International Journal of Dental Research and Allied Sciences
2021, Volume 1, Issue 2, Page No: 66-87

Available online at: www.tsdp.net

ISSN: 3062-3502

Review Article

Innovative Strategies in Minimally Invasive Dentistry for Caries Management: A Literature Synthesis

Mariana Vega[1], Hugo Fuentes[1]*, Valeria Cordero[2], Luis Silva[2], Regina Cabrera[3]

[1]Faculty of Dentistry, Autonomous University of Nuevo León, Monterrey, Nuevo León 64460, Mexico.
[2]Faculty of Dentistry, University of Veracruz, Veracruz, Veracruz, Mexico.
[3]Faculty of Dentistry, Autonomous University of Sinaloa, Culiacán, Sinaloa 80023, Mexico.

***E-mail** ✉ hugofuentes.pro@gmail.com

Received: 02 August 2021; **Revised:** 29 October 2021; **Accepted:** 03 November 2021

ABSTRACT

Over the past several years, a deeper insight into caries pathology alongside innovations in dental biomaterials has sparked growing interest in conservative, non-invasive and minimally invasive alternatives that postpone or eliminate the necessity of conventional restorations. This review evaluates a selection of these modern interventions—such as fluoride varnish, silver diamine fluoride, resin sealants, resin infiltration, chemomechanical removal of decay, and atraumatic restorative treatment—analyzing their underlying chemistry, indications, clinical performance, determinants of success, and inherent constraints. Furthermore, it explores ongoing research aimed at amplifying the antimicrobial potential of these procedures to broaden their clinical utility.

Keywords: Minimally invasive dentistry, Caries therapy, Restorative approaches, Resin infiltration, Sealants, Fluoride

How to Cite This Article: Vega M, Fuentes H, Cordero V, Silva L, Cabrera R. Innovative Strategies in Minimally Invasive Dentistry for Caries Management: A Literature Synthesis. Int J Dent Res Allied Sci. 2021;1(2):66-87. https://doi.org/10.51847/rXhXROt2yc

Introduction

Conventional restorative dentistry for carious lesions traditionally entails significant removal of tooth material to (1) eradicate bacteria driving decay, (2) reshape the cavity for mechanical retention and load resistance, and (3) excise demineralized dentin [1]. However, the evolution of adhesive and bioactive restorative agents that bond micromechanically to dental tissues has rendered such extensive removal largely unnecessary [1]. These materials effectively seal margins, cutting off the lesion from the oral milieu and supporting caries arrest even without full excavation [2–4]. Evidence now indicates that demineralized yet structurally sound dentin can undergo remineralization [5–7]. Consequently, clinicians increasingly practice selective caries removal to conserve remineralizable dentin, which studies suggest reduces pulp exposure risk [8] and enhances treatment success by up to four times compared to conventional excavation [9]. Hence, with improved understanding of caries mechanisms and advanced materials, dentistry is shifting toward non-invasive and minimally invasive care—approaches emphasizing preservation of healthy tissue and breaking the repetitive restoration cycle, often termed the "restorative death spiral" [10].

Non-invasive strategies (e.g., plaque control and fluoride use) aim to reduce biofilm virulence and depend heavily on patient cooperation [11], while minimally invasive techniques (e.g., sealants and resin infiltration) establish protective barriers that require less patient adherence [12]. Their selection and outcomes depend on factors like caries risk profile, lifestyle, lesion size and depth, surface type, and dentition phase. When implemented appropriately, these options demonstrate comparable effectiveness to traditional restorations, showing similar longevity,

reduced chair time [13, 14], decreased patient anxiety [15, 16], and long-term cost benefits [14, 17, 18]. Thus, such conservative measures should be prioritized, with invasive approaches reserved for cases where conservative control proves inadequate. The cumulative success of these techniques underscores the need for continued refinement and innovation in this domain.

Materials and Methods

Relevant publications were collected from the PubMed database using a combination of the following terms: "minimally invasive dentistry", "fluoride varnish", "resin sealants", "resin infiltration", "chemomechanical caries removal", "atraumatic restorative treatment", "caries arrest", and "caries management". Inclusion criteria comprised systematic reviews, meta-analyses, literature reviews, randomized controlled trials, and studies examining the enhancement of antimicrobial features within minimally invasive caries control methods, all published in English within the past decade.

Chemical control of caries with fluoride varnish

Fluoride varnishes (FV) are considered safe [19], non-staining, well tolerated by children [20], and simple for dental practitioners to apply [21]. These varnishes have long been used worldwide to prevent dental caries; however, recent investigations indicate a decline in their effectiveness. This diminished effect may stem from modern children's greater exposure to fluoride through various sources such as water and toothpaste, reducing the additional benefit of FV [22].

A meta-analysis conducted recently found that after a 2–3-year period, there was no statistically significant difference in the rate of occlusal caries on first permanent molars between FV and sealant groups [23]. This aligns with Chestnutt *et al*., who observed slightly higher yet statistically insignificant protection from FV compared to sealants (caries incidence 17.5% vs. 19.6%) after 3 years, though FV proved more cost-efficient [24]. Regarding non-cavitated proximal lesions, pooled data reveal insufficient evidence supporting FV alone for decay arrest. However, combining 5% sodium fluoride with resin infiltration yielded better outcomes than resin infiltration alone [25], suggesting FV may serve effectively as an adjunct measure. Numerous trials have demonstrated that Silver Diamine Fluoride (SDF) performs significantly better than FV in halting caries progression [26], leading the ADA's latest evidence-based guidelines to strongly endorse SDF over FV for managing cavitated carious lesions in primary dentition [27]. Earlier assumptions suggested that FV could reduce caries-related hospital admissions among preschoolers, yet a newer meta-analysis classified its benefits as "modest and uncertain" [22], indicating it likely does not lower hospitalization rates meaningfully.

Silver diamine fluoride (SDF)

Silver Diamine Fluoride is a liquid medication used to arrest caries progression and has been employed for decades in nations such as Japan, China, Argentina, and Brazil [28–31]. In the United States, it was authorized in 2014 for dentin desensitization in adults, and its off-label use for caries management—especially in pediatric dentistry—has since expanded rapidly [32]. Applying 38% SDF twice yearly achieves an 84.8% caries arrest success rate [33], and the American Academy of Pediatric Dentistry (AAPD) supports its application for treating cavitated lesions in primary teeth [34]. It is inexpensive [35], can be used without removing softened dentin [36], and serves as an ideal solution for patients with severe dental anxiety, behavioral challenges, medical complications, or those requiring general anesthesia [16].

SDF consists of silver and fluoride ions stabilized in an ammonia solution. The 38% formulation contains roughly 44,800 ppm of fluoride ions. Although its mechanism is not fully elucidated, it is recognized for inhibiting demineralization, encouraging remineralization, and protecting the dentin's organic framework [37]. Studies demonstrate that it increases enamel mineral content and dentin microhardness [38, 39]. When applied, it precipitates a protective silver chloride layer that curtails mineral loss by reducing calcium and phosphate release. It also facilitates the formation of calcium fluoride, which gradually dissolves in saliva to release fluoride ions. The alkaline pH enhances ion exchange and encourages the transformation of hydroxyapatite into acid-resistant fluorapatite [40]. Furthermore, SDF suppresses matrix metalloproteinases and cysteine cathepsins, limiting collagen breakdown [41–43]. Its alkalinity promotes mineral deposition within exposed collagen networks in demineralized dentin, potentially leading to both inter- and intra-fibrillar remineralization and resulting in greater microhardness [44]. Additionally, SDF exhibits strong antimicrobial activity and effectively reduces cariogenic biofilm accumulation [45, 46].

Caries prevention and arresting efficiency of SDF

Chibinski *et al*.'s meta-analysis on SDF use in primary teeth found that, over 12 months, SDF achieved a caries arrest rate 66% higher than other active treatments (ART and FV) and 154% higher than placebo or no treatment, making it approximately 89% more

effective overall in halting carious lesions [47]. Subgroup analyses revealed that SDF works better on anterior teeth than on posterior teeth [48–52]. The baseline level of oral hygiene significantly impacts outcomes; larger cavities and the presence of visible plaque reduce the likelihood of arrest, particularly with once-yearly applications [51, 52]. Increasing SDF application frequency to twice per year has been shown to enhance its caries-arresting capacity among children with poor oral hygiene [49].

Most clinical evaluations of SDF effectiveness in primary teeth

Most available studies on SDF performance in primary dentition have focused on school-aged cohorts. Mabangkhru *et al*. investigated how SDF compared with 5% sodium fluoride varnish (NaF) for halting lesions associated with severe early childhood caries (SECC) in children aged 1–3 years. They reported that SDF doubled the likelihood of caries arrest compared to NaF. Lesions in front teeth showed a higher tendency to become inactive than those in molars, and occlusal lesions were less responsive than buccal or lingual ones. Dietary factors had a marked effect: children who no longer consumed milk and snacked fewer than three times daily demonstrated the highest arrest rates. The researchers concluded that SDF is an efficient tool for managing SECC [53].

Besides stopping decay, SDF also helps prevent new lesions from forming. Treating four primary teeth was linked to the prevention of one new cavity [54]. A meta-analysis found that, over at least 24 months, the prevented fraction (PF) of SDF reached 77%, while a comparable Cochrane review reported 37% for fluoride varnish. Annual SDF application outperformed quarterly fluoride varnish in reducing new lesions in primary teeth (PF = 54% after 24 months) [55]. Although these findings favor SDF, interpretation must be cautious. Preventive trials typically record decay across all teeth, whereas certain SDF studies only measured selected areas—Llodra *et al*. examined posterior teeth exclusively, while Chu *et al*. assessed anterior surfaces. Such differences hinder direct comparison [56]. In a randomized study comparing SDF with glass ionomer cement (GIC), SDF achieved significantly higher success in primary dentition after 12 months [57]. Nonetheless, longer follow-up studies are necessary for stronger conclusions.

Few investigations have explored SDF in permanent teeth. Llodra *et al*. found 77% of active lesions became arrested in both primary and permanent molars [33]. Braga *et al*. compared SDF, routine toothbrushing, and GIC on early carious lesions and observed that SDF was initially superior within 6 months, though the three methods performed similarly over 30 months [58]. Rosenblatt *et al*. reported that SDF prevented more than 60% of caries in permanent teeth [59]. Conversely, Liu *et al*. observed that sealants, semiannual fluoride varnish, and annual SDF had equivalent preventive efficacy after 24 months [60], while Monse *et al*. recorded better outcomes with GIC sealants than with a single SDF application after 18 months for dentinal decay [61]. At present, solid evidence regarding SDF's preventive and arresting capacity for permanent dentition remains limited [56].

SDF has also been utilized to manage root caries in older adults. Across 24–36 months, the PF values ranged from 24% to 71%. Regarding lesion progression, PF was 725% higher than placebo after 24 months and 100% higher after 30 months [62].

A retrospective analysis of 12-month survival rates among patients at a public clinic revealed that SDF alone showed a 76% survival rate, SDF with sedative fillings 50%, and SDF with same-day restorations 84%. The sedative-filling group failed 2.5 times more often than SDF alone, likely due to the temporary material used. In primary teeth, SDF alone achieved the best outcomes in canines (83–86%) and the lowest in mandibular molars (71%). In permanent teeth, anterior survival rates (50–70%) were lower than posterior ones (75–82%). Overall, survival rates for primary (74%) and permanent (78%) teeth were similar. Among those younger than 6 or older than 41 years, success rates (69% and 68–72%) were lower than in the 6–40-year range (77–84%). When analyzed by caries risk, survival reached 81%, 76%, and 75% for low-, moderate-, and high-risk patients, respectively. Despite the limitations of using insurance claim data—which lacked diagnostic details like lesion type or reason for SDF use—these findings suggest that SDF effectively halts decay progression [63].

Limitations of SDF

Given its high success rate and increasing demand among pediatric patients, SDF has been swiftly integrated into dental training programs at both undergraduate and postgraduate levels. The ADA Code Commission has also established code D1354, enabling reimbursement for SDF as a temporary caries-arresting treatment [26].

A 2016 national survey of U.S. pediatric dental program directors revealed that 89.2% supported using SDF for patients at high caries risk, while only 9.5% opposed its use on primary teeth [26]. Because of its simplicity, SDF is especially beneficial for children who are uncooperative, patients needing behavioral management, and those with limited dental access [26]. However, a major drawback is the permanent black

discoloration of treated enamel and dentin, which raises parental concerns. This aesthetic issue was cited as the most significant barrier by 91.8% of dental educators and 56% of hygienists [26, 64].

Research on parental acceptance shows highly variable attitudes across regions. Cultural expectations and aesthetic values about children's primary teeth influence perceptions [65, 66]. Chu *et al*. reported that nearly all parents were satisfied post-treatment, with only 7% objecting to the color change, whereas Alshammari *et al*. observed near-total parental refusal (with just 3.2% neutral responses) [36, 67]. Access to cosmetic treatment options in private or hospital settings was identified as the main reason behind this resistance [67].

Cultural variations in aesthetic preferences are not the only factors shaping parental attitudes toward SDF. Acceptance also depends on which teeth are treated, the parent's educational background, financial situation, and whether the child requires advanced behavioral management [65]. While many caregivers tolerated the dark discoloration associated with SDF because of its simplicity and the child's comfort during treatment [68, 69], far fewer agreed to its use on front teeth (27%–36%) than on back teeth (54%–69%) due to cosmetic concerns [65, 66, 70]. Families with limited income and public dental insurance demonstrated higher acceptance rates than those with private coverage, likely because they had fewer treatment alternatives [65, 71].

Among parents of toddlers or children who could not cooperate well and might otherwise need sedation or general anesthesia (GA), acceptance rose notably from 54%–62% to 70%–82%. These parents were more inclined to choose SDF when it could prevent pain, infection, or complex behavioral procedures [65, 70, 72, 73]. Given the potential cognitive and developmental risks tied to repeated or extended GA exposure in early childhood, many parents preferred less invasive options that might eliminate or postpone the need for anesthesia [66]. Parents with higher educational levels also tended to approve SDF when presented as an alternative to sedation or GA, possibly because they were more aware of the medical implications of anesthetic exposure [65, 66].

This pattern—higher acceptance among low-income or high-risk populations—could lead to an ethical imbalance: children from disadvantaged backgrounds may receive less aesthetic treatment outcomes, while wealthier groups, with better access to cosmetic restorations, avoid visible staining [26].

Although controlled research on SDF's effectiveness in permanent teeth remains scarce, the American Dental Association (ADA) has issued a conditional guideline supporting its use as a nonrestorative approach for permanent dentition, based on indirect data from studies on primary teeth [27]. Nonetheless, 28.3% of U.S. pediatric dentistry program directors in a 2016 survey expressed opposition, noting that SDF is relatively new and insufficiently studied for permanent teeth [26]. Parents also tended to be less accepting of SDF use in permanent dentition than in primary teeth [66, 70]. Because baby teeth eventually shed, parents were more willing to tolerate discoloration in exchange for avoiding invasive treatments such as GA or sedation. However, when it came to permanent teeth, even parents with limited dental care access were reluctant to accept visibly stained results [70, 73].

Research by Hu *et al*. further revealed that parents of children with autism spectrum disorder had similar esthetic expectations to those of parents of neurotypical children, and both groups were unlikely to select SDF as a substitute for GA [66]. Therefore, SDF continues to face limited parental acceptance for managing decay in older children with permanent dentition.

Resin-based fissure sealants

Resin sealants made from methacrylate derivatives have been in use since the 1960s as a preventive measure against dental caries. These coatings serve as a mechanical barrier that separates tooth enamel from bacterial biofilm **(Figure 1)**, demonstrating superior effectiveness in preventing decay in sealed molars compared with unsealed ones [74].

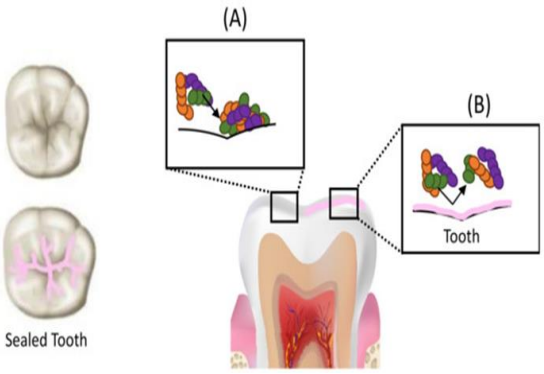


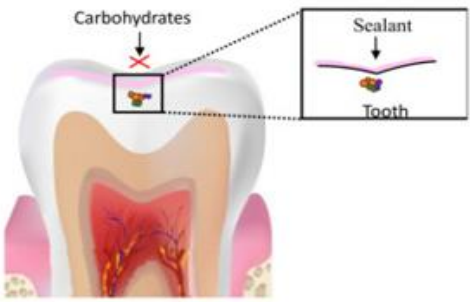
Figure 1. Illustration of how sealants prevent caries. (a) Deep grooves and pits on the chewing surfaces of posterior teeth trap bacteria and debris, promoting decay. (b) Applying a sealant smooths these surfaces, reduces bacterial retention, and creates a protective layer that lowers caries risk.

Clinical studies have shown that sealants can reduce the likelihood of new carious lesions by 87% after 12 months and by 60% after 48–54 months [75]. Over a 10-year period, only 5.7% of sealed first molars developed decay or required restoration [76]. The key

factor influencing long-term success is how well the sealant adheres over time [74, 75]. According to a meta-analysis, the retention rates for light-cured sealants were 68.4%, 83.1%, and 57.8% after 2, 3, and 5 years, respectively [77]. Loss of sealant, either partial or total, allows bacterial invasion, creating new decay-prone areas; hence, reapplication is necessary whenever loss is detected [78]. These results suggest that as sealants wear off, their caries-preventive benefit declines, highlighting the importance of routine dental monitoring following application.

In light of modern dentistry's shift toward minimally invasive care, extending the use of sealants to teeth with early-stage caries has been recommended to stop lesion progression [79, 80]. This concept is not new—studies from the 1970s already showed that trapping bacteria under restorations drastically reduced their numbers [81]. Sealed lesions exhibited at least a 100-fold reduction in Streptococcus mutans and lactobacilli [82, 83]. By forming an airtight seal, the material isolates the decayed site from its nutrient source, leading to fewer viable bacteria and a less aggressive, less diverse biofilm [2, 4, 83]. This biological shift weakens microbial activity, ultimately halting or slowing the advance of caries [74, 84].

a)



b)

Figure 2. Diagram showing how sealants stop caries progression.

When the sealant blocks nutrient flow to the bacteria inside a lesion, their number and virulence decrease, producing a less active biofilm and slowing or preventing further tooth decay.

Clinical trials on sealing occlusal carious lesions

Long-term investigations lasting between 24 and 44 months on sealing carious occlusal surfaces—ranging from non-cavitated to cavitated lesions extending from enamel into the middle third of dentin—have consistently indicated that sealing can effectively halt caries progression, provided proper tooth isolation is maintained during the procedure [85–87]. However, the precise depth limit at which a lesion becomes too extensive to benefit from sealing remains uncertain [84].

The primary issue with sealing deep dentinal decay is that, while the sealant may block external bacterial contamination, it cannot penetrate fully into the lesion to suppress internal bacterial activity. In contrast to the saccharolytic bacteria commonly associated with enamel decay—which depend on sugars from the oral cavity—the microbes inhabiting deep dentin are largely proteolytic, feeding on the organic components of dentin itself [88, 89]. Consequently, even when isolated from external nutrients, these bacteria may stay active and allow the lesion to advance further. Additionally, once caries infiltrates the dentin, the enamel above becomes structurally weakened, and the mechanical limits of the sealant prevent it from adequately protecting this undermined enamel from fracturing under chewing forces [84].

A meta-analysis comparing caries progression between sealed and unsealed lesions (both cavitated and non-cavitated) found a substantial difference: only 5% of sealed sites progressed compared to 16.1% of unsealed ones. Overall, sealing reduced caries advancement by about 70%, performing better than both fluoride varnish and no treatment approaches [90].

In a 10-year clinical study, bonded composite restorations that were placed directly over cavitated dentin lesions—without removing the decayed tissue—demonstrated higher longevity and superior performance than unsealed amalgam fillings where decay was fully excavated first [91]. Another investigation observed similar rates of caries control between sealed lesions and conventionally restored teeth over 2–3 years. In that study, 10% of sealed sites continued to progress, while 88% were fully arrested; none of the composite restorations showed decay, and 14% of the sealants required repair or replacement [85]. Thus, while sealing can substantially slow or stop lesion activity and postpone the need for invasive treatment, sealant loss or reactivation of once-arrested lesions may occur, underscoring the importance of continuous monitoring of treated sites.

Limitations of sealant therapy

Despite strong evidence supporting sealants for controlling pit and fissure caries, their routine use remains debated. Concerns include poor retention, incomplete penetration into fissures, and concealed lesion progression under partially sealed surfaces [92]. Furthermore, polymerization shrinkage can create marginal gaps, promoting plaque accumulation and microleakage [93, 94].

Adhesion of sealants to carious enamel or dentin is often compromised due to demineralization, which limits the material's ability to bond effectively [95]. Such fissures are difficult to clean thoroughly and are ideal environments for biofilm persistence. Residual biofilm and incomplete cleaning interfere with sealant adaptation, preventing full penetration and leaving unfilled voids that enable bacterial regrowth [96]. Inadequate adaptation results in higher microleakage rates and partial filling, both of which can facilitate undetected lesion progression [93]. Additionally, surface wear, matrix degradation, and filler detachment over time can lead to sealant loss, re-exposing teeth to caries risk [97].

Development of antimicrobial sealants

Resin-based sealants face several shortcomings:

1. Microleakage from polymerization shrinkage [98];
2. Increased biofilm accumulation compared with other restorative materials [99];
3. Incomplete filling of deep or carious fissures leading to poor edge sealing [96].

Each of these issues contributes to secondary caries formation. Since clinicians sometimes intentionally or inadvertently apply sealants over early lesions, integrating antibacterial compounds has been explored as a way to strengthen both preventive and arresting effects [98].

Two strategies have been investigated to enhance antibacterial properties—releasing systems and contact-active agents. Fluoride-releasing sealants were designed because fluoride can reduce microbial metabolism, inhibit demineralization, encourage fluorapatite formation, and enhance remineralization [100]. However, current data provide no conclusive proof that fluoride-enhanced sealants outperform standard types in preventing caries [101]. Studies have shown that the frequency of new carious lesions in teeth treated with fluoridated sealants is comparable to those treated with non-fluoridated variants [102, 103], and that their retention rates are either similar [104] or even lower [105, 106].

Another challenge is the decline of fluoride release over time—initial bursts are followed by a rapid decrease, which lessens antimicrobial effects [100, 107]. Dissolution of soluble fluoride salts also tends to weaken mechanical strength, making these sealants less durable [107].

Sealants incorporating chlorhexidine (CHX) have been introduced as an alternative; however, as with fluoride systems, their structural properties degrade over time. The release of CHX increases porosity, leading to staining, reduced wear resistance, and enhanced biofilm retention [108]. In a 6-month in vitro study, Shafiei *et al*. observed that CHX application actually increased microleakage, raising the risk of secondary decay under sealed areas [109].

Contact-killing mechanisms using quaternary ammonium compounds (QACs) have recently drawn significant attention because they can be polymerized directly into the resin matrix without altering the sealant's mechanical integrity or physicochemical characteristics [110]. A number of QACs such as 2-methacryloxylethyl dodecyl methyl ammonium bromide (MAE-DB) [111], 2-methacryloyloxyethyl trimethylammonium chloride (METAC) [112], methacryloxylethyl cetyl dimethyl ammonium chloride (DMAE-CB) [98], dimethylamino-hexadecyl methacrylate (DMAHDM) [113, 114], and 1,3,5-triacryloyl hexahydro-1,3,5-triazine (TAT) [115] have been added to resin formulations to boost their antimicrobial performance **(Figure 3)**.

In vitro assessments of sealants modified with QACs have demonstrated promising antibacterial effects and revealed that incorporating these compounds does not compromise essential parameters such as the degree of conversion, penetration capability, ultimate tensile strength, or micro-shear bond strength [110]. Furthermore, as QACs are covalently bonded within the polymer structure, they are not expected to leach out, which suggests that their antimicrobial activity should persist over time. Nevertheless, it is known that organic debris—such as dead cell matter and salivary protein films—can diminish QAC activity [108]. Over time, resin degradation in the oral cavity might also lead to QAC release, raising potential cytotoxicity issues. Consequently, long-term evaluations of QAC-containing sealants are warranted to determine their stability and safety.

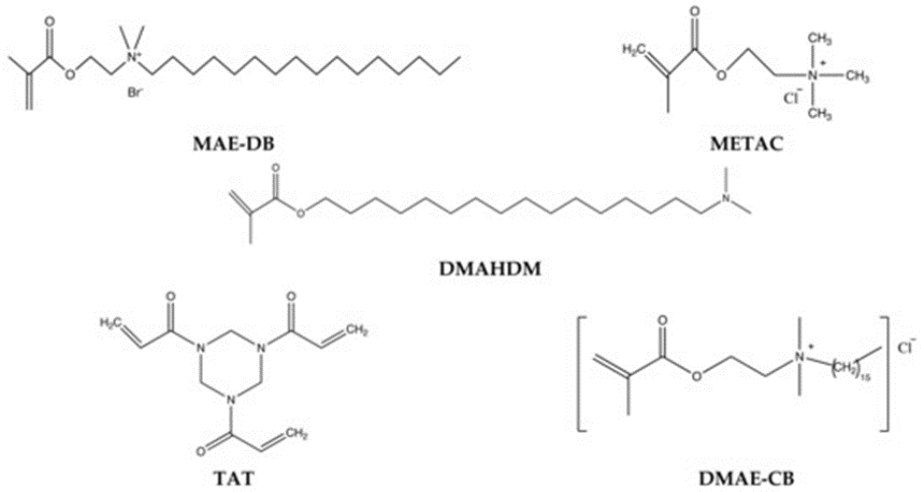


Figure 3. Chemical structures of Quaternary Ammonium Compounds (QACs): 2-methacryloxylethyl dodecyl methyl ammonium bromide (MAE-DB), 2-methacryloyloxyethyl trimethylammonium chloride (METAC), dimethylamino-hexadecyl methacrylate (DMAHDM), 1,3,5-triacryloyl hexahydro-1,3,5-triazine (TAT), and methacryloxylethyl cetyl dimethyl ammonium chloride (DMAE-CB).

Resin infiltration for caries management

Evaluation of its use for non-cavitated and cavitated proximal lesions

Resin infiltration (RI) was conceived as a minimally invasive approach to close the gap between passive observation ("wait and watch") and conventional restorative ("drill and fill") techniques for interproximal carious lesions [116]. RIs are low-viscosity resins primarily composed of triethylene glycol dimethacrylate (TEGDMA) that possess excellent penetration into carious enamel and a high degree of conversion (DC) [117] **(Figure 4)**.

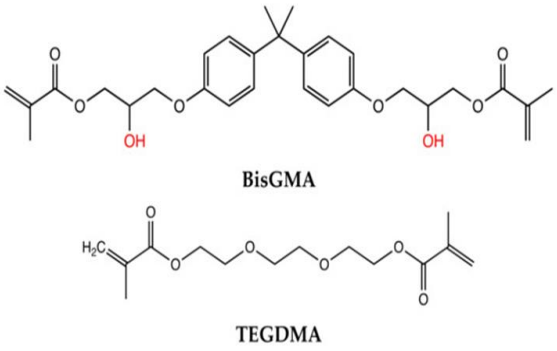


Figure 4. Chemical structures of resin monomers: Bisphenol A-glycidyl methacrylate (BisGMA) and Triethylene glycol dimethacrylate (TEGDMA).

After polymerization, RIs infiltrate demineralized enamel and seal intercrystalline microporosities, generating a polymer scaffold that micromechanically stabilizes the enamel prisms and creates a diffusion barrier against hydrogen ions, thus halting further demineralization and caries progression [117–120] **(Figure 5)**.

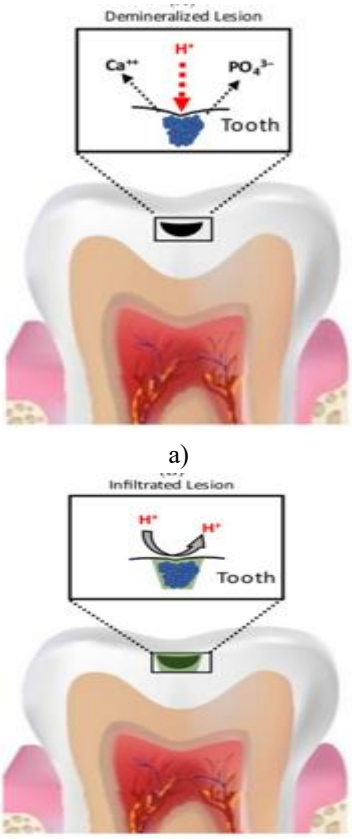


Figure 5. Schematic showing the caries-arresting mechanism of resin infiltration.
(a) Acid-induced enamel demineralization leads to the formation of porosities.
(b) Resin infiltrants penetrate and polymerize within these spaces, forming a solid matrix that blocks ion movement and prevents lesion advancement.

The ability of RIs to prevent lesion progression is governed by their penetration coefficient (PC)—the rate at which a liquid moves through porous material. PC is directly proportional to surface tension and inversely proportional to viscosity and contact angle [121]. While enamel infiltration primarily depends on viscosity, dentinal infiltration may be influenced by both viscosity and hydrophilicity. However, research exploring how hydrophilicity affects resin penetration into dentin remains limited. Efforts to enhance methacrylate resin infiltration have focused on modifying monomer composition and adding solvents.

Compositions rich in TEGDMA—due to their low viscosity—demonstrate superior penetration and enhanced inhibition of caries progression compared with formulations containing high levels of BisGMA [121]. Adding alcohol can reduce viscosity, but it also promotes microgel formation at polymerization sites, limiting free radical mobility and polymer conversion [122, 123]. Reduced polymerization weakens mechanical strength and lessens caries-arresting capability, therefore solvent incorporation is generally discouraged [124].

Meta-analyses evaluating RI's performance in non-cavitated proximal lesions indicate high effectiveness in permanent dentition, particularly when lesions are limited to the enamel and outer third of dentin [125–130]. Over three years, caries progression in infiltrated lesions ranged between 4–14%, compared with 42–48% in control groups [131, 132]. In a seven-year follow-up, Paris *et al*. reported progression rates of 9% for treated lesions versus 45% for controls [133]. Subgroup analysis further revealed that RI was effective in halting enamel lesions, while no significant advantage was observed for dentinal lesions, likely due to differences in tissue structure and disease mechanisms [128].

For primary teeth, earlier meta-analyses found results inconclusive due to variations in methodology and clinical settings [125–127]. However, a 2021 meta-analysis by Chen *et al*. suggested that, despite the need for more research, resin infiltration shows promising outcomes in controlling caries progression over 12–24 months [130]. Across studies, the therapeutic success rate of RI ranged from 21% [134, 135] to 38% [136].

The proven success of resin infiltrants (RIs) in halting non-cavitated proximal carious lesions has prompted researchers to investigate their potential application in cavitated lesions as well. For resin infiltration to be effective in such cases, the RI must be capable of both penetrating the demineralized enamel and filling the cavitated space of the lesion. Investigations evaluating RI performance in deep and micro-cavitated proximal caries (International Caries Detection and Assessment System — ICDAS 3, 4, 5) demonstrated that although the materials can adequately permeate porous enamel at all lesion depths, they are ineffective in fully filling the open cavities in more advanced lesions [137].

This incomplete cavity filling has been linked to three major mechanisms:

1. Porous demineralized enamel exerts strong capillary attraction, allowing RIs to infiltrate easily, while larger cavities exhibit weak capillary forces, reducing resin draw-in;
2. During the cleaning process before polymerization, part of the infiltrant may be washed away from the cavity; and
3. Air entrapment within the lesion generates surface tension, hindering resin penetration.

Consequently, a thin, uneven resin layer forms in deeper lesions (ICDAS 4 & 5) compared with shallower ICDAS 2 & 3 lesions. Since the thickness of the resin layer directly correlates with its caries-arresting ability, the thinner layers in deeper cavities are less effective at preventing demineralization. Moreover, incomplete filling encourages biofilm accumulation, further diminishing RI efficacy in these deeper areas [137].

To enhance the caries-arresting capacity of RIs in deep cavitated lesions, two improvements are proposed:

1. Enhancing cavity-filling potential without compromising penetration ability [138, 139]; and
2. Incorporating antimicrobial functionality to eradicate residual bacteria within partially filled spaces and deter reinfection.

Micro-filled infiltrant resins (MFIR)

Conventional RIs suffer from limited mechanical durability, including low strength, pronounced polymerization shrinkage, and poor wear resistance, mainly due to their low viscosity and insufficient filling capacity. To overcome these drawbacks, micro-filled infiltrant resins (MFIRs) have been engineered by adding inorganic or organic fillers to RIs. The inclusion of fillers has been shown to increase flexural strength, modulus of elasticity, and reduce shrinkage and water absorption [140, 141]. Ideally, an MFIR should retain the infiltration characteristics of traditional RIs while exhibiting filling behavior comparable to flowable composites.

Influence of fillers on RI properties

When fillers are introduced into resin systems, their performance depends on factors such as filler particle size, shape, concentration, and the interaction between

the filler and resin matrix [142]. At low filler concentrations, the particles interact minimally, but as their number increases, particles become densely packed, resulting in stronger inter-particle interactions and higher viscosity [142].

Particle size also plays a crucial role — smaller fillers have larger surface areas, increasing matrix-filler interactions and therefore viscosity. In contrast, larger particles tend to yield heterogeneous mixtures with poor enamel wetting, leading to compromised penetration ability [139, 143].

Determinants of RI mobility in micro-filled infiltrant resins (MFIR)

When MFIR is applied to a carious lesion, two opposing forces influence resin movement:

1. Capillary forces, which draw the resin component into the porous demineralized structure, and
2. Interfacial forces between filler particles and the resin matrix, which resist resin flow.

As the filler surface area increases (inversely proportional to particle size), more resin is required to coat each particle, leaving less free resin available for lesion infiltration [138, 139, 143].

Empirical research assessing MFIRs containing pre-polymerized methacrylate-based fillers (42 μm) in deep lesions (ICDAS 3 & 5) reported no significant difference in penetration depth between RIs and MFIRs. However, MFIRs demonstrated superior filling efficiency (100% in both groups) compared with traditional RIs (25% for ICDAS 3 and 38% for ICDAS 5). MFIRs maintained infiltration comparable to RIs while matching the filling characteristics of flowable composites.

This effect occurs because, during MFIR application, the resin phase infiltrates the porous lesion while the filler particles remain embedded within the surface layer of unpolymerized monomer, which behaves similarly to flowable composite material and fills the cavity [138, 139]. These outcomes indicate that MFIRs represent a promising development for controlling caries progression in deep and cavitated proximal lesions.

Resin infiltrants (RIs) for arresting occlusal carious lesions

Efforts to broaden the clinical use of RIs have led to their evaluation in managing occlusal carious lesions. Nonetheless, because of their limited mechanical strength, RIs alone are not considered adequate for treating occlusal caries [139, 144, 145]. Laboratory research suggests that the best outcomes occur when micro-filled infiltrant resins (MFIRs) or RIs are combined with traditional sealants or flowable composites, which are applied on top of the infiltrated surfaces [139, 145].

Such combinations have demonstrated multiple advantages compared to conventional sealants alone:

1. The diffusion barrier shifts from the enamel's outer surface into the lesion's body, meaning that even if the sealant fails or partially detaches, the infiltrated structure remains sealed, helping to halt lesion advancement.
2. Because RIs possess higher penetration coefficients and employ stronger surface conditioning (15% hydrochloric acid), their ability to infiltrate carious fissures surpasses that of standard sealants [139, 146]. (However, the use of HCl must be carefully controlled in the mouth to prevent soft-tissue injury.)
3. Applying RIs beneath flowable composites has shown to significantly reduce microleakage compared to sealants alone [147].

Hence, the RI–sealant combination may address major limitations of conventional occlusal sealing—such as retention problems, shallow penetration, and microleakage—and represents a minimally invasive treatment option for early fissure caries. Furthermore, incorporating antimicrobial components into RIs may aid in eradicating residual bacteria within deeper cavities and further strengthen their caries-arresting effect.

Clinical evaluations have indicated that dual sealing and infiltration, alongside fluoride varnish, provides substantially greater success in halting carious progression than fluoride varnish alone in primary teeth over 2–3 years [148]. Anauate-Netto *et al.* observed that in permanent teeth, both infiltration and sealing of non-cavitated occlusal lesions were similarly effective across a 3-year period [149]. Conversely, Elkwatehy *et al.* reported that in sound and non-cavitated permanent molars, sealing alone—or sealing combined with infiltration—was more beneficial than using RI by itself [150]. These discrepancies likely stem from differences in lesion depth among studies: the first included mainly deeper lesions (ICDAS 2), while the latter examined sound or incipient lesions (ICDAS 0–2). It appears that RIs offer limited benefit for ICDAS 0–1 fissures, whereas deeper lesions (ICDAS 2) show better infiltration and higher caries-resistance compared with sealants alone.

Limitations of current resin infiltrants

Although RIs provide a conservative and effective therapy, their performance is restricted by certain technical and biological limitations.

Incomplete resin penetration or infiltration

Even though RIs can infiltrate carious tissue efficiently, deep enamel lesions often exhibit uneven or partial resin penetration, leaving unfilled regions [119, 151]. Studies reveal that only around 60% of enamel pore volume becomes sealed in advanced lesions [119, 152], and the resulting microhardness does not match that of healthy enamel [153]. This reduced hardness renders the treated sites more vulnerable to future demineralization [153, 154].

When comparing lesions of different depths, RIs were completely effective (100%) in halting lesions confined to inner enamel, but efficacy dropped to 64% for those reaching outer dentin [131]. In cases where caries extended into dentin, no significant difference in lesion progression was observed between RI-treated and control teeth [128]. The penetration ratio of resin in carious dentin (82%) is lower than in carious enamel (99.1%), which explains the reduced effectiveness of RIs in dentinal tissues [128].

This difference arises from the distinct composition and structure of enamel versus dentin. Enamel, composed mostly of hydroxyapatite, undergoes demineralization by bacterial acids, which enlarge its pores. When RIs are applied, they occlude these pores, creating a diffusion barrier that blocks nutrient flow to bacteria, isolates acids, and helps retain minerals—thus encouraging remineralization once bacteria are deprived of resources [92, 155–157]. This infiltrated layer enhances resistance to demineralization and improves surface hardness, thereby preventing further caries progression [153, 158].

Conversely, dentin contains more water and organic material (≈40%) and features tubular channels that accelerate bacterial invasion. Hence, dentin caries develops faster and involves not only acid-mediated demineralization but also enzymatic degradation of collagen and other organics [88, 89]. These by-products may reduce wettability, and fluid movement through demineralized dentinal tubules can hinder complete drying, making thorough RI infiltration difficult [159]. Finally, while the resin barrier may physically isolate dentinal lesions from external bacteria, its effect on internal bacterial activity remains uncertain and requires further investigation [128].

Surface roughness

Demineralization beneath the enamel surface leads to porosity between enamel prisms, contributing to increased surface roughness. Resin infiltration cannot fully return the lesion's surface texture to that of intact enamel and cannot be polished effectively [160, 161]. Several investigations have reported that the surface roughness of treated enamel remains greater than that of sound enamel, potentially encouraging microbial biofilm buildup [153, 162–164]. When the surface texture of areas treated with adhesives and RIs was analyzed, adhesives showed a smoother, more uniform layer than RIs, attributed to their shallow penetration depth [165]. In an in vitro comparison of fluoride varnish, nano-hydroxyapatite paste, and resin infiltration regarding S. mutans attachment to artificial enamel defects, resin infiltration resulted in the highest bacterial adhesion among the three groups [166].

Polymerization shrinkage and microleakage

Because RIs mainly contain the low–molecular weight monomer TEGDMA, they are prone to substantial polymerization contraction and stress formation during curing. These properties cause microleakage, which can compromise their ability to arrest caries and make the restoration more vulnerable to secondary lesions [138].

Cytotoxicity of leached monomers

It is well known that unreacted monomers continue to leach from restorative surfaces both during and after photopolymerization [167]. Samuelsen *et al*. found that 24-hour exposure to even very low TEGDMA levels (0.5 mM) induced cell death [168]. Similarly, Batarseh *et al*. observed that exposing human pulp fibroblasts to 0.25 mM TEGDMA markedly elevated pro-apoptotic proteins such as Cytochrome c, Caspase 3, and Bim within 24 hours [169]. Although significant TEGDMA release from RIs occurs toward the oral cavity, this leaching happens only during the initial minutes, making 24-hour exposure unlikely [170]. Currently, resin infiltration is restricted to lesions within enamel and the outer third of dentin, reducing the chance of pulp-side diffusion. However, application to deeper lesions (ICDAS 5) may allow inward monomer migration, posing potential pulpal risks. Subtoxic concentrations of TEGDMA (0.3 mM) have been found to suppress mineralization-related gene expression by 5–20% after 4 hours and up to 50% after 12 hours. Consequently, TEGDMA could hinder pulp mineralization and impede reparative dentin formation [171]. Thus, careful use is advised in deeper dentinal restorations.

Degradation of methacrylate resins

Beyond the diffusion of residual monomers, methacrylate-based resins are vulnerable to water absorption, leading to monomer hydrolysis and ester bond cleavage [172]. In an in vitro study, Arslan *et al*. evaluated RI, dental adhesives, and fissure sealants subjected to 10,000 thermocycling rounds

(approximately one year of aging). Results showed that RIs exhibited greater water sorption than the other materials [173], likely due to their higher TEGDMA content, potentially reducing long-term stability in the oral cavity. Moreover, thermal stress can induce microcracks in infiltrated lesions [174], which then serve as entry points for salivary and bacterial enzymes that accelerate TEGDMA degradation [175, 176]. The breakdown product of BisGMA (a typical adhesive monomer) is bisHPPP, while that of TEGDMA (a major RI component) is triethylene glycol (TEG) [177]. BisHPPP slightly suppresses S. mutans proliferation yet heightens its virulence by upregulating genes for attachment and acid resistance [178]. Conversely, TEG promotes S. mutans growth and pathogenicity [179, 180] and enhances esterase production [181]. These enzymes further deteriorate resin surfaces [175, 176], roughening them and encouraging more bacterial buildup [182]. This forms a self-perpetuating cycle of biofilm growth and resin breakdown, potentially leading to recurrent caries.

To counteract these effects and enhance the surface properties of resin-infiltrated enamel, Rai *et al*. applied chlorhexidine (CHX) varnish over RI-treated lesions. Over a 9-month period, combined RI+CHX treatment showed superior caries inhibition for deeper lesions (ICDAS 3) compared with RI alone, whereas no advantage was observed in ICDAS 2 lesions [183]. Meyer-Lueckel *et al*. linked shallow resin penetration with more homogeneous surface layers [132], possibly explaining CHX's benefit only in deeper lesions requiring greater infiltration depth. Further long-term studies are needed to evaluate effects on degradation and leakage. Nevertheless, findings suggest that adding antimicrobial functionality can enhance the performance of RIs in deeper carious sites. Incorporating antimicrobial agents directly into RI formulations could help eradicate bacteria within lesions and raise local antibacterial concentration, limiting colonization on adjacent tooth surfaces. However, such protective effects depend on antimicrobial release kinetics and their diffusion or dilution by saliva.

Enhancing the antimicrobial and anti-degradative performance of resin infiltrants (RI)

Considering the tendency of partially infiltrated advanced lesions to undergo renewed cariogenic attack, the limited capacity of RI to halt dentinal caries, the higher surface roughness of treated enamel, shrinkage-induced microleakage during polymerization, and the gradual degradation of TEGDMA, improving the antibacterial and anti-degradative characteristics of these materials could be an effective strategy. Such improvements may strengthen their ability to arrest caries in deeper regions and extend their service life by minimizing material breakdown within the oral cavity.

Commercially marketed RIs, such as Icon®, primarily utilize TEGDMA as the base monomer. This component is hydrophilic and prone to water uptake and dissolution in saliva, resulting in hydrolytic deterioration that weakens the resin's mechanical integrity and long-term clinical stability [172]. Since the polymer's performance is largely governed by monomer chemistry, several studies have explored modifying RI formulations using alternative monomer mixtures to enhance their strength and antibacterial capability [123, 184–187].

Inagaki *et al*. investigated experimental RIs created by adding hydrophobic monomers—bisphenol A ethoxylate dimethacrylate (BisEMA) and urethane dimethacrylate (UDMA)—to TEGDMA, incorporating different concentrations of chlorhexidine (CHX 0.1% and 0.2%). The resulting materials were compared with Icon® for mechanical, degradative, and antibacterial properties [184, 185] **(Figure 6)**. Degree of conversion (DC) and microhardness (Knoop hardness number, KHN) were measured to evaluate mechanical strength. Incorporating BisEMA and UDMA raised both DC and KHN relative to Icon®, with TEGDMA/UDMA mixtures showing the greatest KHN values. Additionally, CHX addition had no measurable effect on DC or hardness at either concentration [185]. Water sorption in TEGDMA/BisEMA systems was comparable to Icon®, while TEGDMA/UDMA formulations absorbed more water than Icon® [184]. All resin blends demonstrated lower solubility than Icon® [184], and the penetration uniformity (70–100%) was similar to that of Icon® (100%) [123].

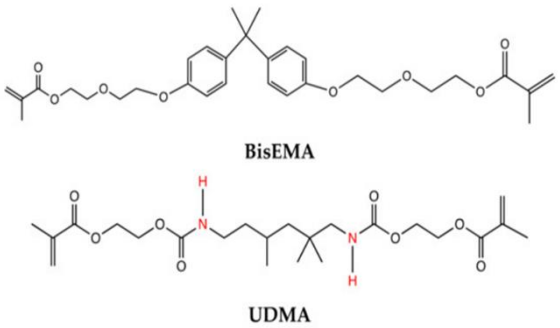


Figure 6. Chemical structures of Bisphenol A ethoxylate dimethacrylate (BisEMA) and Urethane dimethacrylate (UDMA).

Overall, these findings indicate that introducing BisEMA and UDMA to TEGDMA can enhance certain mechanical features without impairing penetration, suggesting that further chemical alterations may help optimize the mechanical stability and biocompatibility of RIs.

In the same studies, CHX supplementation significantly increased the immediate antibacterial effect of all resin variants against S. mutans, whereas Icon® showed none. However, the release pattern and duration of CHX diffusion were not analyzed. Earlier research indicates that releasing systems usually cause a brief burst release [187], while prolonged antimicrobial activity requires slow, sustained discharge. Consequently, long-term trials are needed to confirm the durability of these effects. Even so, the immediate antimicrobial effect of RI application could still help eliminate or deactivate cariogenic microbes trapped beneath the resin. Yet, continued leaching of antimicrobial agents could generate porosities over time, compromising the resin's structural strength [108].

In addition to releasing mechanisms, "contact-active" antimicrobial strategies have been evaluated. Marchi *et al*. worked on improving the mechanical and antibacterial behavior of a TEGDMA/BisEMA-based RI (diluted with HEMA) through incorporation of iodonium salt and chitosan [186] **(Figure 7)**. Onium salts were selected to enhance polymer properties since these ionic, water-soluble compounds promote polymerization of hydrophilic monomers, increasing C=C bond conversion. This results in a denser, cross-linked polymer matrix that resists water sorption and expansion, leading to superior resistance to hydrolytic degradation—even in hydrophilic monomer systems such as TEGDMA [188]. Chitosan, a natural polysaccharide, was introduced for its antibacterial action and ability to suppress demineralization [189]. However, in this experiment, ionic salt addition did not improve DC, likely due to the rapid polymerization rate [186]. A low DC can weaken the long-term mechanical performance of the RI, warranting further investigation.

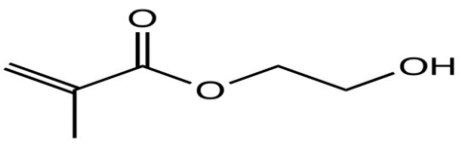
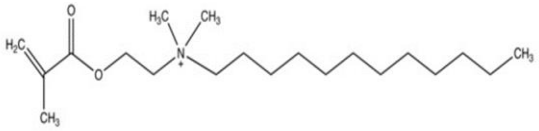


Figure 7. Chemical structure of Hydroxyethyl methacrylate (HEMA).

Yu *et al*. incorporated dimethylaminododecyl methacrylate (DMADDM), a quaternary ammonium monomer (QAM), into RI formulations by copolymerizing it, forming covalent bonds that immobilize the compound within the resin [190] **(Figure 8)**. QAMs are known for bactericidal activity and reduced bacterial adhesion, and because they are fixed within the polymer matrix, their antimicrobial potential should not diminish over time. Nevertheless, their action depends on direct contact with bacterial cell surfaces, and their effect on microorganisms embedded in mature biofilms remains uncertain [187]. Moreover, QAMs tend to exhibit bacteriostatic rather than bactericidal strength, generally weaker than releasing agents. Their surface activity also decreases once an organic pellicle from salivary proteins coats the resin [108]. In this work, QAM incorporation preserved but did not enhance the resin's mechanical characteristics, leaving it prone to water absorption and degradation. Since the QAM is covalently bonded to the polymer backbone, ongoing resin degradation may cause its eventual release into the mouth, potentially reducing antibacterial activity over time and posing cytotoxicity concerns.



DMADDM

Figure 8. Molecular configuration of the quaternary ammonium compound Dimethylaminododecyl methacrylate (DMADDM), n = 11.

Researchers have experimented with incorporating filler components to enhance both mechanical durability and antibacterial efficiency of RIs [159, 191]. Metallic nanoparticles (NPs) are particularly valued for their innate antimicrobial traits [191, 192]. Studies have verified that Zinc Oxide (ZnO) [193] and silver (Ag) [194, 195] NPs inhibit Streptococcus mutans and Lactobacillus. Consequently, ZnO and AgNPs have been integrated into RIs to strengthen their antimicrobial capacity. Kielbassa *et al*. explored how adding fillers influenced infiltration performance, using AgNP-modified RIs. A tunnel method enabled conservative cavity preparation, followed by internal restoration with flowable composite and RI, while the surface was treated with either RI or modified RI. Their findings revealed that lesions were only partially infiltrated in all cases, and AgNP addition did not alter penetration ability [159]. Similarly, Angel Villegas *et al*. observed that ZnO NPs in RIs allowed zinc to diffuse up to 1020 µm below the surface, a penetration

absent when phosphate buffer was used as a vehicle [191]. These findings suggest that fillers can augment antimicrobial effects of RIs without reducing infiltration performance.

Chemomechanical management of caries

Chemomechanical caries removal involves sodium hypochlorite–based Carisolv and papain-derived products like Papacarie and Brix 3000, which selectively remove infected dentin in both deciduous and permanent teeth [196, 197]. Healthy dentin contains alpha-1-antitrypsin that prevents collagen degradation; infected dentin lacks this inhibitor, allowing proteolytic enzymes in these agents to digest denatured collagen and facilitate selective cleaning [198]. A systematic review comparing Papacarie to conventional excavation in primary teeth confirmed Papacarie's effectiveness in carious tissue removal and reduced discomfort, though the process was slower [199]. An in vitro comparison of Papacarie, Brix 3000, and standard excavation also supported these results: all methods removed infected dentin effectively, but conventional excavation was faster (54 s) compared to Papacarie (110.5 s) and Brix 3000 (85 s) [198], albeit with higher pain reports.

Atraumatic restorative treatment (ART)

Atraumatic Restorative Treatment was designed as a resource-friendly method for managing caries in regions with limited dental care access [200]. It entails removing decayed tissue manually—without anesthesia—and restoring cavities with fluoride-releasing materials like glass ionomer cement (GIC) or resin-modified GIC (RMGI) [201]. Fluoride from GIC helps form acid-resistant fluorapatite, decreasing future decay risk [202, 203]. GIC also acts as a rechargeable fluoride source through topical uptake [204, 205]. More recently, the addition of silver diamine fluoride (SDF) has been proposed to further strengthen ART outcomes [206]. The primary drawbacks of ART include marginal imperfections, wear susceptibility, and restoration loss [207, 208].

Meta-analyses report that, for primary posterior teeth, ART survival after two years reached 94.3% (±1.5) for single-surface and 65.4% (±3.9) for multi-surface restorations. For permanent molars, survival rates were 87.1% (±3.2) and 77% (±9.0) for single and multiple surfaces over 3- and 5-year periods, respectively [209]. In Early Childhood Caries (ECC) management, ART's non-invasive nature eliminates the need for general anesthesia, enabling early intervention. Silva *et al*. reported ART success rates of 94%, 87.5%, and 82.9% over 1-, 2-, and 4-year follow-ups in children aged 18–36 months. Faccin *et al*. noted a 72% success rate over 25–48 months in preschoolers (mean age 31 months) [210]. These outcomes affirm ART as a reliable, child-friendly treatment with strong long-term effectiveness. Efforts to boost ART's antibacterial action include adding chlorhexidine (CHX) to GIC to reduce residual microorganisms post-excavation. Laboratory findings showed significant declines in S. mutans and Lactobacillus counts over three months when CHX was incorporated [211]. However, clinical data indicated that while antibacterial performance improved, CHX led to more marginal defects and restoration failures at 9 months [212]. Continued investigation is necessary to optimize ART's antimicrobial benefits without compromising strength.

Conclusion

A range of minimally invasive caries control techniques can effectively stop or reverse early lesion progression. These interventions perform best for non-cavitated, incipient lesions. Once decay extends into dentin, the altered structure and bacterial penetration make current methods less effective, as deep lesions are harder to disinfect or remineralize. The persistence of microorganisms in inner dentin layers adds further challenges without surgical aid. Enhancing the antimicrobial properties of these approaches can therefore improve clinical results.

Over time, materials used in minimally invasive procedures degrade through hydrolytic and enzymatic reactions in the oral cavity, reducing strength and promoting bacterial leakage, biofilm formation, and recurrent decay—ultimately leading to restoration failure. Reinforcing the biostability of these materials may lengthen their service life and delay surgical needs. Future developments should prioritize improving both antimicrobial and anti-degradative characteristics to enhance durability and broaden the applications of these conservative treatment options.

Acknowledgments: None

Conflict of Interest: None

Financial Support: None

Ethics Statement: None

References

1. Banerjee A, Frencken JE, Schwendicke F, Innes NPT. Contemporary operative caries management: consensus recommendations on

minimally invasive caries removal. Br Dent J. 2017;223(3):215–22.
2. Going RE, Loesche WJ, Grainger DA, Syed SA. The viability of microorganisms in carious lesions five years after covering with a fissure sealant. J Am Dent Assoc. 1978;97(3):455–62.
3. Banerjee A, Yasseri M, Munson M. A method for the detection and quantification of bacteria in human carious dentine using fluorescent in situ hybridisation. J Dent. 2002;30(7–8):359–63.
4. Paddick JS, Brailsford SR, Kidd EAM, Beighton D. Phenotypic and genotypic selection of microbiota surviving under dental restorations. Appl Environ Microbiol. 2005;71(5):2467–72.
5. Ogawa K, Yamashita Y, Ichijo T, Fusayama T. The ultrastructure and hardness of the transparent of human carious dentin. J Dent Res. 1983;62(1):7–10.
6. Kreulen CM, De Soet JJ, Weerheijm KL, Van Amerongen WE. In vivo cariostatic effect of resin modified glass ionomer cement and amalgam on dentine. Caries Res. 1997;31(5):384–9.
7. Ngo HC, Mount G, McIntyre J, Tuisuva J, Von Doussa R. Chemical exchange between glass-ionomer restorations and residual carious dentine in permanent molars: an in vivo study. J Dent. 2006;34(8):608–13.
8. Li T, Zhai X, Song F, Zhu H. Selective versus non-selective removal for dental caries: a systematic review and meta-analysis. Acta Odontol Scand. 2018;76(2):135–40.
9. Ali A, Koller G, Foschi F, Andiappan M, Bruce K, Banerjee A, et al. Self-limiting versus conventional caries removal: a randomized clinical trial. J Dent Res. 2018;97(11):1207–13.
10. Qvist V. Longevity of restorations: the "death spiral." 2008 [Internet]. Available from: https://scholar.google.com/scholar_lookup?title=Longevity%20of%20restorations%3A%20the%20death%20spiral&publication_year=2008&author=V.%20Qvist. Accessed 8 Feb 2021.
11. Pitts NB. Are we ready to move from operative to non-operative/preventive treatment of dental caries in clinical practice? Caries Res. 2004;38(3):294–304.
12. Splieth C, Kanzow P, Wiegand A, Schmoeckel J, Jablonski-Momeni A. How to intervene in the caries process: proximal caries in adolescents and adults—a systematic review and meta-analysis. Clin Oral Investig. 2020;24(5):1623–36.
13. Elamin F, Abdelazeem N, Salah I, Mirghani Y, Wong F. A randomized clinical trial comparing Hall vs conventional technique in placing preformed metal crowns from Sudan. PLoS One. 2019;14(6):e0217740.
14. Giacaman RA, Muñoz-Sandoval C, Neuhaus KW, Fontana M, Chałas R. Evidence-based strategies for the minimally invasive treatment of carious lesions: review of the literature. Adv Clin Exp Med. 2018;27(7):1009–16.
15. Frencken JE. Atraumatic restorative treatment and minimal intervention dentistry. Br Dent J. 2017;223(3):183–9.
16. Antonioni MB, Fontana M, Salzmann LB, Inglehart MR. Pediatric dentists' silver diamine fluoride education, knowledge, attitudes, and professional behavior: a national survey. J Dent Educ. 2019;83(2):173–82.
17. Simpson S, Waterhouse PJ. Hall technique: is it superior in success and savings to conventional restorations? Evid Based Dent. 2020;21(4):128–9.
18. Jorge R, Ammari M, Soviero V, Souza I. Randomized controlled clinical trial of resin infiltration in primary molars: 2 years follow-up. J Dent. 2019;90(1):103184.
19. Garcia RI, Gregorich SE, Ramos-Gomez F, Braun PA, Wilson A, Albino J, et al. Absence of fluoride varnish–related adverse events in caries prevention trials in young children, United States. Prev Chronic Dis. 2017;14(1):E17.
20. Oliveira B, Salazar M, Carvalho D, Falcão A, Campos K, Nadanovsky P. Biannual fluoride varnish applications and caries incidence in preschoolers: a 24-month follow-up randomized placebo-controlled clinical trial. Caries Res. 2014;48(3):228–36.
21. Rozier RG, Sutton BK, Bawden JW, Haupt K, Slade GD, King RS. Prevention of early childhood caries in North Carolina medical practices: implications for research and practice. J Dent Educ. 2003;67(8):876–85.
22. Sousa FSDOD, dos Santos APP, Nadanovsky P, Hujoel P, Cunha-Cruz J, de Oliveira BH. Fluoride varnish and dental caries in preschoolers: a systematic review and meta-analysis. Caries Res. 2019;53(5):502–13.
23. Li F, Jiang P, Yu F, Li C, Wu S, Zou J, et al. Comparison between fissure sealant and fluoride varnish on caries prevention for first permanent molars: a systematic review and meta-analysis. Sci Rep. 2020;10(1):2578.
24. Chestnutt IG, Hutchings S, Playle R, Morgan-Trimmer S, Fitzsimmons D, Aawar N, et al. Seal or varnish? A randomised controlled trial to determine the relative cost and effectiveness of pit and fissure sealant and fluoride varnish in

preventing dental decay. Health Technol Assess. 2017;21(40):1–256.
25. Urquhart O, Tampi M, Pilcher L, Slayton R, Araujo M, Fontana M, et al. Nonrestorative treatments for caries: systematic review and network meta-analysis. J Dent Res. 2019;98(1):14–26.
26. Nelson T, Scott J, Crystal YO, Berg JH, Milgrom P. Silver diamine fluoride in pediatric dentistry training programs: survey of graduate program directors. Pediatr Dent. 2016;38(3):212–7.
27. Slayton RL, Urquhart O, Araujo MW, Fontana M, Guzmán-Armstrong S, Nascimento MM, et al. Evidence-based clinical practice guideline on nonrestorative treatments for carious lesions. J Am Dent Assoc. 2018;149(10):837–49.
28. Mauro S, Robles EG, Cinque C, Squassi AF, Bordoni NE. Eficiencia de tres fluoruros concentrados para la estabilización de caries de esmalte. Bol Asoc Argent Odontol Niños. 2004;33(1):4–11.
29. Lo E, Chu C, Lin H. A community-based caries control program for pre-school children using topical fluorides: 18-month results. J Dent Res. 2001;80(12):2071–4.
30. Bijella MFTB, Bijella VT, da Silva MSMB, Lopes ES. Avaliação clínica da aplicação de diamino-fluoreto de prata a 12. Rev Paul Odontol. 1991;13:28–35.
31. Nishino M, Yoshida S, Sobue S, Kato J, Nishida M. Effect of topically applied ammoniacal silver fluoride on dental caries in children. J Osaka Univ Dent Sch. 1969;9:149–55.
32. Hu S, Meyer B, Duggal M. A silver renaissance in dentistry. Eur Arch Paediatr Dent. 2018;19(4):221–7.
33. Llodra JC, Rodriguez A, Ferrer B, Menardia V, Ramos T, Morato M. Efficacy of silver diamine fluoride for caries reduction in primary teeth and first permanent molars of schoolchildren: 36-month clinical trial. J Dent Res. 2005;84(8):721–4.
34. American Academy of Pediatric Dentistry. Policy on the use of silver diamine fluoride for pediatric dental patients. Pediatr Dent. 2018;40(6):51–4.
35. Crystal YO, Niederman R. Silver diamine fluoride treatment considerations in children's caries management. Int J Clin Pediatr Dent. 2016;38(5):466–71.
36. Chu CH, Lo EC, Lin HC. Effectiveness of silver diamine fluoride and sodium fluoride varnish in arresting dentin caries in Chinese pre-school children. J Dent Res. 2002;81(11):767–70.
37. Yu OY, Zhao IS, Mei ML, Lo EC, Chu CH. Caries-arresting effects of silver diamine fluoride and sodium fluoride on dentine caries lesions. J Dent. 2018;78:65–71.
38. Liu BY, Lo EC, Li CM. Effect of silver and fluoride ions on enamel demineralization: a quantitative study using micro-computed tomography. Aust Dent J. 2012;57(1):65–70.
39. Chu CH, Lo EC. Microhardness of dentine in primary teeth after topical fluoride applications. J Dent. 2008;36(5):387–91.
40. Mei ML, Ito L, Cao Y, Li Q, Lo EC, Chu CH. Inhibitory effect of silver diamine fluoride on dentine demineralisation and collagen degradation. J Dent. 2013;41(9):809–17.
41. Mei ML, Li Q, Chu CH, Yiu CK, Lo EC. The inhibitory effects of silver diamine fluoride at different concentrations on matrix metalloproteinases. Dent Mater. 2012;28(8):903–8.
42. Mei ML, Ito L, Cao Y, Li Q, Chu CH, Lo EC. The inhibitory effects of silver diamine fluorides on cysteine cathepsins. J Dent. 2014;42(3):329–35.
43. Mei ML, Chu CH, Lo ECM, Samaranayake LP. Fluoride and silver concentrations of silver diammine fluoride solutions for dental use. Int J Paediatr Dent. 2013;23(4):279–85.
44. Mei ML, Ito L, Cao Y, Lo EC, Li Q, Chu CH. An ex vivo study of arrested primary teeth caries with silver diamine fluoride therapy. J Dent. 2014;42(4):395–402.
45. Mei ML, Li QL, Chu CH, Lo EM, Samaranayake LP. Antibacterial effects of silver diamine fluoride on multi-species cariogenic biofilm on caries. Ann Clin Microbiol Antimicrob. 2013;12(1):4–7.
46. Mei ML, Chu CH, Low KH, Che CM, Lo EC. Caries arresting effect of silver diamine fluoride on dentine carious lesion with S. mutans and L. acidophilus dual-species cariogenic biofilm. Med Oral Patol Oral Cir Bucal. 2013;18(5):e824–31.
47. Chibinski AC, Wambier LM, Feltrin J, Loguercio AD, Wambier DS, Reis A. Silver diamine fluoride has efficacy in controlling caries progression in primary teeth: A systematic review and meta-analysis. Caries Res. 2017;51(5):527–41.
48. Fung MHT, Duangthip D, Wong MCM, Lo ECM, Chu CH. Arresting dentine caries with different concentration and periodicity of silver diamine fluoride. JDR Clin Transl Res. 2016;1(2):143–52.
49. Fung MHT, Duangthip D, Wong MCM, Lo ECM, Chu CH. Randomized clinical trial of 12% and 38% silver diamine fluoride treatment. J Dent Res. 2018;97(2):171–8.

50. Duangthip D, Chu CH, Lo ECM. A randomized clinical trial on arresting dentine caries in preschool children by topical fluorides—18 month results. J Dent. 2016;44(1):57–63.
51. Duangthip D, Wong MCM, Chu CH, Lo ECM. Caries arrest by topical fluorides in preschool children: 30-month results. J Dent. 2018;70(1):74–9.
52. Zhi QH, Lo ECM, Lin HC. Randomized clinical trial on effectiveness of silver diamine fluoride and glass ionomer in arresting dentine caries in preschool children. J Dent. 2012;40(11):962–7.
53. Mabangkhru S, Duangthip D, Chu CH, Phonghanyudh A, Jirarattanasopha V. A randomized clinical trial to arrest dentin caries in young children using silver diamine fluoride. J Dent. 2020;99(1):103375.
54. Horst JA, Heima M. Prevention of dental caries by silver diamine fluoride. Compend Contin Educ Dent. 2019;40(3):158–63.
55. Oliveira BH, Rajendra A, Veitz-Keenan A, Niederman R. The effect of silver diamine fluoride in preventing caries in the primary dentition: A systematic review and meta-analysis. Caries Res. 2019;53(1):24–32.
56. Crystal YO, Niederman R. Evidence-based dentistry update on silver diamine fluoride. Dent Clin North Am. 2019;63(1):45–6.
57. dos Santos VE, de Vasconcelos FMN, Ribeiro AG, Rosenblatt A. Paradigm shift in the effective treatment of caries in schoolchildren at risk. Int Dent J. 2012;62(1):47–51.
58. Braga MM, Mendes FM, De Benedetto MS, Imparato JCP. Effect of silver diammine fluoride on incipient caries lesions in erupting permanent first molars: a pilot study. J Dent Child (Chic). 2009;76(1):28–33.
59. Rosenblatt A, Stamford TCM, Niederman R. Silver diamine fluoride: a caries "silver-fluoride bullet". J Dent Res. 2009;88(2):116–25.
60. Liu BY, Lo ECM, Chu CH, Lin HC. Randomized trial on fluorides and sealants for fissure caries prevention. J Dent Res. 2012;91(7):753–8.
61. Monse B, Heinrich-Weltzien R, Mulder J, Holmgren C, van Palenstein Helderman WH. Caries preventive efficacy of silver diammine fluoride (SDF) and ART sealants in a school-based daily fluoride toothbrushing program in the Philippines. BMC Oral Health. 2012;12(1):52.
62. Hendre AD, Taylor GW, Chávez EM, Hyde S. A systematic review of silver diamine fluoride: effectiveness and application in older adults. Gerodontology. 2017;34(4):411–9.
63. Raskin SE, Tranby EP, Ludwig S, Okunev I, Frantsve-Hawley J, Boynes S. Survival of silver diamine fluoride among patients treated in community dental clinics: a naturalistic study. BMC Oral Health. 2021;21(1):35.
64. Chhokar SK, Laughter L, Rowe DJ. Perceptions of registered dental hygienists in alternative practice regarding silver diamine fluoride. J Dent Hyg. 2017;91(1):53–60.
65. Crystal YO, Janal MN, Hamilton DS, Niederman R. Parental perceptions and acceptance of silver diamine fluoride staining. J Am Dent Assoc. 2017;148(7):510–8.
66. Hu S, Meyer B, Lai BWP, Chay PL, Tong HJ. Parental acceptance of silver diammine fluoride in children with autism spectrum disorder. Int J Paediatr Dent. 2020;30(5):514–22.
67. Alshammari AF, Almuqrin AA, Aldakhil AM, Alshammari BH, Lopez JNJ. Parental perceptions and acceptance of silver diamine fluoride treatment in Kingdom of Saudi Arabia. Int J Health Sci. 2019;13(1):25–9.
68. Clemens J, Gold J, Chaffin J. Effect and acceptance of silver diamine fluoride treatment on dental caries in primary teeth. J Public Health Dent. 2018;78(1):63–8.
69. Cernigliaro D, Kumar A, Northridge ME, Wu Y, Troxel AB, Cunha-Cruz J, et al. Caregiver satisfaction with interim silver diamine fluoride applications for their children with caries prior to operating room treatment or sedation. J Public Health Dent. 2019;79(4):286–91.
70. Bagher SM, Sabbagh HJ, AlJohani SM, Alharbi G, Aldajani M, Elkhodary H. Parental acceptance of the utilization of silver diamine fluoride on their child's primary and permanent teeth. Patient Prefer Adherence. 2019;13(1):829–35.
71. Huebner CE, Milgrom P, Cunha-Cruz J, Scott J, Spiekerman C, Ludwig S, et al. Parents' satisfaction with silver diamine fluoride treatment of carious lesions in children. J Dent Child (Chic). 2020;87(1):4–11.
72. Kyoon-Achan G, Schroth R, Martin H, Bertone M, Mittermuller B, Sihra R, et al. Parents' views on silver diamine fluoride to manage early childhood caries. JDR Clin Transl Res. 2021;6(3):251–7.
73. Kyoon-Achan G, Schroth RJ, DeMaré D, Sturym M, Edwards J, Lavoie JG, et al. Indigenous community members' views on silver diamine fluoride to manage early childhood caries. J Public Health Dent. 2020;80(3):208–16.
74. Wright JT, Tampi MP, Graham L, Estrich C, Crall JJ, Fontana M, et al. Sealants for preventing and

arresting pit-and-fissure occlusal caries in primary and permanent molars. J Am Dent Assoc. 2016;147(8):631–45.
75. Ahovuo-Saloranta A, Forss H, Walsh T, Nordblad A, Makela M, Worthington HV. Pit and fissure sealants for preventing dental decay in permanent teeth. Cochrane Database Syst Rev. 2017;7(1):CD001830.
76. Wendt LK, Koch G. Fissure sealant in permanent first molars after 10 years. Swed Dent J. 1988;12(5):181–5.
77. Kühnisch J, Bedir A, Lo YF, Kessler A, Lang T, Mansmann U, et al. Meta-analysis of the longevity of commonly used pit and fissure sealant materials. Dent Mater. 2020;36(5):e158–68.
78. Jodkowska E. Efficacy of pit and fissure sealing: Long-term clinical observations. Quintessence Int. 2008;39(7):593–602.
79. Crall JJ, Donly KJ. Dental sealants guidelines development: 2002–2014. Pediatr Dent. 2015;37(2):111–5.
80. Splieth CH, Ekstrand K, Alkilzy M, Clarkson J, Meyer-Lueckel H, Martignon S, et al. Sealants in dentistry: Outcomes of the ORCA Saturday Afternoon Symposium 2007. Caries Res. 2010;44(1):3–13.
81. Handelman S, Washburn F, Wopperer P. Two-year report of sealant effect on bacteria in dental caries. J Am Dent Assoc. 1976;93(5):967–70.
82. Oong EM, Griffin SO, Kohn WG, Gooch BF, Caufield PW. The effect of dental sealants on bacteria levels in caries lesions. J Am Dent Assoc. 2008;139(3):271–8.
83. Orhan AI, Oz FT, Ozcelik B, Orhan K. A clinical and microbiological comparative study of deep carious lesion treatment in deciduous and young permanent molars. Clin Oral Investig. 2008;12(4):369–78.
84. Fontana M, Innes N. Sealing carious tissue using resin and glass-ionomer cements. Monogr Oral Sci. 2018;27(1):103–12.
85. Bakhshandeh A, Qvist V, Ekstrand K. Sealing occlusal caries lesions in adults referred for restorative treatment: 2–3 years of follow-up. Clin Oral Investig. 2012;16(2):521–9.
86. Qvist V, Borum M, Møller K, Andersen T, Blanche P, Bakhshandeh A. Sealing occlusal dentin caries in permanent molars. JDR Clin Transl Res. 2017;2(1):73–86.
87. Borges BCD, Borges JDS, Braz R, Montes MAJR, Pinheiro IVDA. Arrest of non-cavitated dentinal occlusal caries by sealing pits and fissures: a 36-month, randomised controlled clinical trial. Int Dent J. 2012;62(5):251–5.
88. Fusayama T, Kurosaki N. Structure and removal of carious dentin. Int Dent J. 1972;22(3):401–11.
89. Pugach M, Strother J, Darling CL, Fried D, Gansky SA, Marshall SJ, et al. Dentin caries zones: Mineral, structure, and properties. J Dent Res. 2009;88(1):71–6.
90. Griffin SO, Oong E, Kohn W, Vidakovic B, Gooch BF; CDC Dental Sealant Systematic Review Work Group. The effectiveness of sealants in managing caries lesions. Centre for Reviews and Dissemination: York, UK. 2008. Available from: https://www.ncbi.nlm.nih.gov/books/NBK76511/ (accessed 2021 Jan 13).
91. Mertz-Fairhurst EJ, Curtis JW, Ergle JW, Rueggeberg FA, Adair SM. Ultraconservative and cariostatic sealed restorations: results at year 10. J Am Dent Assoc. 1998;129(1):55–66.
92. Kielbassa AM, Ulrich I, Schmidl R, Schüller C, Frank W, Werth VD. Resin infiltration of deproteinised natural occlusal subsurface lesions improves initial quality of fissure sealing. Int J Oral Sci. 2017;9(3):117–24.
93. Hevinga M, Opdam N, Frencken J, Bronkhorst E, Truin G. Can caries fissures be sealed as adequately as sound fissures? J Dent Res. 2008;87(5):495–8.
94. Hevinga M, Opdam N, Frencken J, Bronkhorst E, Truin G. Microleakage and sealant penetration in contaminated carious fissures. J Dent. 2007;35(11):909–14.
95. Strassler HE. Bonding to sound vs caries-affected dentin using photo- and dual-cure adhesives. Inside Dentistry. 2006. Available from: https://www.aegisdentalnetwork.com/id/2006/05/bonding-to-sound-vs-caries-affected-dentin-using-photo-and-dual-cure-adhesives (accessed 2021 Jan 25).
96. Fejerskov O, Nyvad B, Kidd E. Dental Caries: The Disease and Its Clinical Management. 3rd ed. Hoboken (NJ): Wiley; 2015. Available from: https://www.wiley.com/en-ca/Dental+Caries%3A+The+Disease+and+its+Clinical+Management%2C+3rd+Edition-p-9781118935828 (accessed 2021 Jan 25).
97. Simonsen RJ, Neal RC. A review of the clinical application and performance of pit and fissure sealants. Aust Dent J. 2011;56(1):45–58.
98. Li F, Li F, Wu D, Ma S, Gao J, Li Y, et al. The effect of an antibacterial monomer on the antibacterial activity and mechanical properties of

a pit-and-fissure sealant. J Am Dent Assoc. 2011;142(2):184–93.
99. Beyth N, Domb AJ, Weiss EI. An in vitro quantitative antibacterial analysis of amalgam and composite resins. J Dent. 2007;35(3):201–6.
100. Wiegand A, Buchalla W, Attin T. Review on fluoride-releasing restorative materials—Fluoride release and uptake characteristics, antibacterial activity and influence on caries formation. Dent Mater. 2007;23(3):343–62.
101. Heifetz SB, Yaari A, Proskin H. Anticaries effectiveness of a fluoride and nonfluoride sealant. J Calif Dent Assoc. 2007;35(8):573–7.
102. Lygidakis NA, Oulis KI. A comparison of Fluroshield with Delton fissure sealant: four-year results. Pediatr Dent. 2000;21(6):429–31.
103. Williams B, Laxton L, Holt RD, Winter GB. Fissure sealants: a four-year clinical trial comparing an experimental glass polyalkenoate cement with a bis-glycidyl methacrylate resin used as fissure sealants. Br Dent J. 1996;180(3):104–8.
104. Jensen OE, Billings RJ, Featherstone JD. Clinical evaluation of Fluroshield pit and fissure sealant. Clin Prev Dent. 1990;12(2):24–7.
105. Yildiz E, Dorter C, Efes B, Koray F. A comparative study of two fissure sealants: A two-year clinical follow-up. J Oral Rehabil. 2004;31(10):979–84.
106. Koch MJ, García-Godoy F, Mayer T, Staehle HJ. Clinical evaluation of Helioseal F fissure sealant. Clin Oral Investig. 1998;1(4):199–202.
107. Fluoride-releasing sealants. J Am Dent Assoc. 1985;110(1):90.
108. Imazato S. Antibacterial properties of resin composites and dentin bonding systems. Dent Mater. 2003;19(6):449–57.
109. Memarpour M, Shafiei F. The effect of antibacterial agents on fissure sealant microleakage: a six-month in vitro study. Oral Health Prev Dent. 2014;12(2):149–55.
110. AlShahrani SS, AlAbbas MAS, Garcia IM, AlGhannam MI, AlRuwaili MA, Collares FM, et al. The antibacterial effects of resin-based dental sealants: a systematic review of in vitro studies. Materials (Basel). 2021;14(3):413.
111. Yu F, Yu H, Lin P, Dong Y, Zhang L, Sun X, et al. Effect of an antibacterial monomer on the antibacterial activity of a pit-and-fissure sealant. PLoS One. 2016;11(9):e0162281.
112. Garcia IM, Rodrigues SB, Balbinot GDS, Visioli F, Leitune VCB, Collares FM. Quaternary ammonium compound as antimicrobial agent in resin-based sealants. Clin Oral Investig. 2019;24(2):777–84.
113. Ibrahim MS, Ibrahim AS, Balhaddad AA, Weir MD, Lin NJ, Tay FR, et al. A novel dental sealant containing dimethylaminohexadecyl methacrylate suppresses the cariogenic pathogenicity of Streptococcus mutans biofilms. Int J Mol Sci. 2019;20(14):3491.
114. Ibrahim MS, Garcia IM, Vila T, Balhaddad AA, Collares FM, Weir MD, et al. Multifunctional antibacterial dental sealants suppress biofilms derived from children at high risk of caries. Biomater Sci. 2020;8(13):3472–84.
115. Monteiro JC, Stürmer M, Garcia IM, Melo MA, Sauro S, Leitune VCB, et al. Dental sealant empowered by 1,3,5-tri acryloyl hexahydro-1,3,5-triazine and α-tricalcium phosphate for anti-caries application. Polymers (Basel). 2020;12(4):895.
116. Anand V, Arumugam SB, Manoharan V, Kumar SA, Methippara JJ. Is resin infiltration a microinvasive approach to white lesions of calcified tooth structures? A systematic review. Int J Clin Pediatr Dent. 2019;12(1):53–8.
117. Paris S, Meyer-Lueckel H, Cölfen H, Kielbassa AM. Resin infiltration of artificial enamel caries lesions with experimental light-curing resins. Dent Mater J. 2007;26(4):582–8.
118. Kielbassa AM, Müller J, Gernhardt CR. Closing the gap between oral hygiene and minimally invasive dentistry: a review on the resin infiltration technique of incipient (proximal) enamel lesions. Quintessence Int. 2009;40(8):663–81.
119. Kielbassa AM, Ulrich I, Treven L, Müller J. An updated review on the resin infiltration technique on incipient proximal enamel lesions. Med Evol. 2010;16(1):3–15.
120. Enan ET, Aref NS, Hammad SM. Resistance of resin-infiltrated enamel to surface changes in response to acidic challenge. J Esthet Restor Dent. 2019;31(4):353–8.
121. Paris S, Meyer-Lueckel H, Cölfen H, Kielbassa AM. Penetration coefficients of commercially available and experimental composites intended to infiltrate enamel carious lesions. Dent Mater. 2007;23(6):742–8.
122. Ye Q, Spencer P, Wang Y, Misra A. Relationship of solvent to the photopolymerization process, properties, and structure in model dentin adhesives. J Biomed Mater Res A. 2007;80(2):342–50.
123. Araújo GSA, Sfalcin RA, Araújo TGF, Alonso RCB, Puppin-Rontani RM. Evaluation of polymerization characteristics and penetration into

enamel caries lesions of experimental infiltrants. J Dent. 2013;41(11):1014–9.
124. Meyer-Lueckel H, Paris S. Infiltration of natural caries lesions with experimental resins differing in penetration coefficients and ethanol addition. Caries Res. 2010;44(5):408–14.
125. Ammari MM, Soviero VM, Fidalgo T, Lenzi M, Ferreira DMT, Mattos CT, et al. Is non-cavitated proximal lesion sealing an effective method for caries control in primary and permanent teeth? A systematic review and meta-analysis. J Dent. 2014;42(10):1217–27.
126. Dorri M, Dunne SM, Walsh T, Schwendicke F. Micro-invasive interventions for managing proximal dental decay in primary and permanent teeth. Cochrane Database Syst Rev. 2015;2015(11):CD010431.
127. Chatzimarkou S, Koletsi D, Kavvadia K. The effect of resin infiltration on proximal caries lesions in primary and permanent teeth: a systematic review and meta-analysis of clinical trials. J Dent. 2018;77:8–17.
128. Liang Y, Deng Z, Dai X, Tian J, Zhao W. Micro-invasive interventions for managing non-cavitated proximal caries of different depths: a systematic review and meta-analysis. Clin Oral Investig. 2018;22(6):2675–84.
129. Elrashid AH, Alshaiji BS, Saleh SA, Zada KA, Baseer MA. Efficacy of resin infiltrate in noncavitated proximal carious lesions: a systematic review and meta-analysis. J Int Soc Prev Community Dent. 2019;9(3):211–8.
130. Chen Y, Chen D, Lin H. Infiltration and sealing for managing non-cavitated proximal lesions: a systematic review and meta-analysis. BMC Oral Health. 2021;21:13.
131. Peters M, Hopkins A, Zhu L, Yu Q. Efficacy of proximal resin infiltration on caries inhibition: results from a 3-year randomized controlled clinical trial. J Dent Res. 2019;98(12):1497–502.
132. Meyer-Lueckel H, Bitter K, Paris S. Randomized controlled clinical trial on proximal caries infiltration: three-year follow-up. Caries Res. 2012;46(6):544–8.
133. Paris S, Bitter K, Krois J, Meyer-Lueckel H. Seven-year efficacy of proximal caries infiltration—Randomized clinical trial. J Dent. 2020;93:103277.
134. Page LF, Beckett D, Ahmadi R, Schwass D, De La Barra SL, Moffat S, et al. Resin infiltration of caries in primary molars in a community setting: 24-month randomized controlled trial findings. JDR Clin Transl Res. 2017;2(3):287–94.
135. Ammari MM, Jorge RC, Souza IP, Soviero VM. Efficacy of resin infiltration of proximal caries in primary molars: 1-year follow-up of a split-mouth randomized controlled clinical trial. Clin Oral Investig. 2017;22(3):1355–62.
136. Ekstrand K, Bakhshandeh A, Martignon S. Treatment of proximal superficial caries lesions on primary molar teeth with resin infiltration and fluoride varnish versus fluoride varnish only: efficacy after 1 year. Caries Res. 2010;44(1):41–6.
137. Paris S, Bitter K, Naumann M, Dörfer CE, Meyer-Lueckel H. Resin infiltration of proximal caries lesions differing in ICDAS codes. Eur J Oral Sci. 2011;119(3):182–6.
138. Askar H, Schwendicke F, Lausch J, Meyer-Lueckel H, Paris S. Modified resin infiltration of non-, micro- and cavitated proximal caries lesions in vitro. J Dent. 2018;74:56–60.
139. Askar H, Lausch J, Dörfer CE, Meyer-Lueckel H, Paris S. Penetration of micro-filled infiltrant resins into artificial caries lesions. J Dent. 2015;43(7):832–8.
140. Bourbia M, Finer Y. Biochemical stability and interactions of dental resin composites and adhesives with host and bacteria in the oral cavity: a review. J Can Dent Assoc. 2018;84:i1.
141. Klapdohr S, Moszner N. New inorganic components for dental filling composites. Mon Chem Chem Mon. 2004;136:21–45.
142. Lee JH, Um CM, Lee IB. Rheological properties of resin composites according to variations in monomer and filler composition. Dent Mater. 2006;22(6):515–26.
143. Beun S, Bailly C, Dabin A, Vreven J, Devaux J, Leloup G. Rheological properties of experimental Bis-GMA/TEGDMA flowable resin composites with various macrofiller/microfiller ratio. Dent Mater. 2009;25(2):198–205.
144. Zhao X, Pan J, Zhang S, Malmstrom HS, Ren YF. Effectiveness of resin-based materials against erosive and abrasive enamel wear. Clin Oral Investig. 2017;21(2):463–8.
145. Lausch J, Askar H, Paris S, Meyer-Lueckel H. Micro-filled resin infiltration of fissure caries lesions in vitro. J Dent. 2017;57:73–6.
146. Paris S, Lausch J, Selje T, Dörfer C, Meyer-Lueckel H. Comparison of sealant and infiltrant penetration into pit and fissure caries lesions in vitro. J Dent. 2014;42(4):432–8.
147. Da Silva VB, De Carvalho RN, Bergstrom TG, Dos Santos TMP, Lopes RT, Neves ADA. Sealing carious fissures with resin infiltrant in association with a flowable composite reduces immediate

microleakage? Pesqui Bras Odontopediatria Clín Integr. 2020;20:e5114.
148. Bakhshandeh A, Ekstrand K. Infiltration and sealing versus fluoride treatment of occlusal caries lesions in primary molar teeth: 2–3 years results. Int J Paediatr Dent. 2015;25(1):43–50.
149. Anauate-Netto C, Neto LB, Amore R, Di Hipólito V, Alpino PHPD. Caries progression in non-cavitated fissures after infiltrant application: a 3-year follow-up of a randomized controlled clinical trial. J Appl Oral Sci. 2017;25(5):442–54.
150. Elkwatehy WMA, Bukhari OM. The efficacy of different sealant modalities for prevention of pits and fissures caries: a randomized clinical trial. J Int Soc Prev Community Dent. 2019;9(2):119–28.
151. Schneider H, Park KJ, Rueger C, Ziebolz D, Krause F, Haak R. Imaging resin infiltration into non-cavitated carious lesions by optical coherence tomography. J Dent. 2017;60:94–8.
152. Yim HK, Min JH, Kwon HK, Kim BI. Modification of surface pretreatment of white spot lesions to improve the safety and efficacy of resin infiltration. Korean J Orthod. 2014;44(4):195–202.
153. Neres ÉY, Moda M, Chiba EK, Briso ALF, Pessan JP, Fagundes TC. Microhardness and roughness of infiltrated white spot lesions submitted to different challenges. Oper Dent. 2017;42(4):428–35.
154. Torres CRG, Rosa P, Ferreira N, Borges AB. Effect of caries infiltration technique and fluoride therapy on microhardness of enamel carious lesions. Oper Dent. 2012;37(4):363–9.
155. Meyer-Lueckel H, Paris S. Improved resin infiltration of natural caries lesions. J Dent Res. 2008;87(12):1112–6.
156. De Sousa FB, Soares JD, Vianna SS. Natural enamel caries: a comparative histological study on biochemical volumes. Caries Res. 2012;47(3):183–92.
157. Silverstone LM. Structure of carious enamel, including the early lesion. Oral Sci Rev. 1973;3:100–60.
158. Prajapati D, Nayak R, Pai D, Upadhya N, Bhaskar VK, Kamath P. Effect of resin infiltration on artificial caries: an in vitro evaluation of resin penetration and microhardness. Int J Clin Pediatr Dent. 2017;10(3):250–6.
159. Kielbassa AM, Leimer MR, Hartmann J, Harm S, Pasztorek M, Ulrich IB. Ex vivo investigation on internal tunnel approach/internal resin infiltration and external nanosilver-modified resin infiltration of proximal caries exceeding into dentin. PLoS One. 2020;15(1):e0228249.
160. Mueller J, Yang F, Neumann K, Kielbassa AM. Surface tridimensional topography analysis of materials and finishing procedures after resinous infiltration of subsurface bovine enamel lesions. Quintessence Int. 2011;42(2):135–47.
161. Ulrich I, Mueller J, Wolgin M, Frank W, Kielbassa AM. Tridimensional surface roughness analysis after resin infiltration of (deproteinized) natural subsurface carious lesions. Clin Oral Investig. 2015;19(6):1473–83.
162. Yazkan B, Ermis RB. Effect of resin infiltration and microabrasion on the microhardness, surface roughness and morphology of incipient carious lesions. Acta Odontol Scand. 2018;76(6):473–81.
163. Arnold WH, Bachstaedter L, Benz K, Naumova EA. Resin infiltration into differentially extended experimental carious lesions. Open Dent J. 2014;8:251–6.
164. Gurdogan EB, Ozdemir-Ozenen D, Sandalli N. Evaluation of surface roughness characteristics using atomic force microscopy and inspection of microhardness following resin infiltration with Icon®. J Esthet Restor Dent. 2017;29(3):201–8.
165. Meyer-Lueckel H, Paris S, Mueller J, Cölfen H, Kielbassa A. Influence of the application time on the penetration of different dental adhesives and a fissure sealant into artificial subsurface lesions in bovine enamel. Dent Mater. 2006;22(1):22–8.
166. Aziznezhad M, Alaghemand H, Shahande Z, Pasdar N, Bijani A, Eslami A, et al. Comparison of the effect of resin infiltrant, fluoride varnish, and nano-hydroxyapatite paste on surface hardness and Streptococcus mutans adhesion to artificial enamel lesions. Electron Physician. 2017;9(7):3934–42.
167. Goldberg M. In vitro and in vivo studies on the toxicity of dental resin components: a review. Clin Oral Investig. 2007;12(1):1–8.
168. Samuelsen JT, Dahl JE, Karlsson S, Morisbak E, Becher R. Apoptosis induced by the monomers HEMA and TEGDMA involves formation of ROS and differential activation of the MAP-kinases p38, JNK and ERK. Dent Mater. 2007;23(1):34–9.
169. Batarseh G, Windsor LJ, Labban NY, Liu Y, Gregson K. Triethylene glycol dimethacrylate induction of apoptotic proteins in pulp fibroblasts. Oper Dent. 2014;39(1):E1–E8.
170. Meyer-Lückel H, Hartwig C, Börner HG, Lausch J. Elution of monomers from an infiltrant compared with different resin-based dental materials. Oral Health Prev Dent. 2020;18(4):337–41.

171. Galler KM, Schweikl H, Hiller KA, Cavender AC, Bolay C, D'Souza RN, et al. TEGDMA reduces mineralization in dental pulp cells. J Dent Res. 2010;90(3):257–62.
172. Chen M, Li JZ, Zuo QL, Liu C, Jiang H, Du MQ. Accelerated aging effects on color, microhardness and microstructure of ICON resin infiltration. Eur Rev Med Pharmacol Sci. 2019;23:7722–31.
173. Arslan S, Lipski L, Dubbs K, Elmali F, Ozer F. Effects of different resin sealing therapies on nanoleakage within artificial non-cavitated enamel lesions. Dent Mater J. 2018;37(6):981–7.
174. Zhao X, Ren YF. Surface properties and color stability of resin-infiltrated enamel lesions. Oper Dent. 2016;41(6):617–26.
175. Finer Y, Santerre JP. Salivary esterase activity and its association with the biodegradation of dental composites. J Dent Res. 2004;83(1):22–6.
176. Huang B, Siqueira WL, Cvitkovitch DG, Finer Y. Esterase from a cariogenic bacterium hydrolyzes dental resins. Acta Biomater. 2018;71:330–8.
177. Stewart CA, Finer Y. Biostable, antidegradative and antimicrobial restorative systems based on host-biomaterials and microbial interactions. Dent Mater. 2019;35(1):36–52.
178. Singh J, Khalichi P, Cvitkovitch DG, Santerre JP. Composite resin degradation products from BisGMA monomer modulate the expression of genes associated with biofilm formation and other virulence factors in Streptococcus mutans. J Biomed Mater Res A. 2009;88A(3):551–60.
179. Sadeghinejad L, Cvitkovitch DG, Siqueira WL, Santerre JP, Finer Y. Triethylene glycol up-regulates virulence-associated genes and proteins in Streptococcus mutans. PLoS One. 2016;11(10):e0165760.
180. Khalichi P. Effect of composite resin biodegradation products on oral streptococcal growth. Biomaterials. 2004;25(23):5467–72.
181. Huang B, Sadeghinejad L, Adebayo OI, Ma D, Xiao Y, Siqueira WL, et al. Gene expression and protein synthesis of esterase from Streptococcus mutans are affected by biodegradation by-product from methacrylate resin composites and adhesives. Acta Biomater. 2018;81:158–68.
182. Nedeljkovic I, De Munck J, Ungureanu AA, Slomka V, Bartic C, Vananroye A, et al. Biofilm-induced changes to the composite surface. J Dent. 2017;63:36–43.
183. Rai P, Pandey RK, Khanna R. Qualitative and quantitative effect of a protective chlorhexidine varnish layer over resin-infiltrated proximal carious lesions in primary teeth. Pediatr Dent. 2016;38(1):6.
184. Inagaki LT, Dainezi VB, Alonso RCB, de Paula AB, Garcia-Godoy F, Puppin-Rontani RM, et al. Evaluation of sorption/solubility, softening, flexural strength and elastic modulus of experimental resin blends with chlorhexidine. J Dent. 2016;49:40–4.
185. Inagaki LT, Alonso RCB, Araújo GSA, de Souza-Junior EJC, Anibal PC, Höfling JF, et al. Effect of monomer blend and chlorhexidine-adding on physical, mechanical and biological properties of experimental infiltrants. Dent Mater. 2016;32(12):e307–13.
186. Flor-Ribeiro MD, Graziano TS, Aguiar FHB, Stipp RN, Marchi GM. Effect of iodonium salt and chitosan on the physical and antibacterial properties of experimental infiltrants. Braz Oral Res. 2019;33:e075.
187. Cheng L, Zhang K, Zhang N, Melo M, Weir M, Zhou X, et al. Developing a new generation of antimicrobial and bioactive dental resins. J Dent Res. 2017;96(8):855–63.
188. Gonçalves LS, Moraes R, Ogliari FA, Boaro L, Braga RR, Consani S. Improved polymerization efficiency of methacrylate-based cements containing an iodonium salt. Dent Mater. 2013;29(11):1251–5.
189. Elsaka SE. Antibacterial activity and adhesive properties of a chitosan-containing dental adhesive. Quintessence Int. 2012;43(8):603–13.
190. Yu J, Huang X, Zhou X, Han Q, Zhou W, Liang J, et al. Anti-caries effect of resin infiltrant modified by quaternary ammonium monomers. J Dent. 2020;97:103355.
191. Villegas NA, Compagnucci MJS, Ajá MS, Rocca DM, Becerra MC, Molina GF, et al. Novel antibacterial resin-based filling material containing nanoparticles for the potential one-step treatment of caries. J Health Eng. 2019;2019:6367919.
192. Martinez-Gutierrez F, Olive PL, Banuelos A, Orrantia E, Niño N, Sanchez EM, et al. Synthesis, characterization, and evaluation of antimicrobial and cytotoxic effect of silver and titanium nanoparticles. Nanomed Nanotechnol Biol Med. 2010;6(5):681–8.
193. Sevinç BA, Hanley L. Antibacterial activity of dental composites containing zinc oxide nanoparticles. J Biomed Mater Res B Appl Biomater. 2010;95B:22–31.
194. Kasraei S, Sami L, Hendi S, AliKhani MY, Rezaei-Soufi L, Khamverdi Z. Antibacterial

properties of composite resins incorporating silver and zinc oxide nanoparticles on Streptococcus mutans and Lactobacillus. Restor Dent Endod. 2014;39(2):109–14.

195. Azarsina M, Kasraei S, Yousefi-Mashouf R, Dehghani N, Shirinzad M. The antibacterial properties of composite resin containing nanosilver against Streptococcus mutans and Lactobacillus. J Contemp Dent Pract. 2013;14(6):1014–8.
196. AlHumaid J, Al-Harbi F, El Tantawi M, Elembaby A. X-ray microtomography assessment of Carisolv and Papacarie effect on dentin mineral density and amount of removed tissue. Acta Odontol Scand. 2018;76(3):236–40.
197. Hegde S, Kakti A, Bolar DR, Bhaskar SA. Clinical efficiency of three caries removal systems: rotary excavation, Carisolv, and Papacarie. J Dent Child. 2016;83(1):22–8.
198. Santos TML, Bresciani E, Matos FDS, Camargo SEA, Hidalgo APT, Rivera LML, et al. Comparison between conventional and chemomechanical approaches for the removal of carious dentin: an in vitro study. Sci Rep. 2020;10:8127.
199. Deng Y, Feng G, Hu B, Kuang Y, Song J. Effects of Papacarie on children with dental caries in primary teeth: a systematic review and meta-analysis. Int J Paediatr Dent. 2018;28(4):361–72.
200. Smales RJ, Yip HK. The atraumatic restorative treatment (ART) approach for primary teeth: review of literature. Pediatr Dent. 2000;22(4):294–8.
201. Holmgren CJ, Roux D, Doméjean S. Minimal intervention dentistry: Part 5. Atraumatic restorative treatment (ART)—A minimum intervention and minimally invasive approach for the management of dental caries. Br Dent J. 2013;214(1):11–8.
202. Tyas M. Cariostatic effect of glass ionomer cement: A five-year clinical study. Aust Dent J. 1991;36(4):236–9.
203. Tam LE, Chan GP, Yim D. In vitro caries inhibition effects by conventional and resin-modified glass-ionomer restorations. Oper Dent. 1997;22(1):4–14.
204. Forsten L. Fluoride release and uptake by glass-ionomers and related materials and its clinical effect. Biomaterials. 1998;19(6):503–8.
205. Donly KJ, Nelson JJ. Fluoride release of restorative materials exposed to a fluoridated dentifrice. ASDC J Dent Child. 1997;64(4):249–50.
206. Crystal YO, Marghalani AA, Ureles SD, Wright JT, Sulyanto R, Divaris K, et al. Use of silver diamine fluoride for dental caries management in children and adolescents, including those with special health care needs. Pediatr Dent. 2017;39(3):135–45.
207. Kemoli AM, Van Amerongen WE. Effects of oral hygiene, residual caries and cervical marginal-gaps on the survival of proximal atraumatic restorative treatment approach restorations. Contemp Clin Dent. 2011;2(4):318–23.
208. Da Franca C, Colares V, Van Amerongen E. Two-year evaluation of the atraumatic restorative treatment approach in primary molars class I and II restorations. Int J Paediatr Dent. 2011;21(3):249–53.
209. De Amorim RG, Frencken JE, Raggio DP, Chen X, Hu X, Leal SC. Survival percentages of atraumatic restorative treatment (ART) restorations and sealants in posterior teeth: an updated systematic review and meta-analysis. Clin Oral Investig. 2018;22(6):2703–25.
210. Faccin ES, Ferreira SH, Kramer PF, Ardenghi T, Feldens CA. Clinical performance of ART restorations in primary teeth: a survival analysis. J Clin Pediatr Dent. 2009;33(4):295–8.
211. Joshi JS, Roshan NM, Sakeenabi B, Poornima P, Nagaveni NB, Subbareddy VV. Inhibition of residual cariogenic bacteria in atraumatic restorative treatment by chlorhexidine: disinfection or incorporation. Pediatr Dent. 2017;39(4):308–12.
212. Kabil NS, Badran A, Wassel MO. Effect of the addition of chlorhexidine and miswak extract on the clinical performance and antibacterial properties of conventional glass ionomer: an in vivo study. Int J Paediatr Dent. 2016;27(5):380–7.