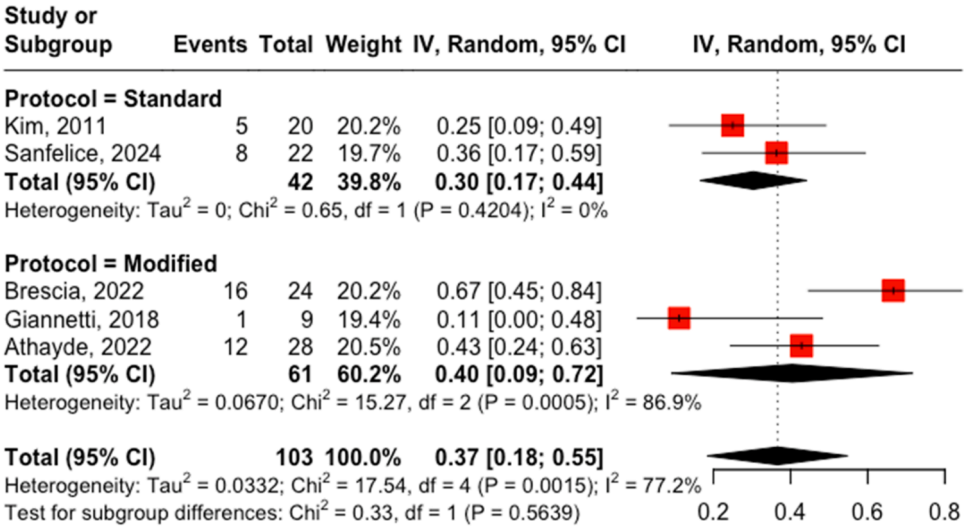


**Fig. 2.** Proportional meta-analysis using random-effects model pooling the studies that evaluated the rate of total masking.

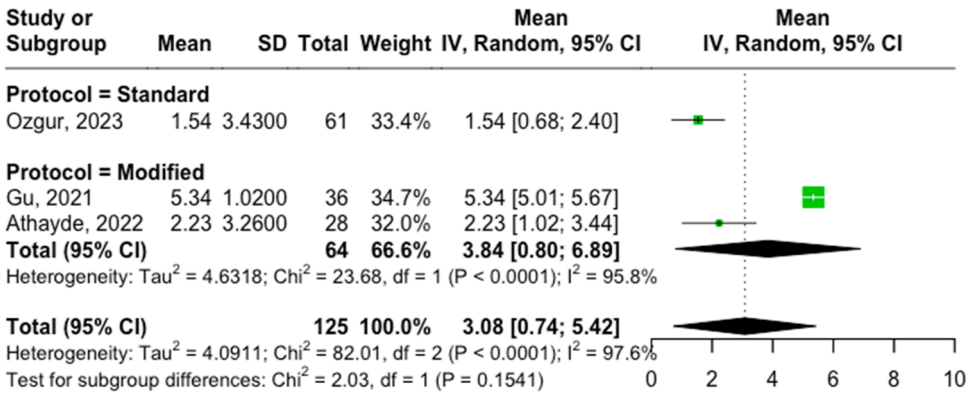


**Fig. 3.** Meta-analysis using random-effects model pooling the studies that evaluated the mean difference in ΔE between the opacity and the surrounding sound enamel pre- and post-treatment.

### *3.10. Certainty of evidence*

According to GRADEpro, the certainty of evidence for both syntheses was compromised (Table S3, Supplemental Material). This was primarily due to the absence of control groups in most studies and significant methodological limitations. Additionally, high heterogeneity ($I^2 >$ 80 %) and concerns about imprecision further impacted the certainty of the evidence.

## 4. Discussion

This systematic review aimed to assess the current evidence regarding the efficacy of resin infiltration in masking MIH opacities in permanent incisors. Moreover, we intended to evaluate whether the application protocol may influence the masking effect. A total of 369 anterior teeth with MIH were treated with resin infiltration in the twelve studies. The studies included in this review collectively showed that resin infiltration can change the appearance of MIH opacities. The treatment effect was observed either by a reduction in the opacity area [34,39,44,47], a decrease in the lightness [30,44,45], or a change in the total color [8,16,30,31,33,34,38,46].

It is important to note that not all changes necessarily indicate that the opacity was masked. The masking effect is achieved when the color difference between the opacity and the surrounding sound enamel is reduced to a level that is barely perceptible to the naked eye. Seven out of the 12 studies in question evaluated the masking effect either by calculating the color difference (ΔE) between the opacity and the surrounding sound enamel before and after treatment [8,16,34,38] or by evaluating the color match qualitatively, with the masking categorized as total, partial or none [8,16,31,33,46]. However, two studies [30,44] that also calculated the ΔE performed that calculation between the opacity before and after treatment, which does not provide sufficient evidence to confirm whether the observed color change resulted in a masking effect.

Alternative methods for assessing the color change included luminosity evaluation and reduction in the opacity area. Three studies [30,44,45] observed a significant decrease in the luminosity of the opacity following treatment. This may indicate that the lesions had darkened to a color closely resembling that of the surrounding natural tooth color [44], but this cannot be confirmed. Furthermore, a reduction in the size of the opacity was observed in four studies [34,39,44,47] following infiltration in comparison to the baseline evaluation. Nevertheless, despite the reduction in area, some opacities may be more deeply infiltrated in the center of the lesion, forming a halo [30]. The heterogeneous nature of the infiltration process may potentially impact the efficacy of masking.

It is hypothesized that a more homogenous and deeper infiltration results in a better masking effect. To ensure proper infiltration, it is necessary to guarantee that the infiltrant has access to the defective enamel in the subsurface and sufficient time to reach the deepest portions of the porosities. In contrast to caries lesions and fluorosis, which are superficial, MIH opacities may be limited to the inner enamel and covered by a relatively intact enamel layer [17]. Based on this assumption, the treatment protocol outlined in five studies [8,31,33,34,47] involved prolonged acid etching. In addition, one study included a microabrasion step prior to infiltration, using an abrasive agent [39] and one study optimized etching by rubbing the acid gel applicator tip for the first 10 s of the etching [8].

Only Alghawe & Raslan (2024) [47] compared a single etching with the multiple etching cycles. The evaluation of the infiltration area revealed an improvement in the multiple application group for white-creamy opacities, although this was not observed in the spectrophotometer analysis. The authors proposed that the color of the opacity may be a more significant factor in masking than the number of etching cycles.

It has been observed that the masking effect of caries lesions during re-wetting with ethanol can serve as a valuable indicator of the number of required etching cycles [48]. In addition to increasing the etching step, Athayde et al. [8] extended the application time of the infiltrant to 30 min for the first application, as suggested by Marouane and Manton [19]. The authors noted that for MIH lesions, longer infiltration time improved the masking effect even in cases where re-wetting with ethanol did not result in complete masking after using a polishing bur and ICON Etch as a pre-treatment protocol. The study indicated that the time required for infiltration could be three times longer when masking was not observed during re-wetting and the opacity was heterogeneous, compared to when masking was observed, and the opacity was homogeneous [19].

Due to several differences in the methods of analysis, the meta-analyses included a limited number of studies. Only three studies [8,34,38] could be pooled to evaluate the ΔE reduction between the opacity and the surrounding sound enamel. Additionally, the results of five studies [16,31,33,46] could be summarized as showing a total or partial/ no masking effect, making it possible to combine them in a meta-analysis. However, the certainty of evidence was very low both for the quantitative and qualitative data. The major concerns were risk of bias, high heterogeneity and an outcome data imprecision.

Overall, a reduction in the color difference between the opacity and the sound enamel, as measured by the calculation of ΔE, was observed independently of the treatment protocol. Interestingly, the ΔE value reached after treatment was significantly lower when a modified protocol was used. This is suggestive that multiple etching cycles and longer application time may enhance the penetration of the infiltrant, resulting in an improved masking effect. In the meta-analysis of the rate of total masking, the tendency for a higher success rate with the modified application protocol was clearly disrupted by a single study [33] with

**Table 3**
Risk of bias of included uncontrolled and non-randomized controlled studies, using the Joanna Briggs Institute (JBI) instrument for quasi-experimental studies (Tufanaru et al., 2020).

| JBI Criteria | Q1 | Q2 | Q3 | Q4 | Q5 | Q6 | Q7 | Q8 | Q9 | Rate of 'yes' | Overall risk of bias* | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Is it clear in the study what is the cause and what is the effect? | Was there a control group? | Were the participants included in any comparisons similar? | Were the participants receiving similar treatment/care, other than the exposure or intervention of interest? | Were there multiple measurements of the outcome both pre and post the intervention/ exposure? | Were the outcomes in any comparisons measured in the same way? | Were outcomes measured in a reliable way? | Was follow up complete and if not, were differences between groups adequately described and analyzed? | Was appropriate statistical analysis used? | n | % | |
| Altan & Yilmaz, 2023 | + | + | – | + | + | – | ? | + | + | 6/9 | 66.7 | Moderate |
| Bandhari et al., 2018 | + | – | – | + | + | NA | + | ? | – | 4/8 | 50.0 | High |
| Brescia et al., 2022 | + | – | ? | + | + | NA | + | + | – | 5/8 | 62.5 | Moderate |
| Elbaz & Mahfouz, 2017 | + | + | + | + | + | + | ? | ? | – | 6/9 | 66.7 | Moderate |
| Giannetti et al., 2018 | + | – | ? | + | + | NA | ? | + | – | 4/8 | 50.0 | High |
| Gu et al., 2021 | + | – | + | + | + | NA | + | ? | – | 5/8 | 62.5 | Moderate |
| Kim et al., 2011 | + | – | ? | + | + | NA | + | + | – | 5/8 | 62.5 | Moderate |
| Ozgur et al., 2023 | + | – | ? | + | + | NA | + | – | + | 5/8 | 62.5 | Moderate |
| Sanfelice et al., 2024 | + | – | + | + | + | NA | + | + | + | 7/8 | 87.5 | Moderate |
| Warner et al., 2022 | + | – | ? | – | + | NA | + | + | – | 4/8 | 50.0 | High |
| n | 11/11 | 2/10 | 3/10 | 9/10 | 10/10 | 1/2 | 6/10 | 6/10 | 3/10 | | | |
| % | 100 | 20.0 | 30.0 | 90.0 | 100 | 50.0 | 60.0 | 60.0 | 30.0 | | | |

Note: + = yes; –= no; ? = unclear; NA = not applicable. * Low risk of bias: rate $\geq$ 80 %; moderate risk of bias: 50 % < rate < 80 %; high rate of bias: rate $\leq$ 50 % - provided that the three most relevant criteria (Q2, Q3 and Q7) were met, otherwise, the risk of bias was also considered moderate.

**Table 4**
Risk of bias of included randomized controlled studies, using the Cochrane risk-of-bias tool version 2 (RoB 2) (Higgins JPT et al., 2023).

| Study | D1 | D2 | D3 | D4 | D5 | Overall risk of bias* |
|---|---|---|---|---|---|---|
| Athayde et al. (2022) | Unclear if size of opacity was evenly distributed | | | | | No domain with high risk, but at least one with some concerns. |
| Alghawe & Raslan (2024) | Unclear if size of opacity was evenly distributed | | Considerable missing data. | | Outcome could not be assessed in some cases due to missing data. | More than one domain is high risk. |

D1: bias due to problems with randomization; D2: bias due to deviation from intended treatment; D3: bias due to missing outcome data; D4: bias in the measurement of the outcome; D5: bias due to selection of reported result. * Low risk of bias: if all domains are judged to be at low risk. Some concern: if there is some concern in at least one domain but does not have a high risk of bias in any domain. High risk of bias: if at least one domain is judged to be at high risk, or if the study has some concerns in multiple domains in a way that substantially reduces confidence in the result. Red: High risk of bias. Yellow: Some concern. Green: Low risk of bias.

high risk of bias, whose results were inferior to those obtained with the standard protocol. More randomized clinical trials are necessary to support specific recommendations for resin infiltration of MIH opacities. Nonetheless, considering the ultrastructure of hypomineralized enamel and the findings of the available studies, it seems plausible that MIH opacities require modifications in the resin infiltration protocol to achieve a proper filling of the porosities within the defective enamel.

From the present review, it seems that the modifications implemented in the studies [8,31,34] included in the meta-analyses improved the infiltration but were not enough to optimize it to an extent where the achievement of total masking was significantly superior. Further studies should be designed to confirm the benefit of prolonged etching, previous microabrasion, or other pre-treatments of the enamel surface prior to infiltration of MIH opacities. Recently, a protocol preconizing the use of polishing stones in low-speed handpiece prior to etching was published [49]. The removal of a very fine layer of enamel was able to facilitate infiltration reducing the etching time to cycles of ten seconds each instead of two minutes. The monitoring of the ethanol penetration with transillumination after each etching cycle allowed the detection of the areas where the lesion still needed to be abraded. The protocol was named infiltration monitoring by transillumination [49] combining a new recommendation of pre-treatment of the enamel surface with the transillumination that was previously suggested by Marouane and Manton [19].

In addition to the outcome of opacity masking, some studies also aimed to assess the short- and long-term color stability [8,30,31,33,34,38,44,45,47] and found that the masking outcomes were stable or even better after a certain period of time. This improvement may be attributed to increased tooth hydration, as the teeth were previously dehydrated by the ethanol and by isolation from saliva under a rubber dam [46]. While the longest evaluation period for MIH lesions was two years, the long-term masking effect for initial caries lesions has been proven to be stable for at least six years [50]. Nonetheless, long-term clinical studies are still needed to confirm the longevity of the esthetic results for MIH lesions.

Almost all studies included in this review [8,16,30,31,34,38,39,45–47] presented a clear diagnostic criterion for MIH. The studies by Altan and Yilmaz [44] and Giannetti et al. [33] lacked a diagnostic criterion, which increases the risk of bias, as the patient selection process was not clearly delineated. Additionally, four studies [30,31,38,44] did not specify the color of the opacity, which could potentially influence the masking results. It is proposed that yellow-brownish opacities are more porous and have a higher protein content than white-creamy ones [51]. Despite the greater porosity of yellow-brownish opacities, which may facilitate resin penetration, the higher protein content may also play a role in preventing the penetration of the infiltrant and consequently affecting the masking result [47].

A comprehensive review of the included studies and the data extracted from them revealed that the authors' classification of the primary studies in some cases differed from what is established in the literature. Uncontrolled studies were classified as those with a single arm, no random allocation and no control group. RCTs were defined as clinical trials with a control group and random allocation. Controlled clinical studies without random allocation were classified as non-RCTs. In Giannetti et al. [33], the article was published in the letter to the editor category, yet it is an original study configured as an uncontrolled clinical study. Warner et al. [39] classified the study as a retrospective laboratory *in vitro* study. Nevertheless, the study is an outcome evaluation based on clinical photographs of teeth before and after resin infiltration, thus characterizing it as an uncontrolled clinical study.

The main limitation of this review relies on the lack of high-quality primary studies. Although relevant information could be retrieved from the available studies, most of them present critical methodological issues that contributed to a very low certainty of evidence. The absence of a control group [16,30,31,33,34,38,39,46], uncertainty regarding participant similarity at baseline [16,30,31,33,38,39,44], absence of a sample size calculation [16,30,31,33,34,39,45], and small sample size [33] were the most critical aspects. Moreover, in some of the studies [33,44,45], there were concerns regarding the reliability the outcome measurement. Nonetheless, from the available literature, it is possible to state that resin infiltration modifies the clinical appearance of MIH opacities. However, more studies properly designed to evaluate the masking effect are necessary to strength the available evidence of the efficacy of resin infiltration on camouflaging MIH opacities.

Future randomized controlled clinical trials should focus on implementing proper measures to assess the masking effect based on reliable methods that assess how much the treatment approximates the opacity to the natural color of the sound enamel, either quantitatively or qualitatively. Only the evaluation of the color difference between the opacity and the surrounding sound enamel can provide a more accurate representation of the masking effect, rather than merely detecting a color change after treatment. Assessment of changes in the level of luminosity and opacity area are valuable but do not properly inform about the masking effect unless combined with an evaluation of the color change in relation to the surrounding sound enamel.

## 5. Conclusion

The studies included in this review indicated that the resin infiltrant is an effective method for reducing the color difference between MIH opacity and normal enamel. The achievement of total masking was not significantly different between the standard and modified resin infiltration protocols. However, the methodology of the studies was heterogeneous, and the absence of randomized clinical studies may limit the certainty of this evidence.

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## CRediT authorship contribution statement

**Natália de Araújo Prado:** Writing – original draft, Methodology, Investigation, Data curation. **Roberta Costa Jorge:** Writing – original draft, Methodology, Investigation, Data curation. **Rudá França Moreira:** Writing – original draft, Investigation. **Susanne Effenberger:** Writing – review & editing, Validation, Investigation, Conceptualization. **Marcus Cebula:** Writing – review & editing, Conceptualization. **Tatiana Kelly da Silva Fidalgo:** Writing – review & editing, Supervision, Formal analysis. **Vera Mendes Soviero:** Writing – review & editing, Supervision, Formal analysis, Conceptualization.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: SE and MC report a relationship with DMG Dental Material Gesellschaft mbH that includes: employment. MC and SE are employees of DMG Dental-Material Gesellschaft mbH, the company that is marketing the commercial resin infiltrate Icon, but do not receive any personal benefit from the sales of the product used in this study. RCJ, TKSF, and VMS are authors of one study included in the meta-analysis. The study was conducted following a strict and clear methodology, limiting the risk of bias due to conflicts of interest. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jdent.2025.105617.

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