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MESTRADO INTEGRADO EM MEDICINA DENTÁRIA

CONVENTIONAL VERSUS NON-CONVENTIONAL CARIES REMOVAL IN DEEP LESIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Trabalho submetido por
Emile Laville
para a obtenção do grau de Mestre em Medicina Dentária

julho 2026

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Trabalho orientado por
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A seguinte tabela apresenta diferentes opções de partilha de dados, incluindo exemplos de formatos e níveis de acessibilidade. Deverá selecionar a(s) opção(ões) que melhor se adequa(m) ao seu projeto, assegurando o cumprimento das diretrizes éticas e científicas aplicáveis.

Tabela 1: Exemplos de declarações de disponibilidade de dados. Onde aparece [nome do repositório, por exemplo, "pure"] deve ser preenchido

Disponibilidade de dados	**Modelo de declaração de disponibilidade de dados**	**Política de partilha**	**Assinale com "x"**
Dados disponíveis num repositório público que emite conjuntos de dados com DOIs	Os dados que apoiam as conclusões deste estudo estão disponíveis em [nome do repositório, por exemplo, "pure"] em http://doi.org/[doi], número de referência [número de referência].	Partilha geral sem pedido	

Disponibilidade de dados	**Modelo de declaração de disponibilidade de dados**	**Política de partilha**	**Assinale com "x"**
Dados abertamente disponíveis num repositório público que não emite DOIs	Os dados que apoiam as conclusões deste estudo estão disponíveis em [nome do repositório] em [URL], número de referência [número de referência].	Partilha geral sem pedido	
Dados derivados de recursos do domínio público	Os dados que apoiam as conclusões deste estudo estão disponíveis em [nome do repositório] em [URL/DOI], número de referência [número de referência]. Estes dados foram obtidos a partir dos seguintes recursos disponíveis no domínio público: [listar recursos e URLs]	Partilha geral sem pedido	
Dados disponíveis no artigo ou nos seus materiais suplementares	Os autores confirmam que os dados que suportam as conclusões deste estudo estão disponíveis no artigo [e/ou] nos seus materiais suplementares.	Básico, partilhar a pedido	**x**
Dados gerados numa instalação central de grande escala, disponíveis mediante pedido	Os dados em bruto foram gerados em [nome da instalação]. Os dados derivados que suportam as conclusões deste estudo estão disponíveis junto do autor correspondente [iniciais], mediante pedido.	Básico, partilhar a pedido	

Disponibilidade de dados	Modelo de declaração de disponibilidade de dados	Política de partilha	Assinale com “x”
Embargo dos dados devido a restrições comerciais	Os dados que suportam os resultados estarão disponíveis em [nome do repositório] em [URL / ligação DOI] após um embargo de [6 meses] a partir da data de publicação para permitir a comercialização dos resultados da investigação.	Básico, Partilhar a pedido	
Dados disponíveis a pedido devido a restrições de privacidade/éticas	Os dados que sustentam as conclusões deste estudo estão disponíveis mediante pedido ao autor correspondente, [iniciais]. Os dados não estão disponíveis ao público devido a [restrições, por exemplo, o facto de conterem informações que podem comprometer a privacidade dos participantes na investigação].	Básico, Partilhar a pedido	
Dados sujeitos a restrições de terceiros	Os dados que suportam as conclusões deste estudo estão disponíveis [junto de] [terceiros]. Aplicam-se restrições à disponibilidade destes dados, que foram utilizados sob licença para este estudo. Os dados estão disponíveis [através dos autores / no URL] com a permissão de [terceiros].	Básico, Partilhar a pedido	

Disponibilidade de dados	Modelo de declaração de disponibilidade de dados	Política de partilha	Assinale com "x"
Dados disponíveis a pedido dos autores	Os dados que suportam as conclusões deste estudo estão disponíveis junto do autor correspondente, [iniciais do autor], mediante pedido razoável.	Básico, Partilhar a pedido	
Partilha de dados não aplicável - não foram gerados novos dados	A partilha de dados não é aplicável a este artigo, uma vez que não foram criados ou analisados novos dados neste estudo.	-	
Dados não digitais disponíveis	Os dados não digitais que suportam este estudo são conservados em [adicionar local].	Básicos	
Dados não disponíveis devido a restrições [éticas/legais/comerciais	Devido à natureza da investigação, os dados de apoio [éticos/legais/comerciais] não estão disponíveis.	-	
Dados não disponíveis - consentimento do participante	Os participantes neste estudo não deram consentimento escrito para que os seus dados fossem partilhados publicamente, pelo que, devido à natureza sensível da investigação, os dados de apoio não estão disponíveis.	-	

O Orientando: Emile Laville Data: 11/06/2001

O Orientador: _____ Data: 11 /*06*/2026

O Coorientador (se aplicável): _____ Data: __ /__/_____

RESUMO

Introdução: A gestão das lesões cariosas profundas constitui um desafio importante em medicina dentária devido ao risco de exposição pulpar. Se a remoção completa da cárie foi durante muito tempo considerada a referência, abordagens conservadoras, tais como a remoção seletiva de cárie e a técnica *stepwise*, foram desenvolvidas com o objetivo de preservar a vitalidade pulpar.

Material e método: O objetivo deste estudo foi comparar a remoção completa de cárie (CCR), a remoção seletiva de cárie (SCR) e a remoção stepwise (SWR) no tratamento de lesões cariosas profundas através de uma revisão sistemática com meta-análise. Realizada segundo PRISMA e registada no PROSPERO (CRD420261321894), incluiu ensaios clínicos randomizados identificados através de várias bases de dados. A análise estatística foi conduzida em "R" com a utilização de um modelo multivariado de efeitos aleatórios (metafor), com estimativa dos efeitos em Risk Ratios (RR) e análises de sensibilidade.

Resultados: Nove pontos de comparação foram incluídos na meta-análise. Não foi observada nenhuma diferença estatisticamente significativa entre as técnicas. Comparativamente à remoção completa de cárie, o RR foi de 1,06 (IC95%: 0,25–4,50) para a remoção seletiva e de 1,29 (IC95%: 0,34–4,83) para a técnica stepwise. Estes resultados foram consistentes apesar de uma heterogeneidade importante.

Discussão: Estes resultados não permitem estabelecer uma hierarquia clara entre as técnicas, mas são coerentes com a literatura científica atual segundo a qual o controlo da lesão depende principalmente da atividade do biofilme e da qualidade do selamento restaurador. Esta ausência de diferença explica-se provavelmente pela imprecisão das estimativas e pela heterogeneidade dos dados disponíveis.

Conclusão: As abordagens conservadoras constituem uma alternativa fiável à remoção completa de cárie no tratamento de lesões cariosas profundas, permitindo reduzir o risco de exposição pulpar sem comprometer o sucesso clínico, embora o nível atual de evidência ainda seja insuficiente para demonstrar a sua superioridade.

Palavras-chave: Remoção de cárie; seletiva; stepwise

ABSTRACT

Introduction: The management of deep carious lesions constitutes a major challenge in dentistry due to the risk of pulp exposure. While complete caries removal has long been considered the standard, conservative approaches, such as selective caries removal and the stepwise technique, have been developed to preserve pulp vitality.

Materials and methods: This study aimed to compare complete caries removal (CCR), selective caries removal (SCR), and stepwise removal (SWR) for treating deep carious lesions through a systematic review and meta-analysis. Conducted according to PRISMA and registered in PROSPERO (CRD420261321894), the study included randomised clinical trials identified across several databases. The statistical analysis was performed in “R” using a multivariate random-effects model (metafor), with effect estimation expressed as Risk Ratios (RR) and sensitivity analyses.

Results: Nine comparison time points were included in the meta-analysis. No statistically significant difference was observed between the techniques. Compared with complete caries removal, the RR was 1.06 (95% CI: 0.25–4.50) for Selective caries Removal and 1.29 (95% CI: 0.34–4.83) for the Stepwise technique. These results were consistent despite substantial heterogeneity.

Discussion: These results do not allow for a clear hierarchy among the techniques but are consistent with the current scientific literature, which indicates that lesion control mainly depends on biofilm activity and the quality of the restorative seal. This absence of difference is probably due to the imprecision of the estimates and the heterogeneity in the available data.

Conclusion: Conservative approaches represent a reliable alternative to complete caries removal for managing deep carious lesions, reducing the risk of pulp exposure without compromising clinical success, although the current level of evidence remains insufficient to establish their superiority.

Keywords: Caries removal; selective; stepwise

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List of Abbreviations

CCR	Complete Caries Removal
SWR	Stepwise Removal technique
SCR	Selective Caries Removal
FDI	World Dental Federation
RCT	Randomized controlled trial
PROSPERO	International prospective register of systematic reviews
RR	Risk Ratio
95% CI	95% Confidence Interval
NMA	Network meta-analysis
REML	Restricted Maximum Likelihood
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses

I. Introduction

Dental caries is a multifactorial and chronic disease involving the interaction of multiple biological, individual, and social risk factors (Takahashi & Nyvad, 2011; Warreth, 2023). According to the Global Burden of Disease 2021, untreated dental caries in permanent teeth is the most common health condition, and oral diseases affect nearly 3.7 billion people (Benzian & Beltrán-Aguilar, 2025). According to the World Health Organisation (2022), dental caries is described as a disease with significant functional, aesthetic, economic, and social consequences.

In his work *Operative Dentistry*, G.V. Black described the different classes of cavities by location. In this work, he stated that carious tissue must be completely removed to ensure successful treatment. This invasive approach reflected an era in which restorative materials were neither adhesive nor biocompatible, necessitating extensive removal of weakened dental tissues for mechanical retention (Black, 1908; Mount, 2001).

From the late twentieth century onward, several studies challenged this invasive philosophy. The pioneering work of Fusayama in 1979 demonstrated that carious dentin is not uniform and consists of two distinct layers: an outer infected layer and an inner “affected” layer with remineralisation potential (Fusayama, 1979a). These findings were confirmed by in vivo ultrastructural and microbiological observations, which highlighted the fundamental difference between infected and affected dentin, showing that only the infected dentin requires complete removal (Massara et al., 2002).

To reinforce this shift in caries management, minimally invasive dentistry emerged, aiming to preserve healthy dental structures whenever possible (Mount, 2001; Tyas et al., 2000). Furthermore, studies have shown that aggressive caries removal may lead to larger, more fragile restorations, thereby reducing long-term durability (Pitts, 2004).

Infected dentin is the outer layer of carious dentin and is characterised by advanced demineralisation, irreversible destruction of the collagen matrix, and heavy bacterial colonisation, with no potential for remineralisation (E. A. M. Kidd, 2004; Massara et al., 2002). It has a soft, often wet consistency and can be easily

removed with manual instruments such as a dentine excavator (Thompson et al., 2008). From a microbiological perspective, infected dentine is dominated by Streptococcus mutans, Actinomyces spp., and Lactobacillus spp. However, it has been demonstrated that any bacteria with acidogenic and aciduric properties and high metabolic activity can contribute to caries progression (Banerjee et al., 2000; Philip & Suneja, 2023; Takahashi & Nyvad, 2011).

In contrast, affected dentin corresponds to the inner layer of carious dentin, located closer to the pulp (Fusayama, 1979b). It is partially demineralised but retains an almost intact collagen structure (Banerjee et al., 2000). It exhibits a lower bacterial load and a real potential for remineralisation, particularly when hermetically sealed with a biocompatible material (Conrado, 2004). Due to its higher collagen content and greater mineralisation, affected dentin is clinically characterised by a firm consistency, a darker brown colour, and resistance to manual caries removal (Warreth, 2023).

Although clinical definitions vary in the literature, deep carious lesions are generally understood as lesions approaching the pulp and associated with an increased risk of pulp exposure (Duncan et al., 2019). Due to this proximity, treating deep carious lesions carries a risk of pulp exposure. For this review, deep carious lesions were operationally defined as lesions radiographically extending into at least half of the dentine without signs of irreversible pulp disease.

Complete caries removal consists of eliminating all altered dentinal tissues until sound, firm, and dry dentin is obtained, both at the peripheral walls and at the cavity floor (Thompson et al., 2008). This approach is historically rooted in the principles of conventional restorative dentistry, which held that complete removal of carious dentin was essential to prevent caries recurrence and ensure long-term restorative success (Black, 1908).

From an operative standpoint, complete caries removal relies mainly on clinical and tactile criteria, such as dentin consistency, resistance to instrumentation, and visual appearance (Bjørndal et al., 2010). Dentin is considered suitable for restoration when it presents a firm, dry texture and resistance to probing, indicating removal of both infected and affected dentin (E. A. M. Kidd, 2004). This strategy aims to obtain homogeneous dentin, and mechanically retentive cavity

forms, in line with the restorative principles available at that time (Thompson et al., 2008).

This shift toward minimally invasive dentistry was also facilitated by the development of adhesive restorative materials. Unlike traditional mechanically retentive cavity designs, adhesive restorations allow greater preservation of sound tooth structure and rely on an adequate peripheral seal. In deep carious lesions, this reinforces the rationale for selective or stepwise caries removal, as lesion control depends not only on dentine removal but also on sealing residual bacteria from nutrient supply (Innes et al., 2016; E. A. M. Kidd, 2004; Ricketts et al., 2013).

In the context of deep carious lesions, the systematic application of conventional caries removal raises significant biological concerns. Several studies have shown that complete removal of carious dentin in deep lesions is associated with a high risk of pulp exposure, even in the absence of clinical signs of pulpal pathology (Dammaschke, 2025; Figundio et al., 2023; Leksell et al., 1996). Such exposure profoundly alters therapeutic management and may compromise long-term pulpal prognosis.

Pulp exposure resulting from CCR often necessitates more invasive pulp treatments, such as pulpectomy, pulpotomy, or root canal treatment. However, several studies have demonstrated that these interventions are associated with variable success rates and reduced tooth survival compared with teeth retaining an intact vital pulp (Landys Borén et al., 2015).

Thus, although conventional caries removal allows maximal removal of carious tissue, it entails a non-negligible biological cost in deep lesions.

Moreover, CCR does not provide a clearly demonstrated clinical benefit in terms of caries control or restorative longevity compared with more conservative approaches, even when effective restorative sealing is achieved (Ricketts et al., 2013). These observations have led to a progressive reconsideration of this strategy as a systematic approach in the management of deep carious lesions (Bjørndal, 2002).

Selective caries removal, also referred to as SCR, is a conservative operative technique for the management of deep carious lesions (Innes et al., 2016;

Thompson et al., 2008). It is based on a differentiated removal of infected and affected dentin according to their location within the cavity: infected dentin is completely removed from the peripheral walls, while residual carious dentin is intentionally preserved at the cavity floor near the dentin–pulp complex (Banerjee et al., 2000; Innes et al., 2016; Maltz et al., 2002). This residual dentin presents a firm or slightly elastic consistency, resisting manual caries removal, without seeking hard, dry, or non-pigmented dentin (Innes et al., 2016).

This technique aims to preserve pulp vitality while enabling a more conservative and biologically oriented approach to patient management.

The fundamental principle of selective caries removal assumes that caries progression can be arrested when residual dentin is isolated from the oral environment by an effective restorative seal, thereby depriving bacteria of nutritional substrates (E. A. M. Kidd, 2004; Paddick et al., 2005). However, the boundary between infected and affected dentin is subjective and relies on visual and tactile criteria (Schwendicke et al., 2013).

This strategy is performed in a single visit, with immediate placement of the definitive restoration, thereby avoiding cavity re-entry and reducing the risk of secondary pulp exposure (Maltz et al., 2018). One objective of selective caries removal is to avoid iatrogenic pulp exposure during deep caries removal (Innes et al., 2016). Thus, partial caries removal, by leaving a dentin layer, helps protect against pulp exposure by limiting cavity depth (Bjørndal et al., 2017; Franzon et al., 2014).

The main limitation of this method lies in the subjectivity of differentiating infected from affected dentin and in the visual and tactile criteria used by clinicians (Banerjee et al., 2000). Furthermore, the quality of the restorative seal is crucial for long-term success, making it a determining factor for restoration longevity (Maltz et al., 2002; Mertz-Fairhurst et al., 1998).

Thus, selective caries removal represents a biologically sound and clinically validated strategy aimed at preserving pulpal vitality while ensuring effective control of caries disease in the management of deep carious lesions (Innes et al., 2016; Schwendicke et al., 2013). Numerous studies have shown that following definitive restoration, biofilm inactivation and arrest of caries progression occur

as a result of reduced bacterial load (Maltz et al., 2002; Paddick et al., 2005). In addition, radiographic success rates are comparable to those of complete caries removal (Maltz et al., 2002; Schwendicke et al., 2013).

SWR is a conservative strategy for managing deep carious lesions to limit the risk of pulp exposure. It is based on an intentionally incomplete initial caries removal at the cavity floor, followed by provisional sealing and a planned second intervention aimed at further caries removal and definitive restoration (Bjørndal et al., 2017; Ricketts et al., 2013).

This technique relies on reducing bacterial load and carious activity through provisional sealing. Several microbiological studies have demonstrated a significant decrease in viable bacteria after sealing, associated with a change in the consistency of residual dentin, which becomes firmer at the second visit (Maltz et al., 2002). This interval also allows an adaptive pulpal response, including stimulation of tertiary dentin formation, which contributes to increased residual dentin thickness (Smith et al., 2001).

Tertiary dentin is newly formed dentin produced by the dental pulp in response to carious or operative aggression (Kalyva et al., 2010). It constitutes a biological defence mechanism that increases the distance between the pulp and the insult, thereby protecting the dentin–pulp complex (Smith et al., 2001). Depending on stimulus intensity, it may be reactionary or reparative (Smith, 2002).

Clinically, the second appointment is classically performed after a delay of 6 to 12 months according to published protocols, during which the cavity is re-entered, caries removal is continued, and a definitive restoration is placed (Bjørndal et al., 2010; Leksell et al., 1996). However, this second stage represents a moment of iatrogenic risk of pulp exposure and requires an additional appointment, with an associated risk of patient loss to follow-up (Ricketts et al., 2013).

Provisional sealing plays a central role by isolating residual carious dentin from the oral environment between the two visits. An effective seal limits nutrient diffusion to residual bacteria, thereby reducing bacterial load and progressively inactivating carious activity (Bjørndal & Larsen, 2000; Maltz et al., 2002). Several studies have shown that sealing effectiveness is a determining factor in lesion stabilization and changes in dentin consistency at re-entry, independently of

complete initial carious dentin removal (Alves et al., 2017; E. Kidd et al., 2015; Paddick et al., 2005).

Materials used for provisional sealing, such as glass ionomer cements or calcium silicate–based cements, are preferred for their adhesive properties, biocompatibility, and ability to provide sufficient sealing during the inter-stage period (Frencken et al., 1996; Talabani et al., 2020).

Although SWR has demonstrated its ability to reduce the risk of pulp exposure compared with one-step CCR, several studies have questioned the need for the second removal stage, emphasising that effective sealing alone may be sufficient to stabilise the lesion (Ricketts et al., 2013; Schwendicke et al., 2013). These limitations have contributed to the emergence of single-visit conservative strategies such as selective caries removal.

The management of deep carious lesions has evolved from an approach historically based on complete carious dentin removal toward more conservative strategies aimed at preserving pulpal vitality. Numerous clinical trials and reviews have shown that non-conventional approaches, such as SCR or SWR, significantly reduce the risk of pulp exposure compared with CCR, without compromising caries control when adequate restorative sealing is achieved (Bjørndal et al., 2010; Maltz et al., 2018; Schwendicke et al., 2013). These findings have progressively challenged the systematic use of complete caries removal in deep carious lesions (Thompson et al., 2008).

Despite the large number of publications, the literature remains marked by substantial heterogeneity in protocols, particularly regarding the definition of deep carious lesions, criteria for caries removal endpoints, and the restorative materials used, thereby limiting comparability of results (Philip & Suneja, 2023; Ricketts et al., 2013).

Institutional and One Health framing

From a One Health perspective, the management of deep carious lesions extends beyond operative dentistry alone, as oral disease is closely linked to human health, behavioural and social determinants, long-term health trajectories, treatment burden, and broader patterns of healthcare use. Strategies that preserve pulp vitality and reduce overtreatment may therefore be understood

within a more integrated, preventive, and resource-conscious model of health (Edwards et al., 2021).

Within the institutional research framework, this thesis may be positioned primarily within the Research Group “Non-Communicable Disease Burden”, as dental caries is a highly prevalent chronic oral disease with important functional, social, and healthcare-related consequences. It also contributes to a line of research focused on minimally invasive restorative dentistry, pulp vitality preservation, and evidence synthesis for clinical decision-making (Innes et al., 2016).

Contribution to the Sustainable Development Goals.

This thesis primarily contributes to Sustainable Development Goal 3 (Good Health and Well-being) by presenting evidence-based strategies to preserve pulp vitality, reduce treatment invasiveness, and support long-term oral health (*Goal 3: Ensure Healthy Lives and Promote Well-Being for All at All Ages,* s. d.). It may also have indirect relevance to the responsible use of healthcare resources (Maltz et al., 2018).

Therefore, the present systematic review was undertaken to clarify the current state of knowledge, distinguish between different caries removal strategies, and rigorously evaluate their clinical impact, particularly regarding pulpal vitality and restorative success.

II. Materials and methods

Protocol and registration

This review was registered in PROSPERO (CRD420261321894). It was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses of 2020 (PRISMA 2020) statement and PRISMA extension for Network Meta-Analyses (PRISMA-NMA).

Eligibility criteria

This systematic review leverages the PICO method to structure the research question.

- **Population** (P): Patients presenting vital permanent teeth affected by deep carious lesions.
- **Intervention** (I): Non-conventional caries removal of deep carious lesions, including:
    - I1: Stepwise Removal technique
    - I2: Selective Caries Removal
- **Comparator** (C): Conventional caries removal, defined as the complete removal of infected and affected dentin performed in a single session.
- **Outcomes** (O) :
    - The primary outcome was treatment failure, defined as a composite of loss of pulp vitality and/or clinical-radiographic failure, according to the reporting criteria of the original studies. Intraoperative pulp exposure was not included in the primary composite outcome when it was excluded from the success analysis of the original study. Instead, pulp exposure was recorded separately and interpreted narratively as an indicator of treatment invasiveness. Therefore, the quantitative meta-analysis was based on post-operative treatment failures reported during follow-up
    - Secondary outcomes included pulp vitality preservation, clinical success, and radiographic success, when reported separately.

Based on this framework, the following research question was formulated:

Does non-conventional caries removal, including selective caries removal and stepwise caries removal, differ from conventional complete caries removal in the management of deep carious lesions in terms of pulp vitality preservation, clinical success, and radiographic success?

Literature Search Strategy

A systematic literature review was conducted to identify relevant studies. The following keywords were used: *"selective caries removal"*, *"complete caries removal"*, *"stepwise"*, *"deep caries"*, and *"vital pulp therapy"*.

The following electronic databases were searched: **PubMed, Scopus, B-on, Embase**, and the **Cochrane Library** from database inception until 20 January 2026. The last search was performed on 20 January 2026. To optimise the search strategy and combine the different terms, the **2D Search** (https://www.2dsearch.com/) tool was used to develop the following search algorithm:

("deep caries lesion" OR "deep cavities" OR "profound carious lesions" OR "deep caries") AND (("partial caries excavation" OR "selective caries removal" OR "selective excavation") OR ("complete caries excavation" OR "non-selective caries removal" OR "total caries removal") OR ("stepwise excavation"))

The search strategy was adapted to the syntax of each database, and the database-specific search strategies are presented in Annex 1.

This strategy aimed to include all studies in English, Portuguese, and French that compared different caries removal techniques for deep carious lesions, both conventional and non-conventional, with no restriction on publication year. Filters for human studies and randomised clinical trials were applied when available within each database. When database filters were not available, eligibility criteria were applied during the screening phase.

Additional searches included backwards and forward citation tracking of all included studies.

Study Selection Process

- *Inclusion Criteria*

Studies were included in this systematic review when they met all of the following five criteria:

- Human patients of any age presenting permanent teeth affected by deep carious lesions, defined as lesions involving at least half of the dentin thickness or appearing radiographically close to the pulp.
- Randomised clinical trials.
- Evaluation of pulp vitality and/or clinical and radiographic outcomes following conventional or non-conventional caries removal of deep carious lesions.
- Studies published in Portuguese, English, or French.
- Studies with a minimum follow-up of 12 months were included. When multiple reports or publications referred to the same study family, eligible follow-up timepoints were retained for the primary multivariate synthesis, as the model accounted for within-family dependence. In addition, sensitivity analyses were performed using only the longest follow-up per study family.

- *Exclusion Criteria*

Studies reporting on teeth with irreversible pulpitis, pulp necrosis, or previous endodontic treatment were excluded. Studies including primary teeth and non-randomised studies were also excluded.

All search results were imported into Rayyan (Ouzzani et al., 2016), and duplicates were removed. Two reviewers independently screened titles and abstracts, and, in a second phase, full texts, against predefined criteria. A third reviewer resolved disagreements. The study selection process followed the PRISMA 2020 guidelines (Page et al., 2021).

Data Collection and Extraction Process

Data extraction from the selected studies was performed independently by two reviewers using a standardised data extraction form (EL; PrAP). The extraction sheet was piloted on a subset of included studies to ensure clarity and completeness before full data extraction. In cases where discrepancies could not be resolved through discussion between the two reviewers, they were settled by

consultation with a third reviewer (PrPM). The collected information included the general characteristics of the studies (i.e., authors, country, and year of publication), study design, number of teeth included in the analysis, diagnosis of the teeth studied, interventions performed, follow-up duration, and number of teeth lost to follow-up.

The main outcomes reported by the studies were also collected, particularly those related to pulp vitality and clinical and radiographic success criteria.

A data extraction table was subsequently developed to construct the comparison network between the different interventions. When data were incomplete or follow-up was lost, analyses were conducted using the available data reported in the original studies.

Data for each therapeutic technique were used to estimate the intervention effect using relative risk (RR) with corresponding 95% confidence intervals (95% CI).

The treated tooth was considered the unit of analysis, as outcomes in the included trials were generally reported at the tooth level. Therefore, when several teeth were treated in the same patient, each tooth was analysed as an independent intervention. This approach was necessary to remain consistent with the structure of the available data, though it may not fully account for potential clustering of multiple teeth within a single patient.

The transitivity assumption implies that indirect comparisons are valid only when studies comparing different treatment pairs are sufficiently similar in their clinical and methodological characteristics. Thus, if treatment A is compared with B and B with C under comparable conditions, an indirect inference between A and C can be considered appropriate.

Risk of Bias

The risk of bias of the included studies was assessed using the ROB 2.0 tool (Sterne et al., 2019) developed by the Cochrane Collaboration, which enables a structured, systematic evaluation of randomised clinical trials.

The ROB 2.0 tool is structured into five domains, each corresponding to a specific type of potential bias evaluated within each study. For each domain, several signalling questions are asked, with the following predefined response options:

Yes (Y), Probably Yes (PY), No (N), Probably No (PN), Not Applicable (NA), or No Information (NI).

Based on the responses to these questions, the Risk of Bias for each domain is classified as *Low Risk, Some Concerns, or High Risk*. A global risk-of-bias judgment is then assigned to each study, taking into account all evaluated domains. Two independent reviewers evaluated all the studies; any disagreements were resolved through discussion and, when necessary, consultation with a third reviewer. The final risk-of-bias judgements were entered into the RobVIS web application (McGuinness & Higgins, 2021) to generate the traffic-light plot illustrating domain-level and overall risk of bias. The RoB 2 domains assessed in this review are summarized in Table 1.

Table 1: Description of the different domains of ROB 2.0

ROB 2.0 domain	**Description**	**Objective of the evaluation**
Domain 1: Bias arising from the randomization process	Assesses how the randomisation was performed and whether allocation to groups was unpredictable	To verify that the compared groups were equivalent at baseline
Domain 2: Bias due to deviations from intended interventions	Evaluates whether participants received the intended intervention and whether deviations could have influenced the outcomes	To assess the impact of protocol deviations on the results
Domain 3: Bias due to missing outcome data	Examines the extent, handling, and justification of losses to follow-up	To determine whether missing data could bias the results
Domain 4: Bias in measurement of the outcome	Assesses how outcomes were measured and whether outcome assessors were blinded to the intervention	To verify the objectivity and reliability of outcome measurements

Domain 5: Bias in the selection of the reported result	Evaluates whether the reported outcomes correspond to those pre-specified in the study protocol	To detect potential selective reporting bias
Overall risk of bias judgment	Synthesis of the five ROB 2.0 domains	To classify the study as Low Risk, Some Concerns, or High Risk of Bias

***Abbreviation**: Rob 2.0: Risk of Bias 2.0*

The criteria used to derive the overall risk-of-bias judgement are presented in Table 2.

Table 2 : Description of the choice of risk of bias

Risk of bias	Interpretation	Within a trial
Low risk of bias	Bias, if present, is unlikely to alter the results seriously	Low risk of bias for all key domains
Some concerns	A risk of bias that raises some doubts about the results	At least one domain has concerns, but none are at high risk.
High risk of bias	Bias may seriously alter the results	High risk of bias for one or more key domains

Data Analysis

All analyses were conducted in “R” using a reproducible script-based workflow. Data import, cleaning, reshaping, and tabulation were performed using *thereadr*, *dplyr*, *tidyr*, *purrr*, *janitor*, and *tibble* packages, while figures were generated with *ggplot2*. Meta-analytic models were fitted using the *metafor* package. Missing covariate values coded as "NA" were treated as missing and were not imputed. Percentage variables were converted to numeric

format, and follow-up duration was retained as a continuous variable and additionally categorised descriptively as ≤18 months, 19–36 months, and >36 months.

Before model fitting, treatment network geometry was assessed descriptively. The network was considered geometrically complete when direct evidence was available for all three pairwise comparisons (*CCR* vs. *SCR*, *CCR* vs. *SWR*, and *SCR* vs. *SWR*). Exchangeability and transitivity were also evaluated descriptively by comparing the distribution of follow-up duration, mean age, and region across the direct contrasts. In practical terms, this assessment aimed to verify whether the different treatment comparisons were sufficiently similar in their clinical and methodological characteristics to allow meaningful indirect comparisons. Although the network was complete, a conventional NMA was not selected as the primary approach because the evidence base was sparse, included repeated follow-up measurements from the same study families, and showed imbalance in clinically relevant study characteristics across contrasts.

Study-level comparative effect sizes were calculated as log risk ratios (log RR) for treatment failure using arm-level event counts and denominators. A continuity correction of 0.5 was applied only when zero cells were present. All comparative results are reported as Risk Ratios (RR) with 95% Confidence Intervals (95% CI) after back-transformation from the log scale. Treatment contrasts were coded with *CCR* as the reference treatment, allowing estimation of the relative failure risks of SCR vs CCR and SWR vs CCR, with SCR vs *SWR* derived as a linear combination of these parameters.

The primary analytical model was a multivariate contrast-based random-effects meta-analysis fitted with "*rma.mv()*" from *metafor*. This model was chosen because it allows simultaneous estimation of treatment contrasts while accounting for dependence among repeated follow-up observations from the same study family. Within-family correlation was handled through a working covariance matrix, and the main model assumed a within-family correlation of rho = 0.50. Sensitivity analyses were conducted with rho = 0.30 and rho = 0.80. Additional sensitivity analyses were performed by retaining only the longest follow-up per study family and by excluding the double-zero comparison. Model fit was summarised using the QE statistic for residual heterogeneity and the QM

statistic for moderator significance. These analyses were intended to test the robustness of the comparative findings under alternative methodological assumptions.

A secondary multivariate meta-regression was fitted with "*rma.mv()*" to adjust treatment effects for follow-up duration, modelled as a common linear effect scaled per 12 months and centred at 24 months for interpretation. Additional one-at-a-time exploratory meta-regressions were fitted for follow-up duration, mean age, male proportion, and molar proportion. These moderator analyses were considered hypothesis-generating only because they were based on a small number of effect sizes. The categorical covariate region was summarised descriptively rather than modelled inferentially because it was structurally confounded with the pattern of available direct treatment contrasts. In other words, some treatment comparisons were only available in specific geographic regions, making it impossible to distinguish a potential regional effect from a treatment-comparison effect.

To complement the primary model, several supplementary analyses were undertaken. First, crude treatment-level failure proportions were calculated descriptively overall and within the predefined follow-up bands. Second, direct pairwise random-effects meta-analyses were fitted separately for each available contrast using "*rma.uni()*" with restricted maximum likelihood (REML) estimation. These direct analyses were interpreted descriptively because they did not account for the within-family dependence induced by repeated follow-up. Third, approximate standardised residuals were computed from the primary multivariate model to identify the study comparisons that contributed most strongly to residual heterogeneity and model misfit.

Graphical outputs included a treatment network plot, plots of follow-up distributions across direct comparisons, observed study-specific forest plots, model-based treatment-effect plots across sensitivity analyses, a follow-up-adjusted forest plot with CCR as the reference, a descriptive subgroup forest plot by region, and bubble meta-regression plots for the continuous covariates. In the meta-regression figures, bubble size was proportional to the inverse of each study-level effect estimate's standard error.

Overall, although the treatment network was geometrically connected, a conventional network meta-analysis was not considered the most appropriate primary approach due to the sparse evidence base, repeated follow-up measurements within the same study families, and imbalances in clinical and methodological characteristics across direct comparisons. Therefore, the multivariate contrast-based model was selected as the primary analytical framework.

III. Results

The literature search identified 1,030 articles. From this, 538 duplicates were removed using the Rayyan tool. The remaining 492 articles underwent an initial screening of titles and abstracts to assess their relevance and eligibility for this systematic review.

Following this screening phase, 28 articles were selected for full-text assessment. Because access to 4 articles was unavailable, 24 full-text articles were thoroughly evaluated against the predefined inclusion and exclusion criteria.

Upon full-text assessment, 14 articles were excluded because they did not meet the predefined eligibility criteria, particularly regarding the study population, the assessed intervention, or the reported outcomes. In total, 10 reports were included in the systematic review. Among these, one report was retained for descriptive synthesis only because its primary outcome was not directly comparable with the composite treatment failure outcome used in the quantitative synthesis. Therefore, the main meta-analysis included nine comparison time points from six independent study families.

The entire study selection process was conducted in accordance with the PRISMA 2020 guidelines (Page et al., 2021) and is summarized in Figure 1.

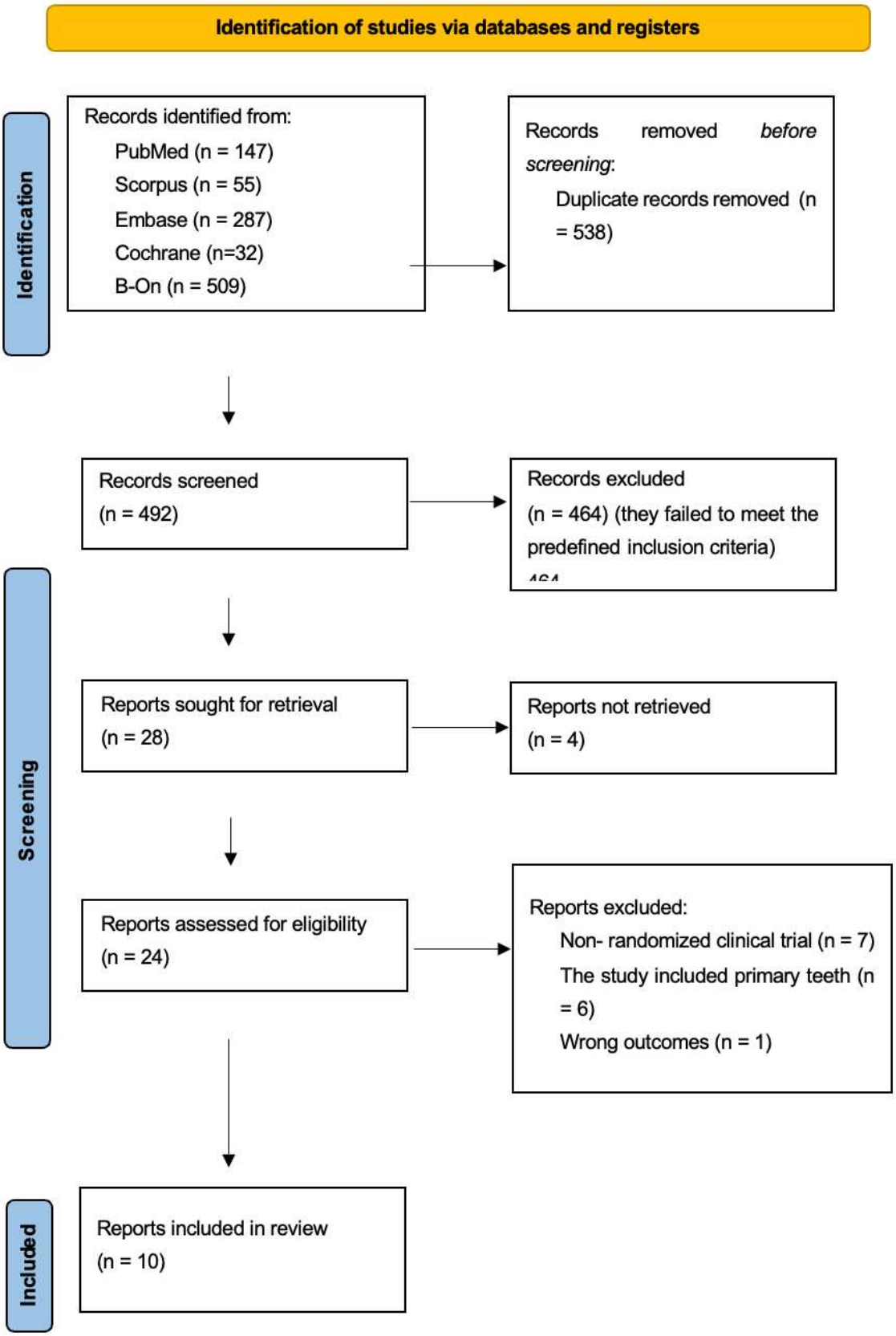

Figure 1 : PRISMA flow diagram of the literature search and study selection

Table 3 presents a general summary of the studies included in the systematic review.

Table 3 : Summary of reports included in the systematic review

Study (Year) / Country	Study design	Number of teeth	Diagnosis	Intervention	Comparator	Follow-up (months)	Drop-outs	Outcomes
(Ahmed et al., 2021)/ Pakistan	RCT	70	Deep carious lesions affecting ≥50% of the dentin without signs of irreversible pulpitis.	SCR	CCR	6,12 and 18	Not reported, although only 60 teeth were included in the final analysis.	At 18 months, the clinical success rate was 100% in the CCR group and 93.3% in the SCR group, with no statistically significant difference between the groups. Pulp exposure occurred in 23.3% of cases in the CCR.

Study (Year) / Country	Study design	Number of teeth	Diagnosis	Intervention	Comparator	Follow-up (months)	Drop-outs	Outcomes
(Bjørndal et al., 2010)/ Denmark, Sweden	Multicenter RCT	314	Carious lesions involving ≥ 75% of the dentin, vital pulp and no signs of irreversible pulpitis or apical pathology.	SWR	CCR	12	22 patients lost to follow-up (13 SWR, 9 CCR)	At 12 months, SWR was significantly higher than CCR (74.1% vs. 62.4%; p = 0.044). There was less pulp exposure in the SWR group than in the CCR (17.5% vs. 28.9%; p = 0.030).
(Bjørndal et al., 2017)/ Denmark, Sweden	Multicenter RCT	314	Carious lesions involving at least 75% of dentin, vital pulp, with no signs of irreversible pulpitis or apical pathology.	SWR	CCR	60	75	At 5-year follow-up, SWR showed a significantly higher success rate than CCR (60.2% vs. 46.3%; p = 0.031). Pulp exposure was significantly lower in the stepwise group (21.2% vs. 35.5%; p = 0.014).

Study (Year) / Country	Study design	Number of teeth	Diagnosis	Intervention	Comparator	Follow-up (months)	Drop-outs	Outcomes
(Khokhar & Tewari, 2018)/ India	RCT	143	Carious lesion involving ≥50% of the dentin with vital pulp and absence of apical radiolucency.	SCR	CCR	18	7	Thirteen pulp exposures occurred exclusively in the CCR group. At 18 months, after exclusion of teeth with pulp exposure, clinical and radiographic success rates did not differ significantly between groups.

Study (Year) / Country	Study design	Number of teeth	Diagnosis	Intervention	Comparator	Follow-up (months)	Drop-outs	Outcomes
(Labib et al., 2019)/ Egypt	RCT	132	Deep carious lesions extending radiographically into >2/3rds of the dentin, vital pulp, no spontaneous or prolonged pain, no apical pathology.	SCR	SWR	12	15	After 12 months, success rates did not differ significantly between selective and stepwise removal (SCR: 89.4% vs SWR: 84.9%; p > 0.05). Pulp exposure occurred only in the stepwise group (0 vs. 5 cases).

Study (Year) / Country	Study design	Number of teeth	Diagnosis	Intervention	Comparator	Follow-up (months)	Drop-outs	Outcomes
(Maltz et al., 2013)/ Brazil	Multicenter RCT	299	Carious lesions extending radiographically over ≥50% of the dentin, vital pulp, absence of spontaneous pain, negative percussion test, and no periapical pathology.	SCR	SWR	18	86 (SCR:41; SWR: 45)	After 18 months, partial caries removal showed a significantly higher success rate than stepwise removal (99% vs 86%; p = 0.016). Pulp exposure occurred only in the stepwise group (4 cases).

Study (Year) / Country	Study design	Number of teeth	Diagnosis	Intervention	Comparator	Follow-up (months)	Drop-outs	Outcomes
(Maltz et al., 2012)/ Brazil	Multicenter RCT	299	Carious lesions extending radiographically over ≥50% of the dentin, vital pulp, absence of spontaneous pain, negative percussion test, and no periapical pathology.	SCR	SWR	36	86	After 3 years, partial caries removal showed significantly higher pulp vitality than stepwise removal (adjusted survival rates: 91% vs 69%; p = 0.004). Failures were mainly due to pulpal complications, particularly in the stepwise group.

Study (Year) / Country	Study design	Number of teeth	Diagnosis	Intervention	Comparator	Follow-up (months)	Drop-outs	Outcomes
(Maltz et al., 2018)/ Brazil	Multicenter RCT	299	Carious lesions extending radiographically over ≥50% of the dentin, vital pulp, absence of spontaneous pain, negative percussion test, and no periapical pathology.	SCR	SWR	60	178	At 5 years, partial caries removal showed significantly greater preservation of pulp vitality than SWR (80% vs. 56%; p < 0.001). Survival analysis demonstrated a significantly lower risk of pulp necrosis in the SCR group (adjusted HR = 0.38; 95% CI: 0.23–0.63). Failures were strongly associated with non-completion of the stepwise protocol.

Study (Year) / Country	Study design	Number of teeth	Diagnosis	Intervention	Comparator	Follow-up (months)	Drop-outs	Outcomes
(Rando Meirelles et al., 2013)/ Brazil	RCT	18	Carious lesions extending to at least the middle 1/3rd of the dentin, vital pulp, absence of spontaneous pain and periapical pathology.	SCR	CCR	24	2	After 24 months, no tooth in either group presented unsatisfactory clinical or radiographic outcomes. All teeth maintained pulp vitality and showed radiographic arrest of the carious process. It is a preliminary study.

Study (Year) / Country	Study design	Number of teeth	Diagnosis	Intervention	Comparator	Follow-up (months)	Drop-outs	Outcomes
(Recchi et al., 2024)/ Brazil	RCT	152	Carious lesions involving ≥50% of the dentin, vital pulp, absence of spontaneous pain, negative percussion, and no periapical pathology.	SCR	SWR	18	17	After 18 months, restoration survival was similar between SCR and SWR. Six restorative failures were observed (4 SCR, 2 SWR), mainly due to marginal fractures or loss of restoration. Pulp necrosis occurred within the first 12 months and was evenly distributed between groups.

Abbreviations: *RCT: Randomised Clinical Trial; CCR: Complete Caries Removal; SCR: Selective Caries Removal; SWR, Stepwise Removal technique; HR: Hazard Ratio; CI: Confidence Interval.*

The analysis of the studies presented in the synthesis table (Table 3) highlights several patterns in the literature regarding the management of deep carious lesions. All included studies are randomised clinical trials comparing three different strategies for carious tissue removal: CCR, SCR, and SWR. The diagnostic criteria are relatively consistent across studies, generally involving deep carious lesions extending at least to half to two-thirds of the dentin in teeth with vital pulp and without signs of irreversible pulpitis or apical pathology. Follow-up periods range from 6 months to 5 years, allowing assessment of both short and long-term outcomes. Overall, high clinical and radiographic success rates are reported for all treatment strategies. However, several studies suggest that conservative approaches are associated with a lower risk of pulp exposure during treatment. In addition, some studies indicate better long-term preservation of pulp vitality with selective or stepwise caries removal. Taken together, these descriptive findings suggest a trend in the literature toward minimally invasive strategies for the management of deep carious lesions.

Risk of bias

The risk-of-bias evaluation results are illustrated in Figures 2 and 3. Among the 10 analysed reports, 2 were judged to be at high risk of bias. Rando Meirelles et al. (2013) was judged as having an overall high risk of bias due to cumulative concerns across several domains, including limited methodological reporting, small sample size, preliminary study design, and insufficient information regarding pre-specified outcome reporting. The remaining studies were rated as presenting some concerns, mainly related to limitations in methodological reporting (Domain 5). In particular, the frequent absence of a pre-specified statistical analysis plan or an accessible study protocol limited the ability to verify whether the reported outcomes and conducted analyses corresponded to the initially defined objectives.

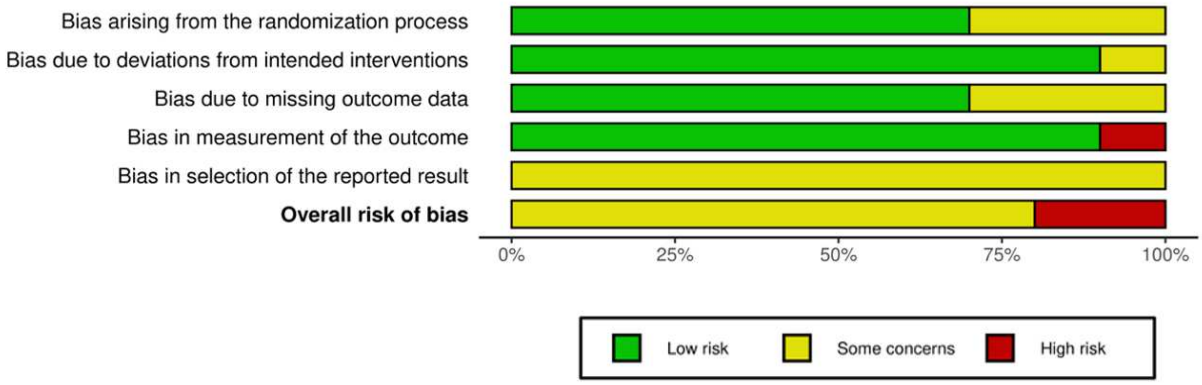

Figure 2 : Graph reviewing authors' judgements of each risk of bias domain across all included studies (in %)

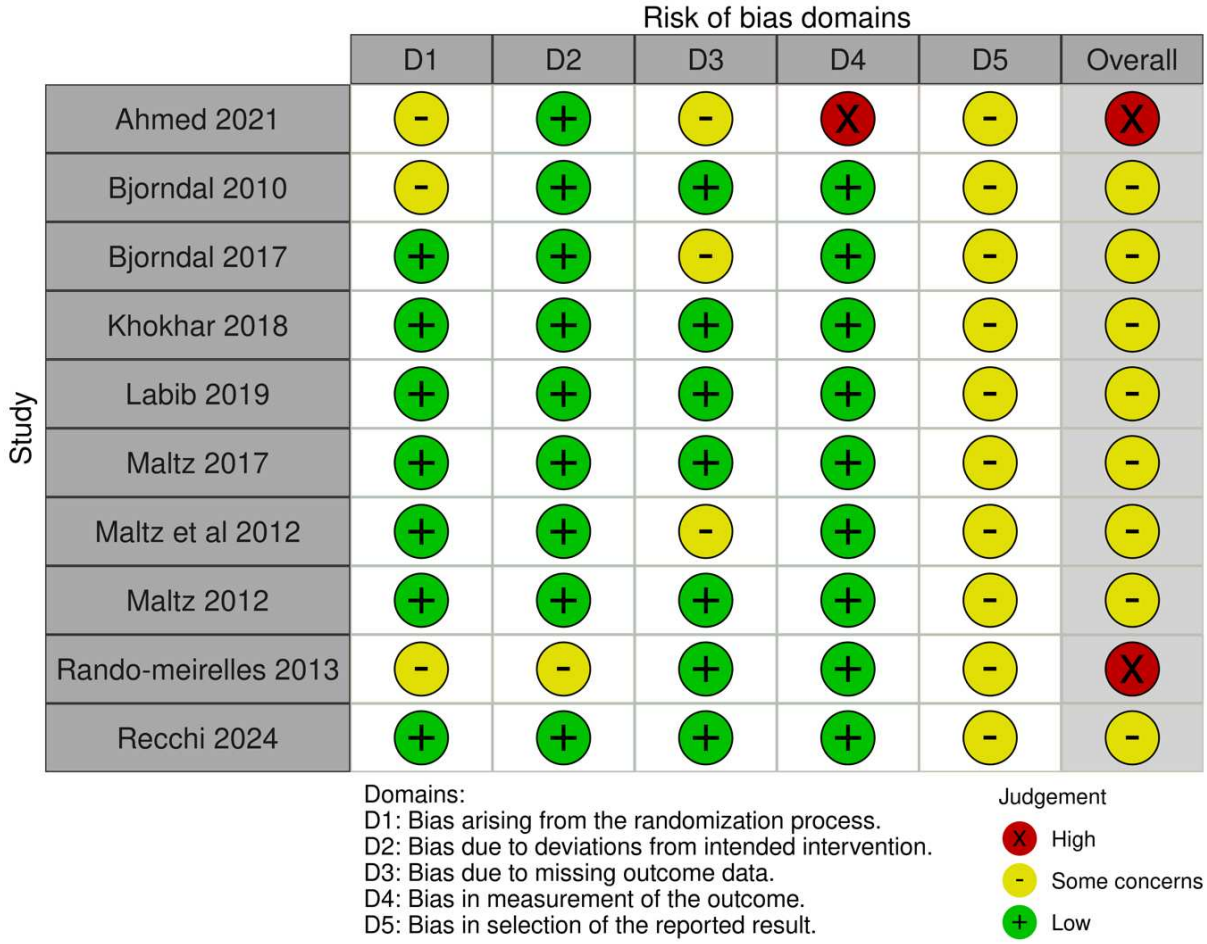

Figure 3 : Risk of bias summary of included studies according to the Cochrane Risk of Bias 2 tool.

Comparative meta-analysis

The primary outcome in the quantitative synthesis was treatment failure, defined as a composite outcome comprising loss of pulp vitality and/or clinical-radiographic failure, according to the reporting criteria of the original studies.

Because pulp vitality preservation and clinical-radiographic success were generally reported together in the included studies, a single meta-analysis was performed using this composite failure outcome.

The study by Recchi et al. (2024) was the only included study to specifically evaluate restoration failure as the primary outcome, according to the FDI criteria for restoration performance. Although pulp necrosis and pulp exposure were reported, these cases were not included in the study's main analysis. Therefore, this study was retained in the systematic review and discussed descriptively. However, it was not included in the primary meta-analysis because its outcome was not directly comparable with the composite treatment failure outcome used in the quantitative synthesis.

The quantitative dataset comprised nine two-arm comparison time points from six independent study families and included the three techniques: CCR, SCR, and SWR.

1. Network structure and exchangeability

The treatment graph was geometrically complete (Table 4), with direct evidence for all three pairwise contrasts. However, the evidence was unevenly distributed across study families and clinical contexts. The CCR vs SWR contrast was informed by only 2 comparison time points from a single study family (Bjørndal). In contrast, SCR vs SWR was based on 4 comparison-timepoints from 2 families, and CCR vs SCR on 3 comparison-timepoints from 3 families.

Table 4: Network geometry and exchangeability summary across direct treatment comparisons.

Direct comparison	Effect sizes	Study families	Follow-up range	Age range	Continent
CCR vs SCR	3	3	18.0-19.9	15.8-24.5	Asia, South America
CCR vs SWR	2	1	12-60	29-34	Europe
SCR vs SWR	4	2	12-60	16.5-29.2	Africa, South America

Abbreviations: *CCR: Complete Caries Removal; SCR: Selective Caries Removal; SWR, Stepwise Removal technique.*

Exchangeability was limited. CCR vs SCR comparisons were observed at approximately 18-19.8 months. They came from Asia and South America, CCR vs SWR ranged from 12 to 60 months and came from Europe only, and SCR vs SWR ranged from 12 to 60 months and came from Africa and South America. These imbalances supported the decision to avoid a standard network meta-analysis as the primary model.

Figure 4 presents the network diagram illustrating the available direct comparisons between the three interventions. The size of the nodes is proportional to the total number of teeth included for each intervention. At the same time, the thickness of the connecting lines represents the number of studies directly comparing the treatments. Because the network was fully connected, both direct and indirect effects among the interventions could be estimated.

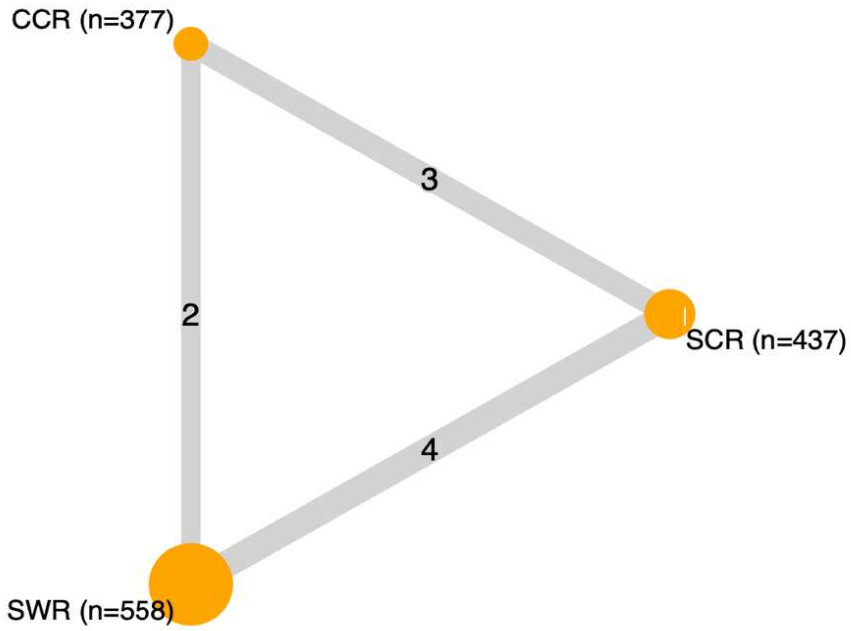

Figure 4: Treatment network for CCR, SCR, and SWR. Edge labels indicate the number of direct comparison time points contributing to each contrast.

Figure 5 presents the distribution of follow-up durations across studies, highlighting heterogeneity in follow-up protocols.

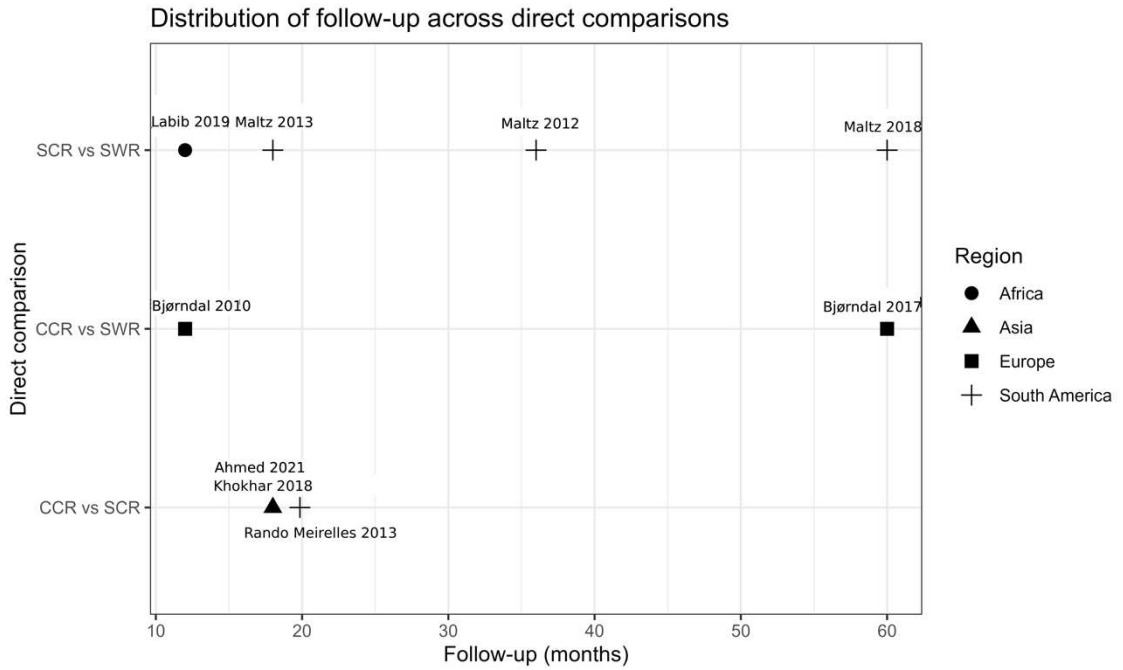

Figure 5 : Distribution of follow-up duration across direct comparisons. Symbols indicate the study region and illustrate the imbalance in design characteristics across the network.

2. Primary multivariate contrast-based meta-analysis

Observed study-specific risk ratios were heterogeneous and often imprecise (Figure 6). The two Bjørndal comparisons consistently favoured SWR over CCR, whereas the SCR vs CCR comparisons were directionally unfavourable to SCR but had wide confidence intervals. The comparisons between SCR and SWR were mixed, though several favoured SCR.

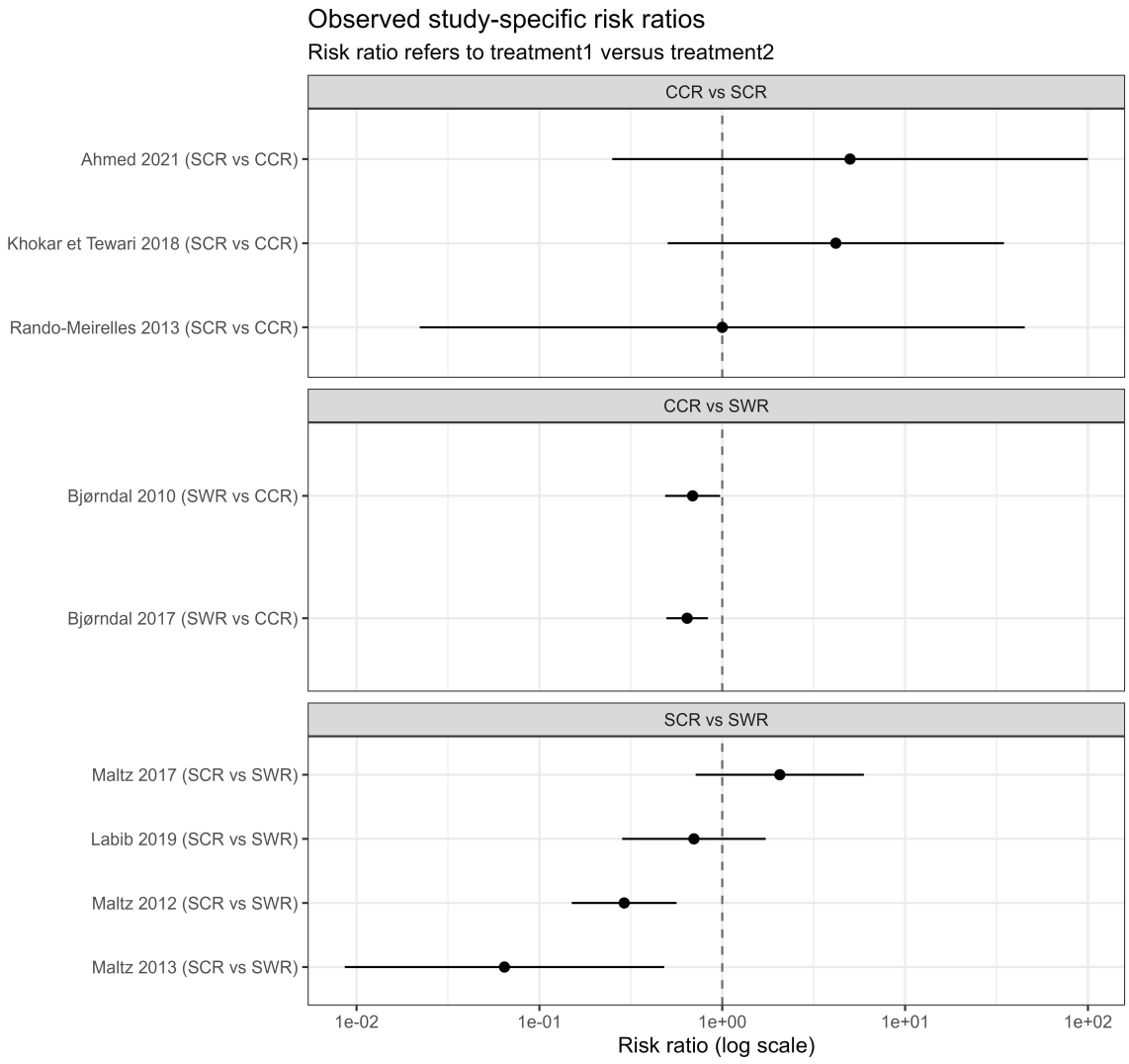

Figure 6 : Observed study-specific risk ratios for treatment failure. Risk ratios are shown on a logarithmic scale and refer to treatment 1 versus treatment 2. Horizontal bars represent 95% confidence intervals.

In the primary multivariate model (rho = 0.50), no statistically significant differences in failure risk were detected among the treatments (Table 5). Compared with CCR, the estimated RR was 1.06 (95% CI, 0.25 to 4.50; p = 0.942) for SCR and 1.29 (95% CI, 0.34 to 4.83; p = 0.709) for SWR. The model-based comparison between SCR and SWR yielded an RR of 0.82 (95% CI, 0.25 to 2.66; p = 0.741).

These non-significant findings should not be interpreted as evidence of equivalence between treatments, but rather as reflecting substantial statistical imprecision within a sparse and heterogeneous evidence base.

Table 5 : Primary and follow-up-adjusted multivariate treatment effects, with CCR specified as the reference treatment.

Contrast	Primary RR (95% CI)	Primary p	24-month adjusted RR (95% CI)	Adjusted p
SCR vs CCR	1.06 (0.25 to 4.50)	0.942	1.21 (0.22 to 6.72)	0.824
SWR vs CCR	1.29 (0.34 to 4.83)	0.709	1.41 (0.27 to 7.48)	0.686
SCR vs SWR	0.82 (0.25 to 2.66)	0.741	0.86 (0.20 to 3.69)	0.840

Abbreviations: *RR: Risk Ratio; CCR: Complete Caries Removal; SCR: Selective Caries Removal; SWR, Stepwise Removal technique; CI: Confidence Interval; p: p-value.*

Model fit indicated substantial unexplained heterogeneity in the primary model (QE = 34.88, df = 7, p < 0.001), whereas the omnibus moderator test for the treatment parameters was not significant (QM = 0.19, df = 2, p = 0.911). These findings indicate substantial imprecision rather than evidence of equivalence. They also suggest residual between-comparison variability not explained by the model.

Figure 7 presents the follow-up-adjusted risk ratios for treatment failure at 24 months, with CCR as the reference treatment.

Model-based risk ratios for treatment failure are shown on a logarithmic scale for SCR and SWR relative to CCR. Points represent adjusted effect estimates, horizontal lines indicate 95% confidence intervals, and the vertical dashed line marks the null value (RR = 1.0). Active treatments are ordered according to the adjusted risk ratio. No statistically significant difference in failure risk was detected between either active treatment or CCR at the 24-month reference follow-up.

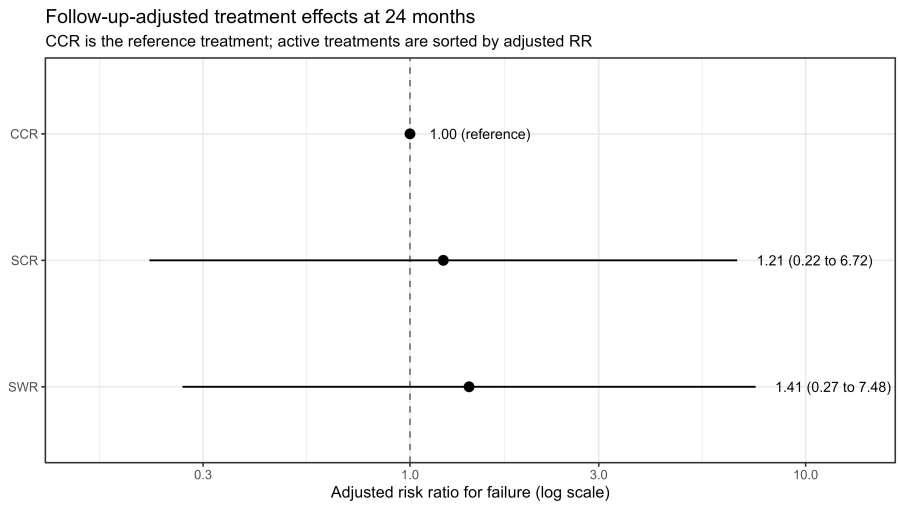

Figure 7 : Follow-up-adjusted treatment effects at 24 months, with CCR as the reference treatment. Horizontal bars represent 95% confidence interval.

3. Sensitivity analyses

Table 6 shows that treatment estimates were highly stable across the assumed within-family correlations of rho = 0.30, 0.50, and 0.80. Restricting the analysis to the longest follow-up per family modestly shifted point estimates and reduced residual heterogeneity, but did not identify a statistically significant treatment difference. Excluding the double-zero comparison also left the conclusions unchanged.

Table 6 : Sensitivity analyses of model-based treatment effects.

Analysis	SCR vs CCR	SWR vs CCR	SCR vs SWR
Primary model (rho = 0.30)	1.07 (0.25 to 4.55)	1.31 (0.35 to 4.98)	0.81 (0.25 to 2.63)
Primary model (rho = 0.50)	1.06 (0.25 to 4.50)	1.29 (0.34 to 4.83)	0.82 (0.25 to 2.66)
Primary model (rho = 0.80)	1.06 (0.24 to 4.63)	1.27 (0.33 to 4.82)	0.84 (0.25 to 2.81)

Longest follow-up only	1.53 (0.45 to 5.15)	0.96 (0.33 to 2.82)	1.59 (0.59 to 4.28)
Exclude double-zero comparison	1.15 (0.22 to 5.98)	1.37 (0.31 to 6.04)	0.84 (0.23 to 3.07)

Abbreviations: *CCR: complete caries removal; SCR: selective caries removal; SWR: stepwise removal; RR: risk ratio; CI: confidence interval; rho: assumed within-family correlation coefficient.*

Figure 8 illustrates the model-based risk ratios for treatment failure across the primary and sensitivity analyses under different methodological assumptions.

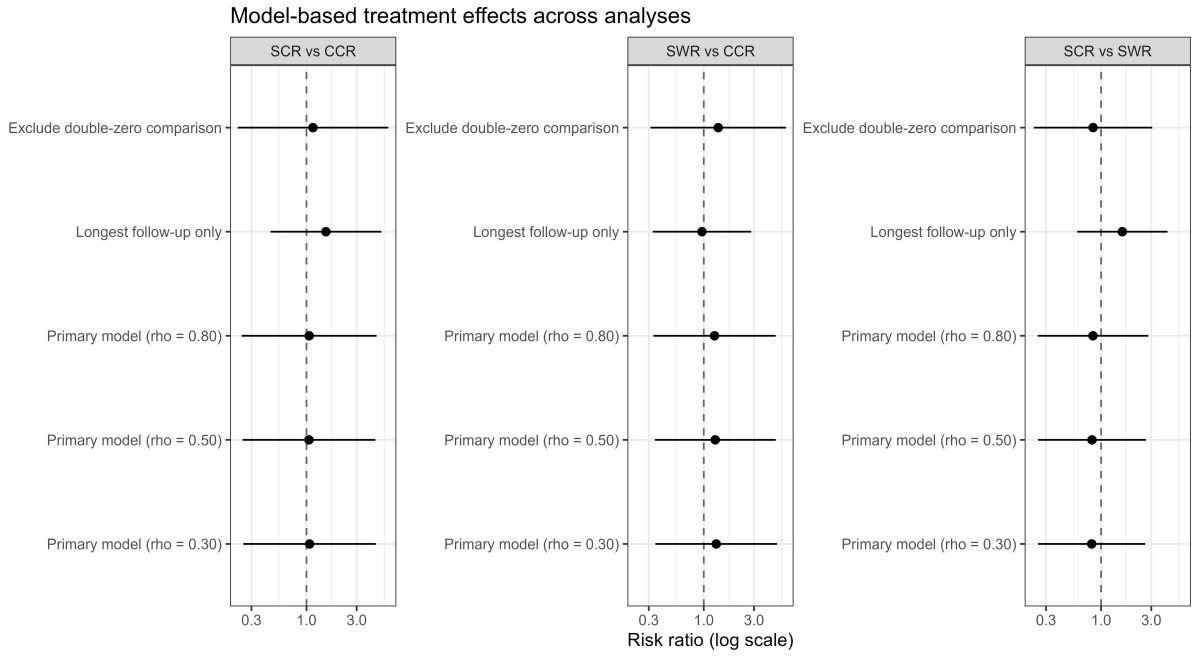

Figure 8 : Model-based treatment effects across primary and sensitivity analyses. Risk ratios are shown on a logarithmic scale. Horizontal bars represent 95% confidence intervals.

The most notable sensitivity finding was observed in the longest-follow-up-only analysis, in which residual heterogeneity decreased to QE = 5.98 (df = 4, p = 0.200). This suggests that part of the variability in the full model was related to repeated follow-up structure rather than to clear treatment separation.

4. Follow-up-adjusted analysis

A secondary meta-regression adjusted treatment effects for follow-up duration by centring the model at 24 months and estimating a common linear effect per 12 months (Figure 9). The adjusted treatment contrasts remained non-significant and were like the primary estimates: RR = 1.21 (95% CI, 0.22 to 6.72; p = 0.824) for SCR vs CCR, RR = 1.41 (95% CI, 0.27 to 7.48; p = 0.686) for SWR vs CCR, and RR = 0.86 (95% CI, 0.20 to 3.69; p = 0.840) for SCR vs SWR.

The common follow-up effect was not significant (RR per 12 months = 1.16 (0.69 to 1.96); p = 0.567), indicating that follow-up duration did not materially explain the between-comparison variation within the limits of this sparse dataset.

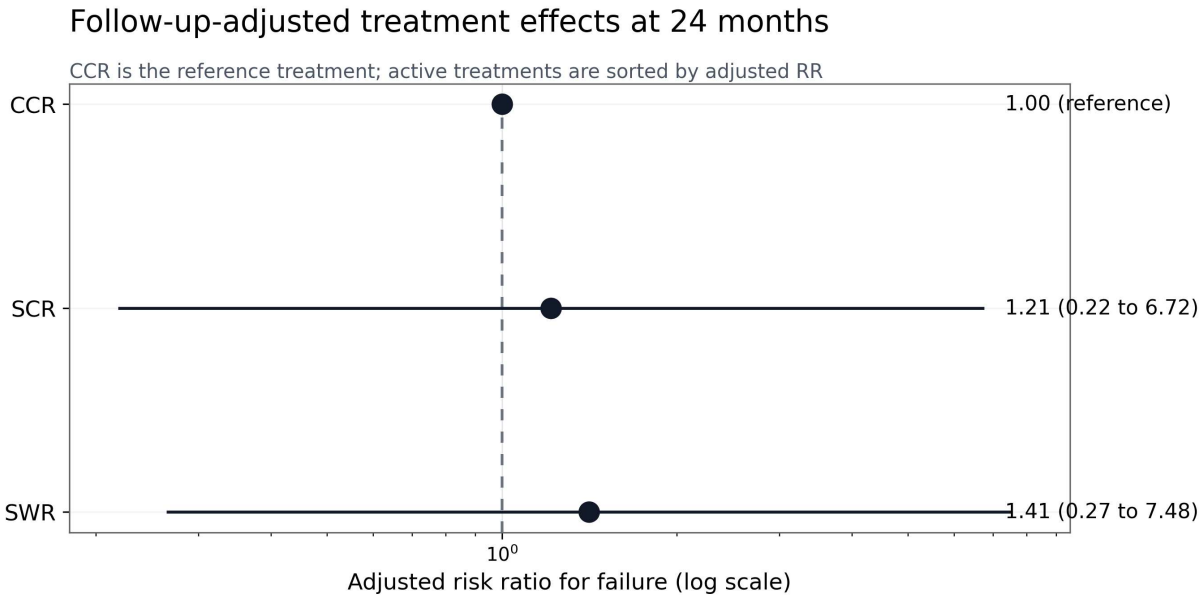

Figure 9 : Follow-up-adjusted treatment effects at 24 months. CCR is the reference treatment, and active treatments are ordered by their adjusted risk ratios. Horizontal bars represent 95% confidence interval.

5. Exploratory moderators

Table 7 shows that the one-at-a-time moderator analyses did not identify any statistically significant associations for follow-up duration, age, male proportion, or molar proportion. These analyses were considered hypothesis-generating only because they were based on 8 to 9 effect sizes and therefore had limited power.

Table 7: Exploratory one-at-a-time moderator analyses.

Moderator	k	RR (95% CI)	p
Follow-up (per 12 months)	9	1.19 (0.71 to 2.01)	0.509
Age (per 5 years)	9	0.91 (0.33 to 2.48)	0.853
Male proportion (per 10 percentage points)	8	2.29 (0.68 to 7.65)	0.179
Molar proportion (per 10 percentage points)	8	1.17 (0.68 to 2.01)	0.566

Abbreviations: *k: number of effect sizes; RR: Risk Ratio; CI: Confidence Interval; p: p-value.*

6. Supplementary descriptive and diagnostic findings

Crude arm-level summaries suggested the lowest observed failure proportion for SCR (8.1%), followed by SWR (24.8%) and CCR (36.3%). These percentages are descriptive only and should not be interpreted as pooled inferential estimates, because they combine repeated follow-up observations and are strongly confounded by differences in follow-up distribution and study characteristics.

Supplementary direct pairwise random-effects meta-analyses also showed an uneven pattern of evidence. The direct CCR vs SWR contrast favoured SWR (RR = 0.66, 95% CI 0.53 to 0.81), but this estimate was based on only two comparison time points from the Bjørndal family. The direct SCR vs CCR and SCR vs SWR contrasts were directionally suggestive but remained very imprecise.

Approximate standardised residuals from the primary multivariate model indicated that the largest departures from model fit were concentrated in the Bjørndal comparisons (CCR vs SWR) and the Maltz comparisons (SCR vs SWR). This reinforces the interpretation that the overall heterogeneity was driven mainly by a small number of influential study families.

Overall, the network was connected and geometrically complete, but the evidence base remained sparse and imprecise. No reliable evidence of differential failure risk among CCR, SCR, and SWR was demonstrated, and clinically relevant differences cannot be excluded.

IV. Discussion

This systematic review and meta-analysis compared conventional complete caries removal with non-conventional approaches, namely selective caries removal and the stepwise technique, in the management of deep carious lesions. The main findings can be summarized in three key points. First, the current evidence does not support a robust comparative hierarchy between CCR, SCR, and SWR. Second, the estimates remained imprecise, with wide confidence intervals and substantial residual heterogeneity. Third, the main contribution of this review is to clarify the current limits of inference in the comparative literature on caries removal strategies and pulp vitality preservation.

Principal Findings

The present synthesis provides a connected three-treatment comparative framework for CCR, SCR, and SWR, but also shows that the current evidence base is not yet sufficiently mature to support a definitive comparative hierarchy. Although the treatment network was geometrically complete, no statistically significant difference in failure risk was observed in the primary multivariate contrast-based model, the follow-up-adjusted model, or the main sensitivity analyses. Importantly, this should not be interpreted as evidence of equivalence. Rather, the overall pattern is one of substantial imprecision, with wide confidence intervals and persistent residual heterogeneity, indicating that clinically relevant differences remain plausible but unresolved.

The main value of the study is not that it identifies a clearly superior treatment, but that it clarifies the current limits of inference in the comparative caries removal and pulp vitality literature. The data are sufficient to support a structured comparative synthesis, but not sufficient to support strong clinical ranking. In that respect, the review provides a more realistic evidence map for clinicians and researchers by distinguishing between a network that is technically connected and a literature base that remains methodologically too sparse and imbalanced for definitive comparative conclusions.

Comparison with existing literature

The absence of statistically significant differences observed between the techniques of caries removal may be explained by current microbiological data.

Indeed, the progression of carious lesions is closely related to an imbalance in the oral biofilm, characterized by acidification of the microenvironment (Marsh, 2010; Takahashi & Nyvad, 2011). Several studies have shown that reductions in microorganisms involved in caries progression, particularly *Streptococcus mutans* and *Lactobacillus* spp., are comparable after conventional or non-conventional restorations, provided that an adequate seal is achieved (Bitello-Firmino et al., 2018; Bjørndal & Larsen, 2000; Maltz et al., 2002). These results suggest that the control of the bacterial environment depends more on the quality of the restorative seal than on the complete elimination of demineralised dentin.

Furthermore, during selective caries removal, the affected dentin that is not removed retains a potential for remineralisation (Maltz et al., 2002). In response to moderate aggression, the dentin–pulp complex forms tertiary dentin, either reactionary or reparative, thereby increasing the remaining dentin thickness and providing pulpal protection (Goldberg, 2011; Vidovic-Zdrilic et al., 2019).

The use of biomaterials such as calcium hydroxide or glass ionomer cements may also contribute to this process due to their biological and antibacterial properties, as well as their ability to promote a durable hermetic seal (Fairbourn et al., 1980; Leung et al., 1980; Paddick et al., 2005).

Thus, the results of this meta-analysis appear consistent with current biological knowledge, suggesting that control of the microenvironment and the quality of the restorative seal play a determining role in the preservation of pulp vitality.

However, biological plausibility should be distinguished from comparative clinical proof. Although the available evidence supports the rationale for conservative caries removal, the present synthesis does not provide sufficiently precise comparative estimates to establish the superiority of SCR or SWR over CCR.

From a clinical perspective, these findings support the consideration of conservative approaches in selected deep carious lesions, while acknowledging that the present evidence does not establish a definitive hierarchy among techniques. Indeed, non-conventional caries removal techniques aim to limit the risk of pulpal exposure, thereby reducing the probability of requiring root canal treatment, a more invasive procedure associated with tooth morbidity.

Selective caries removal may be an attractive single-visit conservative option; however, the present meta-analysis does not establish its superiority over complete caries removal or stepwise removal. Clinically, it may offer a less invasive approach, with potentially shorter operative time and reduced operative stress for both the practitioner and the patient.

Thus, although conservative approaches seem clinically relevant, their success depends closely on case selection and strict adherence to operative protocols.

Many randomized clinical trials (RCTs) have been published on the treatment of deep carious lesions. However, several of them could not be included in the present review due to strict PICO criteria or discrepancies with the predefined inclusion and exclusion criteria.

A large part of the literature concerns primary teeth. These studies consistently report no statistically significant differences among CCR, SCR and SWR in terms of clinical success and pulp preservation. They generally conclude that a non-conventional approach reduces the risk of pulpal exposure and favours conservative techniques (Elhennawy et al., 2021; Franzon et al., 2015; Vaghasiya et al., 2024).

The results of this review are also consistent with previously published literature syntheses. Yao et al. (2023), comparing selective caries removal with the Stepwise technique, reported statistical superiority in favor of the selective approach (Yao et al., 2023). Conversely, Li et al. (2018), comparing SCR with CCR, did not demonstrate any significant difference between the two techniques (Li et al., 2018).

More recently, Ramezanzade et al. (2025) conducted a network meta-analysis comparing the three therapeutic strategies. Their results showed no statistically significant difference between the techniques, although a slight tendency in favor of the stepwise technique was observed in their ranking. However, the authors suggested that selective caries removal could constitute the first therapeutic option, while the stepwise technique could be reserved for patients with assured follow-up (Ramezanzade et al., 2025). It should nevertheless be emphasized that this study included both randomized and non-randomized studies, which may increase the risk of bias and affect effect estimates. The inclusion of studies with

heterogeneous methodological levels may therefore alter the robustness of the conclusions.

Why a Conventional Network Meta-Analysis Was Not the Best Primary Approach

A particularly important strength of this review is that it did not rely on a conventional network meta-analysis merely because the treatment graph was complete. The network had three nodes and direct evidence for all pairwise contrasts, but exchangeability across contrasts was limited. CCR versus SWR was represented only by the Bjørndal family and was European. In contrast, CCR versus SCR and SCR versus SWR arose from different geographic settings and different age and follow-up distributions. Thus, the connected network did not necessarily represent clinically comparable evidence streams.

In addition, repeated follow-up observations within the same study families were present, indicating that a simple contrast-level meta-analysis treating all time points as independent would have been methodologically weaker. The choice of a multivariate contrast-based random-effects model with a working covariance structure was therefore a major methodological asset of the study. This modelling strategy better matched the structure of the evidence and allowed the review to explicitly account for within-family dependence, rather than ignoring it. This approach was therefore methodologically conservative and better suited to the structure of the available evidence.

Interpretation of the Comparative Findings

The primary model, using CCR as the reference treatment, did not detect significant differences between SCR and CCR, SWR and CCR, or SCR and SWR. However, non-significant differences do not demonstrate equivalence between treatments. At the same time, the intervals were broad enough to encompass both potentially meaningful benefit and harm. Accordingly, the current evidence does not permit a confident statement that any one of the three treatment strategies is superior or inferior in terms of failure risk. This distinction is essential because a null finding in a sparse, heterogeneous meta-analysis should not be framed as proof of clinical equivalence.

Although some direct and descriptive comparisons appear to support conservative approaches, the present multivariate synthesis does not establish a statistically robust superiority of SCR or SWR over CCR. The most defensible interpretation is therefore one of persistent uncertainty: conservative strategies remain biologically plausible and clinically relevant, but the available comparative evidence is too sparse and heterogeneous to support a definitive ranking of treatments.

The residual heterogeneity in the primary model remained substantial. That residual heterogeneity is consistent with what was already visible in the direct evidence: different studies favored different contrasts, and the apparent signals were clustered within a small number of study families. The current results, therefore, support a cautious clinical message. The literature is not empty, but it is not yet decisive.

The sensitivity analyses substantially strengthen the credibility of the review. First, the treatment estimates were stable across different assumptions about within-family correlation. This indicates that a single arbitrary dependence parameter was not driving the overall comparative conclusions. Second, excluding the double-zero comparison did not materially change the results, suggesting that this sparse-information study was not responsible for the main findings. Third, restricting the dataset to the longest follow-up per family markedly reduced residual heterogeneity, yet still failed to identify a significant treatment difference.

That last point is especially informative. The drop in heterogeneity in the longest-follow-up-only analysis suggests that part of the apparent between-study variability in the full model reflects repeated longitudinal structure rather than true treatment separation. This is a valuable insight because it identifies one of the mechanisms that makes the current literature difficult to synthesize. In other words, the problem is not only that there are too few studies, but also that the available studies often report multiple dependent follow-up assessments, which complicate comparative pooling.

The follow-up-adjusted analysis was clinically and methodologically worthwhile, even though it did not change the substantive conclusions. After centering

treatment effects at 24 months and modelling a common linear follow-up effect every 12 months, the adjusted treatment contrasts remained non-significant and closely resembled the primary estimates. The common follow-up effect was also not statistically significant. Taken together, these findings suggest that follow-up duration did not materially explain the observed between-comparison differences within the limits of this sparse dataset.

However, this should not be interpreted as proof that follow-up is clinically irrelevant. On the contrary, one of the clearest messages of the review is that an inconsistent follow-up structure is a major barrier to interpretable evidence synthesis in this field. The adjusted model suggests that follow-up alone does not fully account for the lack of treatment separation. However, the broader set of results indicates that harmonized follow-up windows remain essential if future meta-analyses are to become more informative. In practical terms, the field would benefit greatly from routine reporting at common endpoints such as 12, 24, and 60 months.

The exploratory moderator analyses did not identify statistically significant associations for follow-up duration, age, male proportion, or molar proportion. On the surface, these are negative findings, but they remain useful. Their real contribution is not ruling out effect modification but clarifying which clinically plausible modifiers remain unresolved by the current literature. The current evidence base is too sparse, unevenly distributed across contrasts and underpowered for reliable meta-regression of study-level covariates. That is an important message for both readers and future investigators.

Among these covariates, follow-up remains the most important from a design perspective, because repeated and non-harmonized longitudinal reporting was clearly one of the main structural issues in the dataset. Age likewise did not show a detectable study-level association, but the existing evidence is too uneven across contrasts to exclude clinically meaningful age-related differences. The same reasoning applies to molar proportion: the absence of a significant association should not be read as evidence that tooth type is unimportant, but rather as evidence that percentage-based arm-level reporting is too crude to capture tooth-specific comparative effects.

About the male proportion, although not statistically significant, it yielded the largest exploratory point estimate among the tested moderators. That estimate is far too imprecise to support a claim of sex-related effect modification. However, it is sufficient to argue that sex distribution should be reported more systematically and examined prospectively in future trials. In this sense, the covariate analyses do add value: they define which questions remain open and show that future studies should be designed not merely to compare treatments, but to enable covariate-adjusted synthesis.

The descriptive direct pairwise analyses provide an additional layer of interpretation. The direct CCR versus SWR contrast favored SWR and was the strongest individual direct signal in the dataset. However, this contrast was based on only two comparison time points from a single study family. By contrast, the other direct contrasts were either imprecise or directionally mixed. This uneven direct pattern helps explain why the multivariate model produced wide confidence intervals and no definitive separation of treatments. The direct literature contains signals, but they have not yet been sufficiently replicated across independent evidence clusters.

Clinical Implications

From a clinical perspective, the present analysis does not justify a firm hierarchy among CCR, SCR, and SWR based solely on failure risk. Although some descriptive and direct comparisons suggested possible advantages for conservative approaches, these findings remain too imprecise and heterogeneous to support a definitive evidence-based ranking.

Nevertheless, the absence of a clear advantage for complete caries removal is clinically relevant. In deep carious lesions, CCR may increase the risk of pulpal exposure and lead to more invasive treatments, such as pulp therapy or root canal treatment. Therefore, when partial caries removal is clinically feasible, conservative strategies such as SCR and SWR should be considered biologically defensible alternatives.

Treatment choice should remain individualized and based on pulpal diagnosis, lesion depth, operator experience, patient follow-up, and the ability to achieve a durable restorative seal. Selective caries removal may be particularly relevant

when a single-session conservative approach is possible. In contrast, the stepwise technique may be considered when re-entry is clinically justified, and follow-up can be ensured. Until stronger comparative evidence becomes available, clinical decisions should be guided by biological rationale and patient-specific factors rather than by assumptions of superiority between techniques.

Institutional, One Health, and Broader Relevance

From a broader One Health and health-systems perspective, these findings support a more conservative and preventive philosophy of care. Strategies that preserve pulp vitality may reduce treatment burden, prevent escalation to more invasive procedures, and support long-term oral health maintenance within a **r**esource-conscious model of care.

This review also aligns with an institutional line of research focused on minimally invasive restorative dentistry, pulp preservation, and evidence synthesis for clinical decision-making. In this context, the present work contributes to Sustainable Development Goal 3, Good Health and Well-being, by supporting evidence-based, less invasive strategies to preserve oral health, reduce avoidable treatment escalation, and improve patient-centered care.

Strengths of the Present Review

This review has several strengths. First, it assessed network geometry and exchangeability explicitly before model selection, rather than assuming that a connected graph automatically justified a conventional network meta-analysis. Second, it used a multivariate contrast-based approach that accounted for repeated follow-up within study families, a substantial methodological improvement over treating all comparison time points as independent. Third, it included multiple sensitivity analyses, a follow-up-adjusted model, exploratory moderator analyses, and supplementary descriptive and diagnostic analyses, which together provide a fuller picture of both the signal and the uncertainty.

A further strength is that the core inference was stable across major alternative analyses. That consistency matters. Even though the results were non-significant, they were not unstable in a way that would suggest purely arbitrary modelling dependence. This makes the negative finding more credible and

strengthens the manuscript’s central claim that the real limitation lies in the evidence base rather than in the analytical framework.

Limitations

The principal limitations arise from the underlying literature. The total number of comparison time points was small, and the number of independent study families was even smaller. The network was geometrically complete, but direct evidence was unevenly distributed across contrasts, with some comparisons represented mainly by a single family or region. Residual heterogeneity remained substantial in the primary model, indicating that important variability remained unexplained. Furthermore, the moderator analyses were based on only eight to nine effect sizes and therefore had limited statistical resolution.

Another limitation concerns the unit of analysis. The treated tooth was considered the analytical unit because outcomes were reported at the tooth level in the included studies. However, when several teeth originated from the same patient, this approach may have introduced within-patient dependence, which could not be fully accounted for with the available published data.

In addition, the region could not be treated as a meaningful inferential moderator because it was structurally confounded with the available direct contrasts. Similarly, tooth-type composition had to be summarized at the arm level rather than examined through tooth-class-specific comparative outcomes. Finally, the direct pairwise supplementary analyses and crude failure summaries are informative. However, they cannot be interpreted inferentially in the same way as the primary multivariate model because they do not fully resolve the dependence and imbalance problems present in the literature.

Importantly, these limitations do not weaken the value of the review; they define its contribution. The manuscript is strongest when it makes clear that the current uncertainty reflects the field's structure, not merely the outcome of a single statistical method.

Implications for Future Research

The main recommendation arising from this review is that future comparative trials should be designed with evidence synthesis in mind. The field does not simply need more studies; it needs better-aligned studies. Prospective head-to-

head randomized comparisons among CCR, SCR, and SWR with pre-specified, harmonized follow-up windows are the single most important next step. At a minimum, future studies should report comparable endpoints at clinically meaningful common time points, such as 12, 24, and 60 months.

Equally important is the standardization of failure definitions. Future trials should use clear, preferably consensus-based, outcome definitions that incorporate clinical failure, radiographic failure, reintervention, and tooth survival. Without harmonized outcomes, adding more trials may increase volume without substantially improving interpretability.

Future studies should also systematically report potential effect modifiers. Age, sex distribution, tooth type, baseline lesion characteristics, pulpal status, operator characteristics, and restorative protocol should be described in enough detail to permit clinically meaningful subgroup or meta-regression analyses. The current covariate analyses were informative precisely because they showed that these questions remain unresolved rather than irrelevant.

Tooth type deserves special attention. Instead of reporting only arm-level percentages of molars, premolars, or anterior teeth, future trials should provide tooth-class-specific outcomes whenever possible. This would allow future comparative syntheses to address one of the most clinically relevant unresolved questions: whether treatment performance differs systematically by tooth class.

Finally, future evidence should aim for broader geographic and clinical diversity within each direct contrast. At present, some contrasts are too closely tied to specific regions or specific study families. More geographically distributed direct evidence would improve both exchangeability and external validity.

Conducting randomized controlled trials with a follow-up of more than 5 years would allow a more precise evaluation of the long-term stability of the different caries removal techniques.

Furthermore, histological studies could further explore the biological mechanisms involved, particularly regarding tertiary dentin formation and pulpal response after non-conventional caries removal.

Cost-effectiveness analyses would also be useful for evaluating the economic impact of different therapeutic strategies for patients, taking into account the number of sessions, the risk of pulpal exposure, and the potential need for endodontic treatment.

In addition, studies specifically comparing capping biomaterials and restorative materials used in conservative techniques could help identify potential factors influencing clinical success.

V. Conclusion

This study aimed to compare conventional complete caries removal with non-conventional approaches, namely selective caries removal and the stepwise technique, in the management of deep carious lesions, using treatment failure, defined as loss of pulp vitality and/or clinical-radiographic failure, as the primary outcome.

The results of this multivariate contrast-based meta-analysis showed no statistically significant differences in treatment failure among the three techniques across the primary model, follow-up-adjusted analysis, and sensitivity analyses. However, confidence intervals remained wide and residual heterogeneity was substantial, indicating that clinically meaningful differences cannot be excluded. Therefore, the most appropriate interpretation is not that these techniques are equivalent, but rather that the current evidence remains insufficient to establish a definitive comparative hierarchy.

From a clinical perspective, these findings suggest that complete caries removal does not provide a clear advantage when partial caries removal is feasible. Given its more invasive nature and the higher risk of pulpal exposure, which can lead to more complex and costly treatments, complete caries removal should not be assumed to be preferable when partial caries removal is clinically feasible. Conservative approaches, including SCR and SWR, appear clinically credible and biologically defensible alternatives to complete caries removal in carefully selected cases, particularly when the objective is to preserve pulp vitality and reduce unnecessary treatment invasiveness.

This study also highlights key methodological challenges in the existing literature, particularly the impact of multiple follow-up time points and heterogeneous study designs on evidence synthesis. Future research should prioritize adequately powered head-to-head randomized controlled trials with standardized outcome definitions, harmonized follow-up periods, and consistent reporting of clinical variables.

Overall, this work supports the broader development of minimally invasive dentistry, pulp preservation, and evidence-based oral healthcare with relevance for long-term health promotion.

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Conventional versus non-conventional caries removal in deep lesions: a systematic review and meta-analysis

Annex

Database	Search strategy
PubMed	("deep cavities" OR "deep caries lesion" OR "profound carious lesions" OR "deep caries") AND ("stepwise excavation" OR "complete caries excavation" OR "non-selective caries removal" OR "total caries removal" OR "partial caries excavation" OR "selective caries removal" OR "selective excavation")
Cochrane Library	("deep cavities" OR "deep caries lesion" OR "profound carious lesions" OR "deep caries") AND ("stepwise excavation" OR "complete caries excavation" OR "non-selective caries removal" OR "total caries removal" OR "partial caries excavation" OR "selective caries removal" OR "selective excavation")
Embase	('deep cavities' OR 'deep caries lesion' OR 'profound carious lesions' OR 'deep caries') AND ('stepwise excavation' OR 'complete caries excavation' OR 'non-selective caries removal' OR 'total caries removal' OR 'partial caries excavation' OR 'selective caries removal' OR 'selective excavation')
Scopus	("deep cavities" OR "deep caries lesion" OR "profound carious lesions" OR "deep caries") AND ("stepwise excavation" OR "complete caries excavation" OR "non-selective caries removal" OR "total caries removal" OR "partial caries excavation" OR "selective caries removal" OR "selective excavation")
B-on	('deep cavities' OR 'deep caries lesion' OR 'profound carious lesions' OR 'deep caries') AND ('stepwise excavation' OR 'complete caries excavation' OR 'non-selective caries removal' OR 'total caries removal' OR 'partial caries excavation' OR 'selective caries removal' OR 'selective excavation')

Annex 1 : Database Search strategy

Treatment	Total n	Failures	Crude failure proportion
CCR	364	132	36.3%
SCR	469	38	8.1%
SWR	576	143	24.8%

Annex 2 : Crude observed failure summary by treatment

Follow-up band	Treatment	Total n	Failures	Crude failure proportion
19-36 months	CCR	8	0	0.0%
19-36 months	SCR	120	10	8.3%
19-36 months	SWR	101	31	30.7%
<=18 months	CCR	235	57	24.3%
<=18 months	SCR	275	15	5.5%
<=18 months	SWR	310	61	19.7%
>36 months	CCR	121	75	62.0%
>36 months	SCR	74	13	17.6%

>36 months	SWR	165	51	30.9%

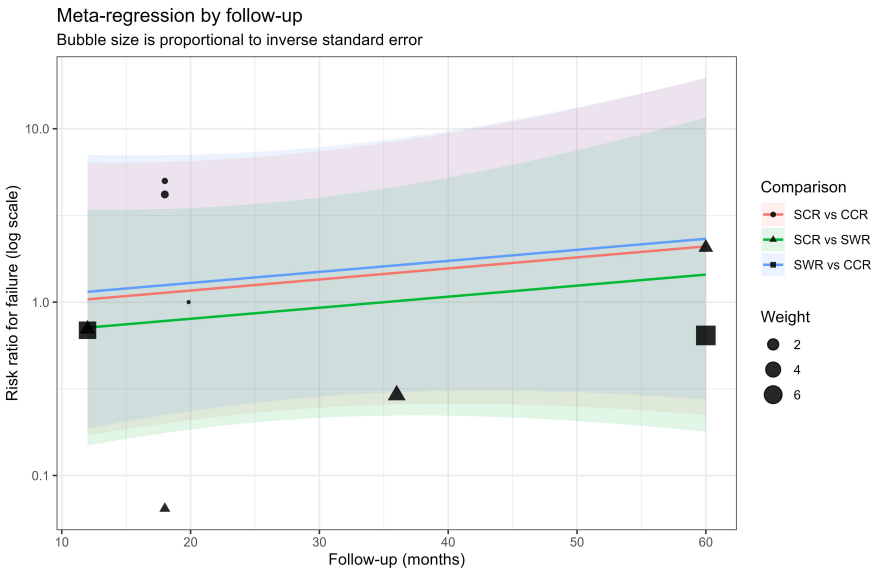
Annex 3 : Crude observed failure summary by treatment and follow-up band.

Direct comparison	k	RR (95% CI)	p
CCR vs SCR	3	3.44 (0.71 to 16.61)	0.124
CCR vs SWR	2	0.66 (0.53 to 0.81)	<0.001
SCR vs SWR	4	0.47 (0.14 to 1.64)	0.238

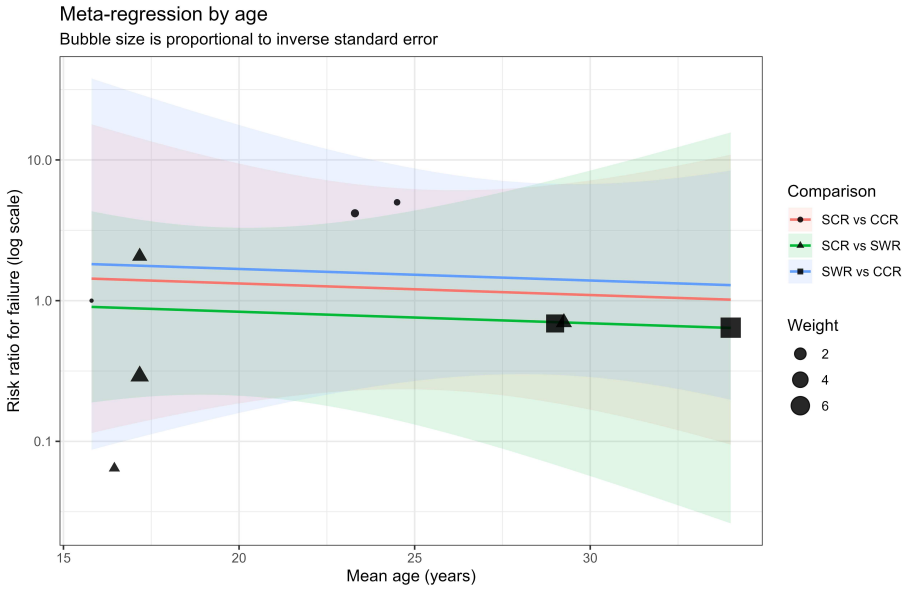
Annex 4 : Direct pairwise random-effects meta-analyses (descriptive supplementary analysis).

Study	Direct comparison	Approx. standardized residual
Bjørndal 2017	CCR vs SWR	-5.19
Bjørndal 2010	CCR vs SWR	-3.54
Maltz 2012	SCR vs SWR	-3.08
Maltz 2013	SCR vs SWR	-2.48
Maltz 2017	SCR vs SWR	1.71

Annex 5 : Largest approximate standardized residuals from the primary multivariate model.

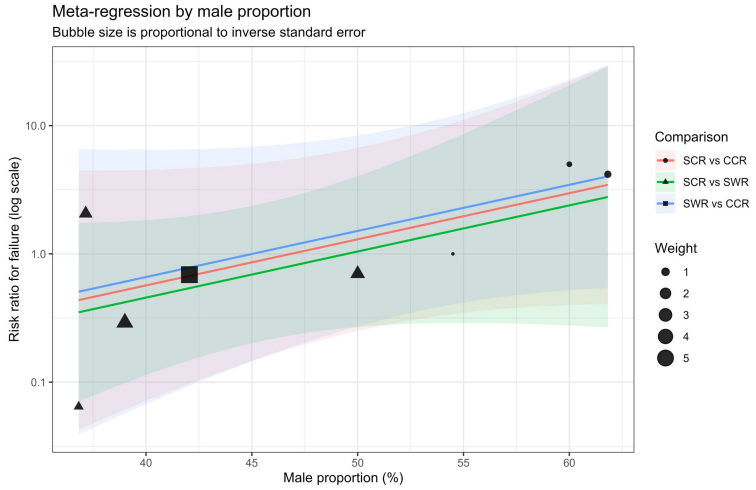


Annex 6 : Meta-regression of treatment effect on follow-up duration Bubble plots display observed study-specific risk ratios for failure against as a function of follow-up time in months, with bubble size proportional to the inverse standard error. Colored lines represent fitted values from the pooled contrast-based random-effects meta-regression, and shaded bands indicate 95% confidence intervals. Separate lines are shown for SCR versus CCR, SWR versus CCR, and SCR versus SWR. The overall slope was positive but not statistically significant, indicating that follow-up duration did not materially explain between-comparison differences in treatment effect.

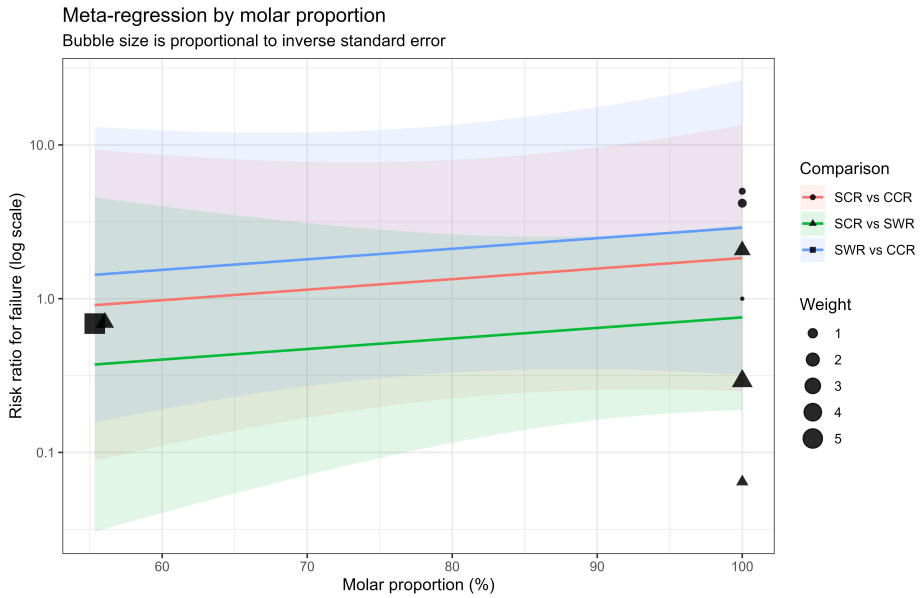


Annex 7 : Meta-regression of treatment effect on mean age. Bubble plots display observed study-specific risk ratios for failure as a function of mean participant age, with bubble size proportional

to the inverse standard error. Colored lines represent fitted values from the pooled contrast-based random-effects meta-regression, and shaded bands indicate 95% confidence intervals. Separate lines are shown for SCR versus CCR, SWR versus CCR, and SCR versus SWR. No statistically significant association was identified between mean age and treatment effect.



Annex 8 : Meta-regression of treatment effect on male proportion. *Bubble plots display observed study-specific risk ratios for failure against the percentage of male participants, with bubble size proportional to the inverse standard error. Colored lines represent fitted values from the pooled contrast-based random-effects meta-regression, and shaded bands indicate 95% confidence intervals. Separate lines are shown for SCR versus CCR, SWR versus CCR, and SCR versus SWR. Although the fitted slope was positive, the association between male proportion and treatment effect was not statistically significant.*



Annex 9 : Meta-regression of treatment effect on molar proportion. *Bubble plots display observed study-specific risk ratios for failure against the percentage of molars, with bubble size proportional to the inverse standard error. Colored lines represent fitted values from the pooled contrast-based random-effects meta-regression, and shaded bands indicate 95% confidence intervals. Separate lines are shown for SCR versus CCR, SWR versus CCR, and SCR versus SWR. The fitted association between molar proportion and treatment effect was weak and not statistically significant.*