Systematic Review

Treatment options for large posterior restorations: a systematic review and network meta-analysis

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Supplemental material is available online.

ABSTRACT

Background. The best treatment option for large caries in permanent posterior teeth is still a matter of uncertainty in dental literature. The authors conducted a network meta-analysis to address the challenges related to rehabilitation of these teeth.

Types of Studies Reviewed. The authors selected prospective and retrospective studies that compared at least 2 different treatment alternatives for permanent teeth with a minimum of 5 years of follow-up. The authors searched databases from MEDLINE, Scopus, Cochrane Library, and Web of Science in October 2019 without language or year of publication restrictions.

Results. From 11,263 studies identified, 43 studies fulfilled the eligibility criteria and were included in the final review. Only 13 studies were randomized controlled trials and were classified as low risk of bias. Gold (annual failure rate of 0.29%) and metal ceramic (annual failure rate of 0.52%) crowns performed better for indirect restorations and direct resin composite performed better for direct restorations (annual failure rate of 2.19%). The most substantial comparisons were between feldspathic and glass ceramics, followed by direct resin composite and amalgam; there were no statistically significant differences between these interventions. Results of the pairwise meta-analysis showed mainly glass ionomer as significantly more prone to failure than amalgam and direct composite resin.

Conclusions and Practical Implications. Reference standard direct and indirect materials except for glass ionomer can be used for restorations of large posterior caries.

Key Words. Restorative materials; dental restorations; dental fillings; dental composites; operative dentistry; clinical studies/trials; evidence-based dentistry.

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There is a tendency for increased expenditures for dental treatment over time,[1] and the major part consists of the placement and replacement of restorations.[2] In this context, although there is some evidence on the indication of composites as the best option for restoring small defects in load-bearing restorations,[3,4] little information is available concerning more extensive restorations. The risk of failure for a posterior restoration increases 30% through 40% for every extra added surface.[5] In addition, the survival of restorations is influenced by several other factors, such as material properties,[6] oral health care providers' choices,[7] and patient characteristics, that is, the presence of caries risk and occlusal stress.[7,8]

Even with the shift of choice from amalgam to composite resin that has occurred in the past several decades,[9] it is still possible to find systematic reviews in the literature supporting both materials.[4-6,10] Indirect restorations are also considered as an alternative for restoring large defects, as they have shown good clinical performance in general practice[11] and a lower need for repair and replacement.[12] Several types of materials for indirect restorations are available, although some ceramic types, such as feldspathic and glass ceramics, might be less suitable for high-functional load

regions.[13] To test differences in the effectiveness of restorative treatments, the outcomes ideally should be measured after long observation times.[14] This is especially important for large restorations, which represent the critical situations in restorative dentistry.[14]

Owing to the extensive number of available materials for both direct and indirect techniques and considering the lack of consensus about the best clinical choice, a network meta-analysis (NMA) of multiple treatment comparisons can be used to predict the best treatment option.[15] A 2016 NMA comparing different restorative treatments and adhesive systems included only prospective studies with direct restorative materials in cervical and load-bearing restorations of permanent and primary molar teeth.[4] Therefore, the aim of our systematic review and NMA was to answer the following question: Which are the best restorative treatment types and materials for large restorations in permanent posterior teeth in adults?

METHODS

For our review, we followed the guidelines of the Cochrane Handbook for Systematic Reviews of Interventions[16] and reported results based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement for Network Meta-Analyses.[17] The protocol was registered in International Prospective Register of Systematic Reviews (PROSPERO) (CRD42016048264).

Eligibility criteria

The participants, interventions, comparisons, and outcomes question was "In adult patients with large tooth preparations, what would be the best treatment option to improve tooth or restoration longevity?"

Large tooth preparation was defined as any preparation involving the need for a restoration that would encompass 2 or more surfaces. This approach was chosen because several of the primary studies made no distinction among the different types of multisurface preparations and did not report on the real extension of the tooth preparation and because there is evidence that a 2-surface restoration has up to 40% higher chance for failure than a 1-surface restoration.[5,18]

Inclusion criteria

The inclusion criteria were clinical studies comparing at least 2 types of restorative materials placed in large tooth preparations in permanent posterior teeth (from 2-surface restorations up to full crowns), studies with survival rate data of the restorations and a minimum of 5 years of follow-up, and randomized controlled trials (RCTs) or non-RCTs, as well as retrospective studies. There were no language or year of publication restrictions.

Exclusion criteria

Studies with the following characteristics were excluded: case-control studies, case reports, reviews, in vitro studies, expert opinions, and studies with no comparison between materials, no information about survival rates, and a follow-up period of less than 5 years.

Literature search and information sources

The literature search strategy for the electronic databases (MEDLINE, Scopus, Cochrane Library, and Web of Science) was created based on Medical Subject Heading terms and adapted for the other databases (eTable 1, available online at the end of this article). The last search was performed on October 2019.

Study selection

Initially, duplicates were removed in EndNote, Version X7 (Thomson Reuters) and 2 independent reviewers (B.M.V., F.L.L.) selected articles by title and abstract for relevance based on the inclusion criteria. In case of disagreement, a third reviewer (T.P.-C.) was recruited to reach consensus. Full texts were obtained for additional screening and, if the same sample was presented in distinguished articles, the one with higher follow-up was considered.

Data collection process and data items

Two reviewers (B.M.V., F.L.L.),collected data in duplicate using Excel spreadsheets (Microsoft). They extracted the following information: author, year, and country of publication; inclusion

ABBREVIATION KEY

AM:	Amalgam.
DR:	Direct resin.
FC:	Feldspathic ceramic.
GC:	Glass ceramic.
GI:	Glass ionomer.
GO:	Gold.
GRADE:	Grading of Recommendations Assessment, Development and Evaluation.
IR:	Indirect resin.
MC:	Metal ceramic.
NMA:	Network meta-analysis.
RCT:	Randomized controlled trial.
RoB:	Risk of bias.
RS:	Resin sandwich.
ZC:	Zirconia-based ceramic.

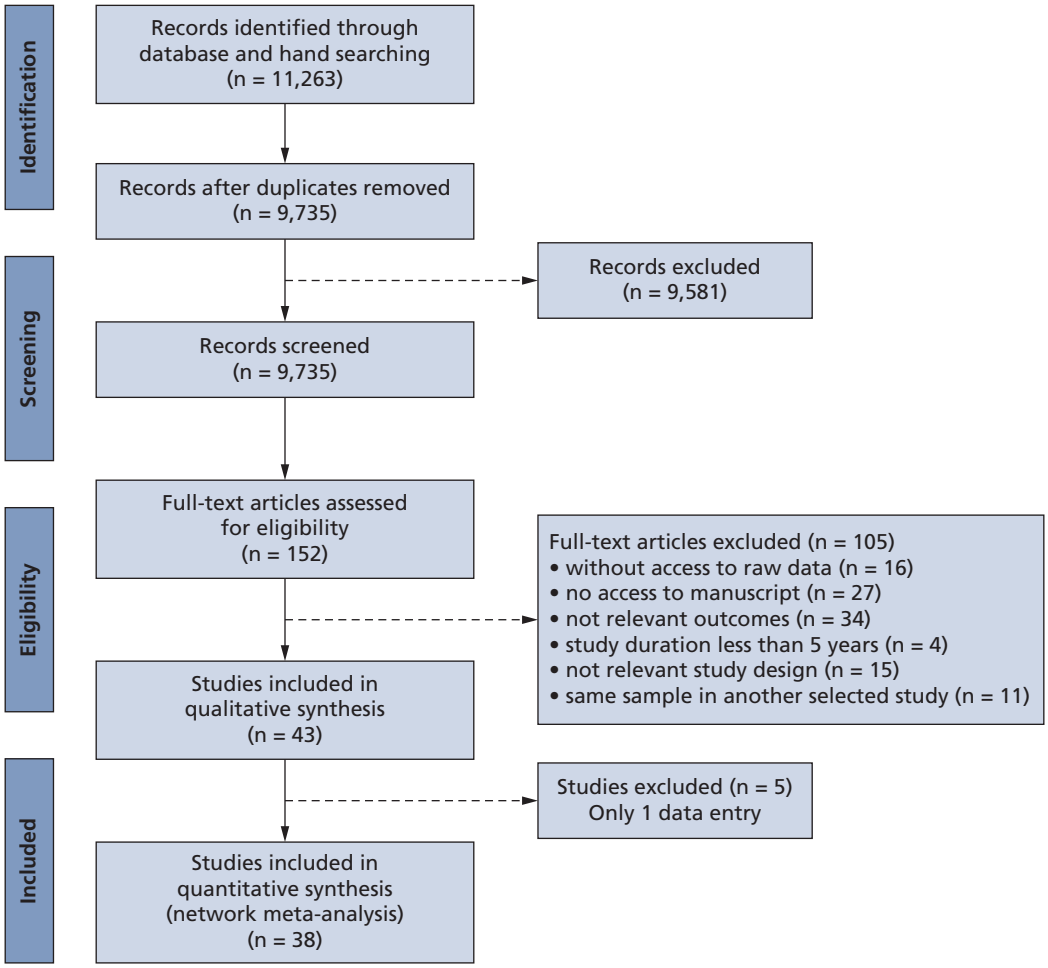


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart of the systematic review.

criteria; patient's age and sex; number of restorations; follow-up and dropout; restorative technique and material; tooth vitality; presence of post; number of failures; survival rate; and evaluation criteria. In case of doubt, the third reviewer's (T.P.-C.) opinion was requested. When data were missing or not clear, for example, when restorations were not divided by size, 2 attempts to request it from the authors were made via e-mail. Considering that most studies, especially on direct materials, reported on the extension of the restoration and not on the extension of the preparation, restoration extension rather than preparation extension was considered to try to have a more homogeneous data collection for the comparisons. Studies were excluded if there was no reply from the authors or if they replied that data were not available.

Summary measures and planned methods of analysis

The primary outcome was restoration survival, recorded either in case of repair or no intervention. Replaced restorations or extracted teeth were considered as failures. The annual failure rate (AFR) of the investigated restorations was calculated according to the following formula: $(1 - y)^z = (1 - x)$, in which y represents mean AFR and x is total failure rate at z years.

All data analysis was performed using R, Version 3.5.1 and the packages "pcnetmeta" and "meta"[19-21] separately for RCTs and nonrandomized prospective and retrospective studies. Pairwise meta-analyses for direct treatment comparisons were performed using the random-effects model, with heterogeneity assessed by calculating the I^2 and τ^2 statistics and its 95% confidence intervals (CIs). Multiarm studies were treated as multiple independent 2-arm studies in pairwise meta-analyses, and the effects were estimated as risk ratios.

The hierarchical model chosen for the NMA was the Bayesian framework[16] using the Markov Chain Monte Carlo method simulation, with 20,000 iterations for adaptation. The random-effects

model was used due to the differences among studies regarding methodology. The convergence was also assessed by the Markov Chain Monte Carlo method.[22] A summary network plot was generated in which the nodes represent the competing interventions, and the edges represent the comparison between the interventions. The surface under the cumulative ranking line for each treatment was calculated. In this approach, the closer to 1 the cumulative probability is, the better the treatment. In the graphic representation of the ranking of probabilities, the darker the treatment is, the better is its performance.

Risk of bias within individual studies and quality of the body of evidence

RCTs were evaluated for risk of bias (RoB) using the Cochrane RoB tool,[23] considering random-sequence generation, allocation concealment, blinding of participants and professionals, blinding of outcomes assessment, incomplete outcomes, selective reporting, and other sources of bias. The assessment of bias of the non-RCTs was performed with the Risk of Bias in Non-randomized Studies-of Interventions tool[24] considering the judgment of confounding, selection of participants, classification of interventions, deviation from intended interventions, missing data, measurement of outcomes, and selection of the reported results. One reviewer rated the studies at first (B.M.V.) and a second reviewer (T.P.-C.) checked them. The quality of evidence was evaluated using the Grading of Recommendations Assessment, Development and Evaluation approach.[25]

RESULTS

Study selection and characteristics

The literature search yielded 11,263 titles and abstracts in October 2019. After duplicates were removed and analysis of titles and abstracts was conducted, 152 articles were selected to access the full-text. The response rate for contact with authors was approximately 62.1%. From the replied e-mails, 11 studies could be included after assessing the original data. Forty-three studies[12,26-67] fulfilled the eligibility criteria and were included in the review (Figure 1; eTables 2 and 3, available online at the end of this article). As each material should appear at least in 2 studies, 5 articles were excluded from this analysis because the materials investigated had been evaluated only once.[26,40,48,56,66] All different types of resin composite were grouped as direct resin composite, which led to 6 additional studies being excluded from the NMA because these studies were comparing 2 types of resin composites.[59-64]

Ranking of probabilities and synthesis of pairwise comparisons results

The NMA results and the AFR values suggest that most of the restorative options have good performance and are suitable for large restorations. Less favorable performances were found for glass ionomer as direct material and glass ceramic and feldspathic ceramic as indirect materials in the ranking of probabilities and surface under the cumulative ranking (Figures 2 and 3). Most of the pairwise comparisons were between feldspathic and glass ceramic (95% CI, 0.84 to 1.77 for non-RCT prospective studies and 95% CI, 0.87 to 1.16 for retrospective studies) and direct resin composite and amalgam (95% CI, 0.65 to 1.15 for RCTs, 95% CI, 0.93 to 1.06 for non-RCT prospective studies, and 95% CI, 0.97 to 1.29 for retrospective studies). Glass ionomer, either alone or in combination with composite, was found to be significantly more prone to failure than amalgam (95% CI, 0.97 to 2.20 for non-RCT prospective studies and 95% CI, 1.36 to 144 for retrospective studies) and direct composite resin in the pairwise meta-analyses (95% CI, 1.06 to 2.14 for non-RCT prospective studies and 95% CI, 1.68 to 1.79 for retrospective studies) (Figure 4).

RoB within individual studies and quality of body evidence

Thirteen RCTs[12,52,53,56-59,61-64,66,67] were included, with a low risk of incomplete outcome data, selective reporting, random-sequence generation, and blinding of outcomes assessment (eFigure 1, available online at the end of this article). There was a moderate confident effect estimate because the RCTs had a high certainty, and the observational studies had a very low certainty about the evidence generated (eFigures 2, 3, and 4, available online at the end of this article). From the included studies, 24 were non-RCTs with a serious RoB,[26-29,32,37-51,54,55,60,65] 5 of the non-RCTS had a moderate RoB[30,31,33,35,36], especially for bias to confounding and measurement of outcomes (Table), and only 1 had a low RoB.[34]

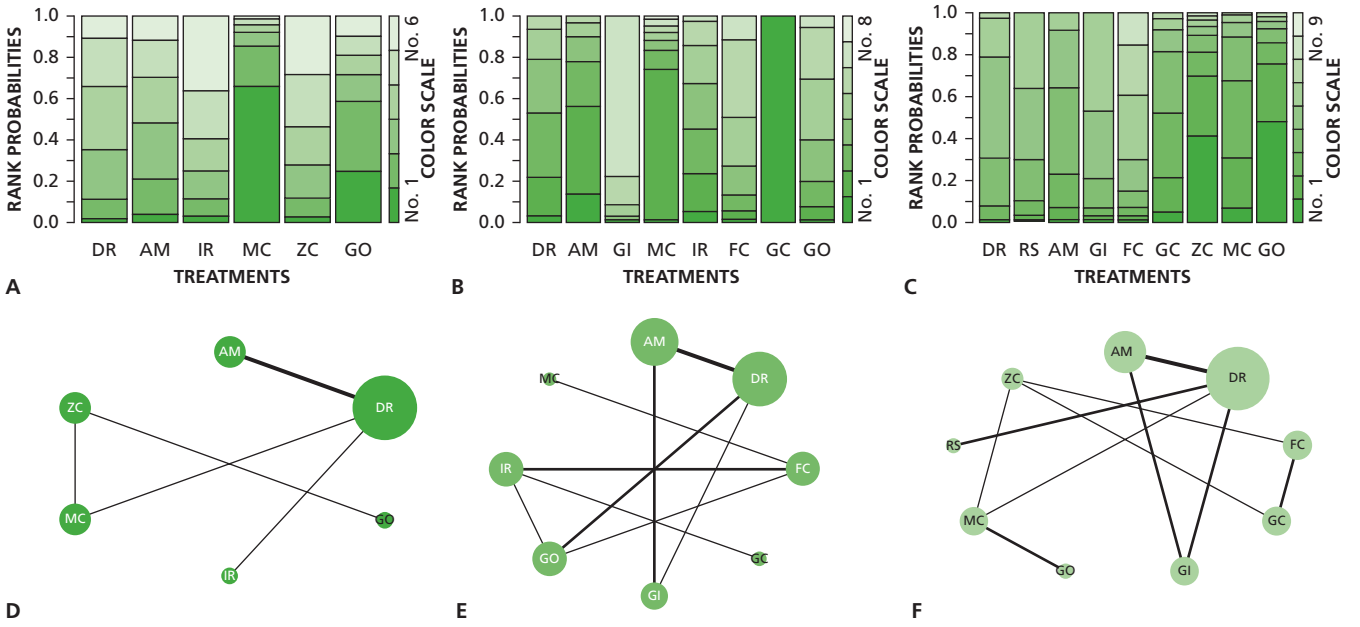


Figure 2. A-C. Ranking of probabilities for the treatments. The darker areas indicates the probability of being the best treatment. **A.** Randomized controlled trials. **B.** Nonrandomized prospective studies. **C.** Retrospective studies. **D-F.** Network graph. Summary of the number of studies and restorations for each treatment. The size of treatment nodes reflects the number of restorations assigned to each treatment. The thickness of lines represents the number of studies underlying each comparison. **D.** Randomized clinical trials. **E.** Nonrandomized prospective studies. **F.** Retrospective studies. AM: Amalgam. DR: Direct resin. FC: Feldspathic ceramic. GC: Glass ceramic. GI: Glass ionomer. GO: Gold. IR: Indirect resin. MC: Metal ceramic. RS: Resin sandwich. ZC: Zirconia-based ceramic.

Results of additional analyses

The Table provides the AFRs for the RCTs and nonrandomized prospective and retrospective studies included in the NMA separately, as well as combined, including the number of studies and number of restorations. The highest AFR was found for glass ionomer restorations (10.02%); composite glass ionomer sandwich restorations had an AFR of 4.24%. Gold and metal ceramic restorations had the lowest AFRs (0.29% and 0.52%, respectively). The best performances were found for direct resin composite as direct restorations (AFR, 2.19%) and gold for indirect restorations (AFR, 0.29%).

DISCUSSION

Dentists have to choose among several restorative options for their patients daily. On small defects, there is a consensus that resin composite is the preferred choice.[3,4,68-70] However, for larger defects, the choice between indirect and direct materials has been investigated in only 1 clinical study.[12] Therefore, in this NMA, we focused on larger defects and compared direct and indirect restorative options. To our knowledge, this is the first review designed as an attempt to help dentists determine the best treatment option for large defects in posterior teeth.

Our overall results showed that gold and metal ceramic crowns perform better in extensively damaged teeth, and resin composite and amalgam perform better for direct restorations. In the data collection, composites were classified as bulk-fill materials, hybrid resin, and others. However, for our analysis, we considered it appropriate to combine the composite groups, as it is challenging to assign most of the restorative materials assessed into a specific classification. For example, a bulk-fill material is also a hybrid composite most of the time. In addition, resin composites were classified in different ways through time and according to different assumptions.

Although nonrandomized studies include more biases,[71] we decided to include them for their closeness to daily practice, and most had a longer follow-up times and larger sample sizes than RCTs. With that, 3 ranking outcomes are shown, and the differences in the results and general conclusion valid for all study types can be seen. In general, indirect restorations (crowns) had the highest probability of showing the best longevity compared with direct restorations, although this was not the case for glass ceramic and zirconium in prospective studies. For direct restorations, composite resin was superior to amalgam in retrospective studies, which was the opposite for

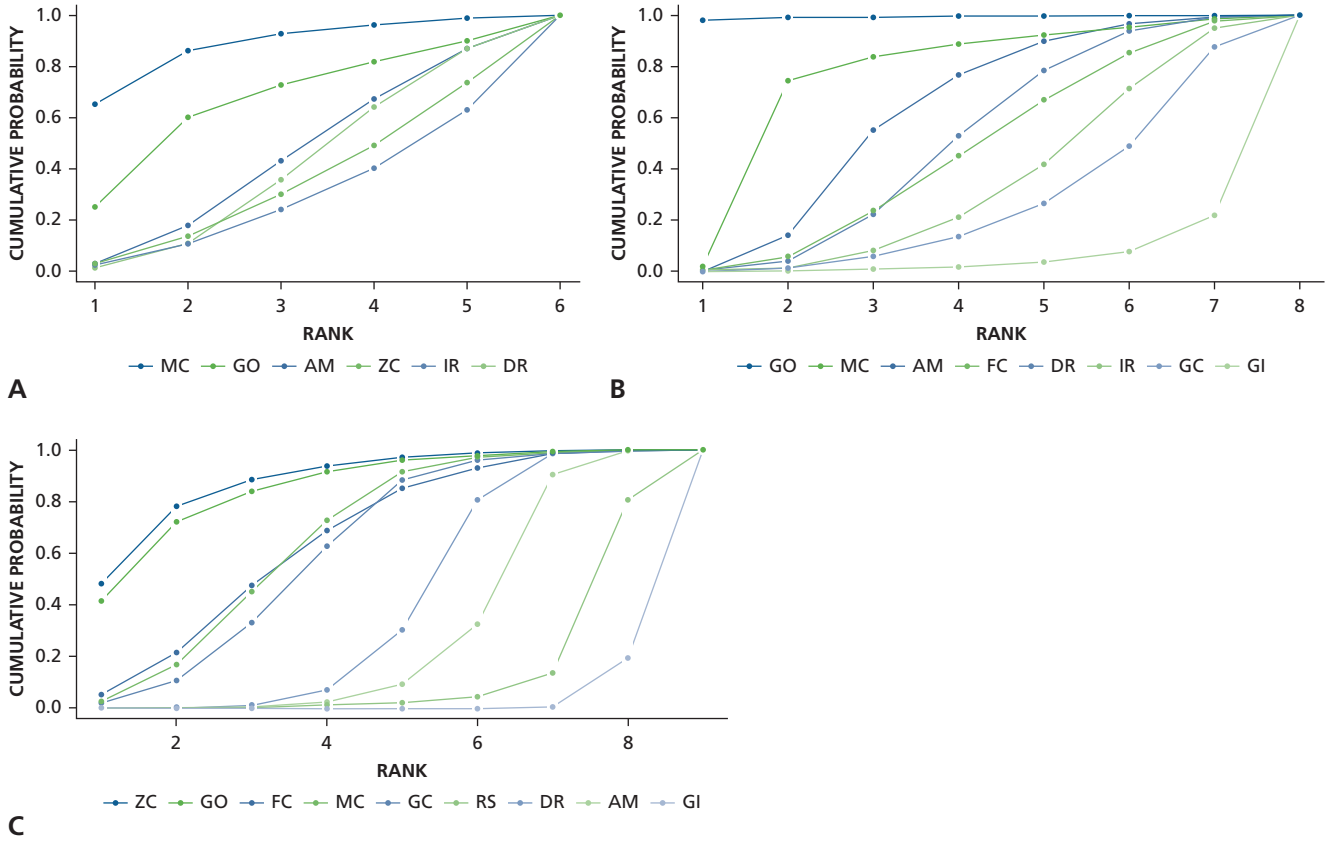


Figure 3. The surface under the cumulative ranking line for each treatment. The closer to 1 the cumulative probability is the better the treatment. **A.** Randomized controlled trials. **B.** Nonrandomized prospective studies. **C.** Retrospective studies. AM: Amalgam. DR: Direct resin. FC: Feldspathic ceramic. GC: Glass ceramic. GI: Glass ionomer. GO: Gold. IR: Indirect resin. MC: Metal ceramic. RS: Resin sandwich. ZC: Zirconia-based ceramic.

prospective studies, randomized or not. Generally, glass ionomer performed worse than other materials in larger restorations. Likewise, composite glass ionomer sandwich restorations had inferior results compared with composite restorations placed without glass ionomer, which was in agreement with a previous systematic review.[5]

For the comparison between amalgam and composite, the explanation for these different results can be found in the differences in study populations. The major contribution to the prospective studies on amalgam (427 restorations) was provided by Bernardo and colleagues,[53] who compared amalgam and composite in a clinical trial with children who likely had active caries. In adult populations, as in the retrospective studies, more patients with active caries were likely included, which could explain the differences between the results in the Table. The differences in AFR between prospective and retrospective studies reflect this, and previous investigators have reported a considerable difference in failure rates between patients with high and low risk of caries.[5]

The relatively bad outcome for glass ceramic crowns in nonrandomized prospective studies (AFR, 3.3%) relies on 136 restorations in 4 studies, and in retrospective studies (n = 3), the number of restorations was 549. For the glass ceramic, some obsolete materials were used, which cannot be compared with contemporary glass ceramic materials. The disadvantage of low sample sizes, old studies, and outdated materials might be less likely in the retrospective research studies, which led to far better results for the glass ceramic group in these studies.

One crucial question is how valuable the NMAs are for comparing restorative techniques in a scenario in which the primary studies have knowledgeable limitations. Lee and Shin[72] analyzed the quality of reporting of 21 NMAs in dentistry and found that most key components from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement for Network Meta-Analyses extension statement were missing.[17] The outcome seems highly dependent on the number of included studies and their sample sizes. Therefore, the inclusion of only RCTs in this NMA could bring a limited answer for the clinical review question.[14]

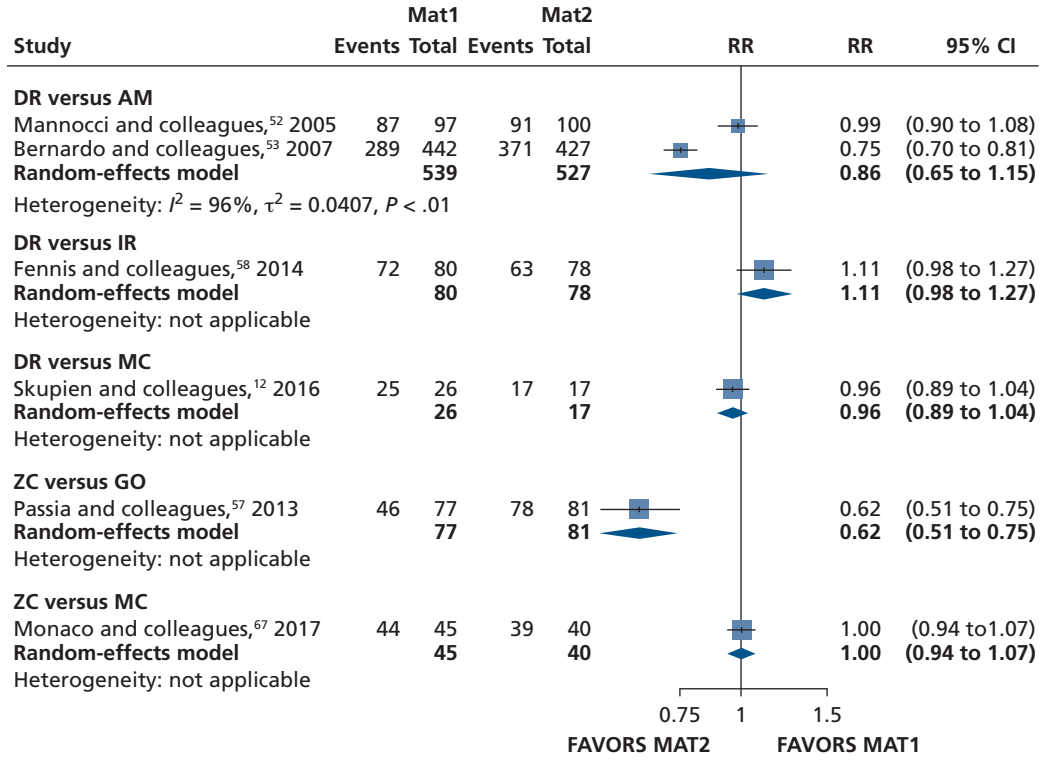
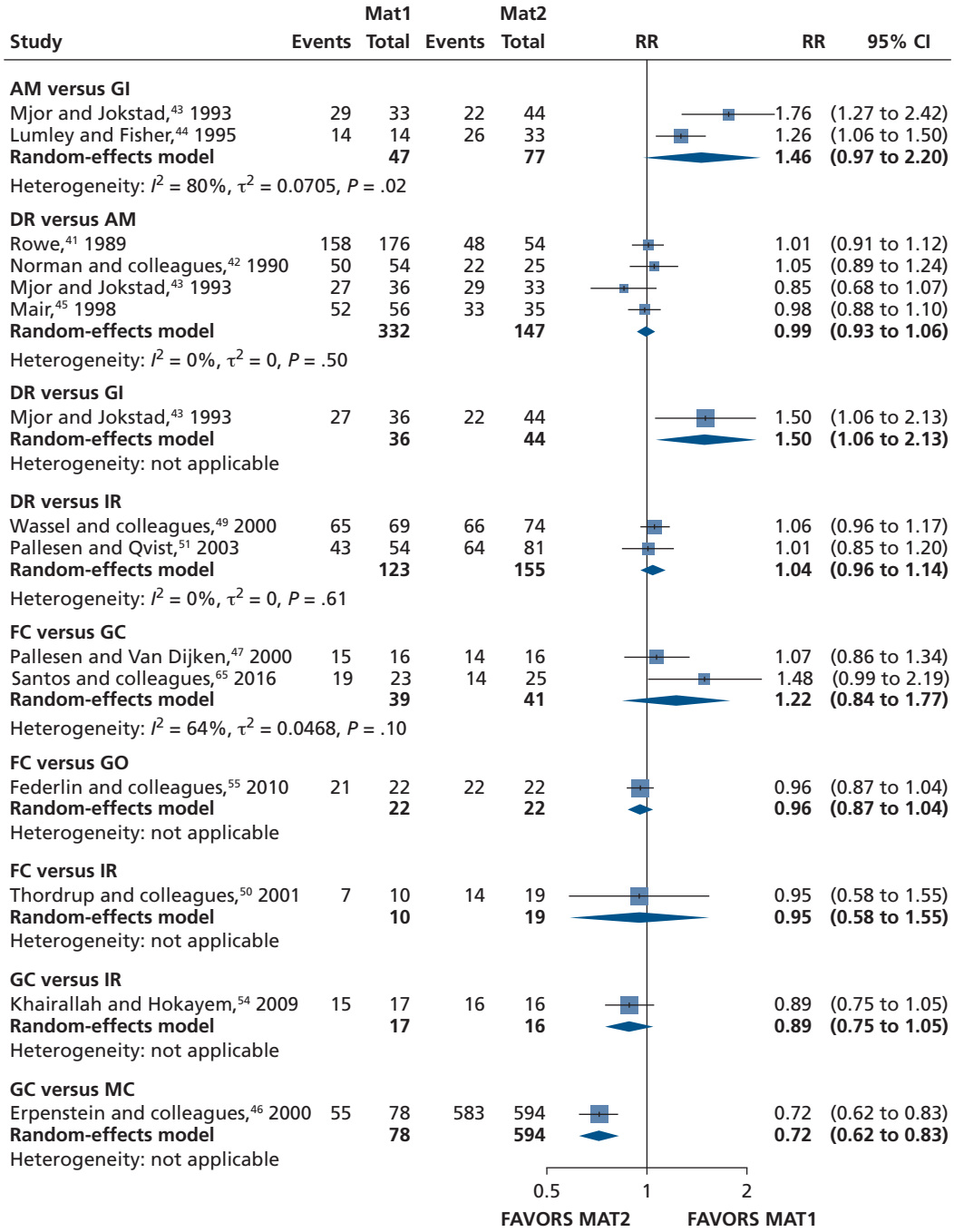


Figure 4. Forest plots of pairwise comparisons for the studies. The events represent the survived restorations. Risk ratio (RR) and 95% confidence interval (95% CI) for the first material group (Mat1) versus the second material group (Mat2). **A.** Randomized controlled trials. **B.** Nonrandomized prospective studies. **C.** Retrospective studies. AM: Amalgam. DR: Direct resin. FC: Feldspathic ceramic. GC: Glass ceramic. GI: Glass ionomer. GO: Gold. IR: Indirect resin. MC: Metal ceramic. RS: Resin sandwich. ZC: Zirconia-based ceramic.

The RoB provided from the specific tools for the different study designs, along with the quality assessment, allows us to see the results of this review as a moderate confident effect because the evidence generated was considered high for RCTs and low for non-RCTs. Still, the RoB assessment does not entirely take into account factors such as external validity, study size, and other aspects that might also influence the interpretation of the studies. Another possible confounding factor is the criteria for failure that are not standardized among primary studies and might produce different results depending on the thresholds used. As a result, failure as defined in retrospective practice-based studies usually stands for the decision taken by the patient and the dentist to intervene. All analyses were split considering these differences in study designs to enable readers to interpret how the different methodologies are influencing the results shown in the current literature.

Our results match those of earlier reviews showing good performance for the direct resin composite.[4,5] The AFR of 2.19% for direct resin composite from our study is similar to the values found in the literature.[73,74] Among the indirect treatment options, our study emphasizes the good performance of gold and metal ceramic restorations, which had the lowest AFR. Although these restorative options require more invasive preparation, higher cost, and perform worse in esthetics than direct procedures, gold and metal ceramics restorations have shown excellent mechanical strength and biocompatibility during the past 50 years.[28,39,57] A previous systematic review on survival rates for single crowns also had a suitable result for gold and metal ceramic (considered as the reference standard) and recommended that feldspathic and glass ceramics should be avoided due to their highest AFR.[13] In our study, the overall AFRs for glass and feldspathic ceramics were 2.48% and 1.62%, respectively. Considering that we should ideally choose the treatment with lower cost, less-invasive tooth preparation, and simpler technique, direct resin composite restorations appear to be a better option than indirect resin composite restorations because there is no difference in longevity.[75]

One limitation of our study was the impossibility of comparing other important options, such as new all-ceramic and resin composite materials. This is explained by the exclusion of studies with less



B

Figure 4. (*continued*).

than 5 years of follow-up, as it is expected that failures like fractures and secondary caries occur after longer follow-up times.[5] Most dental materials used for large restorations lack primary comparative studies with proper follow-up time, but one can consider that these new materials are mainly the evolution of older well-known materials. In this context, although the absence of these new materials might be considered a limitation of our study, good results can be expected for most of these new materials. Another limitation of our study is the lack of clear inclusion criteria in the primary studies, especially regarding the extension of the restoration and confounding factors.

We intended to analyze several criteria at the protocol stage, such as tooth type, cost-effectiveness, and patient risk factors, but those data were rarely available and therefore not sufficient to assess their impact on survival of restorations. In addition, when patient risk factors are not included, the results might be incomplete and lack external validity.

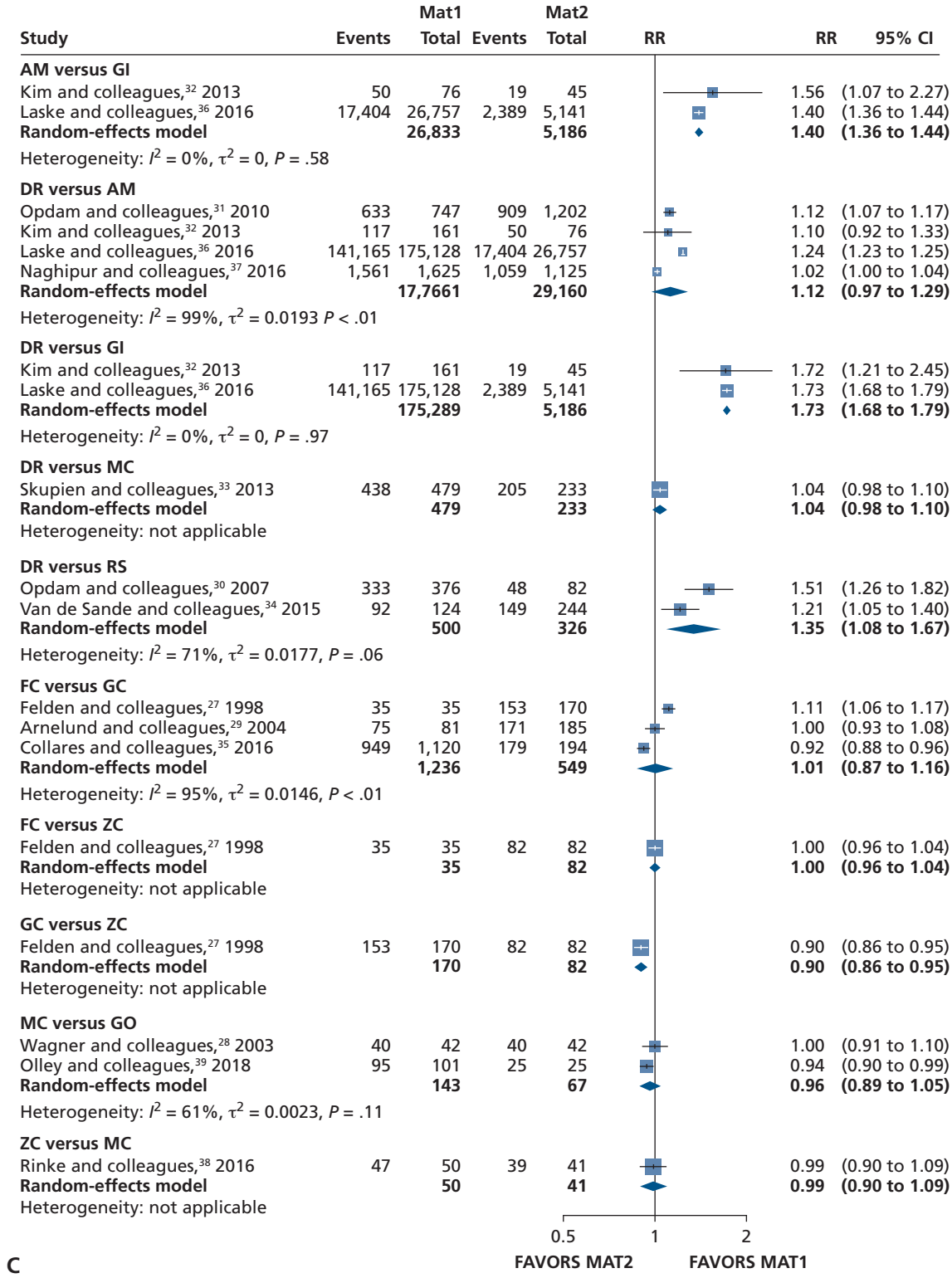


Figure 4. (*continued*).

CONCLUSIONS

We found gold and metal ceramic crowns had the best overall longevity, and resin composites and amalgam performed better for direct restorations, according to AFRs. However, the need for a more invasive preparation, higher costs, and poorer esthetics, especially for gold, should be considered when selecting the material to be used in daily practice. Only glass ionomer and sandwich composite restorations performed worse in the NMA pairwise comparisons. In addition, primary studies

Table. Annual failure rate for direct and indirect materials.

MATERIAL	RANDOMIZED CLINICAL TRIALS			NONRANDOMIZED PROSPECTIVE STUDIES			RETROSPECTIVE STUDIES			OVERALL		
	Studies, No.	Restorations, No	AFR*	Studies, No.	Restorations, No.	AFR	Studies, No.	Restorations, No.	AFR	Studies, No.	Restorations, No.	AFR
Direct												
Direct composite resin	4	645	2.67	6	445	2.11	7	21,110	2.04	17	22,200	2.19
Amalgam	2	527	1.93	5	161	1.59	4	29,154	3.76	11	29,842	2.73
Sandwich (resin and glass ionomer)	NA†	NA	NA	NA	NA	NA	2	326	4.24	2	326	4.24
Glass ionomer	NA	NA	NA	2	77	8.42	2	5,186	11.61	4	5,263	10.02
Indirect												
Gold	1	81	0.75	1	22	0	2	67	0.19	4	170	0.29
Metal ceramic	2	57	0.26	1	594	4.87	4	417	0.78	7	1,068	0.52
Feldspathic ceramic	NA	NA	NA	4	72	1.15	3	1,236	2.08	7	1,308	1.62
Indirect composite resin	1	78	3.5	4	190	1.39	NA	NA	NA	5	268	1.81
Glass ceramic	NA	NA	NA	4	136	3.31	3	549	1.64	7	685	2.48
Zirconia-based ceramic	2	122	5.12	NA	NA	NA	2	132	0.62	4	254	2.87

* AFR: Annual failure rate. † NA: Not applicable.

on the longevity of restorations should follow guidelines to standardize outcome reports to improve future direct and indirect comparisons. ■

SUPPLEMENTAL DATA

Supplemental data related to this article can be found at https://doi.org/10.1016/j.adaj.2020.05.006.

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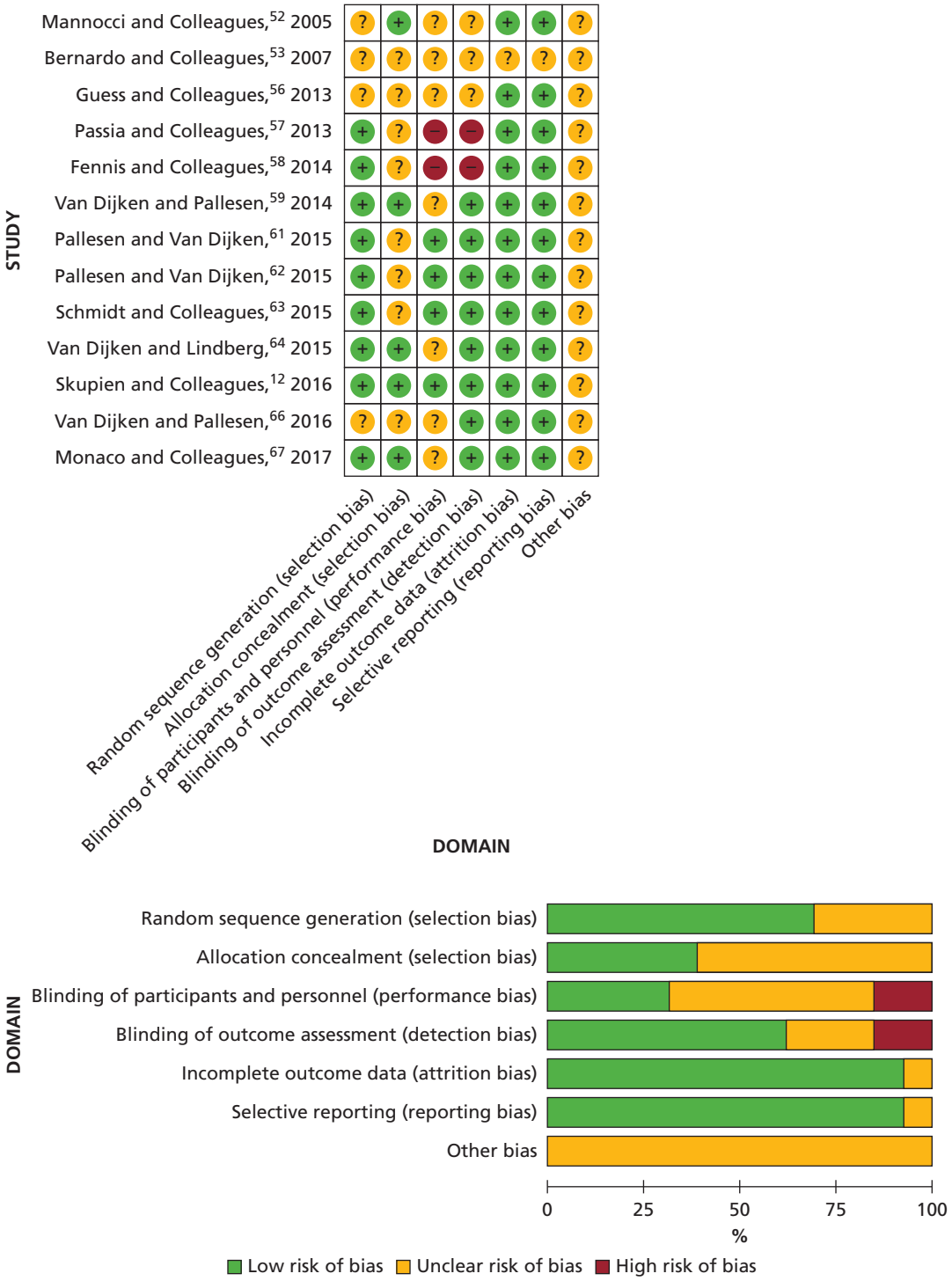

eFigure 1. Risk of bias using the Cochrane risk of bias tool. (+): Low risk of bias. (−): High risk of bias. (?): Unclear risk of bias.

TREATMENT OPTIONS FOR EXTENSIVE POSTERIOR RESTORATIONS			
OUTCOME	RELATIVE EFFECT, RR (95% CI)	NO. OF RESTORATIONS (STUDIES)	CERTAINTY OF EVIDENCE (GRADE)
Survival Rate			
Direct resin [Reference] versus amalgam	**0.86** (0.65 to 1.15)	1,066 (2 RCTs)	⊕⊕⊕⊕ HIGH
Direct resin [Reference] versus indirect resin	**1.11** (0.98 to 1.27)	158 (1 RCT)	⊕⊕⊕⊕ HIGH
Direct resin [Reference] versus metal ceramic	**0.96** (0.89 to 1.04)	43 (1 RCT)	⊕⊕⊕⊕ HIGH
Zirconia-based ceramic [Reference] versus gold	**0.62** (0.51 to 0.75)	158 (1 RCT)	⊕⊕⊕⊕ HIGH
Zirconia-based ceramic [Reference] versus metal ceramic	**1.00** (0.89 to 1.04)	85 (1 RCT)	⊕⊕⊕⊕ HIGH

eFigure 2. Assessment of level of evidence (Grading of Recommendations Assessment, Development and Evaluation [GRADE]) for randomized clinical trials (RCT). GRADE Working Group grades of evidence: High certainty: Very confident that the true effect lies close to that of the estimate of the effect. Moderate certainty: Moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Low certainty: Confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect. Very low certainty: Very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

TREATMENT OPTIONS FOR EXTENSIVE POSTERIOR RESTORATIONS			
OUTCOME	RELATIVE EFFECT, RR (95% CI)	NO. OF RESTORATIONS (STUDIES)	CERTAINTY OF EVIDENCE (GRADE)
Survival Rate			
Amalgam [Reference] versus glass ionomer	**1.46** (0.97 to 2.20)	124 (2 observational studies)	⊕◯◯◯ VERY LOW*†
Direct resin [Reference] versus amalgam	**0.99** (0.93 to 1.06)	469 (4 observational studies)	⊕◯◯◯ VERY LOW*†
Direct resin [Reference] versus glass ionomer	**1.50** (1.06 to 2.13)	80 (1 observational study)	⊕◯◯◯ VERY LOW*†
Direct resin [Reference] versus indirect resin	**1.04** (0.96 to 1.14)	278 (2 observational studies)	⊕◯◯◯ VERY LOW*†
Feldspathic ceramic [Reference] versus glass ceramic	**1.22** (0.84 to 1.77)	80 (2 observational studies)	⊕◯◯◯ VERY LOW*†
Feldspathic ceramic [Reference] versus gold	**0.96** (0.87 to 1.04)	44 (1 observational study)	⊕◯◯◯ VERY LOW*†
Feldspathic ceramic [Reference] versus indirect resin	**0.95** (0.58 to 1.55)	29 (1 observational study)	⊕◯◯◯ VERY LOW*†
Glass ceramic [Reference] versus indirect resin	**0.89** (0.75 to 1.05)	33 (1 observational study)	⊕◯◯◯ VERY LOW*†
Glass ceramic [Reference] versus metal ceramic	**0.72** (0.62 to 0.83)	672 (1 observational study)	⊕◯◯◯ VERY LOW*†

eFigure 3. Assessment of level of evidence (Grading of Recommendations Assessment, Development and Evaluation) for nonrandomized prospective studies. * Nonrandomized studies assessed through Risk of Bias in Non-Randomized Studies-of Interventions tool. † Heterogeneity on methodology and outcomes measurement across the studies.

TREATMENT OPTIONS FOR EXTENSIVE POSTERIOR RESTORATIONS			
OUTCOME	RELATIVE EFFECT, RISK RATIO (95% CONFIDENCE INTERVAL)	NO. OF RESTORATIONS (STUDIES)	CERTAINTY OF EVIDENCE (GRADE)
Survival Rate			
Amalgam [Reference] versus glass ionomer	1.40 (1.36 to 1.44)	32,019 (2 observational studies)	⊕◯◯◯ VERY LOW*†
Direct resin [Reference] versus amalgam	1.12 (0.97 to 1.29)	206,821 (4 observational studies)	⊕◯◯◯ VERY LOW*†
Direct resin [Reference] versus glass ionomer	1.73 (1.68 to 1.79)	180,475 (2 observational studies)	⊕◯◯◯ VERY LOW*†
Direct resin [Reference] versus metal ceramic	1.04 (0.98 to 1.10)	712 (1 observational study)	⊕◯◯◯ VERY LOW*†
Direct resin [Reference] versus resin sandwich technique	1.35 (1.08 to 1.67)	826 (2 observational studies)	⊕◯◯◯ VERY LOW*†
Feldspathic ceramic [Reference] versus glass ceramic	1.01 (0.87 to 1.16)	1,785 (3 observational studies)	⊕◯◯◯ VERY LOW*†
Feldspathic ceramic [Reference] versus zirconia-based ceramic	1.00 (0.96 to 1.04)	117 (1 observational study)	⊕◯◯◯ VERY LOW*†
Glass ceramic [Reference] versus zirconia-based ceramic	0.90 (0.86 to 0.95)	252 (1 observational study)	⊕◯◯◯ VERY LOW*†
Metal ceramic [Reference] versus gold	0.96 (0.89 to 1.05)	210 (2 observational studies)	⊕◯◯◯ VERY LOW*†
Zirconia-based ceramic [Reference] versus metal ceramic	0.99 (0.90 to 1.09)	91 (1 observational study)	⊕◯◯◯ VERY LOW*†

eFigure 4. Assessment of level of evidence (Grading of Recommendations Assessment, Developemnt and Evaluation) for retrospective studies. * Nonrandomized studies assessed through Risk of Bias in Non-Randomized Studies-of Interventions tool. † Heterogeneity on methodology and outcomes measurement across the studies.

eTable 1. Search strategy for the electronic databases.

DATABASE	SEARCH STRATEGY
MEDLINE	(("Dental Restoration, Permanent" [MeSH*] OR "Dental Restoration, Permanent" OR "Permanent Dental Restoration" OR "Restoration, Permanent Dental" OR "Restorations, Permanent Dental" OR "Dental Restorations, Permanent" OR "Permanent Dental Restorations" OR "Dental Permanent Fillings" OR "Fillings, Permanent Dental" OR "Permanent Dental Fillings" OR "Permanent Fillings, Dental" OR "Permanent Filling, Dental" OR "Dental Filling, Permanent" OR "Dental Permanent Filling" OR "Filling, Dental Permanent" OR "Filling, Permanent Dental" OR "Permanent Dental Filling" OR "Fillings, Dental Permanent" OR "Dental Fillings, Permanent" OR "Composite Resins" [MeSH] OR "Composite Resins" OR Resin, Composite OR "Dental Amalgam" [MeSH] OR "Dental Amalgam" OR "Dental Amalgams" OR "Amalgam, Dental" OR "Amalgams, Dental" OR "Ceramics" OR "Compomer" OR "Composite Resins, Polyacid-Modified" OR "Composite Resins, Polyacid Modified" OR "Inlay" OR "Inlay, Dental" OR "Inlays, Dental" OR "Dental Onlay" OR "Onlay, Dental" OR "Onlays" "Dental Restoration Repairs" OR "Repair, Dental Restoration" OR "Failure, Dental Restoration" OR "Restoration Failures, Dental" OR "Failures, Dental Restoration" OR "Failure, Dental Prosthesis" OR "Dental Prosthesis Failures")) AND ((randomized controlled trial[pt†] OR controlled clinical trial[pt] OR randomized controlled trials[mh‡] OR random allocation[mh] OR double-blind method[mh] OR single-blind method[mh] OR clinical trial[pt] OR clinical trials[mh] OR ("clinical trial" [tw§]) OR ((singl*[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask*[tw] OR blind*[tw])) OR ("latin square" [tw]) OR placebos[mh] OR placebo*[tw] OR random*[tw] OR research design[mh:noexp] OR follow-up studies[mh] OR prospective studies [mh] OR cross-over studies[mh] OR control*[tw] OR prospectiv*[tw] OR volunteer*[tw]) NOT (animal[mh] NOT human[mh]) OR (Longitudinal Study) OR (Studies, Longitudinal) OR (Study, Longitudinal) OR (Prospective Study) OR (Studies, Prospective) OR (Study, Prospective) OR (Retrospective Studies) OR (Studies, Retrospective))
Scopus	"Dental Restoration, Permanent" OR "Permanent Dental Restoration" OR "Restoration, Permanent Dental" OR "Restorations, Permanent Dental" OR "Dental Restorations, Permanent" OR "Permanent Dental Restorations" OR "Dental Permanent Fillings" OR "Fillings, Permanent Dental" OR "Permanent Dental Fillings" OR "Permanent Fillings, Dental" OR "Permanent Filling, Dental" OR "Dental Filling, Permanent" OR "Dental Permanent Filling" OR "Filling, Dental Permanent" OR "Filling, Permanent Dental" OR "Permanent Dental Filling" OR "Fillings, Dental Permanent" OR "Dental Fillings, Permanent" OR "Composite Resins" OR resin, AND composite OR "Dental Amalgam" OR "Dental Amalgams" OR "Amalgam, Dental" OR "Amalgams, Dental" OR "Ceramics" OR "Compomer" OR "Composite Resins, Polyacid-Modified" OR "Composite Resins, Polyacid Modified" OR "Inlay" OR "Inlay, Dental" OR "Inlays, Dental" OR "Dental Onlay" OR "Onlay, Dental" OR "Onlays" "Dental Restoration Repairs" OR "Repair, Dental Restoration" OR "Failure, Dental Restoration" OR "Restoration Failures, Dental" OR "Failures, Dental Restoration" OR "Failure, Dental Prosthesis" OR "Dental Prosthesis Failures" AND "randomized controlled trial" OR "controlled clinical trial" OR "randomized controlled trials" OR "random allocation" OR "double-blind method" OR "single-blind method" OR "clinical trial" OR "clinical trials" OR "Longitudinal Study" OR "Studies, Longitudinal" OR "Study, Longitudinal" OR "Prospective Study" OR "Studies, Prospective" OR "Study, Prospective" OR "Retrospective Studies" OR "Studies, Retrospective" OR "Study, Retrospective" OR "Retrospective Study" OR "Cohort Studies" OR "Cohort Study" OR "Studies, Cohort" OR "Study, Cohort"
Cochrane Library	"Dental Restoration, Permanent" or "Permanent Dental Restoration" or "Restoration, Permanent Dental" or "Restorations, Permanent Dental" or "Dental Restorations, Permanent" or "Permanent Dental Restorations" or "Dental Permanent Fillings" or "Fillings, Permanent Dental" or "Permanent Dental Fillings" or "Permanent Fillings, Dental" or "Permanent Filling, Dental" or "Dental Filling, Permanent" or "Dental Permanent Filling" or "Filling, Dental Permanent" or "Filling, Permanent Dental" or "Permanent Dental Filling" or "Fillings, Dental Permanent" or "Dental Fillings, Permanent" or "Composite Resins" or "resin, composite" or "Dental Amalgam" or "Dental Amalgams" or "Amalgam, Dental" or "Amalgams, Dental" or "Ceramics" or "Compomer" or "Composite Resins, Polyacid-Modified" or "Composite Resins, Polyacid Modified" or "Inlay" or "Inlay, Dental" or "Inlays, Dental" or "Dental Onlay" or "Onlay, Dental" or "Onlays" "Dental Restoration Repairs" or "Repair, Dental Restoration" or "Failure, Dental Restoration" or "Restoration Failures, Dental" or "Failures, Dental Restoration" or "Failure, Dental Prosthesis" or "Dental Prosthesis Failures"
Web of Science	TS¶=("Dental Restoration, Permanent" OR "Permanent Dental Restoration" OR "Restoration, Permanent Dental" OR "Restorations, Permanent Dental" OR "Dental Restorations, Permanent" OR "Permanent Dental Restorations" OR "Dental Permanent Fillings" OR "Fillings, Permanent Dental" OR "Permanent Dental Fillings" OR "Permanent Fillings, Dental" OR "Permanent Filling, Dental" OR "Dental Filling, Permanent" OR "Dental Permanent Filling" OR "Filling, Dental Permanent" OR "Filling, Permanent Dental" OR "Permanent Dental Filling" OR "Fillings, Dental Permanent" OR "Dental Fillings, Permanent" OR "Composite Resins" OR "resin, composite" OR "Dental Amalgam" OR "Dental Amalgams" OR "Amalgam, Dental" OR "Amalgams, Dental" OR "Ceramics" OR "Compomer" OR "Composite Resins, Polyacid-Modified" OR "Composite Resins, Polyacid Modified" OR "Inlay" OR "Inlay, Dental" OR "Inlays, Dental" OR "Dental Onlay" OR "Onlay, Dental" OR "Onlays" "Dental Restoration Repairs" OR "Repair, Dental Restoration" OR "Failure, Dental Restoration" OR "Restoration Failures, Dental" OR "Failures, Dental Restoration" OR "Failure, Dental Prosthesis" OR "Dental Prosthesis Failures") AND TS=("randomized controlled trial" OR "controlled clinical trial" OR "randomized controlled trials" OR "random allocation" OR "double-blind method" OR "single-blind method" OR "clinical trial" OR "clinical trials" OR "Longitudinal Study" OR "Studies, Longitudinal" OR "Study, Longitudinal" OR "Prospective Study" OR "Studies, Prospective" OR "Study, Prospective" OR "Retrospective Studies" OR "Studies, Retrospective" OR "Study, Retrospective" OR "Retrospective Study" OR "Cohort Studies" OR "Cohort Study" OR "Studies, Cohort" OR "Study, Cohort")

* MeSH: Medical Subject Heading. † pt: Publication type. ‡ mh: MeSH headings. § tw: Text word. ¶ TS: Topic tag.

eTable 2. Main characteristics of the included studies.

STUDY, YEAR	COUNTRY	INCLUSION CRITERIA*	GENDER	MEAN AGE, Y	MATERIAL TYPE	COMMERCIAL NAME (MANUFACTURER)	RESTORATIONS, NO.	INTERMEDIATE MATERIAL
Retrospective Studies								
Rasmusson and colleagues,[26] 1995[§]	Sweden	Not clearly reported	NR[¶]	NR	Hybrid composite resin	Occlusin (ICI)/P30 (3M)	23	NR
						Ful-Fil (Caulk)	33	
						Profile (Kerr)	20	
					Microfine composite resin	Heliomolar (Vivadent)	23	
						Distalite (J&J)	23	
Felden and colleagues,[27] 1998	Germany	All patients with ceramic restorations placed within 1988-1994	65 female 27 male	37.9	Glass ceramic	Dicor (Dentsply)	44	No
					Leucite-reinforced pressed glass ceramic	IPS Empress (Ivoclar)	126	
					Zirconia-based ceramic	Mirage II (Myron)	82	
					Feldspathic ceramic	Cerec Vita Mark I (Vita)/ Duceram LFC (Ducera)	35	
Wagner and colleagues,[28] 2003	Germany	Patients randomly sampled from groups with cast gold or ceramic partial crowns	18 female 24 male	NR	Gold	NR	42	No
					Leucite-reinforced pressed glass ceramic	IPS Empress (Ivoclar)	42	
Arnelund and colleagues,[29] 2004	Sweden	Patients treated with ceramic restorations within 1992-1996	98 female 55 male	48	Leucite-reinforced pressed glass ceramic	IPS Empress (Ivoclar)	185	Glass ionomer in deep caries
					Alumina-reinforced feldspathic ceramic	Vitadur Alpha (Vita)	81	
Opdam and colleagues,[30] 2007	The Netherlands	Patients with direct posterior restorations placed within 1990-1997	13 female 110 male	49	Hybrid composite resin	Clearfil Photo Posterior (Kuraray)	376	No
					Hybrid composite resin and GIC (sandwich)	Clearfil Photo Posterior (Kuraray) and Vitrebond (3M)/GC (GC)	82	Glass ionomer
Opdam and colleagues,[31] 2010	The Netherlands	Patients with 3- to 5-surface composite or class II amalgam posterior restorations placed within 1983-2003	157 female 116 male	48	Hybrid composite resin	Clearfil Photo Posterior (Kuraray)/Clearfil AP-X (Kuraray)/Others	747	NR
					Amalgam	Dispersalloy (Dentsply/ Caulk)	1,202	
Kim and colleagues,[32] 2013	Republic of Korea	Patients with direct restorations	NR	NR	Amalgam	NR	76	NR
					Direct composite resin		161	
					Glass ionomer		45	

* The inclusion criteria of the studies were reproduced as described by the authors of the article and when not found the information was considered as not clearly reported. † AFR: Annual failure rate. ‡ Non-RCT: Nonrandomized controlled trial. § The study was not included in the network meta-analysis. ¶ NR: Not reported. # S: Serious. ** M: Moderate. †† L: Low. ‡‡ MOD: Mesio-occlusodistal. §§ Randomized clinical trial, the risk for bias is shown in the Supplementary Material (eFigure 1).

eTable 2. (Continued)

PREMOLARS, NO.	MOLARS, NO.	TOTAL, NO.	PULP VITALITY	POST	SURVIVAL RATE, %	AFR[†]	CRITERIAL FOR FAILURE	MEAN FOLLOW-UP, Y	DROPOUT	RISK OF BIAS NON-RCT[‡]
163	13	176	Yes	No	86.9	2.76	Secondary caries, fracture, marginal adaptation	5	29	S[#]
					65.2	15.3				
					86.9	0.89				
					93.7	1.95				
					85.1	0.89				
NR	NR	287	NR	NR	68.2	1.95	Restoration loss or fracture	7	50	S
					97.6	3.16				
					100	1.65				
					100	0.0				
1	41	84	NR	NR	95.2	0.37	Fracture	10	NR	S
15	27				95.2	0.69				
64	121	266	NR	NR	92.3	0.99	NR	5.1	49	S
32	49				93.3	3.97				
NR	NR	458	Yes	No	88.5	1.34	Secondary caries, fracture	9	NR	M**
					58.5	5.78				
234	513	1,949	NR	No	84.7	1.37	Secondary caries, fracture	12	NR	M
389	813				75.6	2.30				
NR	NR	282	NR	NR	66.5	8.03	NR	5	NR	S
					71.6	6.19				
					46.1	15.84				

eTable 2. Main characteristics of the included studies.

STUDY, YEAR	COUNTRY	INCLUSION CRITERIA*	GENDER	MEAN AGE, Y	MATERIAL TYPE	COMMERCIAL NAME (MANUFACTURER)	RESTORATIONS, NO.	INTERMEDIATE MATERIAL
Skupien and colleagues,[33] 2013	Germany	Records from 2000-2011 about endodontically treated teeth with a restoration with at least 6 mo of follow-up; placed within 6 mo after the endodontic treatment; and records containing information about the dentition	NR	40.5	Direct composite resin	NR	479	NR
					Metal ceramic		233	
Van de Sande and colleagues,[34] 2015	Brazil	Patients with full dentition or the restoration should be in occlusion and with at least 1 adjacent tooth; continuous follow-up at least once per year	59 female 34 male	NR	Hybrid composite resin	Z100 (3M)/Tetric Ceram (Ivoclar)	124	Calcium hydroxide
					Hybrid composite resin and GIC (sandwich)	P-50 (3M)/Herculite XR (Kerr)	244	Calcium hydroxide and glass ionomer
Collares and colleagues,[35] 2016	Germany China United States France Chile Spain	Single ceramic restorations placed within 1994-2014	NR	NR	Feldspathic ceramic	Cerec (Sirona)/VITABLOCS (Vita)	1,120	No
					Leucite glass ceramic	HeraCeram (Heraeus)/IPS Empress (Ivoclar)/ProCAD (Ivoclar)/OPC press (Jeneric Pentron)/Imagine PressX (Wieland)	194	
Laske and colleagues,[36] 2016	The Netherlands	Direct restorations placed within 1996-2011	NR	NR	Direct composite resin	NR	175,128	NR
					Amalgam		26,757	
					Glass ionomer		5,141	
					Compomer		664	
Naghipur and colleagues,[37] 2016	Canada	Patients with 2-surface amalgam and composite restorations in premolars placed within 2002-2014	NR	52	Direct composite resin		1,695	NR
					Amalgam		1,125	
Rinke and colleagues,[38] 2016	Germany	Patients in need of restoration with antagonistic teeth in the area; vital abutment or abutment with sufficient endodontic treatment	32 female 21 male	49.6	Zirconia-based ceramic		50	No
					Metal ceramic		41	
Olley and colleagues,[39] 2018	United Kingdom	Patients who received indirect restorations within 1966-2016; with annual follow-up; occlusion with natural teeth or prostheses; excellent oral hygiene	27 female 20 male	49	Metal ceramic	NR	101	No
					Gold	NR	25	

eTable 2. (Continued)

PREMOLARS, NO.	MOLARS, NO.	TOTAL, NO.	PULP VITALITY	POST	SURVIVAL RATE, %	AFR†	CRITERIAL FOR FAILURE	MEAN FOLLOW-UP, Y	DROPOUT	RISK OF BIAS NON-RCT‡
NR	NR	712	No	NR	91.4	0.93	Fracture	9.6	NR	M
					88	1.32				
52	72	368	Yes	No	74.2	1.64	Secondary caries, fracture	18	NR	L††
122	122				61.1	2.7				
790	862	1,652	NR	NR	83.3	2.27	NR	7.2	NR	M
					85.6	1.11				
NR	NR	207,690	Yes/No	NR	80.7	2.13	Restoration replaced or repaired, tooth extraction, endodontic or prosthetic treatment	10	0	M
					65	4.21				
					46.5	7.38				
					54.2	5.94				
1,695	NR	2,820	Yes	No	92.1	0.71	Secondary caries, fracture	12	NR	S
1,125					94.1	0.5				
NR	48	91	Yes/No		94	1.23	Secondary caries, fracture, loss of retention	5	13	S
	43				95.1	1.00				
NR	NR	126	NR	NR	96	0.12	NR	50	NR	S
					100	0.0				

eTable 2. Main characteristics of the included studies.

STUDY, YEAR	COUNTRY	INCLUSION CRITERIA*	GENDER	MEAN AGE, Y	MATERIAL TYPE	COMMERCIAL NAME (MANUFACTURER)	RESTORATIONS, NO.	INTERMEDIATE MATERIAL
Borgia and colleagues,[40] 2019§	Uruguay	Randomly selected sample of direct composite posterior restorations in function for at least 5 y	18 female 10 male	46.8	Nanofiller composite resin	Filtek Z350 (3M)	11	NR
					Microfiller composite resin	Heliomolar (Ivoclar)	9	
				54.6	Microhybrid composite resin	Filtek P60 (3M)/Filtek Z250 (3M)/Tetric Ceram (Ivoclar)/ Prodigy (Kerr)/Prisma APH (Dentsply)	15	
Prospective Studies								
Rowe,[41] 1989	United Kingdom	Patients able to return for 5 y and no need for special management; extensive restorative care; or cuspal replacement	NR	NR	Hybrid composite resin	Occlusin (ICI)	176	NR
					Amalgam	Dispersalloy (Dentsply/ Caulk)/Aristoloy (Englhard)	54	
Norman and colleagues,[42] 1990	United Kingdom	Sound tooth or a sound restored tooth in proximal contact with at least 1 proximal surface of the restoration; a portion of the restoration was required to be in contact with an opposing tooth or restoration	NR	62	Hybrid composite resin	Occlusin (ICI)	54	Calcium hydroxide in deep caries
					Amalgam	Dispersalloy (Dentsply/Caulk)	25	
Mjor and Jokstad,[43] 1993	Norway	Small class II restorations (having enamel surrounding cavity margins and with restricted buccolingual extensions of the interproximal and occlusal sections)	NR	13	Hybrid composite resin	P-10 (3M)	36	No
					Glass ionomer cement	Ketac Silver (ESPE)	44	
					Amalgam	Dispersalloy (Dentsply/Caulk)	33	
Lumley and Fisher,[44] 1995	United Kingdom	Patients able to attend at least 5 y of follow-up; small caries but into dentin	11 male 14 female	29	Glass ionomer cement	Chemfil (Dentsply)/Ketac-Fil (ESPE)	11	Calcium hydroxide
						Ketac Silver (ESPE)	22	
					Amalgam	Sybralloy (Kerr)	14	
Mair,[45] 1998	United Kingdom	Not clearly reported	NR	NR	Amalgam	New True Dentalloy (SS White)/Solila Nova (DeTrey)	35	Calcium hydroxide and zinc phosphate cement in deep caries
					Hybrid composite resin	Clearfil Posterior (Cavex)/ Occlusin (ICI)/P-30 (3M)	56	
Erpenstein and colleagues,[46] 2000	Germany	Crowns placed within 1987-1998 in periodontally healthy patients	123 male 287 female	NR	Glass ceramic	Dicor (Dentsply)	78	No
					Galvano ceramic	AGC (Wieland)	594	
Pallesen and Van Dijken,[47] 2000	Denmark	Patients in need of 2 equal class II restorations	5 male 11 female	40	Feldspathic ceramic	Vita Mark II (Vita)	16	No
					Glass ceramic	Dicor MGC (Dentsply)	16	

eTable 2. (Continued)

PREMOLARS, NO.	MOLARS, NO.	TOTAL, NO.	PULP VITALITY	POST	SURVIVAL RATE, %	AFR[†]	CRITERIAL FOR FAILURE	MEAN FOLLOW-UP, Y	DROPOUT	RISK OF BIAS NON-RCT[‡]
NR	NR	35	Yes/No	No	90.9	0.82	Secondary caries, fracture, endodontic treatment, tooth loss	11.6	0	S
					100	0.0				
					100	0.0				
103	73	230	NR	NR	90	2.1	Secondary caries, fracture	5	NR	S
27	27				90	2.3				
50	29	79	NR	NR	90.7	1.5	Secondary caries	5	NR	S
					88	2.5				
9	27	113	NR	NR	75	5.5	Secondary caries, fracture	5	59	S
14	30				50	13				
11	22				87.8	2.5				
NR	NR	47	NR	No	63.6	7.2	Recurrent caries, fracture or restoration loss	6	0	S
					86.4	2.4				
					100	0.0				
NR	NR	91	NR	NR	94.3	0.5	NR	10	59	S
					92.9	0.7				
NR	NR	672	NR	NR	70.5	4.8	Restoration loss	7	NR	S
					98.1	0.2				
NR	NR	32	Yes	No	90.6	0.8	Fracture	8	0	S
					87.6	1.6				

eTable 2. Main characteristics of the included studies.

STUDY, YEAR	COUNTRY	INCLUSION CRITERIA*	GENDER	MEAN AGE, Y	MATERIAL TYPE	COMMERCIAL NAME (MANUFACTURER)	RESTORATIONS, NO.	INTERMEDIATE MATERIAL
Van Dijken,[48] 2000§	Sweden	Class II amalgam restorations in need of replacement	24 male 16 female	48	Hybrid composite resin (indirect)	Brilliant DI (Coltene)	96	No
					Hybrid composite resin (sandwich)	Fulfil (Dentsply)	33	Glass ionomer cement
Wassel and colleagues,[49] 2000	United Kingdom	Patients able to attend recalls; good oral hygiene; no gingivitis; gingival margin $\geq$ 3 millimeters supragingival; not involving functional cusps and maximum 1 nonfunctional cusp	19 male 54 female	29.6	Hybrid composite resin (direct)	Brilliant Dentin (Coltene)	69	Calcium hydroxide in deep caries
					Hybrid composite resin (indirect)	Brilliant Dentin (Coltene)	74	
Thordrup and colleagues,[50] 2001	Denmark	1-4 posterior teeth needing replacement of large MOD‡‡ restorations; no parafunctional habits; no gingivitis; good oral hygiene; low caries progression; no partial dentures	7 male 30 female	37	Glass ceramic	Cerec (Sirona)	14	NR
					Feldspathic ceramic	VitaDur N (Vita)	11	
					Hybrid composite resin (indirect)	Brilliant DI (Coltene)	10	
					Indirect composite resin	Estilux (Kulzer)	9	
Pallesen and Qvist,[51] 2003	Denmark	Patients requiring 5 medium- to large-sized class II restorations in vital teeth; in functional occlusion teeth with the adjacent teeth	8 male 20 female	35	Hybrid composite resin (direct)	Brilliant Dentin (Coltene)	27	Calcium hydroxide and glass ionomer in deep caries
					Hybrid composite resin (indirect)	Brilliant Dentin (Coltene)	27	
					Direct composite resin	Estilux Posterior (Kulzer)	27	
					Indirect composite resin	Estilux Posterior (Kulzer)	27	
					Indirect composite resin	SR-Isosit (Ivoclar)	27	
Mannocci and colleagues,[52] 2005	Italy	Healthy patients able to return for follow-up; orthodontic class I occlusal scheme; 1 premolar needing endodontic treatment; class II carious lesion and intact cusp structure; in occlusal function and not used as abutment for prostheses	103 male 116 female	45	Hybrid composite resin	Z100 (3M)	97	No
					Amalgam	Valiant PhD (Dentsply)	100	
Bernardo and colleagues,[53] 2007	Portugal	Patients born within 1986-1989; at least 1 carious lesion in a permanent tooth; no prior exposure to dental amalgam; no interfering health condition	NR	NR	Hybrid composite resin	Z100 (3M)	442	NR
					Amalgam	Dispersalloy (Dentsply/Caulk)	427	
Khairallah and Hokayem,[54] 2009	Lebanon	No parafunctional habits; no periodontitis; no removable prostheses	NR	32.4	Leucite-reinforced pressed glass ceramic	IPS Empress (Ivoclar)	17	NR
					Indirect composite resin	Targis (Ivoclar)	16	

eTable 2. (Continued)

PREMOLARS, NO.	MOLARS, NO.	TOTAL, NO.	PULP VITALITY	POST	SURVIVAL RATE, %	AFR†	CRITERIAL FOR FAILURE	MEAN FOLLOW-UP, Y	DROPOUT	RISK OF BIAS NON-RCT‡
NR	NR	129	Yes	Yes	82.3	2.8	Secondary caries, fracture	11	NR	S
					72.7	1.7				
NR	NR	143	Yes	No	94.2	1.1	Fracture, sensitivity	5	NR	S
					89.1	2.2				
NR	NR	44	NR	NR	92.9	0.7	Secondary caries, fracture, sensitivity	5	2	S
					85.1	2.2				
					82.1	2.2				
					91.7	1.1				
NR	NR	135	Yes	No	95.8	1.0	Secondary caries, fracture, loss of proximal contact	11	5.2	S
					74.1	1.4				
					74.1	1.8				
					95.8	1.0				
					77.8	2.2				
97	NR	197	No	Yes	89.7	2.1	Secondary caries, fracture	5	11.8	§§
100	NR				91	1.8				
NR	NR	869	NR	NR	65.6	5.8	Need of replacement	7	NR	§§
					96.9	1.9				
NR	NR	33	NR	NR	88.2	1.9	NR	6.3	NR	S
					100	0.0				

eTable 2. Main characteristics of the included studies.

STUDY, YEAR	COUNTRY	INCLUSION CRITERIA*	GENDER	MEAN AGE, Y	MATERIAL TYPE	COMMERCIAL NAME (MANUFACTURER)	RESTORATIONS, NO.	INTERMEDIATE MATERIAL
Federlin and colleagues,[55] 2010	Germany	Teeth with no pain; the application of rubber dam was possible; tooth mobility was set less than or equal to symbol degree 1; moderate level of oral hygiene	8 male 14 female	37	Feldspathic ceramic	Vita Mark II (Vita)/Cerec 3 (Sirona)	22	NR
					Gold	NR	22	
Guess and colleagues,[56] 2013§	Germany	Patients requiring 2-4 partial-coverage restorations; no removable prostheses in the opposite arch; good oral hygiene; no parafunction	14 male 11 female	NR	Lithium dissilicate pressed ceramic	IPS e.max (Ivoclar)	40	No
					Leucite-reinforced pressed glass ceramic	ProCAD (Ivoclar)/Cerec 3 (Sirona)	40	
Passia and colleagues,[57] 2013	Germany	Vital or successfully endodontically treated tooth; patients > 18 y; periodontally stable after pretreatment; sufficiently treated remaining teeth	104 male 119 female	14.8	Zirconia-based ceramic	NR	77	No
					Gold		81	
Fennis and colleagues,[58] 2014	The Netherlands	Fracture of the buccal or palatal cusp of vital upper premolars along with a class II caries or restoration in the same tooth; the remaining cusp had to be sound; preparation outlines in dentin and subgingival margins were allowed	77 male 80 female	54.9	Hybrid composite resin (direct)	AP-X (Kuraray)	80	NR
					Hybrid composite resin (indirect)	Estenia (Kuraray)	78	
Van Dijken and Pallesen,[59] 2014§	Sweden	Patients in need of 2 or 4 class II restorations; no pregnancy; no partial prostheses; no orthodontic apparatus	25 male 27 female	53	Nanohybrid composite resin	Tetric Evoceram (Ivoclar)	57	No
					Hybrid composite resin	Tetric Ceram (Ivoclar)	57	
Kramer and colleagues,[60] 2015§	Germany	Absence of pain from the tooth to be restored; possibility of using rubber dam; no further restorations planned in other posterior teeth; good oral hygiene; absence of periodontal or pulpal disease; restorations required in 2 different quadrants; aged 18-65 y; no pregnancy	7 male 23 female	32.9	Nanohybrid composite resin	Grandio (Voco)	36	NR
					Hybrid composite resin	Tetric Ceram (Ivoclar)	32	
Pallesen and Van Dijken,[61] 2015§	Denmark	Adult patients in need of 3 of 6 similar-sized class II restorations; no partial prostheses; no orthodontic apparatus	5 male 21 female	38.2	Chemically cured composite resin	Clearfill Posterior (Cavex)	27	Calcium hydroxide
					Hybrid composite resin	Adaptic II (J&J)	29	
					Hybrid composite resin	Occlusin (ICI)	29	

eTable 2. (Continued)

PREMOLARS, NO.	MOLARS, NO.	TOTAL, NO.	PULP VITALITY	POST	SURVIVAL RATE, %	AFR[†]	CRITERIAL FOR FAILURE	MEAN FOLLOW-UP, Y	DROPOUT	RISK OF BIAS NON-RCT[‡]
NR	NR	44	NR	NR	95.4	0.8	Fracture	5.5	NR	S
					100	0.0				
NR	80	80	Yes	No	100	0.0	Secondary caries, fractures, endodontic complications	7	7	§§
					97.5	0.3				
13	109	158	No	Yes	73.2	9.7	Fracture	5	NR	§§
2	97				92.3	0.7				
158	NR	158	Yes	No	91.3	1.8	Fracture	5	18	§§
					84.6	3.5				
NR	NR	114	Yes	No	80.7	2.1	Secondary caries	10	7	§§
					80.7	2.1				
NR	NR	68	Yes	No	100	0.0	NR	10	0	S
					100	0.0				
60	39	99	Yes	No	63	1.7	Secondary caries, fracture, occlusal wear	27	NR	§§
					55.2	2.1				
					51.7	2.4				

eTable 2. Main characteristics of the included studies.

STUDY, YEAR	COUNTRY	INCLUSION CRITERIA*	GENDER	MEAN AGE, Y	MATERIAL TYPE	COMMERCIAL NAME (MANUFACTURER)	RESTORATIONS, NO.	INTERMEDIATE MATERIAL
Pallesen and Van Dijken,[62] 2015§	Denmark	Adult patients in need of 3 of 6 similar-sized class II restorations; no partial prostheses; no orthodontic apparatus	9 male 21 female	30	Chemically cured composite resin	Miradapt (J&J)	27	Calcium hydroxide
					Hybrid composite resin	P10 (3M)	28	
					Hybrid composite resin	P30 (3M)	28	
Schmidt and colleagues,[63] 2015§	Denmark	Patients in need of class II restorations in vital teeth without preoperative symptoms	NR	50.5	Low-shrinkage composite resin	Filtek Silorane (3M-ESPE)	52	NR
					Nanohybrid composite resin	Ceram X (Dentsply)	55	
Van Dijken and Lindberg,[64] 2015§	Sweden	Patients in need of at least 2 class II composite restorations; the teeth had to be in occlusion and should have at least 1 synergist and 1 neighboring tooth; no pregnancy; no partial prostheses; no orthodontic apparatus	28 male 22 female	43	Low-shrinkage composite resin	Inten-S (Ivoclar)	46	No
					Microhybrid composite resin	Point 4 (Kerr)	45	
Santos and colleagues,[65] 2016	Brazil	Patients requiring at least 2 restorations; teeth with occlusal contact; low caries risk; good oral hygiene; no periodontitis; no orthodontic apparatus; no parafunctional habits; no pregnancy	NR	33	Feldspathic ceramic	Duceram Plus (Dentsply)	23	NR
					Leucite-reinforced pressed glass ceramic	IPS Empress (Ivoclar)	25	
Skupien and colleagues,[12] 2016	Brazil	Adult patients in need of endodontic and restorative treatment in teeth with at least 1 entire coronal wall remaining after endodontic procedures; good oral and general health and bilateral occlusal posterior contacts	NR	42.6	Microhybrid composite resin	Filtek Z250 (3M)	26	NR
					Metal ceramic	NR	17	
Van Dijken and Pallesen,[66] 2016§	Sweden	Patients requiring 1 or 2 pairs of similar-sized restorations	44 male 42 female	52.4	Bulk-filled and nanohybrid composite resin	SDR (Dentsply) and Ceram X (Dentsply)	58	NR
					Nanohybrid composite resin	Ceram X (Dentsply)	57	
Monaco and colleagues,[67] 2017	Italy	Patients needing at least 1 molar or premolar fixed prosthesis single crown; aged 18-70 y; minimum of 20 teeth; moderate to good oral hygiene; low to moderate caries risk, and no active periodontal disease	33 male 39 female	44	Zirconia-based ceramic	ZirCad (Ivoclar)	45	No
					Metal ceramic	IPS d.SIGN 91 (Ivoclar) and PoM (Ivoclar)	40	

eTable 2. (Continued)

PREMOLARS, NO.	MOLARS, NO.	TOTAL, NO.	PULP VITALITY	POST	SURVIVAL RATE, %	AFR†	CRITERIAL FOR FAILURE	MEAN FOLLOW-UP, Y	DROPOUT	RISK OF BIAS NON-RCT‡
NR	NR	99	Yes	No	74	1.0	Secondary caries, fracture	30	NR	§§
					69	1.2				
					59	1.8				
29	23	107	Yes	NR	94.2	0.7	Fracture	5	32	††
30	25				94.5	1.1				
NR	NR	91	NR	No	78.3	1.8	Secondary caries, fracture	15	15	§§
					75.6	1.6				
NR	NR	48	NR	NR	95	1.5	Fracture	12	44	S
					76	4.7				
12	14	43	No	Yes	87	0.7	Fracture	5	0	§§
9	8				100	0.0				
NR	NR	115	Yes	No	93.1	1.4	Secondary caries, fracture	5	NR	§§
					89.5	2.0				
NR	NR	85	No	Yes	99.9	0.4	Fracture	5	5.5	§§
					97.5	0.5				

eTable 3. PRISMA* NMA† checklist of items to include when reporting a systematic review involving an NMA.

SECTION/TOPIC	ITEM NO.	CHECKLIST ITEM	REPORTED ON PAGE NO.
Title			
Title	1	Identify the report as a systematic review incorporating a NMA (or related form of meta-analysis).	1
Abstract			
Structured summary	2	Provide a structured summary including, as applicable: Background: main objectives. Methods: data sources; study eligibility criteria, participants, and interventions; study appraisal; and synthesis methods, such as NMA. Results: number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity. Discussion/Conclusions: limitations; conclusions and implications of findings. Other: primary source of funding; systematic review registration number with registry name.	1
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known, including mention of why an NMA has been conducted.	1-2
Objectives	4	Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	2
Methods			
Protocol and registration	5	Indicate whether a review protocol exists and if and where it can be accessed (for example, web address); and, if available, provide registration information, including registration number.	3
Eligibility criteria	6	Specify study characteristics (for example, PICOS, length of follow-up) and report characteristics (for example, years considered, language, and publication status) used as criteria for eligibility, giving rationale. Clearly describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification).	3
Information sources	7	Describe all information sources (for example, databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	3
Search	8	Present full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	3
Study selection	9	State the process for selecting studies (that is, screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	3
Data collection process	10	Describe method of data extraction from reports (for example, piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	3-4
Data items	11	List and define all variables for which data were sought (for example, PICOS, funding sources) and any assumptions and simplifications made.	3
Geometry of the Network	S1	Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers.	4
Risk of bias within individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	4-5
Summary measures	13	State the principal summary measures (for example, risk ratio and difference in means). Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve values, as well as modified approaches used to present summary findings from meta-analyses.	4
Planned methods of analysis	14	Describe the methods of handling data and combining results of studies for each NMA. This should include, but not be limited to: • handling of multiarm trials; • selection of variance structure; • selection of prior distributions in Bayesian analyses; • assessment of model fit.	4
Assessment of Inconsistency	S2	Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment networks studied. Describe efforts taken to address its presence when found.	4
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (for example, publication bias, and selective reporting within studies).	4

* PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses. † NMA: Network meta-analysis.

eTable 3. (Continued)

SECTION/TOPIC	ITEM NO.	CHECKLIST ITEM	REPORTED ON PAGE NO.
Additional analyses	16	Describe methods of additional analyses if done, indicating which were prespecified. This may include, but not be limited to, the following: • sensitivity or subgroup analyses; • meta-regression analyses; • alternative formulations of the treatment network; • use of alternative prior distributions for Bayesian analyses (if applicable).	4
Results			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5-6
Presentation of Network Structure	S3	Provide a network graph of the included studies to enable visualization of the geometry of the treatment network.	5-6
Summary of Network Geometry	S4	Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomized patients for the different interventions and pairwise comparisons in the network, gaps of evidence in the treatment network, and potential biases reflected by the network structure.	5-6
Study characteristics	18	For each study, present characteristics for which data were extracted (for example, study size, PICOS, and follow-up period) and provide the citations.	5
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	6
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: simple summary data for each intervention group, and effect estimates and confidence intervals. Modified approaches may be needed to deal with information from larger networks.	5-6
Synthesis of results	21	Present results of each meta-analysis done, including confidence/credible intervals. In larger networks, authors may focus on comparisons versus a particular comparator (for example, placebo or standard care), with full findings presented in an appendix. League tables and forest plots may be considered to summarize pairwise comparisons. If additional summary measures were explored (such as treatment rankings), these should also be presented.	5-6
Exploration for Inconsistency	S5	Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, *P* values from statistical tests, or summary of inconsistency estimates from different parts of the treatment network.	5-6
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies for the evidence base being studied.	5-6
Results of additional analyses	23	Give results of additional analyses, if done (for example, sensitivity or subgroup analyses, meta-regression analyses, alternative network geometries studied, alternative choice of prior distributions for Bayesian analyses, and so forth).	5-6
Discussion			
Summary of evidence	24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (for example, health care providers, users, and policy-makers).	6-9
Limitations	25	Discuss limitations at study and outcome level (for example, risk of bias), and at review level (for example, incomplete retrieval of identified research, reporting bias). Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any concerns regarding network geometry (for example, avoidance of certain comparisons).	8-9
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	9
Funding			
Funding	27	Describe sources of funding for the systematic review and other support (for example, supply of data); role of funders for the systematic review. This should also include information regarding whether funding has been received from manufacturers of treatments in the network or whether some of the authors are content experts with professional conflicts of interest that could affect use of treatments in the network.	10