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LITERATURE REVIEW

Comparing Fluoride Varnish, Fissure Sealant and Ozone for Children Caries Prevention

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ABSTRACT

Background: *Caries is the most prevalent oral health disease in children globally. Well-known method such as fluoride varnish and fissure sealant has been used to prevent caries overtime. Ozone therapy considered as a new innovation in caries prevention for children which has not been studied much for its effectiveness compared to the other popular method.* ***Objective:*** *This review aimed to compare caries preventive methods with fluoride varnish (FV), fissure sealant (FS) and ozone (O) for children and decide which method is the most effective.* ***Literature Study:*** *PubMed, SpringerLink, EBSCOhost and Science direct were searched from December 2021 to January 2022. The criteria included all randomized controlled trials and clinical trials comparing the caries preventive effect between FV, FS and O on children's permanent teeth.* ***Discussion:*** *A total of 12 articles were included. Regarding dentin caries prevention, 2 studies found resin FS in favour of no FS and 2 studies found FV in favor of controls. 1 study agreed glass ionomer FS and no FS comparable. 3 studies agreed FV and FS were comparable. 1 study agreed resin FS and glass ionomer FS comparable. 1 study also found FV, FS and O comparable. Regarding dentin remineralization, 2 studies found O were comparable with FS dan calcium hydroxide base. These methods are safe for children.* ***Conclusion:*** *Fluoride varnish, fissure sealant and ozone are effective in preventing children's caries with their own benefits and drawbacks. None of the methods is superior over another as there were a variety of the data reported.*

Keywords: *Caries Prevention, Children, Fissure Sealant, Fluoride Varnish, Ozone.*

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INTRODUCTION

Caries is a multifactorial disease that arises from environmental interaction, habits and genetic factors. Caries involve a complex process of remineralization and demineralization of enamel caused by acid produced by microorganisms inhabiting the dental plaque.[1] Caries is the most prevalent oral health disease in children around the world. The World Health Organization (WHO) stated caries incidence in children is around 60-90%.[2] Indonesia Basic Health Research (Riskesdas) also stated that in 2018 as much as 92,6% children aged 5-9 in Indonesia had caries.[3] These events seemed to be far from the target WHO had set in 2020 to achieve 80% of children in the world to be free from caries.[4]

Children tend to be exposed to caries as the anatomical structure of the teeth and early eruption time make it difficult to cleanse by the younger children.[5] As they get older, children with caries in their primary teeth are prone to have higher risk to develop caries in their permanent teeth.[6] Caries prevention is important for children, as the caries experience in children will be a strong indicator for future caries risk.[7] Tickle M divides evidence based intervention to prevent caries into three big categories: lowering the frequency and intake of carbohydrate, maintaining the balance of remineralization and demineralization and sealing the teeth from acid.[8]

An initiation to increase favorable conditions in the oral cavity to prevent caries can be done by the use of fluoride. Topically application of fluor inhibits the absorption of salivary proteins on the enamel surface, thereby inhibiting formation of pellicle and plaque as well as increasing resistance of enamel to acids by creating a fluorapatite layer which is stronger against demineralization.[9] Fluoride varnish is a topical fluoride that is considered sufficient to protect children with moderate to high caries prevalence. It is indicated as a prevention program for children with active caries and as an alternative treatment before fissure sealant placement is adequate.[10] Fluoride varnish is recommended for children as it is easy and fast to apply.[11] It works by releasing fluoride gradually over time and only a little amount of products needed to protect the whole tooth.[12] However, there are some drawbacks of using fluoride varnish including reversible tooth discoloration, risk of acute toxicity and the unpleasant taste that is declined by children.[6]

Other caries prevention initiation can be done by protecting teeth from acids produced by bacteria using fissure sealants. Fissure sealant is a resin material that is placed on the occlusal surface of the tooth as a barrier, preventing the growth of biofilm and accumulation of debris that can form caries in the molars groove.[13] Disadvantages encountered when applying fissure sealants are that proper fluid control techniques are required and there are risk that it will come off and become worn overtime.[14]

In the 21st century new alternatives for caries prevention have emerged, one of which is ozone therapy. Ozone as a caries treatment agent in certain amounts is powerful enough to stop caries, even for a deep caries lesion. Ozone not only kills microorganisms on the tooth surface, but also destroys their biomolecular residues.[15] Ozone application itself does not provide any additional benefit for caries prevention, it only creates a 'clean' environment that can prevent caries from developing further.[13] This therapy can be an option for anxious children and as an alternative to restorative treatment using an invasive bur.[16]

In the past study, Kalnina et al[17] conducted a clinical trial comparing prevention of occlusal caries in Latvia children with interventions of fluoride varnish, fissure sealant and ozone. This study concluded the three caries prevention agents were recommended to prevent occlusal caries, but there was no significant difference in the effectiveness of the three agents. The researcher explained that there is still no literature study that compares the three materials.

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The author is interested to research and seek further information on this topic, because there was still no evidence based study that compared ozone effectiveness with another widely used method for caries prevention, such as fissure sealant and fluoride varnish using literature review approach.

LITERATURE STUDY

The type of research used is literature review with a rapid review approach. The articles reviewed derived from PubMed, SpringerLink, EBSCOhost and Science direct databases that met the following criteria:

1. Articles that discuss the effect of fluoride varnish, fissure sealant and ozone for caries prevention
2. Articles with children having an erupting or fully erupted permanent teeth
3. Articles with randomized controlled trials and clinical trials design
4. Articles published in the last ten years
5. Articles in English

Articles that full text was not available, in the form of narrative review, case report or case series, articles with children who have certain health problems and non-human participants were excluded from this study.

Articles were searched from December 2021 to January 2022 using combination of the keywords “fluoride varnish”, “fissure sealant”, “ozone”, “caries” and “children”, with added conjunctions “AND” and “OR” to specify the search results. Filtering menus in each database were used. The results of the articles obtained were then filtered using the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analysis). Eligible articles are then extracted and analyzed based on the outcomes measured in the study. The strength of recommendations will be evaluated using SORT (Strength of Recommendation Taxonomy).[18]

The subjectivity risk assessment of the articles were reviewed using the Cochrane risk of bias tool version 2.[19] The risk of bias will be assessed based on 5 domains: bias arising from the randomization process, bias due to deviation from intended intervention, bias due to missing outcome data, bias in measurement of the outcome and bias in selection of the reported outcomes. Furthermore, the overall risk of bias will be presented in the form of traffic light graphs.

DISCUSSION

A total of 1,073 articles were obtained from the databases. Thirty-three articles were excluded, as they were duplicates. A total of 1,040 articles were screened from titles and abstracts; 972 articles did not fit the purpose then excluded. Furthermore, 55 articles were read in full text. Twelve articles were found to meet the eligibility criteria then included in qualitative analysis.

Articles covered were mostly from China and Brazil, with three articles each. The study designs included randomized controlled trials, randomized clinical trials, clinical trials and longitudinal clinic studies with parallel or split mouth methods. Research study periods range from 12 to 36 months. The results of the articles identified from this rapid review is illustrated in the PRISMA flow chart in Figure 1.

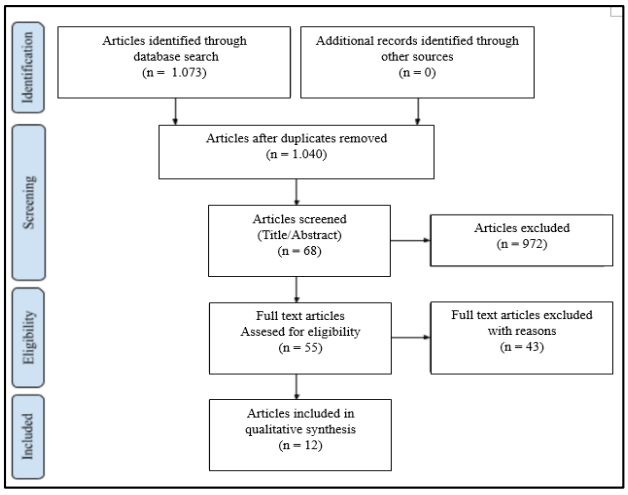

Figure 1. PRISMA flow chart diagram

Based on the evaluation of the quality of evidence using SORT, the strength of

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recommendation for this study was B (moderate). Two articles had good quality, patient-oriented scientific evidence (level 1) and five articles had limited quality scientific evidence, patient-oriented (level 2). Subjectivity risk assessment results showed seven out of twelve articles reviewed had some concerns regarding their overall risk of bias. Summary of the data extracted from the articles reviewed presented in Table 1.

Table 1. Summary of the data extracted from the included study

Researcher (Year)	Title	Location	Study Design	Level of Evidence	Risk of Bias
Arruda et al (2012)	Effect of 5% fluoride varnish application on caries among school children in rural Brazil: A randomized controlled trial	Brazil	Randomized controlled trial	3	Some concerns
Liu et al (2012)	Randomized trial on fluorides and sealants for fissure caries prevention	China	Randomized clinical trial	2	Some concerns
Muller-Bolla et al (2013)	Effectiveness of school-based dental sealant programs among children from low-income backgrounds in France: a pragmatic randomized clinical trial	France	Randomized clinical trial	1	Low risk
Oliveira et al (2013)	Comparison of the caries-preventive effect of a glass ionomer sealant and fluoride varnish on newly erupted first permanent molars of children with and without dental caries experience	Brazil	Longitudinal clinic study	3	High risk
Liu et al (2014)	Glass ionomer ART sealant and fluoride-releasing resin sealant in fissure caries prevention-results from a randomized clinical trial	China	Randomized clinical trial	2	Low risk
Unal et al (2015)	Remineralization Capacity of Three Fissure Sealants with and without Gaseous Ozone on Non-Cavitated Incipient Pit and Fissure Caries	Turkey	Clinical trial	3	Some concerns
Kalnina et al (2016)	Prevention of occlusal caries using a ozone, sealant and fluoride varnish in children	Latvia	Clinical trial	3	High risk
Chestnutt et al (2017)	Fissure Seal or Fluoride Varnish? A Randomized Trial of Relative Effectiveness	UK	Randomized controlled trial	2	Some concerns
Safwat et al (2017)	Clinical Evaluation of Ozone on Dentinal Lesions in Young Permanent Molars using the Stepwise Excavation	Egypt	Randomized controlled clinical trial	3	Some concerns
Wu et al (2020)	Effectiveness of fluoride varnish on caries in the first molars of primary schoolchildren: a 3-year longitudinal study in Guangxi Province, China	China	Randomized controlled trial	2	High risk
Hesse et al (2021)	Atraumatic Restorative Treatment-Sealed versus Nonsealed First Permanent Molars: A 3-Year Split-Mouth Clinical Trial	Brazil	Clinical trial	2	Some concerns
Tahani et al (2021)	Fissure sealant therapy as a portable community-based care in deprived regions: Effectiveness of a clinical trial after 1 year follow-up	Iran	Randomized clinical trial	1	Some concerns

This study included a total of 5.125 randomized participants. Participants' ages ranged from five to fourteen, including both male and female gender. The articles reviewed included children with caries-free permanent first molars or that had early

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caries lesion with ICDAS (International Caries Detection and Assessment Score) code 1-2 which already fully erupted or were in the eruption stage, healthy, cooperative and had high caries risk. The article excluded children who had been under medication in the last 3 weeks, allergic to colophony, using orthodontic appliances and following other clinical trials.

Majority of caries prevention test materials were applied to the permanent first molars. Only one articles applying material on the permanent premolars[17].

The types of fissure sealants studied were resin, fluoride-releasing resin and glass ionomer. Fissure sealant was applied to the occlusal, occlusal-buccal and occlusal-palatal surface. Two articles[20,21] used conventional glass ionomer sealant with finger press technique, while the other two[22,23] used packable glass ionomer sealant.

Fluoride varnish was applied on the entire tooth surface or selective only to the occlusal, occlusal-buccal and occlusal palatal surfaces. The fluoride varnish content covered is 5% sodium fluoride and 0.1% difluorsilane with doses ranging from 0.4 to 0.5 mL per application. Fluoride varnish applications were repeated every follow-up period.

The type of ozone studied in the articles covered was gaseous, which is applied on the entire surface of the molar teeth with a silicone tipped pen-like device. The length of gas exposure ranged between 6 and 40 seconds. After the application, a remineralizing solution was applied on two articles[17,24] studied.

Criteria for assessing caries level for majority of the articles were carried out by recording dentinal caries lesions (ICDAS code 3-6) at the final examination, changes in DMFT (Decayed, Missing and Filled Teeth) or DMFS (Decayed, Missing and Filled Surface for permanent teeth) scores and decreased DIAGNOdent™ score. Articles with fissure sealant intervention also measured sealant retention rates and correlated them with caries rates.

Summary of the characteristics of all the articles reviewed presented in Table 2.

Table 2. Summary of the characteristics of all the articles reviewed

Researcher (year) Duration	Initial Sample (Finals)	Age	Evaluation of the Material Delivery Method	Caries Assessment Criteria/ Index (Calibration)	Type of Material Analyzed	Main Findings
Arruda et al (2012) 12 months	379 (210)	7-14	Tooth brushing, drying, isolation, varnish application on all tooth surface, post application instructions	ICDAS criteria and caries experience in permanent tooth (DFS score) by 4 calibrated examiners (Kappa 0.59-0.93)	Fluoride varnish, 5% NaF–sodium fluoride (Cavity Shield®), 2 times/ year Placebo varnish, 2 times/ year	1. Varnishes group has lower DFS index than placebo group 2. Caries reduction up to 40% with NaF varnish 3. Two annual applications of varnishes reduce caries significantly compared to two annual placebo application 4. None of side effect reported

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Liu et al (2012) 24 months	501 (482)	7-11	Sealant applied to occlusal FPM ICDAS 0-2, light cured Isolation, varnish application on occlusal FPM, post application instructions	Caries development into dentin (ICDAS 4-6) and sealant retention by calibrated examiner (Kappa > 0.9)	Fluoride-releasing resin sealant (Clinpro®), baseline Fluoride varnish, 5% NaF (Duraphat®), 2 times/ year 38% SDF solution (Saforide®), 2 times/ year Placebo control, 2 times/ year	1. Dentinal caries incidence on three intervention groups were lower than control group 2. Caries reduction rate of NaF varnish 39%, SDF 41% and resin sealant 60% 3. The three intervention groups have similar efficacy to prevent pit and fissure caries on FPM 4. Complaints of bitter taste after SDF application
Muller-Bolla et al (2013) 12 months	276 (253)	6-7	Sealant applied on occlusal FPM ICDAS 0-2, given oral hygiene and caries education	Caries incidence (ICDAS 3-6) marked with D_{3-6}MFT and d_{3-6}mft, sealant retention by calibrated examiner (Kappa 0.75 and 0.88)	Resin sealant (Delton Plus®), baseline Control, without intervention	1. FPM with sealant were lower at risk of developing new caries compared to control group 2. Caries reduction as of 74% with resin sealant 3. Sealant retention 52.7%, lower rates on upper jaw 4. None of side effect reported
Oliveira et al (2013) 24 months	80	6-8	Prophylaxis using pumice, sealant applied on occlusal-palatal/ occlusal-buccal FPM using micro brush Varnish applied on occlusal-palatal/ occlusal-buccal 0,5 mL dose/ application	Enamel and dentin caries with visual and tactile methods, sealant retention using Simonsen criteria by 2 examiners. No information of examiner's calibration	Pink glass ionomer sealant (Fuji Triage®), baseline Fluoride varnish NaF 5% (Durafluor®), 2 times a year	1. Teeth sealed using GI sealants develops more caries than fluoride varnish 2. 70% of caries lesions originated from group with previous caries experience (primary teeth) 3. Caries prevention effect of GI sealant and

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						fluoride varnish were comparable 4. GI sealants has bad retention, only one sealant retained fully at the end of studies
Liu et al (2014) 24 months	280 (261)	7-9	Isolation, sealant applied on occlusal FPM ICDAS 0-2, light cured Isolation, sealant applied using finger press technique	Dentinal caries (ICDAS 4-6) and sealant retention by 2 calibrated examiners (Kappa > 0.88)	ART GI sealant (Ketac-Molar Easymix®), baseline Fluoride releasing-resin sealants (Clinpro®), baseline 38% SDF solution, 2 times/ year Fluoride varnish, 2 times/ year	1. More dentin caries proportion on ART GI sealants, compared to resin sealant (not significant) 2. Sealant retention (full and partial) is better significantly on resin sealants (75%) than ART GI sealants (52%) 3. ART sealant and resin sealant are comparable to prevent caries fissure for 24 months 4. None of side effect reported
Unal et al (2015) 12 months	60 (167)	7-9	Gaseous ozone application using HealOzone generator on FPM surface 615 cm^3/min 40 seconds, then remaining gas vacuumed for 10 seconds Aegis® and Helioseal® sealants applied by pressing to tooth surface, Fuji® sealant in packable capsules	Caries remineralization evaluation with DIAGNOdent™, retention sealant by 2 calibrated examiners (Kappa 0.88 and 0.93)	Ozone gas, 40 sec + sealant (Aegis®, Fuji®, Helioseal®), 4 times/ year Control: Sealant only, baselines: Resin sealants amorphous calcium phosphate (Aegis ACP®), GI sealant (Fuji Triage®),	1. Gaseous ozone application followed with Fuji® and Aegis® sealant are effective in caries remineralization (decreased DIAGNOdent™ score), whereas Helioseal® does not 2. Triage® has the worst retention compared to other sealants with resin ingredients significantly (Aegis® and Helioseal®)

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					fluoride-releasing resin sealant (Helioseal®)	3. Gaseous ozone application before sealant placement does not influence sealant retention 4. Sealant with or without gaseous ozone does not have significant influence on dentin and enamel structure
Kalnina et al (2016) 12 months	122 (107)	10	Varnish applied on occlusal premolar permanent for 1 minute, post procedure instruction Prophylaxis, isolation, etching, sealant applied on occlusal premolar permanent Gaseous ozone 6 seconds on occlusal premolar permanent, remineralizatio n agent 1 minutes, post procedure instruction	Occlusal caries with DMFT index changes, OHI-S index, bitewing, sealant retention. No information of examiner's calibration	Fluoride varnish, (Fluocal solute®), 2 times/ year Resin sealant (Clinpro 3M®), baseline Ozone gas (Prozone®) , 6 seconds + remineralizi ng solution, 2 times/ year Control without intervention	1. DMFT index on all group increased after 12 months (not significant) 2. OHI-S index decreased after 12 months 3. Occlusal caries rate among test groups are not significantly different 4. The three test groups are not significantly different on their effectiveness to prevent occlusal caries
Chestnutt et al (2017) 36 months	1016 (835)	6-7	Isolation, sealant applied on occlusal FPM Isolation, varnish applied on entire FPM surface dose <0.4 mL	New caries developed to D_{4-6}MFT, sealant retention by calibrated examiner (Kappa 0.82 and 0.89)	Resin sealant (Delton®), baseline Fluoride varnish, 5% NaF (Duraphat®), 2 times/ year	1. Children proportion with dentin caries on their FPM after 36 months are not significant, FS 19.6% and FV 17.5% 2. Resin sealants has fairly good retention, 75.4% intact 3. FV is comparable with FS resin to prevent caries

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						4. None of side effect reported
Safwat et al (2017) 12 months	81	7-9	Local anesthesia, isolation, tooth cleaning, stepwise excavation, application of ozone gas with HealOzone generator silicon tip for 40 seconds, the remaining gas vacuumed 10 seconds, remineralizing solution (group 2 only)	DIAGNOdent™ score, caries visual and tactile examination by calibrated examiner (Kappa 0.92)	baseline, split mouth divided into: Group I: Ozone gas 40 seconds (Ia), control base $Ca(OH)_2$ (Ib) Group II: Ozone gas 40 seconds + remineralizing solution (pH Balancer®) 2 ml, 5 seconds (IIa), control base $Ca(OH)_2$ (IIb) Intervention temporary sealed until final evaluation	1. No significant difference in dentin color and consistency after ozone application with or without remineralizing solution 2. No significant different among ozone and calcium hydroxide group on dentin color and consistency 3. DIAGNOdent™ value decreased significantly after ozone gas application with and without remineralizing solution 4. Ozone application with or without remineralizing solution has no significant effect to dentin color and consistency after caries excavation
Wu et al (2020) 36 months	2003 (1748)	6-8	Tooth brushing, dried, isolation, applied with 0.4 mL varnish on entire teeth surface, post procedure instruction	Caries prevalence with modified ICDAS, caries development towards dentin (ND01-ND03), DMFT, DMFS by 2 calibrated examiners (Kappa inter-examiner 0.85, intra-examiner 0.84)	Fluoride varnish, 5% NaF (Duraphat®) + oral hygiene instruction, 2 times/ year Control, given oral hygiene education, 2 times/ year	1. Fluoride varnish group has lower caries prevalence, caries development, DMFT and DMFS score compared to control group (significant) 2. None of side effect reported 3. 5% NaF application capable to prevent caries on FPM and recommended as school-based

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						prevention program
Hesse et al (2021) 36 months	187 (153)	6-8	Tooth brushing, isolation, sealant applied with ART technique on occlusal FPM, petroleum jelly application over the sealant	Caries ICDAS 4-6, sealant retention, changes in DMFT/dmft score by 4 calibrated dental students (Kappa inter-examiner 0.85-0.94 and intra-examiner 0.70-0.90)	Vertical split mouth ART GI sealant (Fuji IX®), baseline ART GI sealant (Maxxion®), baseline Control without sealant	1. No significant different on caries development with ART sealants 2. Sealant retention not related with dentinal caries development 3. Children with caries experience at baseline has higher risk on developing caries 4. ART sealant is not more effective than no sealant to reduce FPM dentinal caries
Tahani et al (2021) 12 months	124 (109)	7-9	Prophylaxis, isolation, etching, sealant applied on occlusal-buccal FPM, light cured, fluoride varnish applied on entire teeth, oral hygiene instructions	Caries incidence (ICDAS code 3-6) and sealant retention by 2 calibrated examiners (Kappa 0.82)	Split mouth Resin fissure sealant (Prime Dent®) + fluoride varnish (Asia Chemi Tab®), baseline Control without sealant	1. Caries incidence on teeth without sealant is three times bigger 2. Sealant full retention 41.4% and partially 27.2% 3. There is relationship between sealant retention with new caries incidence 4. Caries reduction by 67% with resin sealant

In this study, the caries prevention effect was categorized based on the measured research outcomes. Based on their ability to prevent dentinal caries, fluoride varnish and fissure sealant (resin and glass ionomer) were effective and comparable in two articles[22,25]. One article[21] showed that resin and glass ionomer fissure sealant were comparable in preventing fissure caries. Two other studies[26,27] showed a significantly higher caries prevention rate with resin sealants compared to teeth without sealants.Two studies showed fluoride varnish had significant effect on caries reduction compared to placebo[27] or oral health education[28] alone. One study[20] showed glass ionomer sealants were not

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significantly different in preventing dentin caries compared to no intervention.

There is only one study[17] which compared caries prevention ability between resin fissure sealant, fluoride varnish and ozone which conclude these three interventions had similar efficacy in preventing occlusal caries. Another study also found resin fissure sealant, fluoride varnish and SDF (silver diamine fluoride)[29] were not much different in preventing caries from progressing into dentin.

Two studies with ozone, measured the caries prevention effect from the degree of remineralization and the state of dentin (hardness and color) changes. Unal et al[23] which studied ozone application prior the placement of three types of fissure sealants (containing fluoride-releasing resin, glass ionomer and amorphous calcium phosphate) showed a decrease in DIAGNOdent™ score, but not significant. When being compared with sealant only control group, there was no significant difference of DIAGNOdent™ score between the sealant group with ozone gas or without ozone gas. Another study by Safwat et al[24], showed ozone gas with or without additional remineralizing solution did not have a major effect on the color and hardness of dentin. DIAGNOdent™ scores decreased in the ozone group, but were not significant compared to the calcium hydroxide base control.

There were no articles that show one intervention is superior over another by significant difference. There is only evidence of effective caries prevention with fluoride varnish and fissure sealant when being compared with no intervention. A total of six articles[15,21,25,26,28,28] reported no complaints or side effects experienced by children after the intervention of fissure sealant, fluoride varnish or ozone.

The outcome results of the articles reviewed are summarized in Table 3.

Table 3. Summary of the research outcome

Research Summary		Effective	Not significantly different
Based on ability to prevent dentinal caries (occlusal/pit and fissure caries)	Resin sealant vs. fluoride varnish		Chestnutt (2017)
	GI (glass ionomer) sealant vs. fluoride varnish		Oliveira (2013) Liu (2014)
	Resin sealant vs. ART GI sealant		
	Resin sealant vs. no intervention	Muller-Bolla (2013), Tahani (2021)	Hesse (2021)
	GI sealant vs. no intervention		
	Fluoride varnish vs. control/placebo	Arruda (2012), Wu (2020)	Kalnina (2016) Liu (2012)
	Resin sealant vs. fluoride varnish vs. ozone gas		
	Resin sealant vs. fluoride varnish vs. SDF		
	TOTAL	**4 studies**	**6 studies**
Based on dentinal remineralization ability	Ozone gas + resin/GI sealant vs. resin/GI sealant		Unal (2015) Safwat (2017)
	Ozone gas + remineralizing solution vs. calcium hydroxide base		
	TOTAL	**-**	**2 studies**

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DISCUSSION

Overall, the findings from this literature review showed that fissure sealant, fluoride varnish and ozone are effective in preventing caries by their own respective ways, especially in children's first permanent molars (FPM). Fissure sealant is the most widely published intervention method in the articles covered in this study.

Fissure sealants have been proven effective in preventing new caries and able to stop caries development. Two studies with randomized split mouth design for 12 months showed that first permanent molars treated with sealants had a lower risk of dentinal caries[26,27] and had three times greater caries risk in the group without sealant[27]. The observed caries reduction rate ranged from 12-74%. Similar results was found in the systematic review by Ahovuo-Saloranta et al[32] which found 11-51% caries reduction on the teeth treated with resin sealants after 24 months. There is a relationship between sealant retention after one year and the incidence of new caries. Sealant retention was found to be good in both studies (52.7% and 41.2%), which could be the reason for the low caries rate in the resin sealant group.

Three clinical trials[22,23,29] comparing fissure sealants with fluoride varnish, concluded that these two methods are comparable in preventing caries. This finding is supported by a recent systematic review by Kashbour et al[33], this study also states that there is no superior method between the two.

Research conducted by Chestnutt et al[25] with resin sealants showed a higher caries rate than Oliveira et al[22] study using glass ionomer sealants, although the retention rate of resin sealants tested better than glass ionomer sealants. This contradicts the statement that there is a relationship between sealant retention and the incidence of caries alone.[27] This could be attributed to differences in the study period conducted. The resin sealant was studied for 36 months, much longer than the 24 months study with glass ionomer sealants. Caries tend develop more on the teeth because of the longer research period.[34]

Effectiveness of glass ionomer sealants in preventing caries does not depend entirely on their retention ability.[35] Glass ionomer sealants also have an advantage to release fluoride over time into the oral cavity.[6] A study in Turkey with 4 years period, concluded an increase in salivary fluoride levels after application of a glass ionomer sealant, which is thought to be capable of preventing caries and induce remineralization.[35] In addition, even when this type of sealant has completely disappeared clinically, a small portion of the sealant will still remain in the fissure's depth and continues to release fluoride.[36]

A study comparing two types of sealants was carried out by Liu et al[21] by comparing fluoride-releasing resin sealants and glass ionomer sealants. In this clinical trial, found that the two types of sealants were comparable in preventing fissure caries with molar survival rates of 93% and 96%, respectively. The caries prevention rate is slightly better on fluoride-releasing resin sealants. This may relate to the fact that fluoride-releasing resin sealants have better retention in this study. However, this does not make fluoride-releasing resin sealants superior to glass ionomer sealants. Similar findings showing that fluoride-releasing resin sealants are slightly superior to glass ionomer sealants have also been reported in other clinical trials.[37,38] There is no high-quality evidence comparing the two types of sealants.

Several things that can be considered when selecting the type of sealant used are whether or not adequate equipment is available and the patient's level of cooperation.[39] Placement of sealant with conventional method (finger press) is the

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most preffered for used in remote areas with limited tools. Other caries prevention methods, such as fluoride varnish can also be carried out under limited equipment conditions.

Application of a fluoride varnish containing 5% sodium fluoride twice a year is an effective and safe method to prevent caries incidence in the first permanent molars of children with high caries risk, compared to controls without intervention.[40] The included 12-month randomized controlled trial showed a decrease in DFS/DMFS score levels up to 49%[28] and 58.9%[30], respectively. The DMFS score decrease of the two studies was greater than the systematic review of Marinho et al[40] which showed an average DMFS score reduction of 43%. This is understandable as a systematic review included many articles with different initial caries levels, hence it may be a confounding variable for the study. The caries prevention rate of fluoride varnish plus oral hygiene education showed better results; therefore, it could be considered as a beneficial additional intervention.

Ozone is a new caries prevention method that has not been widely studied. Clinical trials in children with caries comparing ozone gas with control interventions were included in this study. One study[23] comparing the application of ozone before sealant with control sealant alone in children aged 7-9, found that ozone had no effect on sealant retention success, but was able to prevent incipient caries when used in conjunction with sealants containing calcium phosphate or fluoride. A study by Çelik et al[41] with sectioned third molars showed a similar result. In that study, the application of ozone gas before the placement of fissure sealant was also not affecting the enamel bond strength of a giomer-based fissure sealant and recommend the use of ozone as a pretreatment disinfectant before sealant application.

A study examining ozone with or without remineralizing solution compared to calcium hydroxide base control alone[24], showed that ozone gas applied to dentin after excavation of damaged tissue in deep carious dentin lesions did not significantly affect the hardness and color of the dentin of young permanent molars after 12 month. Similar results were obtained in the in vitro lab tests of Duggal et al[42] and Tahmassebi et al[43]. Those studies reported the application of ozone alone was not effective enough to protect enamel from demineralization and provide remineralization, if not combined with remineralizing solution. There were no recent studies on the effectiveness of ozone as a caries prevention agent in children with better evidence.

Up until this research was conducted, there was only one clinical trial[17] comparing fissure sealant, fluoride varnish and ozone. This study was conducted in a developing country, assessed to have high risk of bias and poor strength of recommendation as the study was disease oriented. That study stated the three methods were effective and not much different to prevent occlusal caries.

This literature study chose good quality evidence derived from randomized controlled trials and clinical trials only to avoid high risk of bias. Interventions were also chosen to be carried out directly on human subjects to provide a factual effect with an actual state of oral cavity and selected the last ten years literature, hence the data obtained had an element of novelty.

Based on the assessment of SORT recommendation, the majority of articles reviewed were limited quality clinical trials with a patient-oriented outcome (Level 2), therefore the strength of recommendation for this study is B (moderate).

Based on the subjectivity risk assessment conducted using Cochrane risk of bias version 2, the overall risk of bias in this study is considered to have some concerns.

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The domain of bias with the worst criteria is bias arising from deviation from intended intervention with 50% (6 of 12 articles) considered to have some concerns. These related to several studies that were not reporting the allocation process and randomization sequences, and not blinding both participants and/or operators.

The result of the subjectivity risk assessment is presented in the traffic light graph reported in Graph 1.

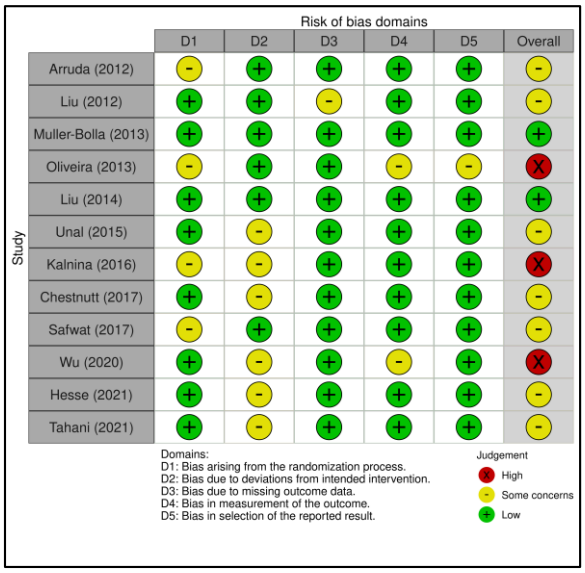

Figure 2. Traffic light of the risk of bias assessment result

The limitations of this rapid review, namely the diversity of data obtained due to combination of various comparisons of interventions and parameters used to measure caries, as well as differences in inclusion and exclusion criteria that varied in all articles. The majority of articles reviewed also reported presence of confounding variables outside the study that could affect the study results. The disproportionate number of articles between interventions also creates some problems. The lack of articles with ozone intervention gives limited results, hence it cannot provide a more valid result.

Majority of articles reviewed are disease oriented and are not focusing on intervention effects directly to the patient's quality of life. In addition, evaluation of subjectivity risk showed more than half of the articles reviewed had some concerns. The presence of bias in a study can cause it to be less reliable and has probability that the following outcome is interfered with by the subjects involved.

The three caries prevention methods using fluoride varnish, fissure sealant and ozone are effective in preventing caries in children with their respective advantages and disadvantages. None of the methods is superior over another as there were a variety of the data articles reported.

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