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Tese

Decisão de tratamento para restaurações extensas em dentes posteriores: revisão sistemática e meta-análise em rede

Ferdinan Luís Leida

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Orientadora: Profª. Drª. Tatiana Pereira Cenci

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Tese apresentada, como requisito parcial, para obtenção do grau de Doutor em Dentística e Cariologia, Programa de Pós-Graduação em Odontologia, Faculdade de Odontologia, Universidade Federal de Pelotas.

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Dedico este trabalho aos meus queridos pais, Sueli e David *(in memoriam).*

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Notas preliminares

A presente tese foi redigida segundo o Manual de Normas para dissertações, teses e trabalhos científicos da Universidade Federal de Pelotas de 2013, adotando o nível de descrição 4- estrutura em artigos, descrita no apêndice D do referido manual. Disponível no endereço eletrônico: http://sisbi.ufpel.edu.br/?p=manu

Resumo

LEIDA, Ferdinan Luís. **Decisão de tratamento para restaurações extensas em dentes posteriores: revisão sistemática e meta-análise em rede**. 2018. 65f. Tese (Doutorado em Dentística) - Programa de Pós-graduação em Odontologia, Faculdade de Odontologia, Universidade Federal de Pelotas, Pelotas, 2018.

O objetivo principal desta tese foi evidenciar, através de uma meta-análise em rede, o melhor tratamento restaurador extenso para dentes posteriores permanentes. Foram utilizadas como base de dados: Pubmed, Scopus, Web of Science e Cochrane Library sem restrição de ano e linguagem. Após a remoção de duplicatas, 9.735 estudos foram selecionados para leitura de título e resumo. Destes, 152 estudos foram selecionados para leitura completa. Foram selecionados para a extração de dados 45 estudos clínicos prospectivos e retrospectivos que tiveram os critérios de elegibilidade com pelo menos cinco anos de acompanhamento e compararam pelo menos dois tipos de tratamentos extensos em dentes permanentes em pacientes de qualquer idade. Para a meta-análise em rede, cinco tiveram de ser excluídos, pois estes estudos só apresentavam uma entrada de dados. A análise foi realizada no software R Studio (Rstudio Inc, Boston, USA). A meta-análise de comparações diretas entre dois tratamentos foi realizada usando um modelo de efeitos randômicos com heterogeneidade avaliada pelo teste estatístico qui-quadrado(I^2) em um intervalo de confiança de 95%. A meta-análise em rede foi avaliada através de dois gráficos sumários (prospectivos e retrospectivos) com demonstração das comparações entre os diferentes estudos primários de acordo com os tipos de materiais e frequência das intervenções. Foram estabelecidas separadamente também duas figuras com um ranking de probabilidades entre as posições dos melhores aos piores materiais. Para a avaliação do risco de viés, foram utilizadas duas ferramentas: a de estudos clínicos randomizados da Cochrane, que demonstrou um baixo risco de viés para os 14 estudos selecionados e a ROBINS-I, de estudos clínicos não-randomizados, que demonstrou um sério risco de viés para 25 estudos, moderado risco para cinco estudos e baixo risco para apenas um estudo. Para avaliar a qualidade de evidência, foi utilizada a ferramenta GRADE que demonstrou um moderado grau de certeza para o desfecho sobrevivência quando todos os estudos foram considerados. As falhas mais frequentes descritas nos estudos foram cárie secundária e fratura. Para a taxa anual de falha, os materiais indiretos em ouro e metalo-cerâmica tiveram os menores valores, de 0,28% e 0,55%, respectivamente. Para os materiais diretos, a menor taxa anual de falha foi para a resina nanohíbrida, com 1,06%. Portanto, o ouro e a metalo-cerâmica tiveram as melhores taxas de sobrevivência em restaurações extensas/coroas. Para restaurações diretas, as resinas diretas nanohíbridas são as melhores indicadas, o que demonstra a evolução nas propriedades mecânicas das resinas e por serem mais favoráveis aos pacientes pelo custo-benefício e por impactar em maior longevidade do dente em longo prazo.

Palavras-chave: restauração dentária permanente; taxa de sobrevivência; estudo clínico

Abstract

LEIDA, Ferdinan Luís. **Decision of treatment for extensive restorations in posterior teeth: a systematic review and network meta-analyses**. 2018. 65f. Thesis (Doctor degree in Dentistry) - Programa de Pós-graduação em Odontologia, Faculdade de Odontologia, Universidade Federal de Pelotas, Pelotas, 2018.

The main objective of this thesis was to demonstrate, through a network meta-analysis, the best extensive restorative treatment for permanent posterior teeth. The following databases were used: Pubmed, Scopus, Web of Science and Cochrane Library without restriction of year and language. After the removal of duplicates, 9,735 studies were selected for title and abstract reading. Of these, 152 studies were selected for complete reading. We selected 45 prospective and retrospective clinical studies that had the eligibility criteria with at least five years of follow-up and compared at least two types of extensive treatments in permanent teeth in patients of any age. For the network meta-analysis, five had to be excluded, since these studies presented only one data entry. The analysis was performed in R Studio software (Rstudio Inc., Boston, USA). The meta-analysis of direct comparisons between two treatments was performed using a random effects model with heterogeneity assessed by the chi-square statistical test (I^2) at a 95% confidence interval. The network meta-analysis was evaluated through two summary graphs (prospective and retrospective) with demonstration of the comparisons between the different primary studies according to the types of materials and frequency of interventions. Two figures with a ranking of probabilities between the positions of the best to the worst materials were also separately established. Two tools were used to assess risk of bias: the Cochrane randomized clinical trials, which demonstrated a low risk of bias for the 14 selected studies and ROBINS-I from non-randomized clinical trials, which demonstrated a serious risk of bias for 25 studies, moderate risk for five studies and low risk for only one study. To evaluate the quality of evidence, we used the GRADE tool that demonstrated a moderate degree of certainty for the survival outcome when all the studies were considered. The most frequent failures described in the studies were secondary caries and fracture. For the annual failure rate, the indirect materials in gold and metal-ceramic had the lowest values, of 0.28% and 0.55%, respectively. For the direct materials, the lowest annual failure rate was for the nanohybrid resin, with 1.06%. Therefore, gold and metal-ceramic had the best survival rates in extensive restorations /crowns. For direct restorations, the direct nanohybrid resins are the best indicated, which demonstrates the evolution in the mechanical properties of the resins and because they are more favorable to the patients for the cost-benefit and for impacting in the longer longevity of the tooth in the long term.

Keywords: permanent dental restoration; survival rate; clinical study

Sumário

1. Introdução Geral

Ao longo da evolução dos materiais restauradores, entre as décadas de 60 e 90, a odontologia focou-se principalmente em tratamentos que pudessem substituir a estrutura dentária que foi acometida por cárie, fratura ou falha de uma restauração já existente, sem levar em consideração necessariamente a preservação de remanescente dentário que seria envolvido no preparo de dentes posteriores, pois as opções disponíveis dependiam, sobremaneira, de retenção adicional para a longevidade dessas restaurações (SMALES;HAWTHORNE,1997; DONLY et al., 1999; VAN NIEUWENHUYSEN et al., 2003; MANHART et al., 2004). Além disso, estratégias de promoção de saúde relacionadas ao controle da doença cárie eram bastante escassas, o que limitava o conhecimento dos profissionais acerca da decisão de tratamento restaurador (MARCENES et al., 2013).

Neste sentido, restaurações “preventivas” em amálgama e ouro eram as mais realizadas e por vários anos foram consideradas como tratamentos padrões de escolha (DONLY et al., 1999). Certamente, estas decisões estavam relacionadas à maior resistência mecânica destes materiais em dentes posteriores, pois as falhas por fraturas e cárie secundária eram menores quando comparadas aos demais materiais existentes da época como as resinas compostas (SMALES;HAWTHORNE,1997; SIMECEK; DIEFENDERFER; COHEN, 2009).

Paralelamente, no início da década de 60, surgiram as resinas quimicamente ativadas e, posteriormente, o desenvolvimento das resinas fotoativadas, mas sempre com o desafio do melhor controle da contração de polimerização. Neste contexto de uma odontologia adesiva, surgiram as resinas macroparticuladas, microparticuladas, híbridas, microhíbridas até as mais recentes nanohíbridas com o intuito de preservar a estrutura dentária através de preparos mais conservadores (BUSATO et al., 2001; FERRACANE, 2012). Como opções de tratamentos restauradores indiretos e com melhores vantagens estéticas, tivemos primeiramente as cerâmicas feldspáticas, em seguida as metalocerâmicas, as cerâmicas vítreas reforçadas por leucita e dissilicato de lítio, até as cerâmicas de zircônia, todas com várias possibilidades de

processamento: sinterizadas, prensadas, infiltradas por vidro ou fresadas (FRIEDL et al., 1996; ANUSAVICE, 2013).

Neste contexto, duas revisões recentes tiveram como ponto-chave indicar o tipo de tratamento restaurador em dentes posteriores de acordo com o número de faces remanescentes em dentes vitais (AFRASHTEHFAR[1] et al., 2017) e não-vitais (AFRASHTEHFAR[2] et al., 2017), mas as conclusões foram bastante limitadas em função da baixa qualidade de padronização dos estudos primários. Além disso, as evidências disponíveis acerca do melhor tratamento restaurador extenso em dentes posteriores permanecem bastante subjetivas e contraditórias (ANGELETAKI et al., 2016; DA VEIGA et al., 2016), o que pode estar relacionado diretamente ao delineamento metodológico dos estudos clínicos (GOSTEMEYER et al., 2016; OPDAM et al., 2018) e por curtos períodos de acompanhamento, pois para detecção das principais falhas e diferenças na sobrevivência entre os tratamentos são necessários, pelo menos, 5 anos de acompanhamento (OPDAM et al., 2014). Uma revisão recente (OPDAM et al., 2018) analisou estudos clínicos publicados entre os anos de 2005 e 2015 e verificou que, entre os prospectivos, apenas 24% apresentavam período de acompanhamento acima de 5 anos quando comparados aos retrospectivos que possuíam 83% dos estudos com 5 ou mais anos. Logo, estudos clínicos retrospectivos refletem melhor as condições da prática clínica real, o que aumenta a validade externa dos resultados (ANGLEMYER et al., 2014; GOSTEMEYER et al., 2016). Por outro lado, os estudos clínicos prospectivos seguem um padrão de randomização com menor risco de viés (OPDAM et al, 2007; GOSTEMEYER et al., 2016; OPDAM et al., 2018; SCHWENDICKE et al., 2016; SCHWENDICKE: OPDAM, 2018).

Outra questão importante está relacionada à experiência clínica do operador e aos fatores inerentes dos pacientes tais como risco de cárie e bruxismo, os quais já foram evidenciados como cruciais para análise da sobrevivência das restaurações e, portanto, devem fazer parte dos critérios de inclusão dos estudos clínicos (VAN DE SANDE et al, 2013; OPDAM et al., 2014; VAN DE SANDE et al., 2016; DEMARCO et al., 2017). Além disso, e de maneira mais contextualizada, fatores sistêmicos dos pacientes como desordens psicológicas, tais como estresse emocional e ansiedade podem ter associação com o bruxismo, o que pode impactar negativamente na saúde bucal dos pacientes e na longevidade dos tratamentos (KUHN; TURP, 2018; GUO et al., 2018).

Adicionalmente, uma revisão da Cochrane (ANGLEMYER A; HORVATH HT; BERO L; 2014) ao selecionar e avaliar criticamente outras 14 revisões que incluíram estudos clínicos prospectivos e observacionais da área médica, não encontraram diferenças significativas entre estes tipos de estudos mesmo após análises de subgrupos. Portanto, Schwendicke e Opdam em 2018 destacaram que as revisões podem incluir ambos os dois tipos de estudos, comparando eficácia versus efetividade, justamente por combinarem todas as vantagens encontradas neles, como maiores tamanhos das amostras, períodos de acompanhamento e redução de custos melhorando, assim, a força da evidência.

Outro fator a ser levado em consideração diz respeito aos critérios utilizados pelos estudos clínicos para identificar e diferenciar o que é “sucesso”, “sobrevivência” e “falha” das restaurações. Um estudo primário (PALLESEN; DIJKEN, 2015) com 30 anos de acompanhamento reportou uma boa taxa de sobrevivência de restaurações em resina composta sendo que as principais causas de falhas das restaurações foram cárie secundária seguida de fratura. Da mesma forma (DA ROSA RODOLPHO et al., 2011 e BALDISSERA et al., 2013) encontraram boas taxas de sobrevivência após 20 anos de acompanhamento sendo fratura a principal razão de falha das restaurações. Contudo, outro estudo retrospectivo (CHRYSANTHAKOPOULOS, 2012) reportou uma baixa taxa de sobrevivência para restaurações em resina composta sendo que após 4 anos de acompanhamento, 39% das restaurações foram substituídas. Entre as principais causas de falhas, estavam manchamento marginal. Por esta razão, é válido levar em consideração que critérios de avaliação estes estudos utilizaram, pois em alguns casos de delineamentos destes estudos, uma superestimação das causas de falhas podem ser observadas (OPDAM et al., 2014).

Em relação aos estudos secundários publicados, os quais normalmente compararam dois tipos de tratamentos tais como resina indireta versus cerâmica (CHABOUIS; FAUGERON; ATTAL, 2013) amálgama versus resina direta (RASINES ALCARAZ et al.2014; MORASQUINI et al., 2015), resina direta versus resina indireta (ANGELETAKI et al., 2016; DA VEIGA et al., 2016; AZEEM; SURESHBABU, 2018) encontraram evidências limitadas em relação à melhor indicação de tratamento restaurador para restaurações extensas em dentes posteriores. Neste sentido, em função dos cuidados da saúde oferecerem mais de dois tratamentos para uma condição particular, há a necessidade de uma abordagem que permita comparações entre múltiplas opções de tratamentos e que compile todas as evidências em uma

síntese – uma meta-análise em rede (CATALÁ-LÓPEZ et al., 2014; WATTAR et al., 2017). Contudo, em odontologia, existem poucas meta-análises em rede publicadas e até o momento a maioria delas não seguiu adequadamente todas as recomendações do PRISMA-NMA *(Extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations)* (HUTTON et al., 2015; LEE; SHIN, 2018).

Recentemente, uma meta-análise em rede de dentes decíduos (PIRES et al.,2018) evidenciou que as decisões restauradoras podem estar mais relacionadas à habilidade dos profissionais e à individualidade dos casos do que aos materiais disponíveis. Outra meta-análise em rede (SCHEWENDICKE et al., 2016), determinou as melhores opções restauradoras comparando materiais exclusivamente adesivos e diretos para dentes decíduos, restaurações classe V e classe I e II de dentes permanentes. Portanto, levando em consideração que há uma maior diversidade de materiais, diretos e indiretos, o objetivo principal deste estudo foi realizar uma meta-análise em rede e encontrar uma evidência mais sólida da melhor opção restauradora extensa para dentes posteriores permanentes com pouca quantidade de remanescente coronário disponível.

2. Capítulo 1 Artigo*

Decision of treatment for extensive posterior restorations: a systematic review and network meta-analysis

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Decision of treatment for extensive posterior restorations: a systematic review and network meta-analysis

Abstract

Although dental restorations are considered one of the most prevalent medical interventions, current evidence is still controversial on the best restorative treatment for severely damaged posterior teeth. The aim of this study was to perform a systematic review and a network meta-analysis to find the best treatment option for these cases. Prospective and retrospective studies comparing at least two different treatment alternatives for permanent teeth and with a minimum of five years of follow-up, with no restriction of year of publication and language were selected. The initial search yielded 11,095 studies, and 45 studies fulfilled the eligibility criteria and were included in the final review. Gold (AFR=0.28%) and metal ceramic (AFR=0.55%) crowns performed better for indirect restorations, while nanohybrid resin composite performed better for direct restorations (AFR=1.06%). According to the network meta-analysis, the largest comparisons were between feldspathic and glass ceramics, direct resin composite and amalgam, and hybrid resin composite and amalgam, with no statistically significant differences between the interventions. Main reasons for failures were secondary caries and restoration fracture. There is a moderate quality of evidence that large posterior cavities should be restored with direct resin composites, preferably nanohybrid composites or indirect gold/metal-ceramic crowns. (CRD4201608264)

Introduction

Impact of oral health on economy and quality of life generates a concern, since there is a tendency for dental treatment to have increased expenditures between 2010 and 2015 (Righolt et al. 2018). This data includes the placement of restorations as one of the most executed procedures in dental practices (Frencken et al. 2012). Whereas evidence is available on longevity of dental restorations and there is a clear indication that composites are the best option for restoring small defects for load-bearing restorations (Schwendicke et al. 2016; Opdam et al. 2016), fewer information is available concerning larger restorations. The risk of failure in larger posterior restorations increase 30 to 40% for every extra surface (Opdam et al. 2014), with properties of the filling material as one of the factors influencing the restoration's survival (Rasines-Alcaraz et al. 2014).

Considering direct restorations, there was a reduction in amalgam restorations placement in the last decades, therefore increasing the choice for composite resin (Eltahlah et al. 2018). However, it is possible to find conflicting results with studies showing higher failure rates for resin composite (Rasines-Alcaraz et al. 2014), while others report higher survival of conventional resin composites for load-bearing restorations (Schwendicke et al. 2016). As an alternative, indirect restorations should also be considered, since they have shown higher acceptable clinical performance and lower need for repair or replacement (Skupien et al. 2016). However, this is not valid for all indirect restorations and ceramic types, as feldspathic and glass ceramics should be avoided in high functional load regions (Sailer et al. 2015).

Due to the large number of available materials for both direct and indirect techniques and considering the lack of consensus about the best clinical choices, a network meta-analysis seems to be a good approach to predict the best treatment option, allowing comparisons between more than two interventions (Jansen and Naci 2013). Until now, few studies using this methodology and with a low quality of reporting (Lee and Shin 2018) have been conducted. Although a recent network meta-analysis (Schwendicke et al. 2016) comparing different restorative treatments was conducted, only prospective studies with direct restorative materials and adhesive systems in cervical restorations, load bearing-posterior cavited of permanent and primary molars teeth were analysed. Thus, the aim of this systematic review was to answer the

following question: Which is the best restorative treatment for extensive restorations in permanent posterior teeth considering adults and any type of material?

Materials and methods

This review followed the guidelines of Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011) and the PRISMA-NMA (Hutton et al. 2015). The procotol was registered in PROSPERO (International prospective register of systematic reviews) (CRD42016082464).

1. Eligibility criteria

Randomized controlled trials (RCTs), controlled clinical trials (CCTs), follow-up studies, retrospective studies, and prospective studies were selected with no language or year of publication restrictions. The PICO question considered which is the best treatment for extensive restorations in permanent posterior teeth considering patients of any age and type of material. The studies should compare at least two types of restorative materials in permanent severely damaged posterior teeth (from two-surface restorations up to full crowns), present survival rate data of the restorations and a minimum of five-years of follow-up, as there is evidence that failures usually occur after 5 years of clinical service (Opdam et al., 2014). Case-control studies, case-series, reviews, and expert opinions were excluded.

2. Search strategy

The literature search strategy for the electronic databases (Medline, Scopus, Cochrane Collaboration's Library and Web of Science) is presented in Table 1 (supplementary material). Duplicates were removed in EndNote Program and data were collected through Excel spreadsheets.

Two independent reviewers (BMV and FLL) selected papers by title and abstract for relevance based on inclusion criteria. In case of disagreement, a third reviewer was recruited to obtain consensus (TPC). Full texts were obtained for further screening and, if the same sample was presented in distinguished paper, the one with higher follow-up was considered.

3. Data extraction

Data extraction included author, year and country of publication; age and gender of patients; number of restorations, follow-up and drop-out; restorative technique and material, tooth vitality, presence of post; survival rate and evaluation criteria. When missing, data were requested to the authors by e-mail.

4. Data analysis

The annual failure rate (AFR) of the investigated restorations was calculated according to the formula: $(1-y)Z = (1-x)$, in which 'y' expresses the mean AFR and 'x' the total failure rate at 'z' years. Survival was recorded when the restoration was repaired or no intervention was necessary, while restorations that were replaced or tooth lost were computed as failure.

All data analysis was performed with R Studio software (Rstudio Inc, Boston, USA) separately for 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 statistic and its 95% CI. Multi-arm studies were treated as multiple independent two-arm studies in pairwise meta-analyses. The NMA was generated through a summary graphic of the size of interventions and comparisons across the studies. The probability of different ranks for each treatments was also assessed through SUCRA (Surface Under the Cumulative Ranking Curve).

5. Risk of bias and quality assessment

Randomized clinical trials were evaluated for risk of bias using the Cochrane risk of bias tool (Higgins 2011) considering random sequence generation, allocation concealment, blinding of participants and professionals, blinding of outcome assessment, incomplete outcomes, selective reporting and other sources of bias. The assessment of bias of the non-randomized trials were performed with the ROBINS-I tool (Sterne et al. 2016) considering the judgement of confounding, selection of participants, classification of interventions, deviation from intended interventions, missing data, measurement of outcomes and selection of the reported result. The quality of evidence was evaluated through GRADE (Grading of Recommendations Assessment, Development and Evaluation) (Guyatt et al. 2008).

Results

The literature search yielded 11,095 titles and abstracts (July, 2018). After duplicates removed and analysis of titles and abstracts, 152 articles were selected to access the full-text. Forty-five studies fulfilled the eligibility criteria and were included in the review (Figure 1; Table 2 and 3– supplementary material). To allow comparisons, each material should appear at least in two studies, which ended up excluding five papers from this analysis because the materials investigated had been evaluated only once (Rasmusson et al.1995; Van Dijken 2000; Guess et al. 2013; Van Dijken et al. 2016; Borgia et al. 2017). The response rate for the contact with authors was of approximately 56%, which represents fifteen of the twenty-six e-mails sent. From the replied ones, two thirds (ten studies) could be included after assessing the original data.

The higher AFR was presented for glass-ionomer restorations alone (10.25%) or in association with resin composite as a sandwich technique (3.84%). Gold and metal-ceramic restorations had the lowest AFR (0.28 and 0.55%, respectively). For direct restorations, the best result was for nano-hybrid direct resin composite with AFR=1.06%, and for indirect restorations gold and metal-ceramic achieved the best performance (Table 4 – supplementary material).

The NMA results suggests in agreement with the AFR values that metal-ceramic and gold are the best options for indirect restorations while nano-hybrid resin composites are better for direct restorations. The worst performances were found in glass-ionomer as a direct material, and glass ceramic and feldspathic ceramic as indirect materials in the rank probabilities (Figure 2). The major comparisons were between feldspathic and glass ceramic, direct resin composite and amalgam, and hybrid resin composite and amalgam, with no statistically significant differences between the interventions (Figures 3 and 4).

From the included studies, twenty five were non-randomized trials with a serious risk of bias, five non-randomized trials with moderate risk of bias especially for bias to confounding and measurement of outcomes (Table 2 and 3 – supplementary material). Only one non-randomized presented low risk of bias (Van de Sande et al. 2015). Fourteen RCTs were included, with a low risk for incomplete outcome data, selective reporting, random sequence generation, and blinding of outcome assessment (Figure 6 – supplementary material). There was a moderate confident effect estimate, since

the randomized trials had a high certainty and the observational studies had a very low certainty about the evidence generated (Figure 5).

Discussion

This review was design as an attempt to help to fill the gap on the literature about what would be the best treatment option for large defects in posterior teeth, since only small defects have a consensus that resin composite is the best choice (Demarco et al. 2012; Lynch et al 2014; Schwendicke et al. 2016; Opdam et a. 2016; Demarco et al., 2017). For that, both direct and indirect materials, were included and up to know, this is the first NMA that also considered retrospective studies, which can show the materials performance through a long-term follow-up in a large population.

The good performance for the direct composite resin was shown in previous studies (Schwendicke et al. 2016; Opdam et al. 2014). The AFR of 2.94% for direct resin composite is the same found in the literature (Manhart et al. 2004; Heintze and Rousson, 2012). The same trend was found for glass-ionomer performance, which appears to have a negative influence on restoration survival even as a single material or in a sandwich technique (Opdam et al.2014). However, there is still controversial results in literature, with low-quality of evidence from one systematic review showing a significantly higher AFR for resin composite, when compared with amalgam (Rasines-Alcaraz et al 2014).

One of the reasons why these failures are deemed to occur is related to technical aspects and polymerization contraction of direct resins. To overcome these technical difficulties, indirect techniques were used to improve mechanical properties, proximal contacts and reduction of occlusal wear (Deliperi and Bardwell 2006; Dukik et al, 2010). Still, recent pairwise reviews comparing both techniques did not find any difference in longevity between direct and indirect composites (Angelataki et al. 2016; da Veiga et al. 2016; Azeem and Sureshbabu, 2018). This is evidenced in our NMA, since we found AFR of 1.81% for indirect restorations in composite resin when compared to AFR of 1.95% for restorations in direct hybrid resin, which have been highly used in clinical studies and therefore considered as gold standard (Schwendicke et al. 2015). This finding was also confirmed in this NMA, where hybrid resin was the material with more direct comparisons between other materials. In addition, other types of direct resins with low polymerization contraction, although presenting a low AFR of 1.4%, did not have significant differences when compared to the conventional hybrid resins.

Considering the indirect treatment options for posterior teeth, this study emphasizes the good performance of gold and metal-ceramic restorations, which presented the lowest AFR. Although these restorative options require more invasive preparation, gold and metal ceramics restorations have demonstrated excellent mechanical strength and biocompatibility over the last 50 years (Wagner et al. 2003; Passia et al. 2013; Olley et al. 2017). A previous systematic review regarding survival rates for single-crowns also showed a suitable result for gold and metal-ceramic (considered as gold standard) and recommended that feldsphatic and glass ceramics should be avoided due to the highest AFR found for these materials (Sailer et al. 2015). Annual failure rates for glass and feldspathic ceramics was 2.67% and 1.64%, respectively. However, there was a important limitation in these findings, since included primary studies comparing these materials did not report (Pallesen and Van Dijken 2000; Felden et al. 1998) or even exclude patients with risk factors such as parafunctional habits (Santos et al. 2015; Thordrup et al. 2006; Khairallah et al. 2009). In addition, some recent studies have shown differences in annual failure rates between patients with low risk and high risk of caries and bruxism (Van de Sande et al. 2013; Opdam et al. 2014; Van de Sande et al. 2016).

The impossibility of comparison of other important options, such as new all-ceramic and resin composite materials was one of the limitations of this study. This is explained by the exclusion of studies with less than five years of follow-up, as it is expected that failures like fractures and secondary caries starts to happen (Opdam et al. 2014). Another factor may be that the number of non-randomized studies was twice the number of RCTs, which can possibly mean a significant risk of bias. However, the number of restorations present should at least show the materials' behaviour in a big scenario.

Despite the methodological problems, we decided to also include non randomized trials due to the fact that the estimated effect provided by these studies sometimes can be larger than for RCT. For example, cohort studies may provide a bigger picture whether a treatment considered "the best" in a RCT has the expected result in a routine practice (Kunz et al. 2007). The risk of bias provided from the specific tools for the different study designs, as well as the quality assessment allows to see the results shown by this review as a moderate confident effect, since the evidence generated was considered high for RCTs and low for non-RCTs. The treatment choice should go for the option with lower cost, less invasive preparation of the cavity and

simpler technique, which lead us to the decision for direct resin composite restorations instead of indirect, since both approaches have no differences on longevity (Veiga et al. 2016).

Conclusions

Based on the present findings, posterior cavities including two or more surfaces should be restored with direct resin composites, preferable nano-hybrid composites, or indirect gold/ metal-ceramics crowns taking into account the low annual failure rate of these treatments.

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Legends:

Table 1. Search strategy

Table 2. Table general of prospective studies included in the review

Table 3. Table general of retrospective studies included in the review

Table 4. AFR of the studies included in the NMA

Figure 1. Flow chart of articles as described in the PRISMA statement

Figure 2. Figure Rank Prob (SUCRA)
Probability of different different ranks for the treatments. The black area indicates the probability of being the best treatment. 1) Prospective studies; 2) Retrospective studies. Materials: DR, Direct resin; HR, Hybrid resin; AM, Amalgam; GI, Glass ionomer; FC, Feldspathic ceramic; GC, Glass ceramic; ZC, Zirconia-based ceramic; MC, Metal-ceramic; GO, Gold; NR, Nanofiller resin; IR, Indirect resin; CR, Chemically-cured Resin; LR, Low-shrinkage Resin; RS, Resin sandwich.

Figure 3. Network Graph:
Summary of the number of studies and the number of restorations for each treatment. The size of treatment nodes reflects the number of patients randomly assigned to each treatment. The thickness of edges represents the number of studies underlying each comparison.
1) Prospective studies;2) Retrospective studies. Materials: DR, Direct resin; HR, Hybrid resin; AM, Amalgam; GI, Glass ionomer; FC, Feldspathic ceramic; GC, Glass ceramic; ZC, Zirconia-based ceramic; MC, Metal-ceramic; GO, Gold; NR, Nanofiller resin; IR, Indirect resin; CR, Chemically-cured Resin; LR, Low-shrinkage Resin; RS, Resin sandwich.

Figure 4. Forest plots of pairwise comparisons for retrospective studies. Risk ratio (RR) and 95%confidence interval (95% CI) of survival in the first material group (Mat1) versus the second (Mat2). Materials: DR, Direct resin; HR, Hybrid resin; AM, Amalgam; GI, Glass ionomer; FC, Feldspathic ceramic; GC, Glass ceramic; ZC, Zirconia-based ceramic; MC, Metal-ceramic; GO, Gold; RS, Resin sandwich.
Forest plots of pairwise comparisons for prospective studies. Risk ratio (RR) and 95% confidence interval (95% CI) of survival in the first material group (Mat1) versus the second (Mat2). Materials: DR, Direct resin; HR, Hybrid resin; AM, Amalgam; GI, Glass ionomer; FC, Feldspathic ceramic; GC, Glass ceramic; ZC, Zirconia-based ceramic; MC, Metal-ceramic; GO, Gold; NR, Nanofiller resin; IR, Indirect resin; CR, Chemically-cured Resin; LR, Low-shrinkage Resin.

Figure 5. GRADE- Assessment of the level of evidence

Figure 6. Risk of bias using the Cochrane Risk of Bias Tool

Table 1. Search strategy

Database	Search strategy
PubMed	(("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")

Table 2. Table general of prospective studies included in the review

Author//Year	Country	Gender	Average of age	Study design	Materials	Material brand	n restorations	Intermediate material	n PM	n M	n total	Pulp vitality Y/N	Post Y/N	Survival rate (%)	AFR	Criteria for failure	Follow-up mean	Drop-out	Risk of Bias Non-RCT
Rowe 1989	UK	.	.	Parallel group	Hybrid composite	Occlusin	176	.	103	73	230	.	.	90	2.1	Secondary caries, fracture	5	.	Serious
					Amalgam	Dispersalloy /Aristoloy	54		27	27				90	2.3				
Norman et al 1990	UK	.	62	Parallel group	Hybrid composite	Occlusin	54	.	50	29	79	.	.	90.7	1.5	secondary caries	5	.	Serious
					Amalgam	Dispersalloy	25							88	2.5				
Mjor and Jokstad 1993	Norway	.	13	Parallel group	Hybrid composite	P-10	36	N	9	27	113	.	.	75	5.5	secondary caries, fracture	5	59	Serious
					Glass-ionomer cement	Ketac Silver	44		14	30				50	13				
					Amalgam	Dispersalloy	33		11	22				87.8	2.5				
Lumley and Fisher 1995	UK	11M 14F	29	Parallel group	Glass-ionomer cement	Chemfil/Ketac -Fil	11	hydroxide cement	.	.	47	.	N	63.6	7.2	recurrent caries, fracture of the marginal ridge or gross loss of restorative material	6	0	Serious
					Cermet	Ketac-Silver	22							86.4	2.4				
					Amalgam	Sybralloy	14							100	0.0				
Mair 1998	UK	.	.	Parallel group	Amalgam	New True Dentalloy/Solila Nova	35	deep: calcium hidroxide liner + zinc	.	.	91	.	.	94.3	0.5	.	10	59	Serious

					Composite (direct)	Clearfil posterior/Occlusin/P-30	56	phosphate cement						92.9	0.7				
Erpenstein et al 2000	Germany	123M 287F	.	Parallel group	Glass-ceramic Galvano-ceramic	Dicor AGC	78 594	N	.	.	672	.	.	70.5 98.1	4.8 0.2	fracture with loss of the fractured segment	7	.	Serious
Pallesen and Van Dijken 2000	Denmark	11 F 5 M	40	Parallel group	Feldspathic ceramic Glass ceramic	Vita Mark II Dicor MGC	16 16	.	.	.	32	Y	N	90.6 87.6	0.8 1.6	fracture	8	0	Serious
*Van Dijken 2000	Sweden	16 F 24 M	48	Parallel group	Composite (indirect) Composite (sandwich closed)	Brilliant DI Fulfill	96 33	N glass ionomer cement base	.	.	129	Y	Y	82.3 72.7	2.8 1.7	secondary caries, fracture	11	.	Serious
Wassel et al 2000	UK	54 F 19 M	29.6	Parallel group	Composite (direct) Composite (indirect)	Brilliant Dentin Brilliant Dentin	69 74	.	.	.	143	Y	N	94.2 89.1	1.1 2.2	fracture, sensitivity	5	.	Serious
Pallesen and Qvist 2003	Denmak	20 F 8 M	35	Parallel group	Composite (direct) Composite (indirect) Composite (direct) Composite (indirect) Composite (indirect)	Brilliant Dentin Estilux Posterior Isosit	27 27 27 27 27	.	.	.	135	Y	N	95.8 74.07 74.07 95.8 77.77	1.0 1.4 1.8 1.0 2.2	fracture, secondary caries, loss of proximal contact	11	5.2	Serious

Van Nieuwenhuysen et al 2003	Belgium	428	.	Parallel group	Composite (direct)	.	89	.	.	.	635	.	.	69.6	4.5	tooth fracture, restoration fracture, secondary caries	10.3	.	Serious
					Amalgam		546							71.9	2.5				
Mannocci et al 2005	Italy	116 F	45	Parallel group	Micro-hybrid composite	Z100	100	N	100	.	209	N	Y	89.6	2.1	secondary caries, fracture	5	11.8	*
		103 M			Amalgam	Valiant PhD	109		109					91.3	1.8			8.3	
Thordrup et al 2006	Denmark	30 F	37	Parallel group	Glass-ceramic	Cerec	14	.	.	.	44	.	.	92.9	0.7	secondary caries, fracture, hypersensitivity	5	2	Serious
		7 M			Feldspathic ceramic	Vita Dur N	11							85.1	2.2				
					Composite (indirect)	Brilliant Direct	10							82.1	2.2				
						Estilux	9							91.7	1.1				
Soncini et al 2007	USA	449	8	Parallel group	Composite (direct)	.	753	.	.	1262	1262	.	.	85.1	3.1	primary or secondary caries	5	.	*
					Amalgam	.	509							89.2	2.2				
Bernardo et al 2007	Portugal	NR	.	RCT parallel group	Composite (direct)	Z100	442	N	.	.	869	.	.	65.6	5.8	need of replacement	7	.	*
					Amalgam	Dispersalloy	427							86.9	1.9				
Khairallah and Hokayem 2009	Lebanon	.	32.4	Parallel group	Leucite-reinforced pressed glass-ceramic	IPS Empress	17	N	.	.	33	.	.	88.2	1.9	.	6.3	.	Serious
					Composite (indirect)	Targis	16							100	0.0				
Federlin et al 2010	Germany	14 F	37	RCT Split mouth	Feldspathic ceramic	Vita Mark II ceramic/ Cerec 3	22	.	.	.	44	.	.	95.4	0.8	fracture	5.5	.	Serious
		8 M			Gold	.	22							100	0.0				

Fennis et al 2013	Netherlands	77M 80F	54.9	RCT parallel group	High filled hybrid composite (direct) Hybrid composite (indirect)	AP-X Estenia	80 78	N	158	.	158	Y	N	91.3 84.6	1.8 3.5	reparable or complete	5	18	*
*Guess et al 2013	Germany	14M 11F	.	RCT split-mouth	Lithium disilicate pressed ceramic Leucite-reinforced pressed glass-ceramic	IPS e.max ProCAD/Cerec 3	40 40	N	.	80	80	Y	N	100 97.5	0.0 0.3	inacceptable fractures, secondary caries, and endodontic complications	7	7	*
Passia et al 2013	Germany	119 F 104 M	41.8	Parallel group	Zirconia-based ceramic Gold	ZrSiO4 .	77 81	.	13 2	109 97	158	N	Y	73.2 92.3	9.7 0.7	fracture	5	.	*
Schmidt et al 2014	Denmark	48	50.5	Parallel group	Low shrinkage composite Hybrid composite	Filtek Silorane Ceram X	52 55		29 30	23 25	107	Y	.	94.2 94.5	0.7 1.1	fracture	5	32	*
Van Dijken and Pallesen 2014	Sweden	27 F 25 M	53	Parallel group	Nano-hybrid composite Hybrid composite	Exite/Tetric Evoceram Exite/Tetric Ceram	57 57	.	.	.	114	Y	N	80.7 80.7	2.1 2.1	secondary caries	10	7	*
Kramer et al 2015	Germany	23F 7M	32.9	Controlled split-mouth	Nano-hybrid composite Micro-hybrid resin composite	Grandio Tetric Ceram	36 32	N	.	.	68	Y	N	100 100	0.0 0.0	.	10	0	Serious
Pallesen and Van Dijken 2015a	Denmark	25 F	38.2	Parallel group	Chemically-cured composite	Clearfil Posterior	27	calcium hydroxide cement	60	39	99	Y	N	63	1.7	secondary caries, restoration fracture,	27	.	*

		5M			Hybrid composite	Adaptic II	29							55.2	2.1	occlusal wear				
						Occlusin	29							51.7	2.4					
Pallesen and Van Dijken 2015b	Denmark	21 F 9 M	30	Parallel group	Chemically-cured composite	MIRADAPT	27	N	.	.	99	Y	N	74	1.0	secondary caries, fracture	30	.	*	
						P10	28							69	1.2					
					Hybrid composite	P30	28							59	1.8					
Santos et al 2015	Brazil	22	33	Parallel group	Feldspathic ceramic	Duceram Plus	23	.	.	.	48	.	.	95	1.5	fracture	12	44	Serious	
					Leucite-reinforced pressed glass-ceramic	IPS Empress	25							76	4.7					
Van Dijken and Lindberg 2015	Sweden	22 F	43	Parallel group	Low shrinkage composite	Inten-S	46	.	.	.	91	.	N	78.3	1.8	secondary caries, fracture	15	16.4	*	
		28 M			Micro-hybrid composite	Point 4	45							75.6	1.6					
Skupien et al 2016	Brazil	47	42.6	Parallel group	Micro-hybrid composite	Filtek Z-250	26	.	12	14	43	N	Y	87	0.7	fracture	5	0	*	
					Metal-ceramic	.	17		9	8				100	0.0					
*Van Dijken and Pallesen 2016	Sweden	42 F	52.4	Parallel group	Bulk-filled + Nano-hybrid composite	SDR + Ceram X	62	.	.	.	124	Y	N	93.5	1.3	secondary caries, fracture	5	.	*	
		44 M			Nano-hybrid composite	Ceram X	62							90.3	2.0					
Monaco et al 2017	Italy	39 F	44	Parallel group	Zirconia-based ceramic	ZirCad	45	.	25	20	88	N	Y	92.6	0.4	tooth or restoration fracture	5	5.5	*	
		33 M			Metal-ceramic	IPS d. SIGN 91 (metal)+ PoM (pressable ceramic)	43		19	24				97.4	0.5					

Author/Year	Country	Gender	Average of age	Materials	Material brand	n rest.	Intermediate material	n PM maxillary/ mandibular	n M maxillary/ mandibular	n total maxillar/mandibular	Pulp vitality (Y/N)	Post (Y/N)	Survival rate (%)	AFR	Criteria for failure	Follow-up mean	Drop-out	Risk of Bias Non-RCT
*Rasmusson et al 1995	Sweden	.	.	Hybrid composite	Oclusin/ P30	23	.	163	13	176	Y	N	86.9%	2.76	secondary caries	5	29	Serious
					Ful-Fil	33							65.2	15.3	fracture			
					Profile	20							86.9	0.89	marginal adaptation			
				Microfine composite	Heliomolar	23							93.7	1.95	appr contact			
					Distalite	23							85.1	0.89				
Felden et al 1998	Germany	65F	37.9	Glass-ceramic	Dicor	44	N	.	.	287	.	.	68.2	1.95	loss or fracture of the restoration	7	50	Serious
				Leucite-reinforced pressed glass-ceramic	IPS Empress	126							97.6	3.16				
				Zirconia based ceramic	Mirage II	82							100	1.65				
		27M		Feldspathic ceramic	Cerec Vita Mark I/Ducera m LFC	35							100	0.0				
Wagner et al 2003	Germany	18F	.	Gold	.	42	N	1	41	84	.	.	95.2	0.37	fracture	10	.	Serious
				Leucite-reinforced pressed glass-ceramic	IPS Empress	42		15	27				95.2	0.69				
		24M																

Arnelund et al 2004	Sweden	98F 55M	48	Leucite-reinforced pressed glass-ceramic Alumina-reinforced feldspathic ceramic	IPS Empress Vitadur Alpha	185 81	N	64 32	121 49	266	.	.	92.3 93.3	0.99 3.97	.	5.1	49	Serious
Opdam et al 2007	Netherlands	13F 110M	49	Hybrid composite Hybrid composite + GIC (Sandwich)	Clearfil Photo Posterior Clearfil Photo Posterior + Vitrebond/GC	376 82	N Y	.	.	458	Y	N	88.5 58.5	1.34 5.78	secondary caries, fracture	9	.	Moderate
Opdam et al 2010	Netherlands	157 F 116 M	48	Hybrid composite Amalgam	Clearfil Photo Posterior /AP-X/Others Dispersalloy	747 1202		234 389	513 813	1949	.	N	84.7 75.6	1.37 2.30	secondary caries, fracture	12	.	Moderate
Kim et al 2013	Korea	.	.	Amalgam Composite (direct) Glass-ionomer	. .	76 161 45	N	.	.	282	.	.	66.5 71.6 46.1	8.03 6.19 15.84	.	5	.	Serious
Skupien et al 2013	Germany	.	40.5	Composite (direct) Metal-ceramic	. .	304 124	.	.	.	428	N	.	97.6 88.7	0.24 1.24	tooth fracture	9.6	.	Moderate

Van de Sande et al 2015	Brazil	62F 35M	.	Hybrid composite Hybrid composite + GIC (Sandwich)	Z100/ Tetric Ceram P-50/Herculite XR	270 362	calcium hydroxide calcium hydroxide +glass-ionomer cement	105 168	165 194	632	Y	N	68.3 71	2.1 1.9	fracture,, secondary caries	18	.	Low
Collares et al 2016	Germany/China/USA/France/Chile/Spain	.	.	Feldspathic ceramic Leucite glass-ceramic	CEREC/ VITABLOCS HeraCeram/IPS Empress /ProCAD /OPC press/Imagine PressX	1120 194	N	790	862	1652	.	.	83.3 85.6	2.27 1.11	.	7.2	.	Moderate
Laske et al 2016	Netherlands	.	.	Composite (direct) Amalgam Glass-ionomer Compomer	.	175128 26757 5141 664	.	.	.	207690	Y/N	.	80.7 65 46.5 54.2	2.13 4.21 7.38 5.94	restoration replaced or repaired, tooth extraction, endodontic or prosthetic treatment	10	0	Moderate
Naghipur et al 2016	Canada	.	52	Composite (direct) Amalgam		1444 1002	.	1444 1002	.	2820	Y	N	86 91.5	0.81 0.57	secundary caries fracture	12	.	Serious
Rinke et al 2016	Germany	32F 21M	49.6	Zirconia-based ceramic Metal-ceramic		50 41	.	.	48 43	91	Y/N		94 95.1	1.23 1.00	secondary caries, loss of retention, fracture	5	13	Serious

		18F	46.8	Nano-filler composite (direct)	Filtek Z350	11							90.9	0.82				
				Micro-filler composite (direct)	Heliomolar	9							100	0.0	tooth or restoration fracture, secondary caries, endodontic treatment, tooth loss	11.6	0	Serious
***Borgia et al 2017**	Uruguay				Filtek P60/Filtek Z250/Tetric Ceram/Prodigy/Prisma APH		N	.	.	35	Y/N	N						
		10M	54.6	Micro-hybrid composite (direct)		15							100	0.0				
Olley et al 2017	UK	27F	49	Metal-ceramic	.	101		.	.	123			96	0.12		50	.	Serious
		20M		Gold	.	22							100	0.0				

***Author/year - studies excluded NMA (only one data entry)**

Table 4. AFR of studies included in the NMA

Material	Studies (n)	AFR
Glass-ionomer	4	10.25
Sandwich (Resin+Glass-ionomer)	2	3.84
Direct composite resin	6	2.94
Zirconia-based ceramic	4	2.87
Glass ceramic	8	2.67
Amalgam	12	2.49
Hybrid composite resin	19	1.95
Indirect composite resin	5	1.81
Feldspathic ceramic	7	1.64
Chemically-cured composite resin	2	1.42
Low shrinkage composite resin	2	1.4
Nano-hybrid composite resin	2	1.06
Metal-ceramic	7	0.55
Gold	4	0.28

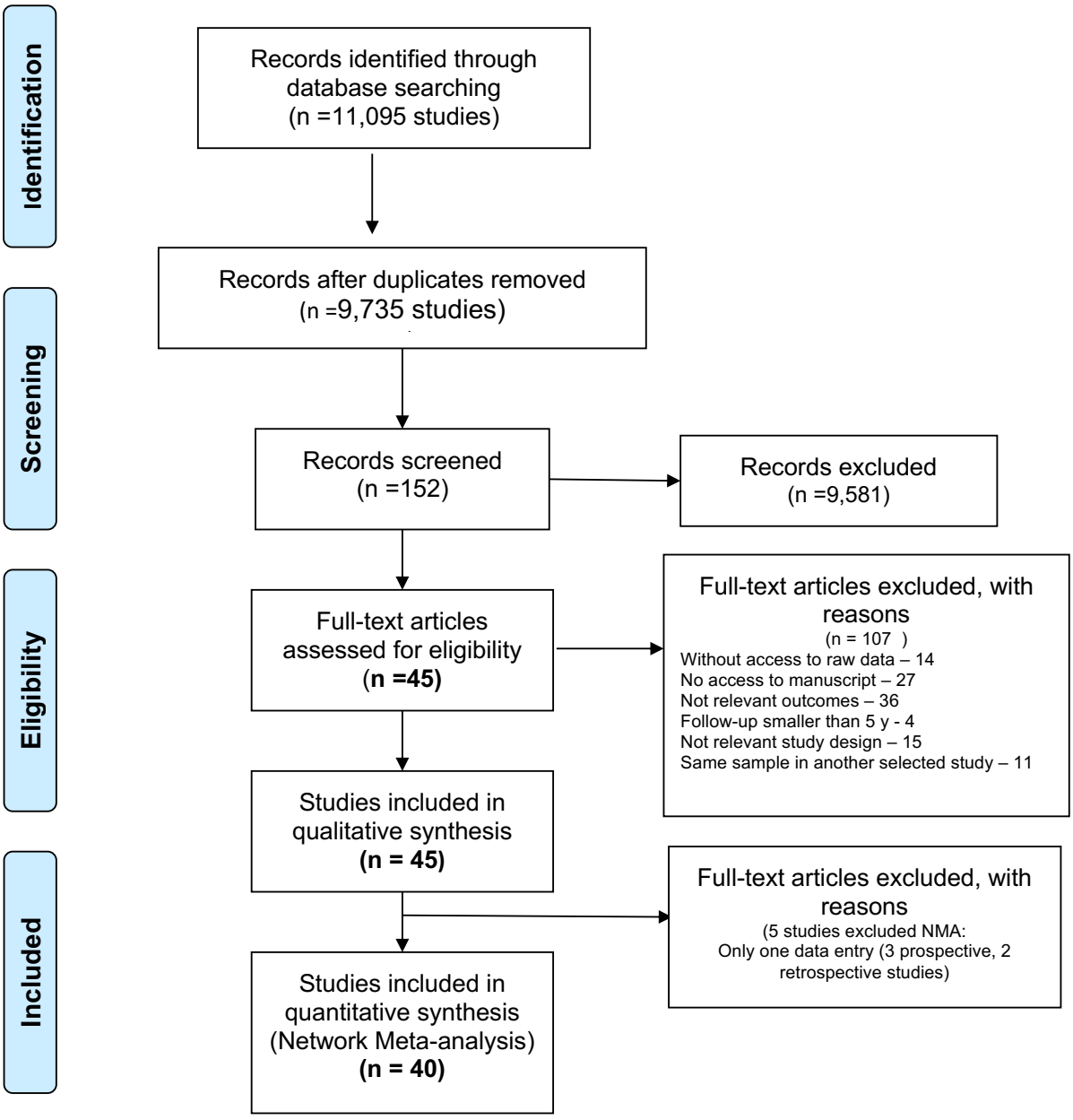

Figure 1. Flow chart of articles as described in the PRISMA statement

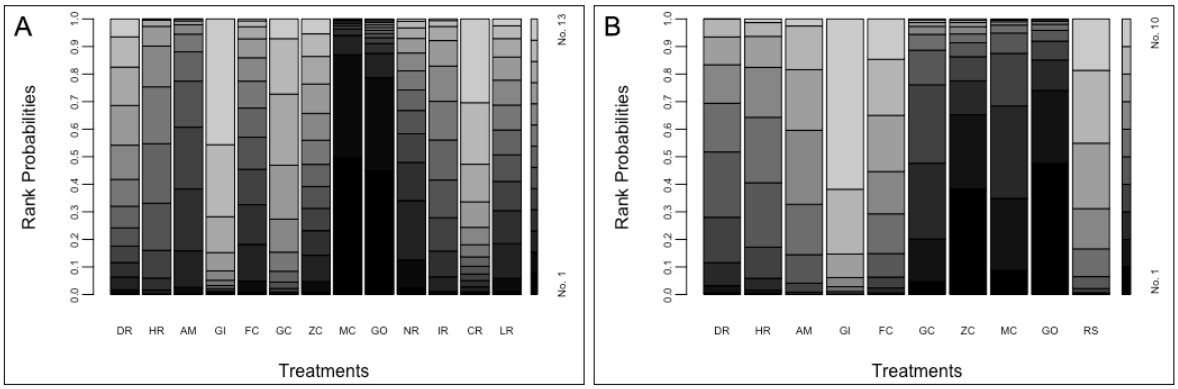

Figure 2. Figure Rank Prob:
Probability of different different ranks for the treatments. The black area indicates the probability of being the best treatment. 1) Prospective studies; 2) Retrospective studies. Materials: DR, Direct resin; HR, Hybrid resin; AM, Amalgam; GI, Glass ionomer; FC, Feldspathic ceramic; GC, Glass ceramic; ZC, Zirconia-based ceramic; MC, Metal-ceramic; GO, Gold; NR, Nanofiller resin; IR, Indirect resin; CR, Chemically-cured Resin; LR, Low-shrinkage Resin; RS, Resin sandwich.

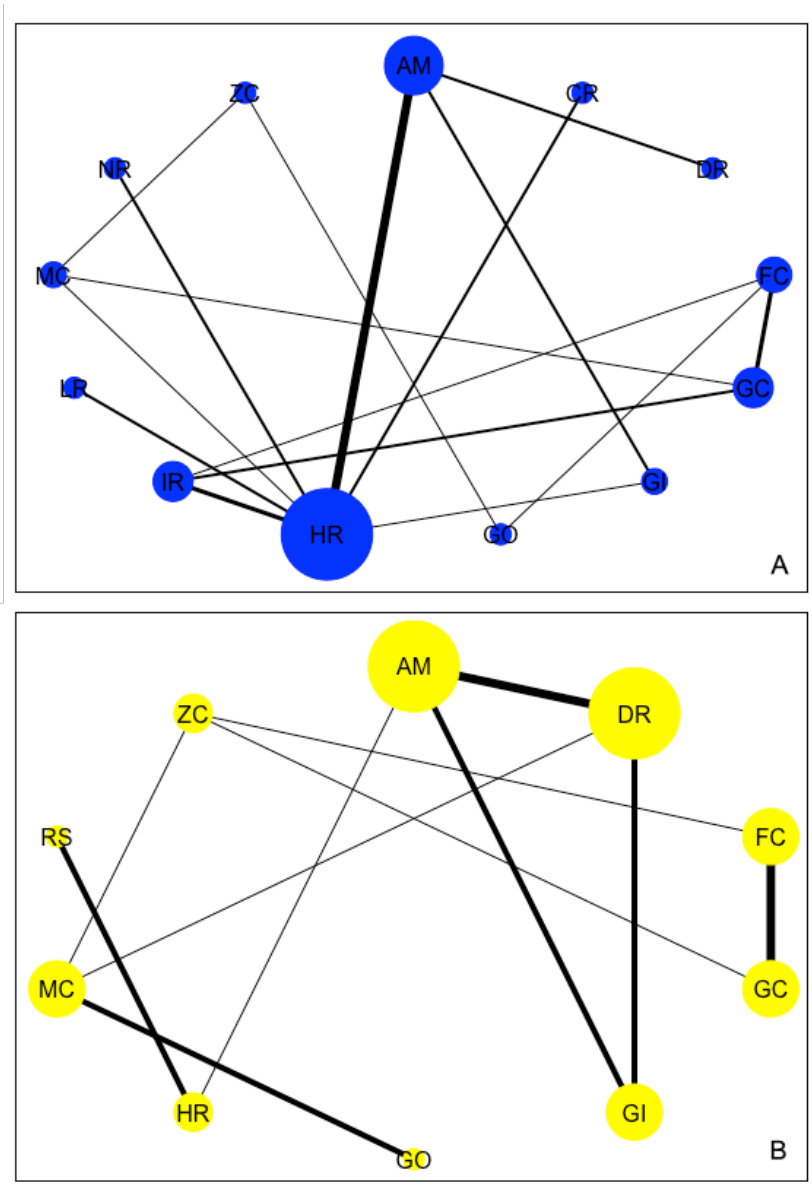

Figure 3. Network Graph:
Summary of the number of studies and the number of restorations for each treatment. The size of treatment nodes reflects the number of patients randomly assigned to each treatment. The thickness of edges represents the number of studies underlying each comparison.
1) Prospective studies;2) Retrospective studies. Materials: DR, Direct resin; HR, Hybrid resin; AM, Amalgam; GI, Glass ionomer; FC, Feldspathic ceramic; GC, Glass ceramic; ZC, Zirconia-based ceramic; MC, Metal-ceramic; GO, Gold; NR, Nanofiller resin; IR, Indirect resin; CR, Chemically-cured Resin; LR, Low-shrinkage Resin; RS, Resin sandwich.

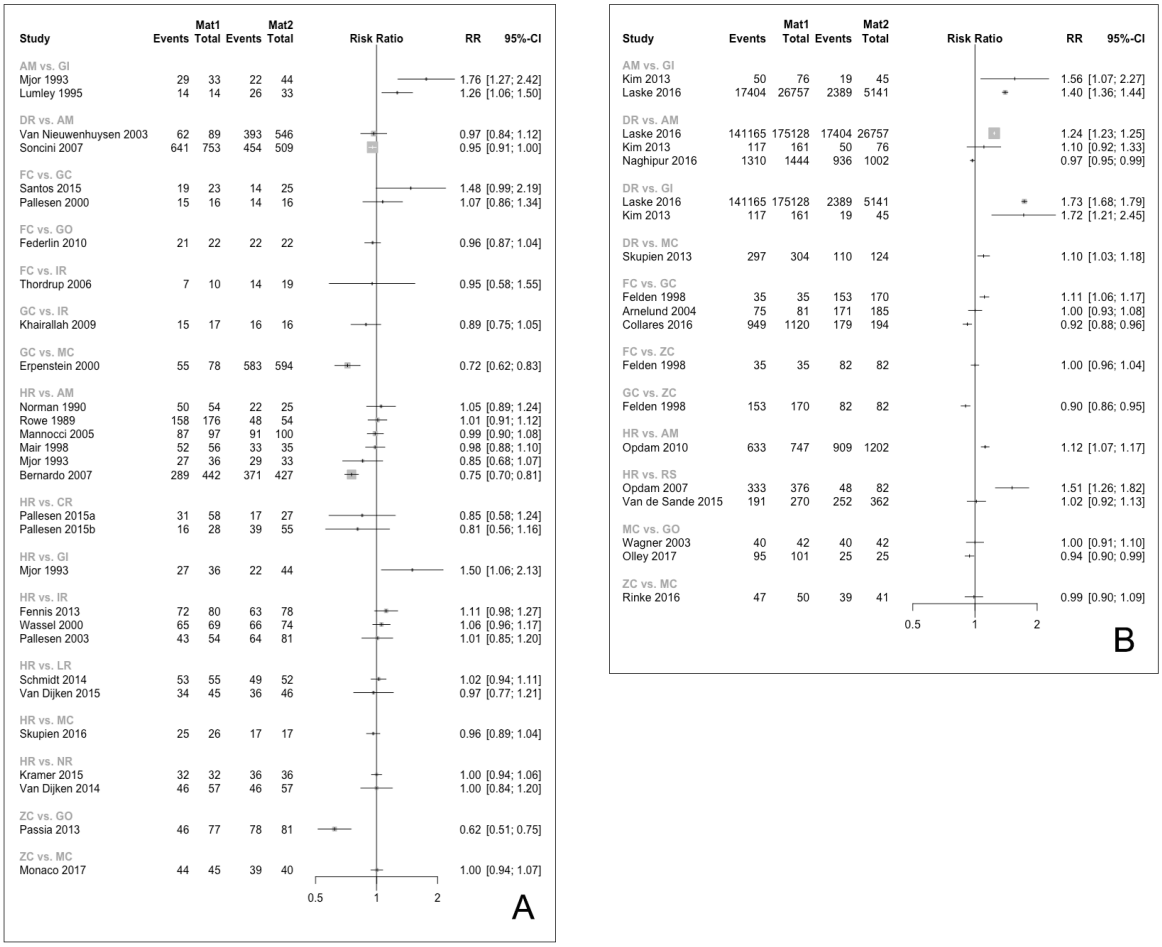

Figure 4. Forest plots of pairwise comparisons for retrospective studies. Risk ratio (RR) and 95%confidence interval (95% CI) of survival in the first material group (Mat1) versus the second (Mat2). Materials: DR, Direct resin; HR, Hybrid resin; AM, Amalgam; GI, Glass ionomer; FC, Feldspathic ceramic; GC, Glass ceramic; ZC, Zirconia-based ceramic; MC, Metal-ceramic; GO, Gold; RS, Resin sandwich.
Forest plots of pairwise comparisons for prospective studies. Risk ratio (RR) and 95% confidence interval (95% CI) of survival in the first material group (Mat1) versus the second (Mat2). Materials: DR, Direct resin; HR, Hybrid resin; AM, Amalgam; GI, Glass ionomer; FC, Feldspathic ceramic; GC, Glass ceramic; ZC, Zirconia-based ceramic; MC, Metal-ceramic; GO, Gold; NR, Nanofiller resin; IR, Indirect resin; CR, Chemically-cured Resin; LR, Low-shrinkage Resin.

Summary of findings

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)
Survival rate (Survival rate) assessed with: %	(14 RCTs)	⨁⨁⨁⨁ HIGH
Survival rate (Survival rate) assessed with: %	(31 observational studies)	⨁◯◯◯ VERY LOW [a,b]

Explanations:
a. Non-randomized studies assessed through ROBINS-I tool.
b. Heterogeneity on methodology and outcome measurement across the studies.

Figure 5. GRADE- Assessment of the level of evidence

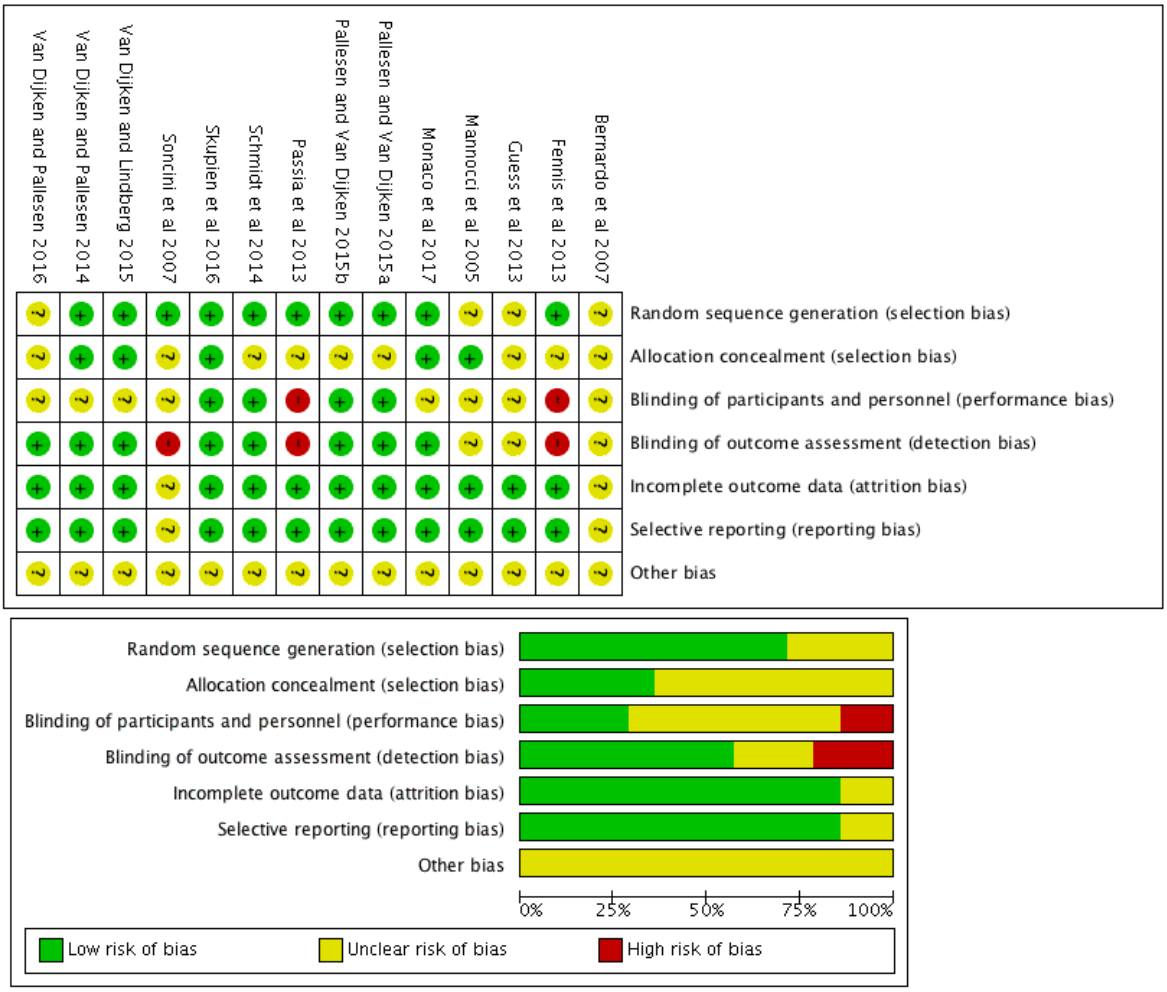

Figure 6. Risk of bias using the Cochrane Risk of Bias Tool

Supplementary material

PRISMA NMA Checklist of Items to Include When Reporting A Systematic Review Involving a Network Meta-analysis

Section/Topic	Item #	Checklist Item	Reported on Page #
TITLE			
Title	1	Identify the report as a systematic review *incorporating a network meta-analysis (or related form of meta-analysis).*	**Pgs. 19, 20**
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 network meta-analysis.* **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.	**Pg. 20**
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known*, including mention of why a network meta-analysis has been conducted.*	**Pg. 21,22**
Objectives	4	Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	**Pg.22**
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists and if and where it can be accessed (e.g., Web address); and, if available, provide	**Pg. 22**

		registration information, including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, 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).*	**Pg. 22**
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	**Pgs.22, 24**
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	**Pgs.22, 31,32**
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	**Pgs. 22, 23, 43**
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	**Pg. 22, 23**
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	**Pg. 22**
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.	**Pgs. 24, 45**
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.	**Pgs. 23, 24,33-41, 48**
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means). *Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified*	**Pgs. 23,44**

		approaches used to present summary findings from meta-analyses.	
Planned methods of analysis	14	Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to: • *Handling of multi-arm trials;* • *Selection of variance structure;* • *Selection of prior distributions in Bayesian analyses; and* • *Assessment of model fit.*	**Pg. 23**
Assessment of Inconsistency	**S2**	Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address its presence when found.	**Pg. 23**
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	**Pg. 47**
Additional analyses	16	Describe methods of additional analyses if done, indicating which were pre-specified. This may include, but not be limited to, the following: • Sensitivity or subgroup analyses; • Meta-regression analyses; • *Alternative formulations of the treatment network; and* • *Use of alternative prior distributions for Bayesian analyses (if applicable).*	**----------**
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.	**Pgs. 24, 43**
Presentation of network structure	**S3**	Provide a network graph of the included studies to enable visualization of the geometry of the treatment network.	**Pg. 45**
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	**Pg. 24**

		network, gaps of evidence in the treatment network, and potential biases reflected by the network structure.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	**Pg.24**
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	**Pgs. 24, 33-41, 47**
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data for each intervention group, and 2) effect estimates and confidence intervals. *Modified approaches may be needed to deal with information from larger networks.*	**Pgs. 24, 46**
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 (e.g. 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.	**Pgs.24, 44, 46**
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.	**---------**
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies for the evidence base being studied.	**Pg.47**
Results of additional analyses	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression analyses*, alternative network geometries studied, alternative choice of prior distributions for Bayesian analyses,* and so forth).	**-------**
DISCUSSION			
Summary of evidence	24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g.,	**Pgs. 25, 26**

		healthcare providers, users, and policy-makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., 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 (e.g., avoidance of certain comparisons).*	**Pg. 26**
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	**Pg.27**
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., 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 and/or whether some of the authors are content experts with professional conflicts of interest that could affect use of treatments in the network.	**Pg.27**

PICOS = population, intervention, comparators, outcomes, study design.
* Text in italics indicateS wording specific to reporting of network meta-analyses that has been added to guidance from the PRISMA statement.
† Authors may wish to plan for use of appendices to present all relevant information in full detail for items in this section.

3. Considerações Finais

Diante do trabalho apresentado, evidenciou-se que, após a realização de uma meta-análise em rede, os materiais disponíveis para restaurações extensas e ou coroas podem ser indicados de acordo com a quantidade de remanescente dentário envolvido no preparo. Apesar de uma diversidade de materiais restauradores indiretos terem sido desenvolvidos ao longo dos últimos anos, restaurações em ouro e metalo-cerâmica tiveram as menores taxas anuais de falhas. Em relação às restaurações diretas, a menor taxa anual de falha foi para a classificação de resinas nanohíbridas, o que mostra a melhora na composição e evolução favorável destes materiais.

Contudo, para melhorar o nível de evidência, fatores inerentes aos pacientes tais como risco de cárie, bruxismo e, como sugestão, a inclusão da análise de condições psicológicas como estresse e ansiedade, podem impactar diretamente na sobrevivência das restaurações.

. E, por fim, permanece como o maior desafio nas pesquisas, o desenvolvimento de materiais mais simplificados, com menores chances de sensibilidade pós-operatória e menores riscos de falhas por fraturas e cárie secundária, com foco principal na longevidade do dente.

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Apêndices

Apêndice A. Dados de sobrevivência por material nos estudos prospectivos.

Treatments	direct resin		hybrid resin		nanofiller resin		indirect resin		chemically-cured resin		low shrinkage resin		amalgam		glass-ionomer		feldspathic ceramic		glass ceramic		zirconia-based ceramic		metal-ceramic		gold	
Study name	# n surv.	# n rest.	# n surv	# n rest;	# n surv.	# n rest.	# n surv.	# n rest.	# n surv.	# n rest.	# n survi.	# n rest.	# n surv.	# n rest.	# n surv.	# n rest.	# n surv.	# n rest.	# n surv.	# n rest.	# n surv.	# n rest.	# n surv.	# n rest.	# n surv.	# n rest.
Rowe 1989			158	176									48	54												
Norman et al 1990			50	54									22	25												
Mjor and Jokstad 1993			27	36									29	33	22	44										
Lumley and Fisher 1995													14	14	26	33										
Mair 1998			52	56									33	35												
Erpenstein et al 2000																			55	78			583	594		
Pallesen and Van Dijken 2000																	15	16	14	16						
Wassel et al 2000			65	69			66	74																		
Van Nieuwenhuysen et al 2003	62	89											393	546												
Manocci et al 2005			87	97			91	100																		
Thordrup et al 2006							14	19									7	10	8	12						
Pallesen and Qvist 2003			43	54			64	81																		
Bernardo et al 2007			289	442									371	427												
Soncini et al 2007	641	753											454	509												
Khairallah and Hokayem 2009							16	16											15	17						
Federlin et al 2010																	21	22							22	22
Kramer et al 2015			32	32	36	36																				
Fennis et al 2013			72	80			63	78																		
Passia et al 2013																					46	77			78	81
Schmitt et al 2014			53	55							49	52														
Pallessen and Van Dijken 2015a			31	58					17	27																
Pallesen and Van Dijken 2015b			16	28					39	55																
Santos et al 2015																	19	23	14	25						
Van Dijken and Pallesen 2014			46	57	46	57																				

Van Dijken and Lindberg 2015	34	45			36	46						
Skupien et al 2016	25	26									17	17
Monaco et al 2017									44	45	39	40

Apêndice B. Dados de sobrevivência por material nos estudos retrospectivos.

Treatments	direct resin		hybrid resin		resin sandwich (closed)		amalgam		glass-ionomer		feldspathic ceramic		glass ceramic		zirconia-based ceramic		metal-ceramic		gold	
Study name	# n surv.	# n rest.	# n surv.	# n rest.	# n surv.	# n rest.	# n surv.	# n rest.	# n survi.	# n rest.	# n surv.	# n rest.	# n surv.	# n rest.	# n surv.	# n rest.	# n surv.	# n rest.	# n surv.	# n rest.
Felden et al 1998											35	35	153	170	82	82				
Wagner et al 2003																	40	42	40	42
Arnelund et al 2004											61	75	135	142						
Opdam et al 2007			333	376	48	82														
Opdam et al 2010			633	747			909	1202												
Kim et al 2013	117	161					50	76	19	45										
Skupien et al 2013	297	304															110	124		
Van de Sande et al 2015			191	270	252	362														
Laske et al 2016	141165	175128					17404	26757	2389	5141										
Collares et al 2016											949	1120	179	194						
Naghipur et al 2016	1310	1444					936	1002												
Rinke et al 2016															47	50	39	41		
Olley et al 2017																	95	101	25	25