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SYSTEMATIC REVIEW

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Evaluation of vital pulp therapy with Biodentine in young permanent teeth: a systematic review and meta-analysis

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Abstract

Background: Vital pulp therapy (VPT) is essential for preserving the vitality of young permanent teeth. This systematic review and meta-analysis aimed to compare the efficacy of Biodentine with other bio-ceramic materials, specifically evaluating clinical success, radiographic success and tooth discoloration outcomes. **Methods**: A comprehensive literature search was performed in PubMed, Embase, Web of Science and The Cochrane Library databases for randomized controlled trials (RCTs) comparing Biodentine with other bio-ceramic materials in VPT for permanent teeth until 01 November 2024. Two independent reviewers screened studies based on predefined inclusion and exclusion criteria. Eligible RCTs were assessed for risk of bias, following data were extracted and the meta-analysis was performed. **Results**: A total of 8 RCTs met the inclusion criteria. The meta-analysis revealed that clinical success rates for Biodentine were 99.38% at 6 months, 94.20% at 12 months and 87.38% at 18 months. Other bio-ceramic materials achieved clinical success rates of 98.15%, 92.59% and 88.35% at the same time intervals. Radiographically, Biodentine demonstrated an overall success rate of 93.87%, compared to 91.04% for other bio-ceramic materials. No significant differences were observed in clinical or radiographic success rates between Biodentine and other materials over 6–18 months of follow-up ($p > 0.05$). However, Biodentine exhibited a significantly lower tooth discoloration rate compared to mineral trioxide aggregate (MTA) at the final follow-up ($p < 0.05$). **Conclusions**: Biodentine showed clinical and radiographic success rates comparable to other bio-ceramic materials in VPT for young permanent teeth, with the added advantage of significantly reducing the incidence of tooth discoloration. **The PROSPERO Registration**: number CRD42024599307.

Keywords

Biodentine; Calcium silicate; Dental pulp capping; Meta-analysis; Pulpotomy; Pulp capping and pulpectomy agents

1. Introduction

Young permanent teeth are particularly vulnerable to deep caries, trauma or mechanical irritation due to their lower degree of mineralization and higher permeability, often resulting in pulpitis [1]. Pulpitis is an inflammatory condition of the dental pulp that occurs when the pulp becomes irritated or infected by bacteria. Prolonged inflammation can disrupt the continued development of the root canal system in young permanent teeth, necessitating the preservation of pulp vitality to support root maturation and overall tooth health [1–3]. Thus, maintaining pulp vitality not only ensures root development but also preserves the tooth's proprioceptive functions and fracture resistance, both critical for long-term function and structural integrity [4].

Vital pulp therapy (VPT) is performed to manage deep caries and pulpal pathology while preserving pulp vitality in young permanent teeth [5]. VPT encompasses several approaches, including indirect pulp therapy (*e.g.*, selective caries removal, stepwise techniques and indirect pulp capping), direct pulp capping, partial pulpotomy, and full pulpotomy [6, 7], which involve the use of bioactive materials as capping agents to stimulate mineralized tissue or dentin bridge formation, thereby promoting the healing of damaged pulp [8]. The success of VPT depends on the regenerative potential of the dentin-pulp complex [9], which initiates a cascade of biological responses, such as progenitor cell recruitment, immune modulation and reparative dentinogenesis, creating an environment conducive to hard tissue formation at the site of injury [10, 11].

The choice of pulp capping material is an important determinant of VPT success. Ideal capping materials should possess anti-inflammatory and antibacterial properties, exhibit

excellent biocompatibility and marginal sealing, and promote reparative dentin formation [8, 12]. The American Association of Endodontics (AAE) recommends silicate-based cements (CSCs), a group of bio-ceramic materials with favorable physical and biological properties, as capping agents for VPT [13]. The commonly used CSCs include calcium silicate-based bioceramics such as Mineral Trioxide Aggregate (MTA), TheraCal LC and Biodentine. Among these, MTA, the first bioceramic material introduced, has been extensively used in clinical practice due to its demonstrated success in treating pulpal diseases [14–16].

To improve the properties of MTA, modified formulations such as White MTA and fast-setting MTA have been developed, which effectively improve its aesthetics and reduce setting time. Despite these advancements, several researchers [17–20] have noted that MTA still has certain limitations for clinical use, including tooth discoloration, prolonged setting time, handling difficulties, technique sensitivity and high cost [20]. Among these shortcomings, the prevention of tooth discoloration remains an important factor affecting treatment success and patient quality of life. Current research indicates that even the white version of MTA exhibits a higher potential for discoloration compared to Biodentine [21, 22]. Biodentine, a dentin substitute derived from MTA, shares many biological properties with MTA, including excellent sealing ability, adequate compressive strength and antimicrobial effects [23, 24]. Its pre-mixed capsule formulation further enhances chairside handling, making it more convenient than manually mixed MTA. The primary objective of VPT is to induce the formation of a hard tissue barrier at the site of pulpal exposure through the application of capping materials, thereby preserving the remaining vital pulp tissue [17, 25]. It has also been reported that Biodentine can promote dentin bridge formation, indicating its potential for remineralization [26, 27]. While extensive research has been conducted on applying bio-ceramics in VPT, most studies focus primarily on either primary or permanent teeth and MTA. There is a lack of systematic evaluations comparing the clinical outcomes of Biodentine and other bioceramics, specifically in the VPT of young permanent teeth.

This study aims to address this gap by performing a meta-analysis to assess the efficacy of Biodentine and other bioceramic materials as capping agents in VPT for young permanent teeth, thereby providing evidence-based guidance for clinical decision-making.

2. Materials and methods

The study protocol was registered in the Prospective Register of Systematic Reviews (PROSPERO) database with the registration number CRD42024599307 (https://www.crd.york.ac.uk/prospero).

2.1 Study selection

This manuscript follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The PRISMA checklist is provided in **Supplementary material 1**. A systematic search of databases, including PubMed, Embase, Web of Science and the Cochrane Library was conducted up to 01 November 2024. Additionally, the reference sections of included articles were manually reviewed to identify potentially relevant studies.

The literature search utilized a combination of Medical Subject Headings (MeSH) terms and free-text keywords. For illustrative purposes, the search strategy used in PubMed is presented in Table 1, and the comprehensive search strategies for all databases are detailed in **Supplementary material 2**.

2.1.1 Inclusion criteria

The inclusion criteria were defined according to the PICOS framework:

P (Population): Studies involving young permanent teeth with pulp exposure due to trauma, mechanical factors or caries, including cases with deep dentin caries. Both the experimental and control groups were required to have at least 10 cases.

I (Intervention): Studies using Biodentine as a pulp capping agent for VPT in young permanent teeth.

C (Comparison): Studies comparing Biodentine with MTA or other bio-ceramic materials.

O (Outcomes): The primary outcome was the clinical success rate. Secondary outcomes included the incidence of tooth discoloration and the radiographic success rate. Studies were required to have a follow-up period of at least 12 months, and must be published in English.

S (Study design): Randomized controlled trials (RCTs).

TABLE 1. Search strategy template applied in PubMed.

Database	Search Strategy
PubMed	#1 (((“Pulpotomy” (Mesh)) OR (pulpotomies)) OR (pulp therapy)) OR (pulp treatment OR pulp exposure) #2 (((“Dental Pulp Capping/methods” (Mesh)) OR (direct pulp capping)) OR (indirect pulp capping)) OR (pulp capping) #3 (selective caries removal) OR (stepwise techniques) #4 Vital Pulp Therapy #5 (“tricalcium silicate” (Supplementary Concept)) OR (((EndoSequence Root Repair Material) OR (Biodentine)) OR (pulpotomy agent)) #6 ((immature permanent teeth) OR (young permanent teeth)) OR (open apex) #7 #1 OR #2 OR #3 OR #4 #8 #5 AND #6 AND #7

2.1.2 Exclusion criteria

The exclusion criteria included the following: (1) studies involving primary teeth or adult permanent teeth; (2) studies with fewer than 10 cases in either the experimental or control groups; (3) cases with non-vital pulp, sinus tract, swelling, internal or external root resorption, or periapical radiolucency on radiographs; (4) studies with follow-up periods shorter than 12 months; (5) non-randomized controlled trials, retrospective studies, case reports, reviews, animal studies and meeting reports.

2.2 Study selection and data collection

Two researchers independently screened the literature and extracted the literature data based on the inclusion and exclusion criteria. Each study was individually verified, and discrepancies were resolved through mutual discussion. When necessary, a third pediatric dentist was consulted. Customized data collection forms were used to record the following information: study characteristics (title, first author and year of publication), population characteristics (age and sample size), materials and methods, treatments and outcome measures. For studies with missing data, efforts were made to contact the authors.

2.3 Quality evaluation

The methodological quality of the included studies was independently assessed by two reviewers using Cochrane's Risk of Bias Tool 2.0 [28]. The evaluation comprised seven domains: Random sequence generation (selection bias); Allocation concealment (selection bias); Blinding of participants and personnel (performance bias); Blinding of outcome assessment (detection bias); Incomplete outcome data (attrition bias); Selective reporting (reporting bias) and other bias.

2.4 Data synthesis and statistical analyses

A narrative synthesis was conducted to summarize the findings. Statistical analyses and forest plots were performed using Review Manager 5.4 (the Review Manager software 5.4, The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark). Relative risk (RR) and 95% confidence intervals (CI) were calculated to assess outcomes. Heterogeneity was evaluated using the I^2 statistic. An I^2 value of $\leq$ 50% indicated low heterogeneity, for which a fixed-effects model was used. In cases of high heterogeneity ($I^2 \geq 50\%$), a random-effects model was applied, along with sensitivity analysis. Publication bias was assessed using funnel plots generated by Review Manager 5.4. A p-value of < 0.05 was considered statistically significant.

3. Results

3.1 Search results

A total of 322 relevant articles were identified through a combination of electronic and manual searches. After removing duplicates, 202 articles remained. Upon reviewing titles and abstracts, 27 articles were shortlisted for further evaluation. Full-text screening by two independent reviewers resulted in the inclusion of 8 randomized controlled trials (RCTs) from an initial pool of 16 full-text articles [29–36]. The detailed process of literature selection is illustrated in Fig. 1. The excluded studies and the reasons for their exclusion are detailed in **Supplementary Table 1**.

3.2 Study characteristics

Among the 8 included RCTs that evaluated bio-ceramic materials for VPT, 7 compared Biodentine with MTA, while 1 examined Biodentine versus Theracal. Studies employed various VPT techniques, with 3 focusing on direct pulp capping [31–33], 1 on indirect pulp capping [34], 2 on pulpotomy [29, 30] and 2 on partial pulpotomy [35, 36]. In total, 563 affected teeth were assessed across the studies, with follow-up durations ranging from 6 months to 6 years. The pulp capping agents used included MTA, Biodentine, calcium hydroxide (CH) and Theracal. The descriptive characteristics of the included studies are summarized in Table 2 (Ref. [29–36]).

3.3 Quality assessment

The Cochrane Risk of Bias assessment was performed for all included RCTs. Three studies were classified as having a low risk of bias, while three other studies were categorized as having an unclear risk due to insufficient descriptions of the random sequence generation process. Two studies were rated as high risk of bias: one due to the absence of blinding of outcome assessors and the other because of a high participant attrition rate. The primary factor affecting the validity of the included studies was the unclear risk of selection bias. However, most studies were assessed as having a low risk of performance bias and detection bias. Nearly all studies were evaluated as having a low risk of attrition and reporting bias. Studies with no reported dropouts or those that adequately compensated for dropouts were generally rated as having a low risk of attrition bias. Conversely, the study by Brizuela *et al*. [31] was identified as having a high risk of bias due to a significant dropout rate. The quality assessment results are summarized in Fig. 2.

3.4 Studies comparing VPT using Biodentine and other medicaments

3.4.1 Comparison of clinical outcomes

Among the 8 included RCTs, 6 reported the clinical success rates of VPT at 6 months postoperatively. The studies were found to be homogeneous ($I^2 = 0\%$), allowing for fixed-effects analysis. The analysis revealed that both Biodentine and other bio-ceramic materials achieved high clinical success rates at 6 months, with no statistically significant difference between them (RR = 1.00, 95% CI (0.97, 1.04), $p = 0.83$) (Fig. 3A). Specifically, Biodentine exhibited a success rate of 99.38%, while other bio-ceramic materials achieved a success rate of 98.15%.

Similarly, 6 studies reported success rates at 12 months postoperatively, again showing homogeneity ($I^2 = 0\%$). The fixed-effects analysis indicated that both Biodentine and other bio-ceramic materials maintained high clinical success rates at 12 months, with no statistically significant difference (RR =

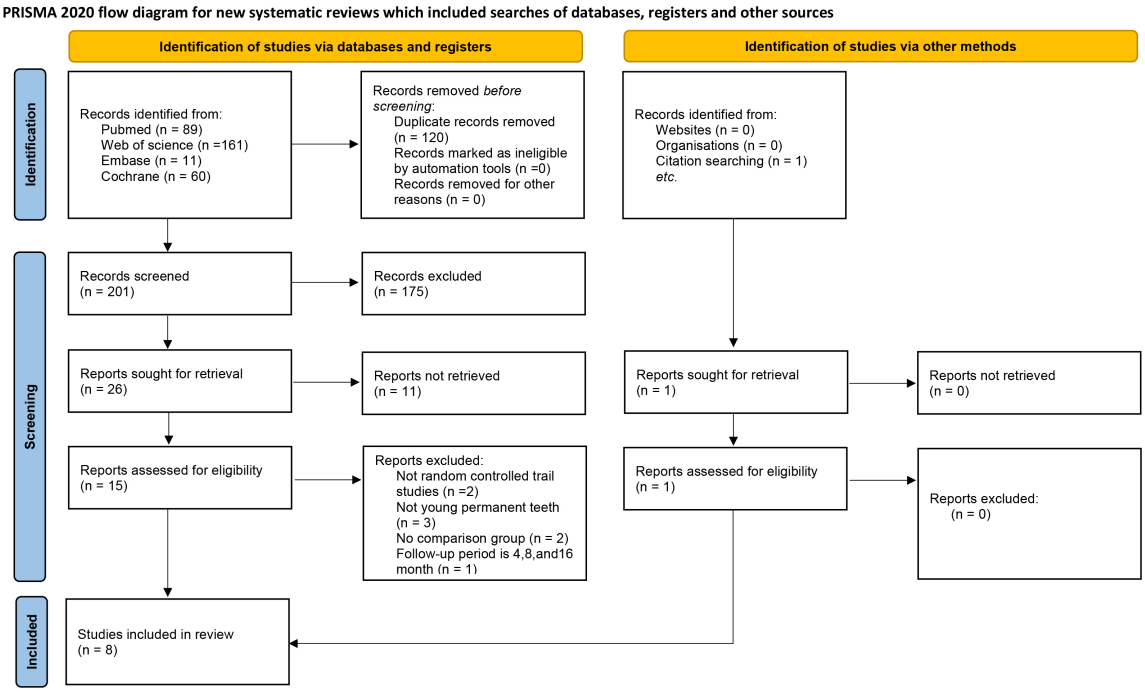

FIGURE 1. Flow diagram of study selection.

TABLE 2. Characteristics of eight included studies in the systematic review.

Study, year	RCT Design	Age range (yr)	Treatment	Medicaments (number of teeth treated)	Follow-up (mon)	Outcome measures
Abuelniel GM, 2020 [29]	Parallel	7.5–9	Full pulpotomy	MTA (25) Biodentine (25)	6, 12 and 18 mon	Clinical success rate Discoloration Radiographic success rate
Abuelniel GM, 2021 [30]	Split-mouth	7–8	Full pulpotomy	MTA (30) Biodentine (30)	6, 12 and 18 mon	Clinical success rate Radiographic success rate
Brizuela C, 2017 [31]	Parallel	7–16	Direct pulp capping	CH (53) MTA (56) Biodentine (60)	1, 3, 6 and 12 mon	Clinical success rate Radiographic success rate
Katge FA, 2017 [32]	Split-mouth	7–9	Direct pulp capping	Biodentine (21) grey MTA (21)	6 and 12 mon	Clinical success rate Radiographic success rate
Parinyaprom N, 2018 [33]	Parallel	6–18	Direct pulp capping	ProRoot MTA (30) Biodentine (29)	every 6 mon	Clinical success rate Discoloration Radiographic success rate
Rahman B, 2021 [34]	Parallel	7–15	Indirect pulp capping	Biodentine (20) Theracal (20) Dycal (20)	3 wk, 3, 6, 12, 18 and 24 mon	Clinical success rate Radiographic success rate
Uesrichai N, 2019 [35]	Parallel	6–18	Partial pulpotomy	ProRoot MTA (37) Biodentine (32)	every 6 mon, for up to 6 yr	Clinical success rate Discoloration Radiographic success rate
Uyar DS, 2021 [36]	Parallel	6–13	Partial pulpotomy	CH (18) MTA (18) Biodentine (18)	1, 3, 6 and 12 mon	Clinical success rate Radiographic success rate

MTA: mineral trioxide aggregate; CH: calcium hydroxide; RCT: randomized controlled trials.

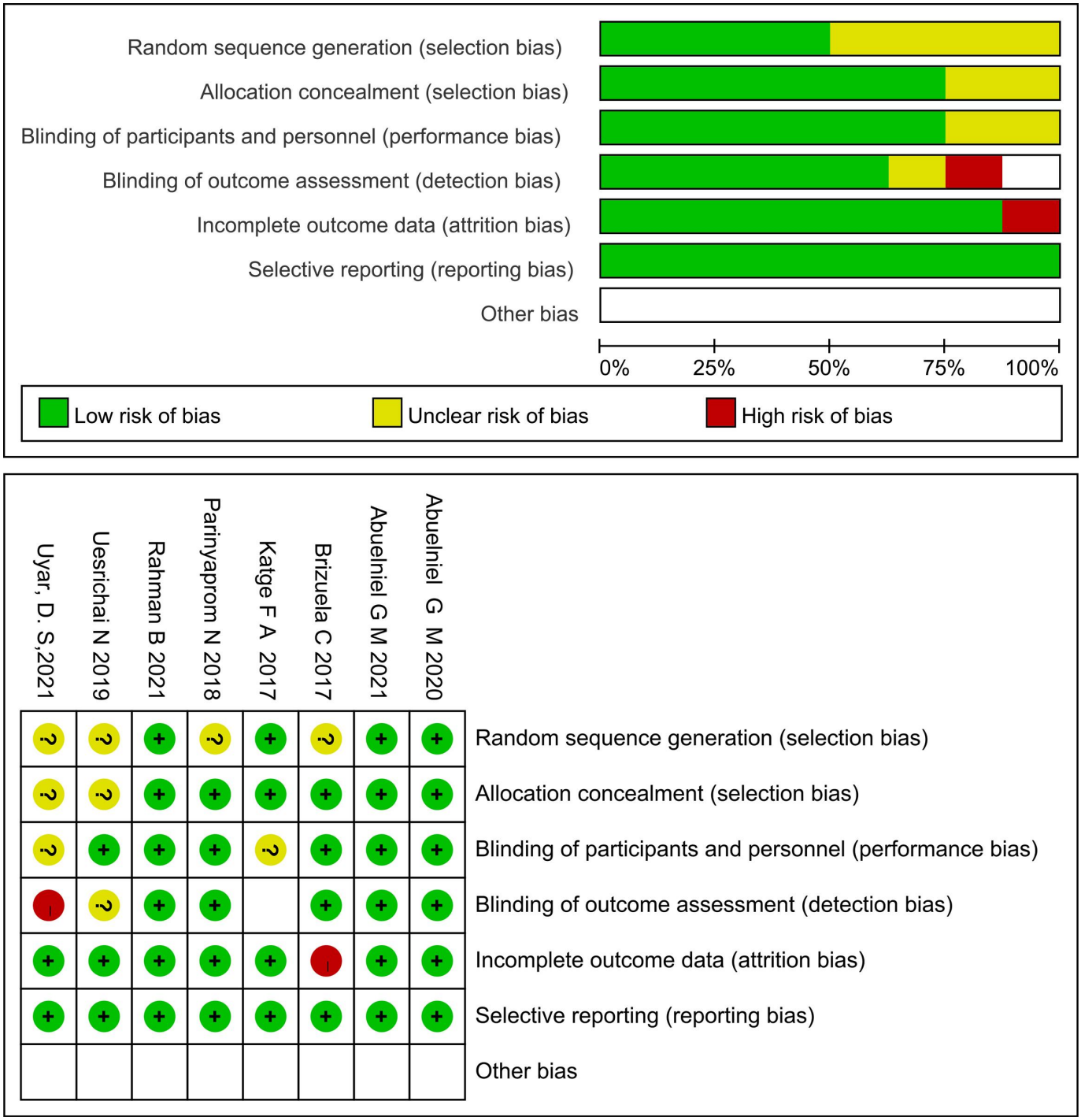

FIGURE 2. Risk of bias of included studies. The figure uses different colors (green, red, yellow) and symbols "+", "-", "?" to represent "low risk of bias", "high risk of bias" and "unclear", respectively.

1.02, 95% CI (0.95, 1.09), p = 0.61) (Fig. 3B). At this time point, Biodentine achieved a success rate of 94.20%, compared to 92.59% for other bio-ceramic materials.

For 4 studies with follow-up at 18 months, homogeneity was also observed (I^2 = 0%). Fixed effects analysis showed that both Biodentine and other bio-ceramic materials continued to demonstrate high clinical success rates at 18 months, with no observed statistically significant difference (RR = 0.99, 95% CI (0.90, 1.09), p = 0.83) (Fig. 3C). Biodentine achieved a success rate of 87.38%, while other bio-ceramic materials reported a success rate of 88.35%. In summary, the clinical success rates of VPT using Biodentine and other bio-ceramic materials were comparable at 6, 12 and 18 months postoperatively, with no statistically significant differences observed.

To determine publication bias, funnel plots were generated for each time point (Fig. 4A–C). The results showed that the points were distributed symmetrically within the inverted funnel and centered around the baseline, indicating no evidence of publication bias.

3.4.2 Secondary outcomes

The secondary outcome measures included the rate of tooth discoloration and the radiographic success rate. Three RCTs reported discoloration rates for Biodentine compared to MTA

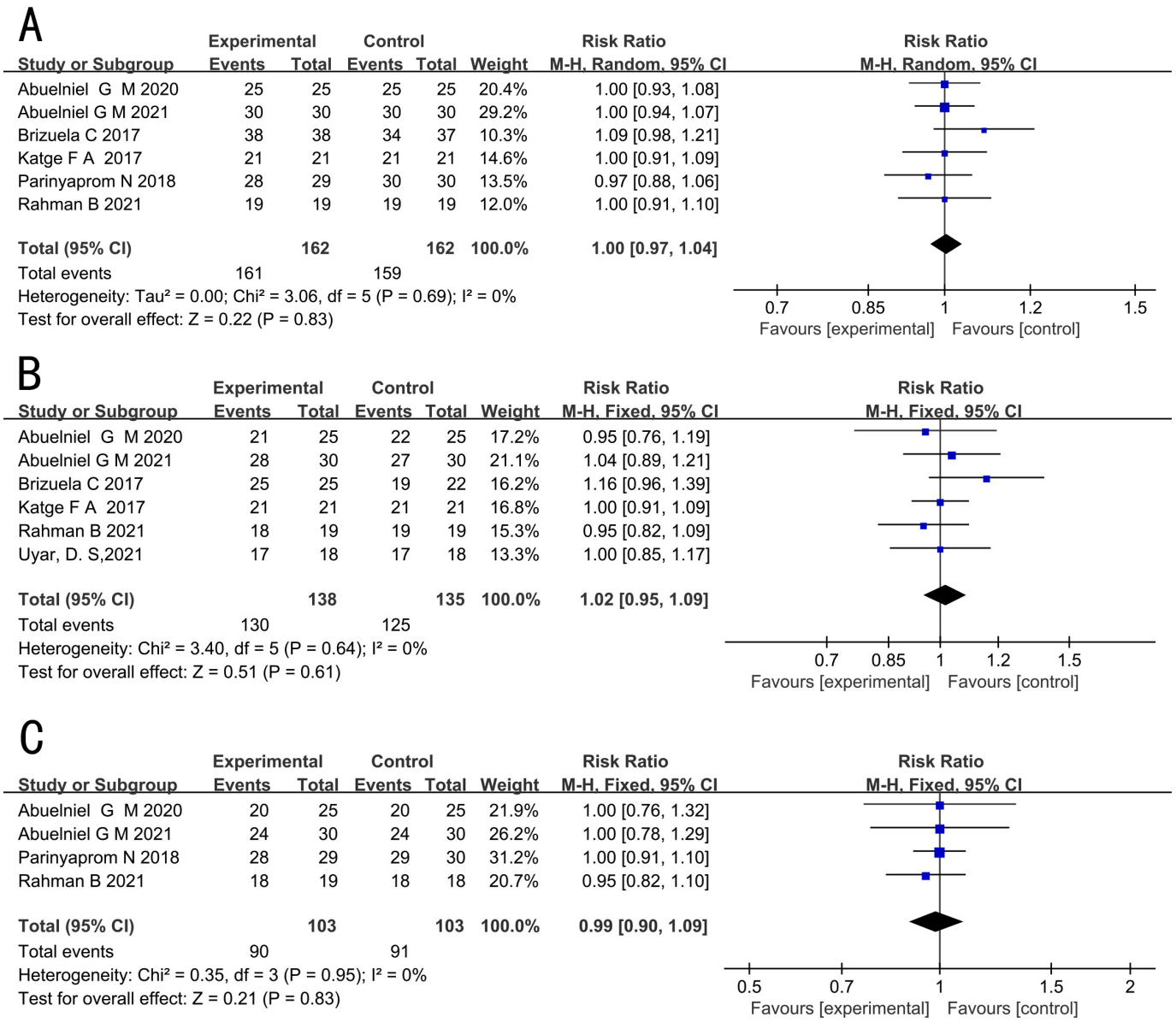

FIGURE 3. Forest plots for clinical success of Biodentine and other biomaterials at 6, 12 and 18 months. (A) 6 months. (B) 12 months. (C) 18 months. CI: confidence intervals; M-H: Mantel-Haenszel method.

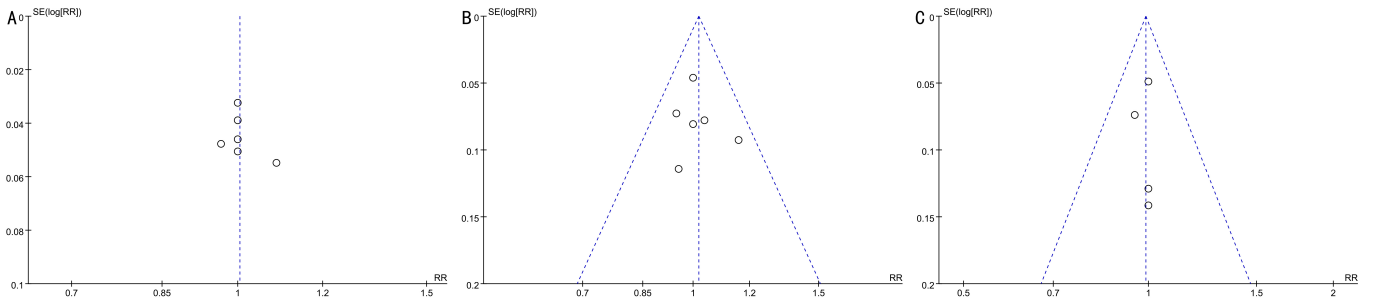

FIGURE 4. Funnel plots for clinical success of Biodentine and other biomaterials at 6, 12 and 18 months. (A) 6 months. (B) 12 months. (C) 18 months. RR: Relative Risk; SE: Standard Error.

at the last follow-up. These studies demonstrated heterogeneity (I^2 = 73%). Random-effects modelling revealed that the incidence of tooth discoloration was significantly lower with Biodentine than with MTA, with a statistically significant difference (RR = 0.16, 95% CI (0.09, 0.31), $p < 0.00001$) (Fig. 5). Sensitivity analysis indicated that excluding the study by Uesrichai reduced the I^2 statistic to 0%, without altering the meta-analysis results, thereby suggesting that while Uesrichai's study contributed to heterogeneity, it did not affect the overall findings, and thus it was retained in the analysis.

Radiographic success rates were reported in all 8 studies at the last follow-up, with the included studies exhibiting homogeneity (I^2 = 0%). Three studies specifically monitored the continued development of the root. Fixed-effects analysis demonstrated that the radiographic success rates were high for both Biodentine and other bio-ceramic materials, with no statistically significant difference between them (RR = 1.03, 95% CI (0.97, 1.09), p = 0.28) (Fig. 6). Moreover, the radiographic success rate of Biodentine was 93.88%, compared to 91.04% for other bio-ceramic materials.

3.4.3 Subgroup analysis

Subgroup analysis was conducted to evaluate clinical success rates at the last follow-up based on the type of VPT procedure by categorizing them into three subgroups: pulp capping, partial pulpotomy and pulpotomy. The analysis revealed high clinical success rates for both Biodentine and other bio-ceramic materials across all VPT procedures, with low intergroup heterogeneity (p = 0.62, I^2 = 0%). Overall, these findings suggest that when the procedural indications are strictly followed, the type of VPT procedure does not significantly influence success rates (Fig. 7).

4. Discussion

The studies included in this review focused on young permanent teeth diagnosed with deep caries, reversible pulpitis and irreversible pulpitis, with the primary outcome of comparing the clinical success rates of Biodentine and other bio-ceramic materials. The results showed that the clinical success rates for Biodentine at 6, 12 and 18 months were 99.38%, 94.20% and 87.38%, respectively, while the corresponding rates for other bio-ceramic materials were 98.15%, 92.59% and 88.35%. No statistically significant differences were observed in clinical success rates between Biodentine and other bio-ceramic materials across the same follow-up periods ($p > 0.05$). Radiographic success rates for all bio-ceramic materials exceeded 90% at the final follow-up, with no significant differences detected ($p > 0.05$). However, it was observed that Biodentine's radiographic success rate, as well as its clinical success rates at 6 and 12 months, were slightly higher than those of other bio-ceramic materials, although these differences were not statistically significant ($p > 0.05$), and this may be attributed to the limited sample size of the included studies. Conversely,

FIGURE 5. Forest plots for tooth discoloration of Biodentine and other biomaterials. CI: confidence intervals; M-H: Mantel-Haenszel method.

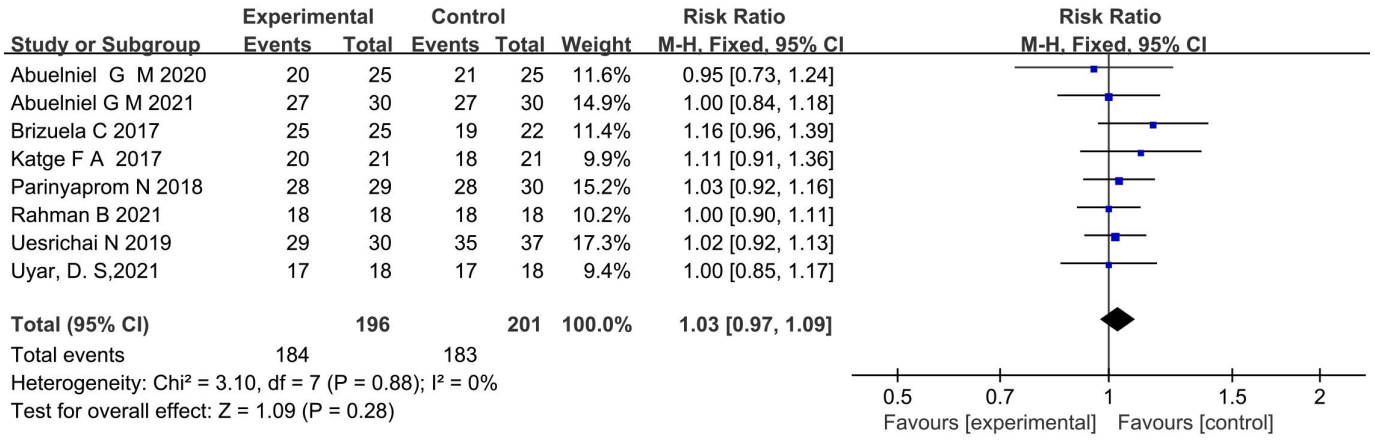

FIGURE 6. Forest plots for radiographic success of Biodentine and other biomaterials. CI: confidence intervals; M-H: Mantel-Haenszel method.

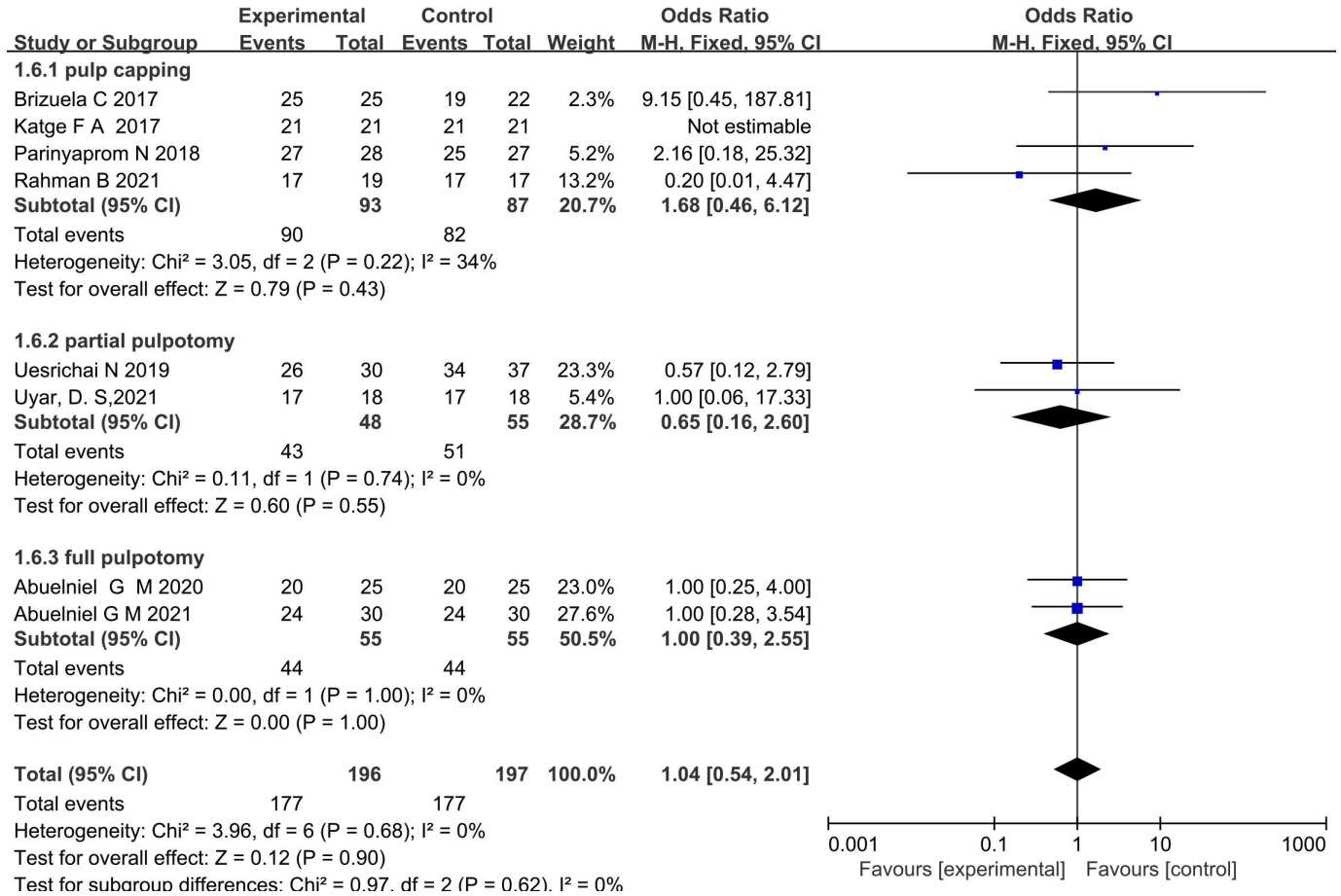

FIGURE 7. Subgroup analysis for various treatment performed. CI: confidence intervals; M-H: Mantel-Haenszel method.

Biodentine's clinical success rate at 18 months was marginally lower than other bio-ceramic materials, which could also be related to the small sample size analyzed. The most common clinical failure was pain, while radiographic failures frequently involved periapical pathology, such as including incomplete root development and the loss of the apical lamina dura [37, 38]. Secondary outcomes revealed a significantly lower rate of crown discoloration with Biodentine compared to MTA ($p < 0.05$). This finding aligns with the meta-analysis by Stringhini Junior *et al.* [39], which compared MTA and Biodentine in pulpotomy for primary teeth.

The formation of dentin bridges is an important measure of the effectiveness of pulp capping materials. Histological evaluation is widely regarded as the gold standard for assessing pulp status and dentin bridge formation [40]. An ideal hard tissue barrier should possess characteristics similar to natural dentin; however, none of the currently available capping materials fully meet this standard [41]. The process of hard tissue formation is generally considered reparative rather than regenerative [42]. The quality of the hard tissue formed reflects the health status of the pulp following direct pulp capping [41], and is regarded as a critical marker of the success of VPT [1]. Previous studies have demonstrated that MTA promotes a high rate of dentin bridge formation at the pulp interface [43, 44]. However, the mineralized tissue formed is often amorphous and irregularly calcified, lacking the tubular structure characteristic of natural dentin [41]. Both Biodentine and MTA have shown substantial potential for promoting the recruitment and differentiation of human dental pulp stem cells [45], which play an essential role in dentin regeneration and the formation of dentin bridges [46]. Histological analyses have been conducted to document and grade parameters such as the location and severity of inflammatory responses and the presence and quality of dentin bridge formation, and the findings suggest that Biodentine-induced reparative dentin often receives higher grades compared to MTA, and the underlying pulp tissue appears more similar to normal pulp tissue, indicating a reduced inflammatory response post-treatment [47]. These observations have led researchers to conclude that Biodentine demonstrates superior reparative dentin formation quality. Clinically, the formation and quality of dentin bridges are typically assessed using radiographic examinations. Bui *et al.* [1] reported that teeth treated with Biodentine for direct pulp capping exhibited dentin bridge formation during follow-up, indicating a favorable healing response. Some studies suggest that Biodentine induces thicker [48, 49] and denser dentin bridges compared to MTA [50]. However, Kim reported contrasting findings, indicating that dentin bridges formed in the MTA group were more regular and homogeneous in thickness [51]. In the present study, radiographic success rates for both MTA and Biodentine exceeded 90%, with no statistically significant difference between the two materials ($p > 0.05$). However, the limited number of quantitative studies on dentin bridge formation restricts the ability to conduct sub-

group analyses to identify which materials are more effective in promoting consistent and high-quality dentin bridges, thereby highlighting need for further research to explore the formation rates and quality of dentin bridges induced by different pulp capping materials.

A notable advantage of Biodentine over MTA is its color, which more closely matches that of natural teeth and demonstrates its superior color stability [29, 52]. The discoloration associated with MTA is primarily attributed to the presence of bismuth oxide, a radiopacifier [53]. When in contact with collagen in the dentin matrix, bismuth oxide molecules can destabilize, undergoing reduction to form metallic bismuth or oxidation to produce bismuth carbonate. Both processes lead to the formation of dark precipitates, resulting in tooth discoloration [54]. In Biodentine, zirconium oxide is used as a radiopacifier instead of bismuth oxide, significantly reducing the incidence of discoloration and enhancing the aesthetic outcomes of the treatment. In this study, Biodentine exhibited significantly fewer instances of discoloration at the final follow-up compared to MTA ($p < 0.05$), a finding consistent with previous research [27, 29]. The aesthetic impact of discoloration is particularly critical in anterior teeth, where the visual appearance of restorations plays a pivotal role in patient satisfaction. This characteristic underscores the importance of Biodentine in clinical practice, especially for treatments involving anterior teeth. Tooth discoloration may also be influenced by several factors, including the detection method, the area of contact between the capping material and the pulp, the duration of follow-up and the presence of blood contamination [35, 53]. Taken together, these variables highlight the need for further clinical studies employing various types of VPT and extended follow-up periods to validate the current findings and refine clinical protocols.

The success rate of VPT is closely related to the health status of the pulp, the size and position of pulp exposure, and adherence to aseptic techniques [6, 38, 49, 55]. In the studies included in this review, strict aseptic protocols were employed to enhance the success rate of VPT. Moisture control was achieved using a rubber dam, physiological saline was used for irrigation, and sodium hypochlorite was applied for disinfection. Traditionally, VPT has been considered appropriate only for teeth with reversible pulpitis or without pulp symptoms. However, some researchers have reported a poor correlation between clinical symptoms and pulp sensitivity tests with the actual histological condition of the pulp [56, 57]. Specifically, teeth clinically diagnosed with irreversible pulpitis may not always exhibit a completely irreversible histological state [58]. In some cases, the microbial infection associated with irreversible pulpitis is confined to the carious exposure area and does not involve the entire pulp [59]. Based on these observations, recent studies have suggested expanding the indications for VPT to include teeth diagnosed with irreversible pulpitis but without periapical pathology [13, 60–62]. In this review, one study employed indirect pulp capping, while six studies addressed teeth with reversible pulpitis or no pulp symptoms. One study included both reversible and irreversible pulpitis but did not differentiate success rates based on pulp status. Therefore, a subgroup analysis of how pulp status affects VPT success could not be performed. Despite this limitation, the consistently high success rates reported across the included studies support the inclusion of both reversible and irreversible pulpitis (without periapical inflammation) within the indications for VPT. Among the eight included studies, one utilized indirect pulp capping without pulp exposure, while the remaining seven performed direct pulp capping or pulpotomy. Of these, six studies quantified the size of the pulp exposure during inclusion, but none provided information about the location of the exposure Generally, larger pulp exposure areas are associated with higher risks of bacterial contamination and compromised pulp vitality, which can negatively impact treatment outcomes. However, due to significant variability in exposure sizes across the studies and consistently high success rates, no definitive conclusions could be drawn regarding the relationship between pulp exposure size and VPT success. This variability complicates direct comparisons and may obscure the actual impact of exposure size on treatment outcomes. Regarding root development status, five studies focused exclusively on young permanent teeth with open apices, while three included both open and closed apices. It is widely accepted that teeth with open apices exhibit richer vascularization and a higher density of cells, which may enhance their regenerative capacity and positively influence VPT success rates. However, a randomized clinical trial by Kang *et al*. [16] reported no significant difference in the efficacy of partial pulpotomy between permanent teeth at different stages of root development. In this review, the final success rates were not categorized based on root development status, preventing a subgroup analysis of this parameter. Such analyses are essential, as the stage of root development may significantly influence healing responses and overall treatment success. The inability to assess this aspect limits the generalizability of these findings and may affect the reliability of the overall conclusions.

This review included only randomized clinical trials, as specified by the inclusion criteria. One significant limitation was that nearly half of the studies were assessed as having an unclear risk of bias due to insufficient descriptions of the randomization methods. The lack of standardization in randomization can introduce bias, as imbalances between baseline characteristics in small sample size studies may inadvertently skew the results. Future studies should prioritize rigorous randomization techniques and provide detailed reporting of the randomization processes to enhance transparency and reproducibility. Blinding, another critical aspect of study design, could also be essential for minimizing detection bias. However, the distinct physical characteristics and varied application methods of the materials made operator blinding challenging, potentially increasing the risk of performance bias. To mitigate detection bias, most of the included studies ensured that operators were not involved in outcome assessments. Although sensitivity analysis indicated that the findings related to discoloration rates were stable, the observed high heterogeneity and potential biases remain important considerations. These limitations highlight the need for further validation through more comprehensive clinical trials, incorporating rigorous study designs to reduce bias and ensure robust conclusions.

This study had several limitations. First, the limited number

of included studies reduces the robustness and generalizability of the findings. A small sample of studies inherently increases the risk of potential biases and diminishes the strength of the evidence, emphasizing the need for more comprehensive future research. Additionally, only three studies reported outcomes related to discoloration, resulting in high heterogeneity and introducing potential bias. Therefore, these findings require further validation with additional data. Moreover, the assessment of tooth discoloration is highly subjective and influenced by factors such as lighting conditions, light sources, clothing, makeup and individual color perception, which reduces the accuracy and repeatability of color assessments, further contributing to potential bias in the reported outcomes. Second, the baseline conditions among the included studies varied significantly. Differences in factors such as reasons for pulp exposure, size and position of the exposure, and pulp status complicated comparisons and influenced the interpretation of results, introducing heterogeneity between studies. For example, teeth with varying exposure sizes and positions may exhibit different healing responses to treatment. However, due to the lack of detailed subgroup data in the included studies, subgroup analyses to evaluate the individual impact of these baseline differences could not be performed. Furthermore, the criteria used to determine treatment success were inconsistent across studies. While some studies assessed only clinical symptoms and periapical radiolucencies, others also included measures such as root development and dentin bridge formation. This variability in outcome evaluation standards introduced experimental heterogeneity. Third, the follow-up periods in most studies ranged from 6 to 18 months, which may be insufficient to assess long-term outcomes. The incidence of pulp pathology and discoloration following VPT could increase over time, and the absence of data for longer follow-up durations limits the ability to evaluate the long-term effectiveness of the treatment. Future research should aim to standardize the criteria for assessing clinical and radiographic success outcomes and to evaluate discoloration rates in a more objective and reproducible manner. Additionally, studies with extended follow-up periods are needed to assess the long-term outcomes of VPT. Future investigations could also explore the effects of pulp capping agents on teeth with varying pulp statuses or stages of root development. By addressing these variables, research could provide a clearer understanding of how these factors influence treatment outcomes, ultimately enabling the development of more personalized and effective treatment strategies.

5. Conclusions

The findings of this meta-analysis showed that Biodentine can achieve high clinical and radiographic success rates, comparable to those of other bio-ceramic materials, such as MTA and TheraCal, when utilized as a capping material for VPT in young permanent teeth. One of Biodentine's significant advantages is its lower rate of tooth discoloration, which enhances aesthetic outcomes and broadens its applicability in clinical settings. Despite these promising results, further research is needed to validate these findings and address existing limitations. In addition, higher quality, multicenter studies with long-term follow-up periods are needed to provide more robust evidence regarding Biodentine's prognosis in VPT and deeper insights into the factors influencing treatment success, which would contribute to optimizing clinical strategies.

ABBREVIATIONS

AAE, American Association of Endodontics; VPT, vital pulp therapy; PROSPERO, Prospective Register of Systematic Reviews; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; MeSH, Medical Subject Headings; MTA, Mineral Trioxide Aggregate; CSCs, silicate-based cements; RCTs, randomized controlled trials; RR, Relative risk; CI, confidence intervals; CH, calcium hydroxide; M-H, Mantel-Haenszel method; SE, Standard Error.

AVAILABILITY OF DATA AND MATERIALS

The data that support the findings of this study are openly available in PubMed, Embase, Web of Science and the Cochrane Library.

AUTHOR CONTRIBUTIONS

LJL and WYZ—designed the research study and independently conducted the literature screening and data extraction. LJL—analyzed the data and wrote the manuscript. WYZ—provided help and advice. Both authors contributed to editorial changes in the manuscript. Both authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at https://oss.jocpd.com/files/article/1917110009426001920/attachment/Supplementary%20material.zip.

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