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The preventive effect of glass ionomer cement restorations on secondary caries formation: A systematic review and meta-analysis



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ARTICLE INFO	A B S T R A C T							
Keywords: Glass ionomer cement Restoration Caries Prevention Systematic review	Objective: The objective is to compare the preventive effect on secondary caries of glass ionomer cement (GIC) restorations with amalgam or resin-composite restorations.Methods: Two independent researchers conducted a systematic search of English publications in PubMed, Web of Science, Cochrane and Scopus. They selected randomized clinical trials comparing secondary caries incidences around GIC restorations (conventional GIC or resin-modified GIC) with amalgam or resin-composite restorations. Meta-analysis of the secondary-caries incidences with risk ratio (RR) and 95% confidence interval (95% CI) as the effect measure was performed. <i>Results</i> : This review included 64 studies. These studies included 8310 GIC restorations and 5857 amalgam or resin-composite restorations with a follow-up period from 1 to 10 years. Twenty-one studies with 4807 resto- rations on primary teeth and thirty-eight studies with 4885 restorations on permanent teeth were eligible for meta-analysis. The GIC restorations had a lower secondary caries incidence compared with amalgam restorations in both primary dentition [RR= 0.55, 95% CI:0.41–0.72] and permanent dentition [RR= 0.20, 95% CI:0.11–0.38]. GIC restorations showed similar secondary caries incidence compared with resin-composite restorations in primary dentition [RR= 0.92, 95% CI:0.77–1.10] and permanent dentition [RR= 0.77, 95% CI:0.39–1.51]. Conventional GIC restorations showed similar secondary caries incidence compared with resin- modified GIC-restored teeth in both primary dentition [RR= 1.12, 95% CI:0.67–1.87] and permanent denti- tion [RR= 1.63, 95% CI:0.34–7.84]. Conclusions: GIC restorations showed a superior preventive effect against secondary caries compared to amalgam 							

1. Introduction

Secondary caries, or recurrent caries, refers to caries lesions occurring adjacent to an existing restoration [1]. Secondary caries is responsible for 60% of restoration failure in dental practice [2]. The treatment for secondary caries has historically involved the replacement of restoration [3]. The repetitive operative procedure of restoration replacement causes the removal of more tooth hard tissue, weakens the remaining tooth, and eventually leads to tooth loss [3]. Moreover, the replacement of restorations placed a heavy burden on health care expenditure [4]. In the Delphi survey on restorative dentistry, the prevention of secondary caries was recognized as an oral health issue with the highest importance over the next 20 years [5]. The selection of restorative materials may affect the incidence of secondary caries [6,7]. Amalgam, resin-composite and glass ionomer cement (GIC) are commonly used dental restorative materials [8]. Dental amalgam has been used as a dental restorative material for over 150 years [9]. It is strong, durable, easy to operate, and cost-effective [10]. Because amalgam contains several metal contents such as silver and copper, it was believed that the amalgam restoration has a preventive effect on secondary caries formation [11]. Resin-composite is another common restorative material with great physical and aesthetic properties [12]. The major limitation of resin-composite is the polymerization shrinkage, which could cause microleakage between the tooth and the restoration and lead to secondary caries [13]. GIC includes conventional GIC or resin-modified GIC [14]. As a restorative material,

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it has moderate mechanical and aesthetic properties compared to resin-composite. Because of the remineralizing effects on dental hard tissue, GIC was believed to have the potential to prevent secondary caries [15].

GIC has several favourable properties for secondary caries prevention. GIC can release and recharge fluoride sustainably, which promotes remineralization. Its remineralizing effects on dental hard tissue have been reported in several laboratory and clinical studies [15,16]. GIC demonstrates antibacterial properties that contribute to its cariostatic effects, although these antibacterial effects significantly weaken after the material sets [17–19]. The physiochemical bond between the GIC and the tooth structure may prevent microleakage between GIC and cavity walls [20]. *In vitro* studies have concluded that GIC shows inhibitory effects on secondary caries formation [21]. Moreover, clinical studies found that GIC restoration failures are seldom caused by secondary caries [22].

The World Health Organization (WHO) have added GIC to the WHO Model List of Essential Medicines since 2021, which represents the most efficacious, safe and cost-effective medicines for priority conditions [23]. Although the physical property of GIC raised some concern on its use in occlusal loading areas [24], the replacement of defective restoration in primary teeth is not always necessary [25]. With this recent WHO endorsement, an increase in the use of GIC is plausible. Thus, an updated systematic quantitative evaluation focusing on the preventive effect of GIC restorations on secondary caries, compared with amalgam or resin-composite restorations of will lend continuing scientific support for GIC use. Therefore, this review aimed to evaluate the preventive effect of GIC restorations (conventional GIC or resin-modified GIC) on secondary caries compared with amalgam or resin-composite restorations in primary and permanent teeth.

2. Methods

2.1. Research questions and protocols

This systematic review evaluates the clinical evidence on the research question, 'What is the effectiveness of glass ionomer cement (conventional GIC or resin-modified GIC) restorations on preventing secondary caries formation in primary or permanent teeth compared with amalgam or resin-composite restorations of dental restorations?'.

This systematic review was reported following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) Statement. It was registered in the International Prospective Register of Systematic Reviews (PROSPERO Registration ID: CRD42022380959).

2.2. Search strategy

A comprehensive literature search was conducted to identify the available studies evaluating the caries preventive effect of GIC restorations (conventional GIC or resin-modified GIC) with no limits of publication year. The literature search was conducted in four databases, including PubMed/ Medline, Web of Science, Cochrane and Scopus. The last search was performed on 3rd Jan 2023.

The search strategy was developed as follows.

1 "caries" "carious" OR "tooth decay" OR "teeth decay" OR "dental caries" OR "caries susceptibility" OR "secondary caries" OR "recurrent caries"

2 "glass ionomer cement" OR "glass ionomer" OR "GIC" "glass polyalkenoate cement" OR "glass-ionomer cement" OR "ART" OR "atraumatic restorative procedure" OR "RMGIC" OR "resin-modified glass ionomer cement"

3 "#1' AND "#2'.

Two independent reviewers (KXG & OYY) conducted the study selection. Both authors independently screened titles, compared findings and included full texts after de-duplication. The third author (CHC) was consulted when there was disagreement. Studies with the consensus being reached through discussion were included.

2.3. Eligibility criteria

The inclusion criteria were developed based on population, intervention, comparison, outcome and study design (PICOS) strategy.

The PICOS strategy was as follows:

Population (P) - Studies with participants of all ages were included. Intervention (I) - GIC restorations (conventional GIC or resimmodified GIC) for restorative application.

Comparison (C) - Amalgam or resin-composite restorations.

Outcome (O) - Secondary caries incidences at various follow-up periods.

Study design (S) – Randomized controlled clinical trials (RCTs). The exclusion criteria of the studies were:

- To be the in vitro studies, animal studies, reviews, letters to the editor, case reports/series retrospective clinical and observational studies.
- 2. To investigate amalgam or resin-composite restorations but did not include the GIC restorations (conventional GIC or resin-modified GIC).
- 3. To investigate GIC for nonrestorative application in the clinic (i.e., fissure and sealant, liners/bases or cement).
- 4. To output data that did not contain the secondary caries incidence.

2.4. Data extraction

Two independent reviewers (KXG & OYY) performed data extraction of the eligible studies independently and in duplicate. They reviewed each paper and extracted systematically the data. The data included publication details (authors name, publication year and duration), tooth characteristics (type of teeth and number of restorations for each type of restoration), outcome information (assessment and caries incidence) and patients' information (risk of caries).

2.5. Assessment of the quality and risk of bias assessment of the studies

Two independent reviewers performed the risk of bias assessment of the study following the Cochrane Handbook for Systematic Reviews of Interventions 5.4.1 for assessing the risk of bias in RCTs. Six domains of bias were evaluated: selection bias-random sequence generation and allocation concealment; performance bias-blinding of participants and personnel; detection bias-blinding of outcome assessment; attrition biasincomplete outcome data; reporting bias-selective outcome reporting; other bias-other possible sources of bias. In case of disagreements between the reviewers, a consensus was reached through discussion, and if needed, by consulting a third reviewer (CHC).

2.6. Data synthesis and analysis

Meta-analysis of the secondary caries incidence after GIC restorations (conventional GIC or resin-modified GIC) was carried out from the selected studies and analysed using Review Manager 5.4. Data on secondary caries incidence of the eligible studies were extracted for metaanalysis. The results of the intervention effect were presented as risk ratio (RR) utilizing 95% confidence intervals (95% CI). Fixed-effects models were applied, and heterogeneity was tested using Cochran's Q test and the I² index. P < 0.05 was considered statistically significant. The follow-up periods were classified as short- (1 year), medium- (2–4 years) or long-term (\geq 5 years).

3. Results

3.1. Search result and study selection

A total of 5458 records were found in the initial search. 2586 duplicates were identified and removed. 2872 studies were eligible for screening. After the screening of titles and abstracts, 2275 studies other than randomized controlled clinical trials were excluded. Full texts of 337 articles were assessed. Finally, 64 studies that reported the secondary caries preventive effect of the GIC restorations were included in this review. Among them, 21 studies on primary teeth and 38 studies on permanent teeth were eligible for meta-analysis, while 5 studies were

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excluded from the meta-analysis. 4 of the excluded studies employed Danish Public Dental Health Service (Danish PDHS) criteria (3 studies) [26–28]or radiograph (1 study) [29] for the diagnosis of secondary caries. However, the details of Danish PDHS and radiograph were not provided in the original studies. In addition, studies using different criteria to assess outcomes may introduce methodological heterogeneity into the meta-analysis. Therefore, we excluded these 4 articles to reduce the heterogeneity of the included studies and enhance the certainty of evidence. Additionally, 1 study [30] was excluded from meta-analysis because it was the only study that employed FDI criteria for the diagnosis of secondary caries in permanent teeth. As a result, we are unable to compare and synthesize the results of this study with other studies.



Fig. 1. Flow diagram of the systematic review on glass ionomer cement (GIC). Danish PDHS: Danish Public Dental Health Service criteria.

The details of the literature search are presented in a flowchart (Fig. 1).

3.2. Study characteristics

A total of 64 included studies were published between 1997 and 2022, with a follow-up period of 1–10 years. Details about 64 articles selected for this review are shown in Tables 1 and 2. All included studies were randomized controlled clinical trials. The included studies involved 14,167 restorations, including 5073 conventional GIC, 3273

resin-modified GIC, 2282 amalgam and 3575 resin-composite restorations. The number of restorations involved in the systematic review is shown in Table 3.

Secondary caries incidence was the main outcome of interest of this systematic review, which was assessed with Modified United States Public Health Service (USPHS) criteria in 56 studies, FDI World Dental Federation (FDI) criteria in 5 studies and Danish Public Dental Health Service (Danish PDHS) criteria in 3 studies.

Table 1

Randomized controlled clinical trials of glass ionomer cements (GIC) in primary teeth (n = 26).

Authors, Year [Ref]	Groups (n = number of restorations): Caries incidence in $\%$	Duration In years	Assessment method	Significance (p < 0.05)	Include meta- analysis	ed Risk of caries
Daou et al. 2009[31]	Conventional GIC (n = 23):13.0% vs Amalgam (n = 21):14.3%	0	USPHS	No	Yes	Low
Fuks et al. 2000[32]	Conventional GIC (n = 9): 0 vs Amalgam (n = 9):11.1%	2	USPHS	No	Yes	Unclear
Hilgert et al. 2014[33]	Conventional GIC (n = 386): 3.6% vs Amalgam (n = 386): 6.2%	2	USPHS	No	Yes	Low
Taifour et al. 2002[34]	Conventional GIC (n = 1086): 4.9% vs Amalgam (n = 805): 9.5%	3	USPHS	Yes	Yes	Unclear
Qvist et al. 1997[26]	Conventional GIC (n = 515): 0.2% vs Amalgam (n = 543): 2.0%	3	Danish PDHS	Yes	No	Unclear
Qvist et al. 2004[27]	Conventional GIC (n = 281): 1.4% vs Amalgam (n = 309): 2.8%	3	Danish PDHS	No	No	Unclear
Arora et al. 2022[35]	Conventional GIC (n = 77):0 vs Resin-composite (n = 77):0	0	USPHS	No	Yes	Low
Gok Baba et al. 2021[36]	Conventional GIC (n = 168):0 vs Resin-composite (n = 83):0	1	USPHS	No	Yes	Low
Akman et al. 2020[37]	Conventional GIC (n = 34):0 vs Resin-composite (n = 100):0	1	USPHS	No	Yes	Low
De Medeiros et al. 2019	Conventional GIC (n = 79):20.2% vs Resin-composite (n = 79):7.6%	1	Radiograph	Yes No		Low
[29] Marks et al. 2000[38]	Conventional GIC (n = 52):1.9% vs Resin-composite (n = 48):4.2%	1	USPHS	No	Yes	Unclear
Passaro et al. 2022[39]	Conventional GIC (n $= 78$):6.4% vs Resin-composite (n $= 83$): 3.6%	1	USPHS	No	Yes	Unclear
Pani et al. 2018[40]	Conventional GIC (n = 106): 67.0% vs Resin-composite (n = 146):	2	USPHS	No	Yes	Unclear
Daou et al. 2009[31]	Conventional GIC (n = 23): 13.0% vs Resin-composite (n = 26):15.4%	2	USPHS	No	Yes	Low
Ersin et al. 2006[41]	Conventional GIC (n $=70$): 27.1% vs Resin-composite (n $=73$): 24.7%	2	USPHS	No	Yes	Unclear
Fuks et al. 2000[32]	Conventional GIC (n = 9): 0 vs Resin-composite (n = 8): 12.5%	2	USPHS	No	Yes	Unclear
Kupietzky et al. 2019[42]	Conventional GIC (n = 58): 0 vs Resin-composite (n = 58): 3.4%	2	USPHS	No	Yes	Unclear
Mufti et al. 2014[43]	Conventional GIC(n = 20): 45.0% vs Resin-modified GIC (n = 20):	3	USPHS	No	Yes	Unclear
Daou et al. 2009[31]	Conventional GIC (n = 23):13.0% vs Resin-modified GIC (n = 23): 17.40	1	USPHS	No	Yes	Low
Hubel et al. 2003[44]	Conventional GIC (n = 56): 7.1% vs Resin-modified GIC (n = 56):0	2	USPHS	No	Yes	Unclear
Espelid et al. 1999[45]	Conventional GIC (n = 39): 10.2% vs Resin-modified GIC (n = 44):	2	USPHS	No	Yes	Unclear
Qvist et al. 2004[46]	Conventional GIC (n = 451): 3.0% vs Resin-modified GIC (n = 543): 2.004	0	Danish PDHS	No No		Unclear
Daou et al. 2009[31]	Resin-modified GIC (n = 23):17.4% vs Amalgam (n = 21):14.3%	0	USPHS	No	Yes	Low
Donly et al.1999[47]	Resin-modified GIC (n = 19): 21.1% vs Amalgam (n = 19): 31.6%	2	USPHS	No	Yes	Low
Daou et al. 2009[31]	Resin-modified GIC ($n = 23$):17.4% vs Resin-composite ($n = 26$):15.4%	3	USPHS	No	Yes	Low
Ei-Houssei et al. 2019[48]	Resin-modified GIC (n = 54): 0 vs Resin-composite (n = 54): 0	2	USPHS	Yes	Yes	Unclear
Casagrande et al. 2013[49]	Resin-modified GIC (n = 38): 0 vs Resin-composite (n = 94): 0	1	USPHS	No	Yes	Low
Dermata et al. 2018[50]	Resin-modified GIC (n = 54): 7.4% vs Resin-composite (n = 47): 12.7%	2	USPHS	No	Yes	Unclear
Sengul et al. 2015[30]	Resin-modified GIC (n = 32): 0 vs Resin-composite (n = 78): 5.1%	2	FDI	Yes	No	High
Andersson et al. 2006[51]	Resin-modified GIC (n = 50): 0 vs Resin-composite (n = 50): 10%	2	USPHS	No	Yes	Low
Qvist et al. 2004[28]	Resin-modified GIC (n = 1191): 1.1% vs Resin-composite (n = 374): 1.39	% 7	Danish PDHS	No No		Unclear

Randomized controlled clinical trials of glass ionomer cements (GIC) in permanent teeth (n = 38).

Authors, Year [Ref]	Groups (n = number of restorations): Caries incidence in $\%$	Duration in year	Assessment method	Significance (p < 0.05)	Included meta- analysis	Risk of caries
Haveman et al. 2003[52]	Conventional GIC (n = 61): 13.1% vs Amalgam (n = 34): 44.0%	2	USPHS	Yes	Yes	High
Mandari et al. 2003[53]	Conventional GIC (n = 274): 1.1% vs Amalgam (n = 156): 10.2%	6	USPHS	Yes	Yes	Unclear
Fatma et al. 2020[54]	Conventional GIC (n = 67): 0 vs Resin-composite (n = 67): 0	1	USPHS	No	Yes	High
Menezes et al. 2019[55]	Conventional GIC (n = 71): 2.8% vs Resin-composite (n = 74): 0	1	USPHS	No	Yes	Low
Gladys et al. 1998[56]	Conventional GIC (n = 122): 0.8% vs Resin-composite (n = 32): 0	1	USPHS	No	Yes	Low
Molina et al. 2021[57]	Conventional GIC (n = 136): 0 vs Resin-composite (n = 136): 0	2	USPHS	No	Yes	Low
Balkaya et al. 2020[58]	Conventional GIC (n = 34): 0 vs Resin-composite (n = 75): 0	2	USPHS	No	Yes	Low
Menezes et al. 2021[59]	Conventional GIC (n = 62): 4.8% vs Resin-composite (n = 66): 3.0%	2	USPHS	No	Yes	Low
Hatirli et al. 2021[60]	Conventional GIC ($n = 56$): 0 vs Resin-composite ($n = 56$): 1.8%	2	USPHS	No	Yes	Low
Diem et al. 2014[61]	Conventional GIC (n = 134): 1.5% vs Resin-composite (n = 64): 1.5%	3	USPHS	No	Yes	Low
Gurgan et al. 2015[62]	Conventional GIC ($n = 70$): 0 vs Resin-composite ($n = 70$): 0	4	USPHS	No	Yes	Low
Gurgan et al. 2017[63]	Conventional GIC ($n = 70$): 0 vs Resin-composite ($n = 70$): 0	6	USPHS	No	Yes	Low
Gurgan et al. 2020[64]	Conventional GIC ($n = 70$): 0 vs Resin-composite ($n = 70$): 0	10	USPHS	No	Yes	Low
Celik et al. 2015[65]	Conventional GIC ($n = 67$): 0 vs Resin-composite ($n = 67$): 0	1	FDI	No	Yes	Low
Mc comb et al. 2002[66]	Conventional GIC (n = 4): 0 vs Resin-composite (n = 26): 30.8%	2	FDI	No	Yes	High
Fotiadou et al. 2019[67]	Conventional GIC ($n = 42$): 0 vs Resin-composite ($n = 43$): 0	3	FDI	No	Yes	Unclear
Celik et al. 2019[68]	Conventional GIC (n = 67): 0 vs Resin-composite (n = 67): 0	3	FDI	No	Yes	Low
Gladys et al. 1998[56]	Conventional GIC (n = 122): 0.8% vs Resin-modified GIC (n = 33): 3.0%	1	USPHS	No	Yes	Low
Dulgergil et al. 2005[69]	Conventional GIC (n = 39): 0 vs Resin-modified GIC (n = 52): 0	1	USPHS	No	Yes	Low
Ercan et al. 2009[70]	Conventional GIC (n = 39): 5.1% vs Resin-modified GIC (n = 52): 0	2	USPHS	No	Yes	High
Mc comb et al. 2002[66]	Conventional GIC (n = 4): 0 vs Resin-modified GIC (n = 9): 11.1%	2	FDI	No	Yes	High
Gladys et al. 1998[56]	Resin-modified GIC (n = 33): 3.0% vs Resin-composite (n = 32): 0	1	USPHS	No	Yes	Low
Van Dijken et al. 2019[71]	Resin-modified GIC (n = 82): 3.7% vs Resin-composite (n = 82): 0	1	USPHS	No	Yes	High
De Medeiros et al. 2015 [72]	Resin-modified GIC (n = 30): 0 vs Resin-composite (n = 30): 0	1	USPHS	No	Yes	Low
Perdigão et al. 2012[73]	Resin-modified GIC (n = 26): 0 vs Resin-composite (n = 27): 7.4%	1	USPHS	No	Yes	Low
De Oliveria et al. 2012 [74]	Resin-modified GIC (n = 41): 0 vs Resin-composite (n = 40): 0	1	USPHS	No	Yes	Low
Adeleke et al. 2012[75]	Resin-modified GIC (n = 170): 0 vs Resin-composite (n = 168): 0	1	USPHS	No	Yes	Unclear
Chinelatti et al. 2004[76]	Resin-modified GIC (n = 29): 0 vs Resin-composite (n = 58): 1.7%	1	USPHS	No	Yes	Unclear
Santiago et al. 2003[77]	Resin-modified GIC (n = 35): 0 vs Resin-composite (n = 35): 0	1	USPHS	No	Yes	Low
Popescu et al. 2016[78]	Resin-modified GIC ($n = 73$): 0 vs Resin-composite ($n = 74$): 0	2	USPHS	No	Yes	Low
Santiago et al. 2010[79]	Resin-modified GIC ($n = 35$): 0 vs Resin-composite ($n = 35$): 0	2	USPHS	No	Yes	Low
Onal et al. 2004[80]	Resin-modified GIC (n = 24): 0 vs Resin-composite (n = 106): 0	2	USPHS	No	Yes	Unclear
Brackett et al. 2003[81]	Resin-modified GIC (n = 37): 0 vs Resin-composite (n = 37): 0	2	USPHS	No	Yes	Unclear
Brackett et al. 2001[82]	Resin-modified GIC (n = 32): 0 vs Resin-composite (n = 32): 9.4%	2	USPHS	No	Yes	Unclear
Goncalves et al. 2021[83]	Resin-modified GIC ($n = 100$): 0 vs Resin-composite ($n = 100$): 0	3	USPHS	No	Yes	Low
Ozgunaltay et al. 2002 [84]	Resin-modified GIC ($n = 50$): 0 vs Resin-composite ($n = 48$): 0	3	USPHS	No	Yes	Low
Folwaczny et al. 2001[85]	Resin-modified GIC (n = 82): 0 vs Resin-composite (n = 115): 0	3	USPHS	No	Yes	Unclear
Alessandro et al. 2003 [86]	Resin-modified GIC (n = 16): 0 vs Resin-composite (n = 16): 0	5	USPHS	No	Yes	Low
Van Dijken et al. 1999[87]	Resin-modified GIC (n = 41): 0 vs Resin-composite (n = 49): 2.0%	5	USPHS	No	Yes	Unclear
Van Dijken et.al 2001[88]	Resin-modified GIC (n = 41): 0 vs Resin-composite (n = 49): 2.0%	6	USPHS	No	Yes	Unclear
Fagundes et.al 2014[89]	Resin-modified GIC (n = 23): 0 vs Resin-composite (n = 13): 7.7%	7	USPHS	No	Yes	Low
Mc comb et al. 2002[66]	Resin-modified GIC (n = 9): 11.1% vs Resin-composite (n = 26): 30.8%	2	FDI	No	Yes	High

3.2.1. Studies on primary teeth

26 included studies published between 1999 and 2022 investigated the preventive effect of the GIC-restored primary teeth on secondary caries. The included studies involved 9282 restorations, including 3588 conventional GIC, 2124 resin-modified GIC, 2092 amalgam and 1478 resin-composite restorations.

3.2.2. Studies on permanent teeth

38 included studies published between 1997 and 2022 investigated the preventive effect of GIC-restored permanent teeth on secondary caries. The included studies involved 4885 restorations, including 1485 conventional GIC, 1113 resin-modified GIC, 190 amalgam and 2097 resin-composite restorations.

3.3. Risk of bias of the studies

The risk of bias of the 64 studies included in the systematic review

was assessed (Fig. 2 and Table 3). 17 studies presented a low risk of bias. 2 studies showed an unclear risk of bias. 45 studies had a high risk of bias. Specifically, 41 studies did not report random sequence generation, and 28 studies did not report allocation concealment. 13 studies and 23 studies did not perform the blinding of participants and outcome assessment, respectively. No attrition bias, reporting bias or other bias was noticed in any of the included studies.

3.4. Meta-analysis

3.4.1. GIC vs other restorations

Generally, teeth with GIC restorations showed a lower secondary caries incidence compared to teeth with amalgam or resin-composite restorations in primary dentition [RR=0.74, 95% CI:0.63-0.86] (Fig. 3A) and permanent dentition [RR=0.38, 95% CI:0.25-0.60] (Fig. 3B). The risk ratio of secondary caries incidence of different types of materials was summarized in Tables 5 and 6.

Number of restorations and restorative materials included in the review.

Restoration material	toration Glass ionomer cement terial			Resin- composite	Total
No. of restoration (No. of studies)	Conventional				
No. of restoration in primary teeth (26 studies)	3588	2124	2092	1478	9282
No. of restorations in permanent teeth (38 studies)	1485	1113	190	2097	4885
Total no. of restorations (64 studies)	5073	3237	2282	3575	14,167

3.4.1.1. *GIC vs amalgam*. GIC-restored teeth exhibited a lower secondary caries incidence compared with amalgam-restored teeth in primary dentition [RR=0.55, 95% CI:0.41–0.72] (Fig. 3A) and permanent dentition [RR=0.20, 95% CI:0.11–0.38] (Fig. 3B).

3.4.1.2. GIC vs resin-composite. GIC-restored teeth showed a similar secondary caries incidence compared with composite restored teeth in primary dentition [RR= 0.92, 95% CI:0.77–1.10] (Fig. 3A) and permanent dentition [RR= 0.77, 95% CI:0.39–1.51] (Fig. 3B).

3.4.2. Conventional GIC/Resin-modified GIC vs amalgam with different follow-up periods

3.4.2.1. Conventional GIC vs amalgam. Conventional GIC-restored primary teeth presented a lower secondary caries incidence compared to amalgam-restored primary teeth in 2–4 years follow-up period [RR= 0.54, 95% CI:0.40–0.72] (Fig. 4A). A similar trend was observed in conventional GIC-restored permanent teeth in 2–4 years [RR= 0.30, 95% CI:0.14–0.63] and \geq 5 years [RR= 0.11, 95% CI:0.03–0.36] follow-up period (Fig. 4B).

3.4.2.2. Resin-modified GIC vs amalgam. Resin-modified GIC-restored primary teeth showed similar secondary caries incidence compared with amalgam-restored primary teeth in 2–4 years [RR= 0.75, 95% CI:0.31–1.81] (Fig. 5). No studies on resin-modified GIC-restored permanent teeth were included in this study.

3.4.3. Conventional GIC/Resin-modified GIC vs resin-composite with different follow-up periods

3.4.3.1. Conventional GIC vs resin-composite. Conventional GIC-restored primary teeth showed no statistical difference in secondary caries incidence compared to resin-composite-restored primary teeth in 1 year [RR= 0.46, 95% CI:0.04–4.93] and 2–4 years [RR= 0.98, 95% CI:0.82–1.17] (Fig. 6A). A similar outcome was identified in conventional GIC-restored permanent teeth in 1 year [RR= 2.49, 95% CI:0.33–18.59] and 2–4 years [RR= 1.02, 95% CI:0.30–3.52] (Fig. 6B).

Conventional GIC-restored permanent teeth assessed by FDI criteria showed no statistical difference in secondary caries incidence compared to resin-composite-restored permanent teeth in 2–4 years [RR=0.32, 95% CI:0.02–4.67] (Fig. 6C).

3.4.3.2. Resin-modified GIC vs resin-composite. Resin-modified GICrestored primary teeth presented no statistical difference in secondary caries incidence compared to resin-composite-restored primary teeth in 2–4 years [RR= 0.35, 95% CI:0.12–1.03] (Fig. 7A). A similar outcome was observed in resin-modified GIC-restored permanent teeth in 1 year [RR= 1.37, 95% CI:0.41–4.63], 2–4 years [RR= 0.14, 95% CI:0.01–2.66] and \geq 5 years [RR= 0.26, 95% CI:0.04–1.56] (Fig. 7B).

3.4.4. Conventional GIC vs Resin-modified GIC with different follow up periods

Conventional GIC-restored teeth showed similar secondary caries incidence compared with resin-modified GIC-restored teeth in primary dentition [RR= 1.12, 95% CI:0.67–1.87] (Fig. 8A) and permanent dentition [RR= 1.63, 95% CI:0.34–7.84] (Fig. 8B).

Conventional GIC-restored primary teeth showed no statistical difference in secondary caries incidence compared to resin-modified GIC-restored primary teeth in 1 year [RR= 0.69, 95% CI:0.39–1.24] and 2–4 years follow-up period [RR= 2.16, 95% CI:0.82–5.70] (Fig. 8A). A similar observation was noted in conventional GIC-restored permanent teeth in 1 year [RR= 0.27, 95% CI:0.02–4.21] and 2–4 years follow-up period [RR= 6.63, 95% CI:0.33–134.20] (Fig. 8B).

Conventional GIC-restored permanent teeth assessed by FDI criteria showed no statistical difference in secondary caries incidence compared to resin-modified GIC-restored permanent teeth in 2–4 years [RR= 0.67, 95% CI:0.03–13.60] (Fig. 8C).

4. Discussion

In this study, we found that overall GIC restorations were more effective in preventing secondary caries compared to amalgam or resincomposite restorations in primary dentition and permanent dentition. GIC contains silicon aluminum fluoride glasses and can release fluoride [90] [91]. The dentinal walls underneath a GIC restoration may contain up to 5000–6000 ppm fluoride [92]. Previous studies reported that fluoride at a concentration of as low as 0.03–0.07 ppm can stop mineral loss and promote mineral deposition in dental hard tissue [93]. Therefore, the fluoride release may contribute to the preventive effect of GIC secondary caries formation by decreasing demineralization and enhancing remineralization of dental hard tissues [15]. In addition, GIC materials are "rechargeable", they take up and re-release fluoride and prolonged the fluoride release [92]. The sustainable fluoride release may enhance the secondary caries preventive effect of GIC [94,95].

GIC restorations were more effective in preventing secondary caries compared to amalgam restoration in primary dentition and permanent dentition. GIC restoration includes conventional GIC and resin-modified GIC restoration. Only one study on primary teeth (and no study on permanent teeth) was included in this review that compared the secondary caries incidence of resin-modified GIC restorations and amalgam restorations [96]. The meta-analysis of this study [96] did not rule out a difference in secondary caries preventive effect between resin-modified GIC restoration and amalgam restoration with the statistical power. Therefore, the superior preventive effect of GIC on secondary caries compared to amalgam may be due to the effect of conventional GIC in the pool of the collected data. Further high-quality randomized control trials on the secondary caries preventive effect of resin-modified GIC are needed to support the results.

GIC-restored teeth showed similar secondary caries incidence compared with resin-composite restored teeth in primary dentition and permanent dentition. A previous review found that GIC restorations resulted in a lower primary caries incidence in other teeth of the dentition compared to resin-composite restorations [95]. In comparing GIC to resin-composite, GIC restorations seem to have a greater preventive effect on new primary lesions in the surrounding dentition versus preventing secondary caries at their own margins. It could be associated with the specific characteristics of secondary caries compared to primary caries. Secondary caries follows the same pathogenesis pattern as primary caries except that it is modified by the presence of a restoration margin [6]. A defective restoration margin allows the

Risk of bias of the included studies (n = 64).

Authors, year [Ref]	Selection bias	Selection bias	Performance	Detection	Attrition	Reporting	Overall
Adeleke et al. 2012 (75)	(Random)	(Allocation)					
Arora et al. 2022 [35]	•		•	•		•	•
Balkaya et al. 2020 [58]			•	•			
Celik et al. 2015 [65]	•	•	۲	٠	•	•	•
Celik et al. 2019 [68]	•	•	•	•	•	•	•
De Oliveria et al. 2012 [74]	•	•	•	•		•	•
Ercan et al. 2009 [70]		•	•	•		•	•
Fotiadou et al. 2019 [67]	•	•	•				
Gok Baba et al. 2021 [36]		•					
Goncalves et al. 2021 [83]			•				
Gurgan et al. 2013 [02]	•	•	•	•	•	•	•
Gurgan et al. 2020 [64]			•			•	•
Hubel et al. 2003 [44]	٠	٠	۲	٠	٠	٠	
Mandari et al. 2003 [53]	•	•	•	•	•	•	•
Menezes et al. 2019 [55]			•	•		٠	
Molina et al. 2021 [57]	•	•	۲	•	•	۲	٠
Dermata et al. 2018 [50]		?	•	•		•	?
Qvist et al. 2004 [46]	?	?	•	•	•	•	?
Akman et al. 2020 [37]	•	•	•	•	•	•	•
Alessandro et al. 2003 [86]	•		•	•	•	•	•
Brackett et al. 2003 [81]			•	•		•	
Brackett et al. 2001 [82]		•	•			•	
Casagrande et al. 2013 [49]							
De Medeiros et al. 2015 [/2							
De wederros et al. 2019 [29							
Ersin et al. 2014 [01]							
Eran et al. 2000 [41] Fagundes et al 2014 [89]	•		•			•	•
Folwaczny et al. 2001 [85]			•	•			•
Kupietzky et al. 2019 [42]	•	٠	۲	۲		٠	•
Mufti et al. 2014 [43]			•	•			•
Van Dijken et al. 2019 [71]	•	•	۲	۲	•	•	•
Andersson et al. 2006 [51]	•	?	•	•	•	•	•
Ei-Houssei et al. 2019 [48]	•	?	۲	•	•	•	•
Onal et al. 2004 [80]	•	?	•	•	•	•	•
Ozgunaltay et al. 2002 [84]	•	?	•	•	•	•	•
Qvist et al. 2004 [28]		?	•	•	•	•	
Van Dijken et al. 1999 [87]		2	•		•	•	
Santiago et al. 2010 [/9]							
Entra at al. 2004 [76]							
Hatirli of al 2020 [54]			•			•	
Mc comb et al. 2002 [66]	•	•	•	•	•	•	
Menezes et al. 2021 [59]			•	•		•	•
Pani et al. 2018 [40]	•	•	۲	۲	•	•	•
Passaro et al. 2022 [39]	•	•	•	•	•	•	•
Santiago et al. 2003 [77]	•	•	۲	۲		٠	•
Daou et al. 2009 [31]	•	?	•	•	•	•	•
Marks et al. 2000 [38]	•	?	•	•		•	•
Popescu et al. 2016 [78]	•	?	•	•	•	•	•
Dulgergil et al. 2005 [69]	•	•	•	•	•	•	•
Donly et al.1999 [47]	•	•	•	•	•	•	•
Espelid et al. 1999 [45]	•	•	-	•	•	•	
Gladys et al. 1998 [56]		•	•	-			
Fuks et al. 2000 [32]		2					
Perdiga o et al. 2014 [33]		2					
Ovistetal 1997 [26]	•	2	•		•	•	•
Sengul et al. 2015 [30]	•	?	•	•	•	•	•
Van Dijken et.al 2001 [88]	•	7	•	•		•	•
Haveman et al. 2003 [52]	•	•	•	•	•	•	•
Qvist et al. 2004 [27]	•	•	•	•			•
Taifour et al. 2002 [34]	•	•	•	•			•

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Fig. 2. Risk of bias assessment of the included studies.

cariogenic biofilm to grow in the gap of the restoration-tooth interface and cause secondary caries. Therefore, the incidence of secondary caries is related to the marginal seal of the restorative material. Since the mechanical strength of GIC is lower compared to resin-composite, fracture is easier to occur in GIC restoration and may cause microleakage around the restoration [97,98]. In addition, in the meta-analysis comparing GIC and resin-composite, we noted that 27 of 49 included studies did not report secondary caries cases in both GIC and resin-composite restored teeth. The follow-up period of these 27 studies ranges from 1 to 5 years, which is relatively short. The low incidence of secondary caries due to the short follow-up period might affect the results of the review.

Conventional GIC restorations showed similar preventive effect on secondary caries compared with resin-modified GIC restorations in primary dentition and permanent dentition. Previous studies found less microleakage around resin-modified GIC than conventional GIC [98] because of the presence of 2-hydroxyethyl methacrylate in resin-modified GIC. It leads to a hygroscopic expansion of up to 6% at 24 h. The expansion of the restoration may counteract the tendency of microleakage in the restoration margin [99]. Besides, resin-modified GIC shows a higher mechanical strength than conventional GIC and is less likely to fracture. These favourable properties of resin-modified GIC may promote its preventive effect on secondary caries compared with conventional GIC. We noted that resin-modified GIC restoration tends to be more effective in preventing secondary caries with medium-term follow-up (2-4 years) than with short-term (1 year). However, no statistical difference was observed (Fig. 8A, B). No long-term studies (more than 5 years) comparing the secondary caries preventive effect of conventional GIC and resin-modified GIC were available.

Out of 64 included studies on the secondary caries of GIC in this review, only 9 studies were on amalgam restorations while 51 studies were on resin-composite restorations. Studies on amalgam were published between 1997 and 2009, and studies on resin-composite were published between 1998 and 2022. It may be due to the decreased use of amalgam in recent years. Amalgam has been used as dental restorative material since the 1800 s [100]. Because of the negative effect of the mercury content in the amalgam on the environment, the Minamata Convention was approved in 2013, aiming to phase out the use of mercury. Dental amalgam has been required to be phased down under the convention [101]. In addition, amalgam restorations normally require extensive tooth preparation. Because the philosophy of caries management has shifted to minimal intervention dentistry, restorative materials which allow for a more conservative tooth preparation have been predominating in restorative dentistry [102]. Since the introduction of a resin-composite in the late 1960 s [103], conventional GIC in 1971 [104] and resin-modified GIC in the 1980 s [105], the selection and application of restorative material have been changing dramatically [106]. Resin-composite and GIC are more popular options [107].

We analyzed the secondary caries incidence in primary and permanent teeth separately, because the caries risk of primary and permanent teeth could be distinct [108]. Generally, the primary teeth are uniquely vulnerable to caries. Around 30% of caries occurs in the primary teeth despite their relatively short residual period in the mouth [109]. In addition, some primary teeth are restored during the mixed dentition phase, when the caries risk was relatively high [109]. The differences in caries risk may have influences on secondary caries incidences. Although the caries risk patterns may be different, the meta-analysis comparing secondary caries incidence among different types of restorative materials showed similar results in primary and permanent teeth in this study.

We analyzed the risk ratio of secondary caries incidence of teeth with different types of restorations in defined follow-up periods. We categorized the studies based on the follow-up times to obtain more reliable results at different time points. The follow-up periods were categorized as short-term (1 year), medium-term (2–4 years) or long-term (≥ 5 years). Clinical trials have shown that the incidence of secondary carious lesions increases with a longer follow-up period [110]. Nedeljkovic et al. reported that the highest mean incidence of secondary caries development was recorded after 5 years compared to less than 5 years follow-up period [3]. Therefore, we set 5 years as a long-term follow-up period for the meta-analysis with defined follow-up periods.

Only 10 of the 64 included studies had a follow-up period of \geq 5 years. Fernandes et al. reported that amalgam showed the highest survival rates (22.5 years) with an average survival rate of 95% over 10 years, followed by resin-composite (90% over 10 years), and GIC (65% over 5 years) [12]. The shorter longevity of GIC restorations could be caused by restoration fracture due to its low fracture toughness and strength [97]. This may be the reason why the follow-up period of most included GIC studies are short. In addition, the follow-up periods are limited in primary teeth due to the natural exfoliation of the primary teeth. Further randomized control trials with longer follow-up periods are needed to confirm these results.

Secondary caries was not found in 27 of the included 64 studies. Because no case of secondary caries was found in these studies, it was not feasible to compare the difference between GIC and amalgam or resin-composite restorations within the single study. We presented the results of these studies as "Not estimable" in the forest plot. But these data were included for the overall analysis of the risk ratio of secondary caries incidence around different restorative materials. The low incidence of secondary caries in these studies might be attributed to the relatively short follow-up period, the difficulty in the diagnosis of secondary caries and the low caries risk of the patient population. Among the 64 included studies, 33 featured patients with low caries risk, 28 had unclear caries risk, and 3 involved high caries risk.

Only one study out of the 64 included studies used the radiological assessment [29], while the other 63 used the visual and tactile

Α		Experime	ental	Contro	ol		Risk Ratio	Risk Ratio
· · ·	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% Cl
		2	22	2	21	1 20/	0.01 [0.21 4.04]	
	Euks et al. (2009)	5	23	3	21	1.5%	0.33 [0.02 7 24]	
	Hildert et al. (2000)	14	386	24	386	9.6%	0.58 [0.31 1 11]	
	Taifour et al. (2002)	54	1086	77	805	35.5%	0.52 [0.37, 0.73]	
	Donly et al. (1999)	4	19	6	19	2.4%	0.67 [0.22, 1.99]	
	Subtotal (95% CI)		1523		1240	49.3%	0.55 [0.41, 0.72]	◆
	Total events	75		111				
	Heterogeneity: $Chi^2 = 0.82$	1, df = 4 (P	P = 0.94); $I^2 = 0\%$	5			
	Test for overall effect: Z =	4.21 (P <	0.0001)					
	1.1.2 Resin-composite							
	Arora et al. (2022)	0	77	0	77		Not estimable	
	Cok Baba et al. (2021)	ő	168	ő	83		Not estimable	
	Akman et al. (2020)	õ	34	õ	100		Not estimable	
	Marks et al. (2000)	1	52	2	48	0.8%	0.46 [0.04, 4.93]	
	Passaro et al. (2022)	5	78	3	83	1.2%	1.77 [0.44, 7.17]	
	Pani et al.(2018)	71	106	101	146	34.1%	0.97 [0.82, 1.15]	+
	Daou et al. (2009)	3	23	4	26	1.5%	0.85 [0.21, 3.40]	
	Ersin et al. (2006)	19	70	18	73	7.1%	1.10 [0.63, 1.92]	
	Fuks et al. (2000)	0	9	1	8	0.6%	0.30 [0.01, 6.47]	
	Fi Houssoi et al. (2019)	0	58	2	58	1.0%	0.20 [0.01, 4.08]	•
	Casagrande et al. (2013)	0	38	0	04 04		Not estimable	
	Dermata et al. (2018)	4	54	6	47	2.6%	0.58 [0.17, 1.93]	
	Andersson et al. (2006)	0	50	4	50	1.8%	0.11 [0.01, 2.01]	· · · · · · · · · · · · · · · · · · ·
	Subtotal (95% CI)	-	871	-	947	50.7%	0.92 [0.77, 1.10]	
	Total events	103		141				
	Heterogeneity: $Chi^2 = 6.04$	4, df = 8 (P	9 = 0.64); $I^2 = 0\%$	6			
	Test for overall effect: Z =	0.94 (P =	0.35)					
	Total (95% CI)		2304		2187	100.0%	0.74 [0.63 0.86]	▲
	Total events	178	2394	252	2107	100.0%	0.74 [0.03, 0.80]	•
	Heterogeneity: $Chi^2 = 21^{-3}$	1/0	P = 0	$(07) \cdot 1^2 =$	39%			
	Test for overall effect: $Z =$	3.88 (P = 1)	0.0001	07),1 =	3370			0.01 0.1 1 10 100
	Test for subgroup differen	ices: Chi ² =	= 9.47, 0	df = 1 (P)	= 0.00	()2), $I^2 = 8$	9.4%	Favours [GIC] Favours [Control]
_				_				
В	Study or Subgroup	Experim	ental	Contr	ol	Woight	Risk Ratio	Risk Ratio
	1.2.1 Amalgam	Events	TOLAI	Events	TOLAI	weight	M-H, FIXed, 95% CI	
	Haveman et al. (2003)	8	61	15	34	32.8%	0 30 [0 14 0 63]	_ _
	Mandari et al. (2003)	3	274	16	156	34.7%	0.11 [0.03, 0.36]	
	Subtotal (95% CI)		335		190	67.5%	0.20 [0.11, 0.38]	◆
	Total events	11		31				
	Heterogeneity: $Chi^2 = 2.11$	l, df = 1 (P	= 0.15)	$ 1^2 = 53$	%			
	Test for overall effect: Z =	4.95 (P <	0.00001	.)				
	1 2 2 Resin-composite							
	Estma et al. (2020)	0	67	0	67		Not estimable	
	Balkava et al. (2020)	õ	34	ŏ	75		Not estimable	
	Menezes et al. (2019)	2	71	Ő	74	0.8%	5.21 [0.25, 106.63]	
	Gladys et al. (1998)	1	122	0	32	1.3%	0.80 [0.03, 19.31]	
	Molina et al. (2021)	0	136	0	136		Not estimable	
	Balkaya et al. (2020)	0	34	0	75		Not estimable	
	Menezes et al. (2021)	3	62	2	66	3.3%	1.60 [0.28, 9.24]	
	Hatirli et al. (2021)	0	56	1	56	2.6%	0.33 [0.01, 8.01]	
	Diem et al. (2014)	2	134	1	64	2.3%	0.96 [0.09, 10.34]	
	Gurgan et al. (2015)	0	70	0	70		Not estimable	
	Gurgan et al. (2017)	0	70	0	70		Not estimable	
	Alessandro et al. (2020)	0	16	0	16		Not estimable	
	Van Dijken et al. (2019)	3	82	õ	82	0.9%	7.00 [0.37, 133,41]	,
	De Medeiros et al. (2015)	0	30	0	30		Not estimable	
	Perdiga o et al. (2012)	0	26	2	27	4.2%	0.21 [0.01, 4.12]	
	De Oliveria et al. (2012)	0	41	0	40		Not estimable	
	Adeleke et al. (2012)	0	170	0	168		Not estimable	
	Chinelatti et al. (2004)	0	29	1	58	1.7%	0.66 [0.03, 15.61]	
	Santiago et al. (2003)	0	35	0	35		Not estimable	
	Popescu et al. (2016)	0	73	0	74		Not estimable	
	Santiago et al. (2010)	0	24	0	106		Not estimable	
	Brackett et al. (2003)	ő	37	ő	37		Not estimable	
	Brackett et al. (2001)	0	32	3	32	6.0%	0.14 [0.01, 2.66]	· · · · · · · · · · · · · · · · · · ·
	Goncalves et al. (2021)	0	100	0	100		Not estimable	
	Ozgunaltay et al. (2002)	0	50	0	48		Not estimable	
	Folwaczny et al. (2001)	0	82	0	115		Not estimable	
	Van Dijken et al. (1999)	0	41	1	49	2.3%	0.40 [0.02, 9.49]	
	Van Dijken et al. (2001)	0	41	2	49	3.9%	0.24 [0.01, 4.82]	
	Fagundes et al. (2014)	0	23	1	13	3.2%	0.19 [0.01, 4.46]	
	Total events	11	1993	14	1909	32.3%	0.77 [0.59, 1.51]	
	Heterogeneity: Chi ² = 8 17	7. df = 11.0	P = 0.70	14 = 0	%			
	Test for overall effect: Z =	0.76 (P =	0.45)	, i – 0	~			
								.
	Total (95% CI)		2228		2159	100.0%	0.38 [0.25, 0.60]	◆
	Total events	22	(0	45	1 70/			
	Test for overall effect: 7 -	4 28 (P	(P = 0.1)	27); 1" =	1/%			0.01 0.1 1 10 100
	Test for subgroup differen	20 (P < 1	• 8.20, d	lf = 1 (P	= 0.00	4), $I^2 = 82$	7.8%	Favours [GIC] Favours [Control]

Fig. 3. Meta-analysis of secondary caries incidence in teeth with GIC restorations vs amalgam or resin-composite restorations in the primary dentition (A) and permanent dentition (B).

The risk ratios of secondary caries in primary teeth when using different types of materials assess by the United States Public Health Service (USPHS) criteria. The risk of failure of the strategy in each row is compared against the ones in each column. * p < 0.05.

		Glass ionomer cement	restoration	Amalgam restoration	Resin-composite restoration
		Conventional	Resin-modified		
Glass ionomer cement restoration Conventional		-	0.89 [0.53,1.48]	1.79 [1.35, 2.39]*	1.03 [0.87, 1.23]
	Resin-modified	1.12 [0.67, 1.87]	-	1.33 [0.55, 3.21]	2.82 [0.97, 8.20]
Amalgam restoration		0.54 [0.40,0.72]*	0.75 [0.31,1.81]	-	-
Resin-composite restoration		0.97 [0.81,1.16]	0.35 [0.12,1.03]	-	-

Table 6

The risk ratios of secondary caries in permanent teeth when using different types of materials were assessed by the United States Public Health Service (USPHS) criteria. The risk of failure of the strategy in each row is compared against the ones in each column. * p < 0.05.

		Glass ionomer cement	restoration	Amalgam restoration	Resin-composite restoration
		Conventional	Resin-modified		
Glass ionomer cement restoration	Conventional	-	0.61 [0.13, 2.94]	5.02 [2.65, 9.50]*	0.75 [0.27, 2.12]
	Resin-modified	1.63 [0.34, 7.84]	-	-	1.67 [0.71, 3.94]
Amalgam restoration		0.20 [0.11, 0.38]*	-	-	-
Resin-composite restoration		1.33 [0.47,3.74]	0.60 [0.26,1.42]	-	-

•		Experim	ental	Contr	rol		Risk Ratio	Risk Ratio
А	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
	2.1.1 2-4 years							
	Daou et al. (2009)	3	23	3	21	2.7%	0.91 [0.21, 4.04]	
	Fuks et al. (2000)	0	9	1	9	1.3%	0.33 [0.02, 7.24]	
	Hilgert et al. (2014)	14	386	24	386	20.5%	0.58 [0.31, 1.11]	
	Taifour et al. (2002)	54	1086	77	805	75.5%	0.52 [0.37, 0.73]	H
	Subtotal (95% CI)		1504		1221	100.0%	0.54 [0.40, 0.72]	◆
	Total events	71		105				
	Heterogeneity: Chi ² =	0.68, df =	= 3 (P =	0.88); I ²	= 0%			
	Test for overall effect:	Z = 4.15	(P < 0.0	0001)				
	Total (95% CI)		1504		1221	100.0%	0.54 [0.40, 0.72]	•
	Total events	71		105				
	Heterogeneity: Chi ² =	0.68, df =	= 3 (P =	0.88); I ²	= 0%			
	Test for overall effect:	Z = 4.15	= 4.15 (P < 0.0001)					[Conventional CIC] [Amalgam]
	Test for subgroup diff	ferences: N	Not appl	icable				[conventional dicj [Analgani]

_		Experim	ental	Contr	rol		Risk Ratio	Risk Ratio	
в	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI	
-	3.1.1 2-4 years								
	Haveman et al. (2003) Subtotal (95% CI)	8	61 61	15	34 34	48.6% 48.6%	0.30 [0.14, 0.63] 0.30 [0.14, 0.63]		
	Total events	8		15					
	Heterogeneity: Not appl	icable							
	Test for overall effect: Z	= 3.18 (P	9 = 0.00	1)					
	3.1.2 ≥ 5 years								
	Mandari et al. (2003) Subtotal (95% CI)	3	274 274	16	156 156	51.4% 51.4%	0.11 [0.03, 0.36] 0.11 [0.03, 0.36]		
	Total events	3		16				-	
	Heterogeneity: Not appl	icable							
	Test for overall effect: Z	= 3.60 (P	9 = 0.00	03)					
	Total (95% CI)		335		190	100.0%	0.20 [0.11, 0.38]	◆	
	Total events	11		31					
	Heterogeneity: $Chi^2 = 2$.	.11, df = 1	1 (P = 0)	.15); I ² =	53%				ł
	Test for overall effect: Z	= 4.95 (P	9 < 0.00	001)				[Conventional CIC] [Amalgam]	,
	Test for subgroup differ	ences: Ch	$i^2 = 1.9$	7, df = 1	(P = 0)	.16), $I^2 =$	49.3%	[conventional ofc] [Annaigani]	

Fig. 4. Meta-analysis of secondary caries incidence in teeth with Conventional GIC restorations vs amalgam with defined follow-up period in the primary dentition (A) and permanent dentition (B).



Fig. 5. Meta-analysis of secondary caries incidence in teeth with resin-modified GIC restorations vs amalgam with defined follow-up period in the primary dentition.

examination for secondary caries detection. The early detection of secondary caries is important, as it allows for less invasive treatment options to prevent further loss of dental tissues [6]. However, it is difficult to diagnose secondary caries in clinical settings. Oral examination based on visual and tactile examination combined with radiological assessment is commonly used for clinical diagnosis of secondary caries. These techniques have certain limitations. It is difficult to distinguish secondary caries from marginal discolouration or so-called "amalgam tattoos" by visual and tactile examination [111,112]. Furthermore, for tactile examination, sharp probes can be inserted even into non-carious marginal gaps or overhangs, which may not reliably predict the presence of secondary caries [113]. Radiological assessment may be influenced by the radiopacity of the restorative material when testing secondary caries [114]. The detection methods and standards may affect the reported incidence of secondary caries. Brouwer et al. reported that visual and radiographic examination for secondary caries detection had similar sensitivities (mean values, 0.53 and 0.59, respectively) and specificities (mean values, 0.78 and 0.83, respectively). The tactile examination had low accuracy, with mean values of sensitivity and specificity of 0.28 and 0.86, respectively [115]. Therefore, the incidence of secondary caries in the included studies could be underestimated or overestimated. This limitation was caused by the nature of the difficulty in the detection of secondary caries with regular clinical procedures.

The studies included in this review used 3 types of criteria to assess secondary caries incidence. Modified United States Public Health Service (USPHS) criteria were adopted in 56 studies. FDI World Dental Federation (FDI) criteria were adopted in 5 studies. Danish Public Dental Health Service (Danish PDHS) criteria were adopted in 3 studies. The USPHS criteria are commonly used for the assessment of secondary caries around restorations [116]. The USPHS criteria score the restorations as Alpha for no secondary caries and Bravo for the existence of secondary caries. It was designed to reflect differences in acceptability (Yes/No) rather than in degrees of success [117]. USPHS is highly specific, which can avoid false positive diagnoses. On the contrary, using USPHS may lead to missing many secondary caries lesions [115]. The USPHS criteria were recommended to be used in long-term clinical studies [118]. The FDI criteria were recommended in clinical trials assessing dental restorations in terms of materials, operative technique and clinical practice [119]. The FDI criteria score the restoration in 5 levels. The restorations can be scored 1-5, where 1-3 means clinically acceptable, while 4 or 5 represents failure [120]. Kim et al. reported that FDI criteria present a high intra-examiner and a slight to fair inter-examiner reliability [121]. As FDI criteria have more scoring options, it gives more sensitive results than USPHS [118]. It should be noted that high sensitivity is often accompanied by a high risk of false positive diagnoses [115]. The FDI criteria were more suitable for short-term clinical evaluation of restorations than USPHS [122,123]. Danish Public Dental Health Service (Danish PDHS) criteria were used in oral health education programs [124]. The Danish PDHS criteria were adopted in 3 studies and the authors could not find more details about the criteria.

In this systematic review, a total of 64 studies were included. Among them, 59 studies were deemed eligible for meta-analysis. In the metaanalysis, we grouped studies that were as similar as possible in terms of methodology and outcome measures. It reduces the heterogeneity of the studies and enhances the certainty of the evidence [125]. Because of the difference in the assessment criteria, studies using USPHS and FDI criteria were analyzed separately to perform the meta-analysis. 5 studies were excluded from the meta-analysis. 4 of the excluded studies employed Danish Public Dental Health Service (Danish PDHS) criteria (3 studies) [26,27] [28] or radiograph (1 study) [29] for the diagnosis of secondary caries. However, the details of Danish PDHS and radiograph were not provided in the original studies. In addition, studies using different criteria to assess outcomes may introduce methodological heterogeneity into the meta-analysis. Therefore, we excluded these 4 articles to reduce the heterogeneity of the included studies and enhance the certainty of evidence. Additionally, 1 study [30] was excluded from meta-analysis because it was the only study that employed FDI criteria for the diagnosis of secondary caries in permanent teeth. As a result, we are unable to compare and synthesize the results of this study with other independent studies.

Some studies showed high performance bias and detection bias as these studies did not perform the blinding of participants and outcome assessment. Because the nature and presentation of the used materials are different and easily identified by participants and dentists. Meanwhile, some studies showed an unclear bias for selection bias and selection bias, as they did not report the random sequence generation and allocation concealment. It should be noted that the overall risk of bias in the study was not considered as a ground for meta-analysis exclusion.

The limitation of the review was that we analyzed the data based on the type of restorations, the type of dentition and the assessment criteria for secondary caries. Secondary caries is also influenced by several other factors such as the location of the lesion, the patient's caries risk, the patient's age, socioeconomic status, and operator's skills variation [126]. In addition, the subtypes or the brands of restorative material may also affect the incidence of secondary caries. However, due to the limited information provided in the included studies, we could not include these factors in our analysis.

This systematic review indicates the potential of GIC restoration in preventing secondary caries.

In this review, we evaluated the available clinical evidence of the secondary caries preventive effect of different types of restorations. Secondary caries are a major reason for the replacement of restorative materials worldwide [127]. Secondary caries development may be related to the type of restorative materials [128]. Several studies observed significantly more caries around resin-composite restorations



Fig. 6. Meta-analysis of secondary caries incidence in teeth with conventional GIC restorations vs resin-composite with defined follow-up period by USPHS in the primary dentition (A) and permanent dentition (B) and by FDI criteria in permanent dentition (C).

Α		Experim	ental	Contro	ol		Risk Ratio	Risk Ratio
_	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M–H, Fixed, 95% Cl
-	4.2.1 1 year							
	Ei-Houssei et al. (2019)	0	54	0	54		Not estimable	
	Casagrande et al. (2013)	0	38	0	94		Not estimable	
	Subtotal (95% CI)		92		148		Not estimable	
	Total events	0		0				
	Heterogeneity: Not applica	ble						
	lest for overall effect: Not	applicable	2					
	4.2.2 2-4 years							
	Dermata et al. (2018)	4	54	6	47	53.8%	0.58 [0.17, 1.93]	
	Andersson et al. (2006)	0	50	5	50	46.2%	0.09 [0.01, 1.60]	
	Subtotal (95% CI)		104		97	100.0%	0.35 [0.12, 1.03]	
	Total events	4		11				
	Heterogeneity: $Chi^2 = 1.51$	df = 1 (F	P = 0.22	?); $I^2 = 34$	%			
	Test for overall effect: Z =	1.91 (P =	0.06)					
	Total (95% CI)		196		245	100.0%	0 35 [0 12 1 03]	
	Total events	4	150	11	245	100.070	0.55 [0.12, 1.05]	
	Heterogeneity: $Chi^2 = 1.51$	df = 1 (F	P = 0.22	2): $I^2 = 34$	%			
	Test for overall effect: Z =	1.91 (P =	0.06)	,,				0.01 0.1 1 10 100
	Test for subgroup differen	ces: Not a	pplicab	le				[Resin-modified GIC] [Resin-composite]
		Experim	ental	Contr			Rick Ratio	Risk Ratio
в	Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Fixed, 95% Cl	M-H, Fixed, 95% CI
-	5.1.1 1 year							
	Gladys et al. (1998)	1	33	0	32	3.8%	2.91 [0.12, 68.95]	
	Van Dijken et al. (2019)	3	82	0	82	3.7%	7.00 [0.37, 133.41]	
	De Medeiros et al. (2015)	0	30	0	30		Not estimable	
	Perdiga [~] o et al. (2012)	0	26	2	27	18.2%	0.21 [0.01, 4.12]	
	De Oliveria et al. (2012)	0	41	0	40		Not estimable	
	Chinelatti et al. (2012)	0	29	1	58	7.5%	0.66.10.03 15.611	
	Santiago et al. (2003)	Ő	35	0 0	35	7.370	Not estimable	
	Subtotal (95% CI)	Ŭ	446	Ŭ	472	33.1%	1.37 [0.41, 4.63]	
	Total events	4		3				
	Heterogeneity: $Chi^2 = 3.13$, df = 3 (P	9 = 0.37); $I^2 = 4\%$				
	Test for overall effect: Z =	0.51 (P =	0.61)					
	5.1.2 2-4 years							
	Popescu et al. (2016)	0	73	0	74		Not estimable	
	Santiago et al. (2010)	Ő	35	ŏ	35		Not estimable	
	Onal et al. (2004)	0	24	0	106		Not estimable	
	Brackett et al. (2003)	0	37	0	37		Not estimable	
	Brackett et al. (2001)	0	32	3	32	25.9%	0.14 [0.01, 2.66]	· • • • • • • • • • • • • • • • • • • •
	Goncalves et al. (2021)	0	100	0	100		Not estimable	
	Ozgunaltay et al. (2002)	0	50	0	48		Not estimable	
	Folwaczny et al. (2001) Subtotal (95% CI)	0	433	0	115 547	25.9%	Not estimable	
	Total events	0	433	3	547	23.370	0.14 [0.01, 2.00]	
	Heterogeneity: Not applica	ble		5				
	Test for overall effect: Z =	1.30 (P =	0.19)					
	$5.1.4 \ge 5$ years							
	Alessandro et al. (2003)	0	16	0	16	10.10	Not estimable	
	Van Dijken et al. (1999)	0	41	1	49	10.1%	0.40 [0.02, 9.49]	
	Facundes et al. (2001)	0	23	2	49	10.9%	0.24 [0.01, 4.82]	·
	Subtotal (95% CI)	0	121	1	127	41.0%	0.26 [0.04, 1.56]	
	Total events	0		4				
	Heterogeneity: $Chi^2 = 0.10$, df = 2 (P)	9 = 0.95); $I^2 = 0\%$				
	Test for overall effect: Z =	1.47 (P =	0.14)					
	Total (05% CI)		1000		1146	100.0%	0.60 [0.25 1.42]	
	Total events	4	1000	10	1140	100.0%	0.00 [0.23, 1.42]	
	Heterogeneity: $Chi^2 = 5.96$	4 df = 7 (P	= 0.54	10^{11}				· · · · · · · · · · · · · · · · · · ·
	Test for overall effect: Z =	1.17 (P =	0.24)	,,, = 0/0				0.01 0.1 1 10 100
	Test for subgroup differen	ces: Chi ² =	= 3.48,	df = 2 (P	= 0.18), $I^2 = 42$	6%	[kesin=modified GIC] [kesin=composite]

Fig. 7. Meta-analysis of secondary caries incidence in teeth with resin-modified GIC restorations vs resin-composite with defined follow-up period in the primary dentition (A) and permanent dentition (B).

۸		Experime	ntal	Contro	bl .		Risk Ratio	Risk Ratio
Α_	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M–H, Fixed, 95% Cl
	2.3.1 1 year Mufti et al. (2014) Subtotal (95% CI)	9	20 20	13	20 20	70.5% 70.5%	0.69 [0.39, 1.24] 0.69 [0.39, 1.24]	-
	Total events Heterogeneity: Not app Test for overall effect:	9 blicable Z = 1.24 (P = 0.22	13 2)				
	2.3.2 2-4 years							
	Daou et al. (2009) Hubel et al. (2003)	3	23	4	23	21.7%	0.75 [0.19, 2.98]	
	Espelid et al. (1999) Subtotal (95% CI)	4	39 118	1	44 123	5.1% 29.5%	4.51 [0.53, 38.68] 2.16 [0.82, 5.70]	
	Total events Heterogeneity: Chi ² = 3 Test for overall effect: 3	11 3.64, df = Z = 1.55 (2 (P = 0) P = 0.12	5 0.16); I ² : 2)	= 45%			
	Total (95% CI)		138		143	100.0%	1.12 [0.67, 1.87]	+
	Total events	20		18				
	Heterogeneity: Chi ² = 6 Test for overall effect: Test for subgroup diffe	6.59, df = Z = 0.45 (erences: Cl	3 (P = 0) P = 0.6 $hi^2 = 3.5$	0.09); I ² = 5) 88, df =	= 54% 1 (P =	0.05), I ² =	= 74.2%	0.01 0.1 1 10 100 [Conventional GIC] [Resin-modified GIC]
D	Study on Submoun	Experin	nental	Cont	rol	Waiaha	Risk Ratio	Risk Ratio
Р_	3 3 1 1 year	Events	Total	Events	Total	weight	M-H, Fixed, 95% Cl	м-н, Fixed, 95% Сі
	Dulgergil et al. (2005)	0	30	0	52		Not estimable	
	Gladys et al. (1998) Subtotal (95% CI)	1	122 161	1	33 85	78.5% 78.5%	0.27 [0.02, 4.21] 0.27 [0.02, 4.21]	
	Total events Heterogeneity: Not app Test for overall effect: 2	1 olicable Z = 0.93 (l	P = 0.35	1				
	3.3.2 2-4 years							
	Ercan et al. (2009) Subtotal (95% CI)	2	39 39	0	52 52	21.5% 21.5%	6.63 [0.33, 134.20] 6.63 [0.33, 134.20]	
	Total events Heterogeneity: Not app	2 licable		0				
	Test for overall effect:	Z = 1.23 (1	P = 0.22	?)				
	Total (95% CI)		200		137	100.0%	1.63 [0.34, 7.84]	
	Total events Heterogeneity: Chi ² = 2	3 2.48, df =	1 (P = 0)	1).12); I ² =	= 60%			
	Test for overall effect: 2 Test for subgroup diffe	Z = 0.61 (learning contracts)	P = 0.54 $ni^2 = 2.3$	4) 87. df = 1	1 (P = 0	$(1, 12), 1^2 =$	57.8%	[Conventional GIC] [Resin-modified GIC]
				.,		,, .		
0		Experin	nental	Cont	rol		Risk Ratio	Risk Ratio
U -	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
	Mc comb et al. (2002) Subtotal (95% CI)	0	4 4	1	9 9	100.0% 100.0%	0.67 [0.03, 13.60] 0.67 [0.03, 13.60]	
	Total events	0		1	_		_	
	Heterogeneity: Not app Test for overall effect: 2	olicable Z = 0.26 (I	P = 0.79	9)				
	Total (95% CI)		4		9	100.0%	0.67 [0.03, 13.60]	
	Total events	0		1				
	Heterogeneity: Not app	licable						0.01 0.1 1 10 100

Fig. 8. Meta-analysis of secondary caries incidence in teeth with conventional GIC restorations vs resin-modified GIC with defined follow-up period by USPHS in primary dentition (A) and permanent dentition (B) and by FDI criteria in permanent dentition (C).

than amalgam restorations [3]. The result of this review affirmed the inhibitory effect of GIC on secondary caries compared with amalgam or resin-composite restorations, mainly amalgam restorations.

Test for overall effect: Z = 0.26 (P = 0.79)

Test for subgroup differences: Not applicable

5. Conclusion

GIC restorations showed a better preventive effect on secondary caries compared with amalgam restorations with a follow-up period of 2–6 years. GIC restorations showed a similar preventive effect on secondary caries compared to resin-composite restorations in permanent

[Conventional GIC] [Resin-modified GIC]

and primary teeth with a follow-up period of 1-7 years.

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