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Does the Type of Solvent in Dental Adhesives Influence the Clinical Performance of Composite Restorations Placed in Noncarious Cervical Lesions? A Systematic Review and Meta-analysis

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Clinical Relevance

According to the clinical and scientific evidence presented in this systematic review and meta-analysis, dental adhesives containing either organic solvent (acetone or alcohol) can be used to achieve similar clinical performance and longevity of composite restorations.

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SUMMARY

Objectives: This systematic review and meta-analysis compared the clinical performance and survival rates of composite restorations placed in noncarious cervical lesions (NCCLs) using dental adhesives containing acetone or alcohol-based solvents.

Methods and Materials: PubMed, Scopus, Web of Science, Virtual Health Library (VHL) LILACS, Cochrane Library, OpenGrey, Clinical Trials, and Rebec were searched. MeSH terms, supplementary concepts, synonyms, and free keywords were used in the search strategy. All references were crosschecked by two independent investigators following the PICOS strategy (population, NCCLs; intervention, acetone-based bonding agent; comparison, alcohol-based bonding agent; outcome, clinical evaluation parameters and survival rates; study design, randomized controlled clinical trials).

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Cochrane Collaboration's tool was used to assess risk of bias, and two distinct meta-analyses were performed using the RevMan software. The prevalence of success and the total number of restorations for each group (acetone- or alcohol-based) were used to calculate the risk difference at a confidence interval of 95%. Random-effects models were applied, and heterogeneity was assessed using the I^2 index in the pooled and subgrouped meta-analyses. The certainty of evidence was evaluated through the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach.

Results: A total of 7876 studies were retrieved, from which 27 studies were selected for the systematic review. Ten studies were classified as "low risk of bias" and included in the meta-analyses. Overall heterogeneity was not significant ($I^2 = 0.00\%$). The clinical performance of restorations placed with bonding agents based on both solvents for each of the available parameters presented no statistical significance for any of the meta-analyses ($p>0.05$).

Conclusion: Scientific evidence suggests composite restorations placed with acetone or alcohol-based dental adhesives present similar clinical performance and survival rates in NCCLs.

INTRODUCTION

A solvent is the component of a solution that is present in the greatest amount,[1] and it is capable of dissolving or dispersing other substances.[2] Water, ethanol, and acetone are the most commonly added solvents in the composition of dental adhesives,[3,4] in which they will dissolve monomers and consequently help reduce the viscosity of adhesive primers and/or resins, improving their diffusion through etched dentin.[5] Therefore, solvents are included in the formulations of dental adhesives to facilitate the establishment of micro-retention with both enamel and dentin, regardless of adhesive mode of application, either etch-and-rinse or self-etch, or pH of adhesive formulation (mild/intermediately strong or strong, in the case of self-etch adhesives).[3,5,6]

Alcohol and water are polar solvents that can create strong hydrogen bonds with collagen fibrils, maintaining the interfibrillar spaces, which improves monomer diffusion along etched dentin.[4] Moreover, hydrogen bonds between ethanol and water increase evaporation rates, leading to more surface water removal compared with pure water.[5] Acetone-based solvents might be a great choice for bonding agents that contain hydrophilic and hydrophobic monomers in the same bottle, as acetone can dissolve both polar and nonpolar substances because of its high dipole moment and low dielectric constant.[5]

Conflicting information is available regarding the laboratory performance of composite restorations placed using acetone-based bonding agents: whereas some studies report higher nanoleakage and lower bond strengths,[4,7-9] others describe similar results compared with ethanol-based adhesives.[10,11] A randomized clinical trial (RCT)[12] reported better clinical performance for restorations placed with an ethanol/water-based bonding agent compared with an acetone-based one over 36 months of evaluation. Conversely, other clinical trials showed no differences between the clinical performance of restorations using bonding agents containing the aforementioned solvents for 24- or 36-month follow-up periods.[13-15] Nonetheless, there are very few clinical trials designed to specifically compare acetone and alcohol-containing bonding agents.

Dental adhesives that use acetone might be expected to perform worse than water/alcohol-based systems, as they require a greater amount of water for optimal hybridization,[4] and therefore are more sensitive to air-drying.[16] This limitation occurs because, due to the absence of hydroxyl groups in the chemical structure of acetone, it cannot re-expand the collapsed collagen matrix,[17] hindering adhesive resin diffusion. Additionally, acetone-based bonding agents are likely to form thinner adhesive layers that are more prone to polymerization inhibition by oxygen compared with ethanol and/or water.[12] However, acetone evaporates much more residual water from the tooth surface because of its higher vapor pressure and water-chasing effect,[16,18] which has been suggested to cause less collagen degradation at the hybrid layer over time.[18]

In addition to the significant contributions of laboratory assessments about dental adhesives, randomized clinical trials of composite restorations in noncarious cervical lesions (NCCLs) are considered the best clinical condition to evaluate resin-based materials subjected to mechanical and chemical challenges.[12,13,19,20] Thus, a systematic review and meta-analysis of the clinical evidence regarding the effect of the solvent type contained in dental adhesives on the performance of composite restorations in NCCLs might be important to guide future research and practice involving adhesive procedures. Therefore, this systematic review and meta-analysis aimed

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to answer the following PICO (population, intervention, comparison, outcome) question: "does the type of solvent in dental adhesives influence the clinical performance of composite restorations placed in non-carious cervical lesions?" The null hypotheses were as follows: 1) there would be no difference in the clinical performance of composite restorations placed in NCCLs using acetone-based dental adhesives compared with alcohol-based dental adhesives; and 2) there would be no difference in the survival rates over several follow-up periods of composite restorations placed in NCCLs using acetone-based dental adhesives compared with alcohol-based dental adhesives.

METHODS AND MATERIALS

Study Protocol and Registration

The protocol of this study was registered in the International Prospective Register of Systematic Reviews (PROSPERO-CRD 42018106544) database, and its reporting followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[21]

Databases, Search Strategy, and Eligibility Criteria

An electronic search was carried out during the week of August 9, 2018 in the following databases: PubMed, Scopus, Web of Science, Virtual Health Library (VHL) LILACS, Cochrane Library, OpenGrey, Clinical Trials, and Rebec. The MeSH terms, supplementary concepts, synonyms, and free keywords used for the search strategy are presented in Table 1. A handmade search was also performed to find relevant articles that had not been retrieved in the electronic search of the selected databases. No restriction of date, language, or any other search filters were applied.

The selection criteria were defined based on the elements of the PICOS strategy[22] described as follows:

Population (P): adult patients with NCCLs (class V);
Intervention (I): composite restorations performed with dental adhesives containing acetone-based solvents;
Comparison (C): composite restorations performed with dental adhesives containing alcohol-based solvents;
Outcome (O): clinical evaluation parameters of composite restorations (retention, marginal adaptation, marginal discoloration, surface texture, color, postoperative sensitivity, secondary caries, anatomic form, pulp vitality), and overall survival rates, considering different follow-up periods (the "outcome" criterion was not used in the search strategy, because it would limit the number of retrieved studies);
Study design (S): randomized controlled clinical trials (the "study design" criterion was included in the search strategy to avoid a high number of laboratory studies).

RCTs with follow-ups shorter than 18 months, nonrandomized clinical trials, laboratory studies, and reviews were excluded. Additionally, studies performed on animals, primary teeth, carious or non-cervical cavities, or with restorative materials other than resin-based composites were also excluded.

Study Selection and Data Extraction Process

All references found on electronic databases were transferred to the EndNote X9 software (Clarivate Analytics, Philadelphia, PA, USA). Duplicates were excluded by the software considering title and year similarities and further by manual revision by two independent investigators (RBEL and MS). After title and abstract screening, all papers that could potentially be included in the systematic review were fully read to determine their eligibility. A third reviewer (MBM) was consulted in case the two main investigators could not reach an agreement.

Details of the studies (authors, year, country, and study design), participants (age—mean and range, number of NCCLs, and restored teeth), tested bonding agents (acetone or alcohol-based), methodologies (outcomes, follow-up in months, and overall survival rates), and results (success, failure rates, and statistical analyses) were extracted from the selected papers. Additionally, a classification regarding mode of action (etch and rinse [E&R] or self-etch [SE] with their respective number of application steps) and pH assessment (mild or intermediately strong, with a $pH \geq 1.5$, or strong, with a $pH < 1.5$) was also taken into consideration.[6] If a certain study presented missing data, its corresponding or first author was contacted by email to obtain the necessary information so a decision could be made whether it should be included in the review. If no response was obtained after three attempts of contact by email, the manuscript was excluded.

Risk of Bias in Individual Studies

Quality and risk of bias of the eligible studies were assessed by two independent investigators (RBEL

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Table 1: *Electronic Databases Searched and Strategies Used (up to August 9, 2018)*

Electronic Database	Strategy Used
PubMed (n=1615)	#1 Tooth erosion[MeSH Terms] OR Tooth abrasion[MeSH Terms] OR Tooth wear[MeSH Terms] OR Dental restoration, permanent[MeSH Terms] OR Erosion*, tooth[Title/Abstract] OR Tooth erosion*[Title/Abstract] OR Abrasion, dental[Title/Abstract] OR Abrasion, tooth[Title/Abstract] OR Teeth abrasions[Title/Abstract] OR Tooth abrasion*[Title/Abstract] OR Teeth abrasion[Title/Abstract] OR Wear*, dental[Title/Abstract] OR Dental wear[Title/Abstract] OR Wear*, tooth[Title/Abstract] OR Tooth wear*[Title/Abstract] OR Teeth abfraction*[Title/Abstract] OR Restoration, permanent dental[Title/Abstract] OR Dental restoration, permanent[Title/Abstract] OR Restorations, permanent dental[Title/Abstract] OR Dental restorations, permanent[Title/Abstract] OR Permanent Filling, Dental[Title/Abstract] OR Permanent Fillings, Dental[Title/Abstract] OR Dental Filling, Permanent[Title/Abstract] OR Dental Fillings, Permanent[Title/Abstract] OR Permanent dental fillings[Title/Abstract] OR Dental permanent filling*[Title/Abstract] OR Cervical lesion*[Title/Abstract] OR Class V[Title/Abstract] OR NCCL*[Title/Abstract] OR Cervical filling[Title/Abstract] OR Non-carious cervical lesion*[Title/Abstract] OR Noncarious cervical lesion*[Title/Abstract] OR Cervical restoration[Title/Abstract] OR Class V lesion*[Title/Abstract] OR Cervical fillings[Title/Abstract])); #2 Bis-GMA, BPDM, HEMA dental-bonding resin[Supplementary Concept]) OR Dental bonding[MeSH Terms]) OR Dentin-Bonding Agents[MeSH Terms]) OR hydroxyethyl methacrylate[Supplementary Concept]) OR Bisphenol A-Glycidyl Methacrylate[MeSH Terms]) OR Dental Cements[MeSH Terms]) OR Solvents[MeSH Terms]) OR Ethanol[MeSH Terms]) OR Acetone[MeSH Terms])) OR (((((((Bonding, Dental[Title/Abstract]) OR Dental Cements Curing[Title/Abstract]) OR Dental Cement* Curing[Title/Abstract]) OR Agent*, Dentin Bonding[Title/Abstract]) OR Curing, Dental Cement*[Title/Abstract]) OR Dental Cement Curing[Title/Abstract]) OR Bonding Agents, Dentin[Title/Abstract]) OR Bonding Agent*, Dentin[Title/Abstract])) OR (((((((Bonding Agent, Dentin[Title/Abstract]) OR Bis-GMA[Title/Abstract]) OR Adhesive system*[Title/Abstract]) OR Dentin bonding system*[Title/Abstract]) OR HEMA[Title/Abstract]) OR hydroxyethyl methacrylate[Title/Abstract]) OR 2-hydroxyethyl methacrylate[Title/Abstract]) OR glycol methacrylate[Title/Abstract])) OR ((((((“Bisphenol A-Glycidyl Methacrylate”[Title/Abstract]) OR Solvent*[Title/Abstract]) OR Methacrylate, Bisphenol A-Glycidyl[Title/Abstract]) OR BisGMA[Title/Abstract]) OR “Bisphenol A Glycidyl Methacrylate Polymer”[Title/Abstract]) OR Dentin bonding[Title/Abstract])) OR ((((((Ethanol[Title/Abstract]) OR Alcohol, Ethyl[Title/Abstract]) OR Alcohol, Absolute[Title/Abstract]) OR Alcohol, Grain[Title/Abstract]) OR Absolute Alcohol[Title/Abstract]) OR Acetone*[Title/Abstract])) OR (((((Cement*, Dental[Title/Abstract]) OR Cement, Dental[Title/Abstract]) OR Adhesive*, Dental[Title/Abstract]) OR Self-etch adhesive*[Title/Abstract]) OR Self-etching adhesive*[Title/Abstract])) OR Etch-and-rinse adhesive[Title/Abstract] OR Adhesive material*[Title/Abstract] OR Universal adhesive*[Title/Abstract] OR Total-etch adhesive*[Title/Abstract] OR All-in-one adhesive*[Title/Abstract] OR One-bottle adhesive*[Title/Abstract]))) OR (((Etch-and-rinse bonding agents[Title/Abstract]) OR Total-etch bonding agents[Title/Abstract]) OR Self etching bonding agent*[Title/Abstract])) OR Multimode adhesive*[Title/Abstract]) OR Self-etch bonding agent*[Title/Abstract]) OR Universal bonding agent*[Title/Abstract]) OR One-bottle bonding agent*[Title/Abstract]) OR “All-in-one bonding agent"[Title/Abstract]) OR Total-etch bonding agent[Title/Abstract])) OR “all in one bonding agents"[Title/Abstract] OR “all in one bonding agent"[Title/Abstract] #3 Clinical[Title/Abstract] OR Randomized[Title/Abstract] OR Intervention Study[Title/Abstract] OR Intervention Studies[Title/Abstract] OR Controlled Trial*[Title/Abstract] OR Prospective[Title/Abstract] OR Follow-up*[Title/Abstract] OR follow up[Title/Abstract] OR Trial*[Title/Abstract] OR Longitudinal[Title/Abstract] OR Quasi-Experimental[Title/Abstract] OR Non-Randomized[Title/Abstract] OR Nonrandomized[Title/Abstract]; #1 AND #2 AND #3

and MS) using the Cochrane Collaboration's tool for assessing risk of bias in randomized controlled clinical trials.[23] The evaluators compared and discussed the results of the selected papers, and a third investigator was consulted (LCM) when necessary. Assessment criteria were divided into seven domains: 1) random sequence generation; 2) allocation concealment; 3) blinding of participants and personnel; 4) blinding of outcomes assessment; 5) incomplete outcome data; 6) selective reporting; and 7) other bias. All domains were considered key domains, except for 3, and were classified as low, unclear, or high risk of bias for each study, following recommendations described in the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0.[24] For a study to be considered low risk of bias, all of its key domains had to be classified as low. If a study presented any key domains registered as unclear, the corresponding or first author was contacted to request additional information that could enable a precise risk of bias evaluation.

Meta-analyses

Clinical performance parameters and overall survival rates of composite restorations placed using acetone- or alcohol-based bonding agents presented in the low risk of bias studies were analyzed using the Revman 5.3 Software (Review Manager v. 5, The Cochrane Collaboration, Copenhagen, Denmark). Two separate meta-analyses were performed for 1) clinical evaluation parameters (retention, marginal adaptation, marginal discoloration, surface texture, color, postoperative sensitivity, secondary caries, anatomic form, and pulp vitality) and 2) survival rates (overall and at different evaluation periods: 6, 12, 18, 24, 36, 60, and 72 months). Clinical outcomes and overall survival rates were dichotomized as

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Table 1: *Electronic Databases Searched and Strategies Used (up to August 9, 2018) (cont.)*

Electronic Database	Strategy Used
Cochrane Library (n=839)	#1MeSH descriptor: [Tooth Erosion] explode all trees #2(Erosion*, tooth OR Tooth erosion*):ti,ab,kw #3MeSH descriptor: [Tooth Abrasion] explode all trees #4("Abrasion, dental" OR "Abrasion, tooth" OR "Teeth abrasions" OR Tooth abrasion* OR "Teeth abrasion"):ti,ab,kw #5MeSH descriptor: [Tooth Wear] explode all trees #6(Wear*, dental OR Wear*, tooth OR "Dental wear" OR Tooth wear* OR Teeth abfraction*):ti,ab,kw #7MeSH descriptor: [Dental Restoration, Permanent] explode all trees #8("Restoration, permanent dental" OR "Restorations, permanent dental" OR "Dental restorations, permanent" OR "Permanent Filling, Dental" OR "Permanent Fillings, Dental" OR "Dental Filling, Permanent" OR "Dental Fillings, Permanent" OR "Permanent dental fillings" OR Dental permanent filling* OR "Dental restoration, permanent"):ti,ab,kw #9(Cervical lesion* OR "Class V" OR NCCL* OR "Cervical filling" OR Non-carious cervical lesion* OR Noncarious cervical lesion* OR "Cervical restoration" OR Class V lesion* OR "Cervical fillings"):ti,ab,kw #10#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 #11("Bis-GMA, BPDM, HEMA dental-bonding resin"):ti,ab,kw #12MeSH descriptor: [Dental Bonding] explode all trees #13("Bonding, Dental" OR "Dental Cements Curing" OR Dental Cement* Curing OR Curing, Dental Cement* OR "Dental Cement Curing"):ti,ab,kw #14MeSH descriptor: [Dentin-Bonding Agents] explode all trees #15("Bonding Agents, Dentin" OR Bonding Agent*, Dentin OR Agent*, Dentin Bonding OR "Bonding Agent, Dentin" OR Adhesive system* OR Dentin bonding system*):ti,ab,kw #16("hydroxyethyl methacrylate"):ti,ab,kw #17(HEMA):ti,ab,kw #18("2 hydroxyethyl methacrylate"):ti,ab,kw #19("glycol methacrylate"):ti,ab,kw #20MeSH descriptor: [Bisphenol A-Glycidyl Methacrylate] explode all trees #21("Bis-GMA" OR "Methacrylate, Bisphenol A-Glycidyl" OR "Bisphenol A Glycidyl Methacrylate Polymer" OR "Bisphenol A-Glycidyl Methacrylate" OR "Dentin bonding" OR BisGMA):ti,ab,kw #22MeSH descriptor: [Solvents] explode all trees #23(Solvent* OR Ethanol):ti,ab,kw #24MeSH descriptor: [Ethanol] explode all trees #25("Alcohol, Ethyl" OR "Alcohol, Absolute" OR "Alcohol, Grain" OR "Absolute Alcohol"):ti,ab,kw #26MeSH descriptor: [Acetone] explode all trees #27(Acetone*):ti,ab,kw #28MeSH descriptor: [Dental Cements] explode all trees #29(Cement*, Dental OR "Cement, Dental" OR Adhesive*, Dental):ti,ab,kw #30(Self-etch adhesive* OR Self-etching adhesive* OR "Etch-and-rinse adhesive" OR Adhesive material* OR Universal adhesive* OR Total-etch adhesive* OR All-in-one adhesive* OR One-bottle adhesive* OR "Etch-and-rinse bonding agents" OR "Total-etch bonding agents" OR Self-etching bonding agent* OR Multimode adhesive* OR Self-etch bonding agent* OR Universal bonding agent* OR One-bottle bonding agent* OR "All-in-one bonding agent" OR "All-in-one bonding agents" OR "All in one bonding agent" OR "Total-etch bonding agent"):ti,ab,kw #31#11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 #32("Intervention Study" OR "Intervention Studies" OR Clinical OR Follow-up* OR "Follow up" OR Trial* OR Randomized OR Controlled Trial* OR Prospective OR Longitudinal OR "Quasi-Experimental" OR "Non-Randomized" OR Nonrandomized):ti,ab,kw #33#10 AND #31 AND #32

success or failure according to the criteria used by each of the selected studies. The prevalence of success and the total number of restorations for each group (acetone- or alcohol-based) were used to calculate the risk difference at a confidence interval of 95%. Random-effects models were applied, and heterogeneity was tested using the I^2 index.

Certainty of Evidence Assessment

The quality of evidence (certainty in the estimates of effect) was determined for the outcomes using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach,[25] whereby randomized controlled clinical trials start as high evidence, and the quality or certainty of the body of evidence decreases to moderate, low, or very low evidence if serious or very serious issues related to risk of bias, inconsistency, indirectness, imprecision, and publication bias are present. Additionally, the quality of evidence of a study may be upgraded if the magnitude of effect is large or very large or if the effect of all plausible confounding factors would be to reduce or suggest a false effect. Therefore, the

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Table 1: *Electronic Databases Searched and Strategies Used (up to August 9, 2018) (cont.)*

Electronic Database	Strategy Used
Lilacs VHL (n=268)	#1 (mh:(Tooth erosion)) OR (mh:(Tooth abrasion)) OR (mh:(Tooth wear)) OR (mh:(Dental restoration, permanent)) OR (tw:(Erosion$, tooth)) OR (tw:(Tooth erosion$)) OR (tw:(Abrasion, dental)) OR (tw:(Abrasion, tooth)) OR (tw:(Teeth abrasions)) OR (tw:(Tooth abrasion$)) OR (tw:(Teeth abrasion)) OR (tw:(Wear$, dental)) OR (tw:(Dental wear)) OR (tw:(Wear$, tooth)) OR (tw:(Tooth wear$)) OR (tw:(Teeth abfraction$)) OR (tw:(Restoration, permanent dental)) OR (tw:(Dental restoration, permanent)) OR (tw:(Restorations, permanent dental)) OR (tw:(Dental restorations, permanent)) OR (tw:(Permanent Filling, Dental)) OR (tw:(Permanent Fillings, Dental)) OR (tw:(Dental Filling, Permanent)) OR (tw:(Dental Fillings, Permanent)) OR (tw:(Permanent dental fillings)) OR (tw:(Dental permanent filling$)) OR (tw:(Cervical lesion$)) OR (tw:(Class V)) OR (tw:(NCCL$)) OR (tw:(Cervical filling)) OR (tw:(Non-carious cervical lesion$)) OR (tw:(Noncarious cervical lesion$)) OR (tw:(Cervical restoration)) OR (tw:(Class V lesion$)) OR (tw:(Cervical fillings)) #2 (mh:(Bis-GMA, BPDM, HEMA dental-bonding resin)) OR (mh:(Dental bonding)) OR (mh:(Dentin-Bonding Agents)) OR (mh:(hydroxyethyl methacrylate)) OR (mh:(Bisphenol A-Glycidyl Methacrylate)) OR (mh:(Dental Cements)) OR (mh:(Solvents)) OR (mh:(Ethanol)) OR (mh:(Acetone)) OR (tw:(Bonding, Dental)) OR (tw:(Dental Cements Curing)) OR (tw:(Dental Cement$ Curing)) OR (tw:(Agent$, Dentin Bonding)) OR (tw:(Curing, Dental Cement$)) OR (tw:(Dental Cement Curing)) OR (tw:(Bonding Agents, Dentin)) OR (tw:(Bonding Agent$, Dentin)) OR (tw:(Bonding Agent, Dentin)) OR (tw:(Bis-GMA)) OR (tw:(Adhesive system$)) OR (tw:(Dentin bonding system$)) OR (tw:(HEMA)) OR (tw:(hydroxyethyl methacrylate)) OR (tw:(2-hydroxyethyl methacrylate)) OR (tw:(glycol methacrylate)) OR (tw:("Bisphenol A-Glycidyl Methacrylate")) OR (tw:(Solvent$)) OR (tw:(Methacrylate, Bisphenol A-Glycidyl)) OR (tw:(BisGMA)) OR (tw:("Bisphenol A Glycidyl Methacrylate Polymer")) OR (tw:(Dentin bonding)) OR (tw:(Ethanol)) OR (tw:(Alcohol, Ethyl)) OR (tw:(Alcohol, Absolute)) OR (tw:(Alcohol, Grain)) OR (tw:(Absolute Alcohol)) OR (tw:(Acetone$)) OR (tw:(Cement$, Dental)) OR (tw:(Cement, Dental)) OR (tw:(Adhesive$, Dental)) OR (tw:(Self-etch adhesive$)) OR (tw:(Self-etching adhesive$)) OR (tw:(Etch-and-rinse adhesive)) OR (tw:(Adhesive material$)) OR (tw:(Universal adhesive$)) OR (tw:(Total-etch adhesive$)) OR (tw:(All-in-one adhesive$)) OR (tw:(One-bottle adhesive$)) OR (tw:(Etch-and-rinse bonding agents)) OR (tw:(Total-etch bonding agents)) OR (tw:(Self etching bonding agent$)) OR (tw:(Multimode adhesive$)) OR (tw:(Self-etch bonding agent$)) OR (tw:(Universal bonding agent$)) OR (tw:(One-bottle bonding agent$)) OR (tw:("All-in-one bonding agent")) OR (tw:(Total-etch bonding agent)) OR (tw:("all in one bonding agents")) OR (tw:("all in one bonding agent")) #3 (tw:(Clinical)) OR (tw:(Randomized)) OR (tw:(Intervention Study)) OR (tw:(Intervention Studies)) OR (tw:(Controlled Trial$)) OR (tw:(Prospective)) OR (tw:(Follow-up$)) OR (tw:(follow up)) OR (tw:(Trial$)) OR (tw:(Longitudinal)) OR (tw:(Quasi-Experimental)) OR (tw:(Non-Randomized)) OR (tw:(Nonrandomized)) #1 AND #2 AND #3

quality of evidence may vary from very low to high. Two GRADEs were performed: one for each clinical parameter and overall clinical performance and another for overall survival rates.[25]

RESULTS

Study Selection

After an electronic search on all the aforementioned databases, 7876 studies were exported: 2826 duplicates were removed, and 4907 studies were excluded by title and abstract screening. One hundred forty-three studies were analyzed regarding eligibility. Four laboratory studies, 17 conference papers, 33 studies comparing two or more bonding agents with the same solvent composition, 52 studies that used only one bonding agent, and 10 studies that compared bonding agents containing alcohol/acetone/water with another water-based adhesive system were excluded. Thus, 27 remaining studies were included in the present systematic review, and 10 of these were used for the meta-analyses (Figure 1).[14,26-34] Also, the handmade search returned no relevant papers.

Characteristics of the Selected Studies

Information about the 27 studies included in this systematic review is presented in Table 2 (supplemental material). All studies followed the randomized controlled clinical trial design, and they were developed in Australia, Belgium, Brazil, Egypt, Germany, Italy, Japan, Sweden, the United States, and Turkey. The selected papers were published between 2001 and 2019, comprising a total of 3959 dental restorations in 1087 patients, with follow-up periods ranging from 18 to 72 months. Twenty-two of the included studies used the modified United States Public Health Service (USPHS) criteria to evaluate dental restorations,[12,14,19,26-31,34-46] whereas four studies used the FDI World Dental Federation criteria,[15,20,32,33] and one study used its own customized criteria.[13] All studies compared composite restorations performed using at least one bonding agent with acetone-based solvent against one bonding agent with alcohol-based solvent. Table 3 (supplemental material) presents the composition of the dental adhesives from the studies included in the meta-analyses, as well as adhesive classification: six 2E&R, one 3E&R, one 4E&R, seven 1SE, and two

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Table 1: *Electronic Databases Searched and Strategies Used (up to August 9, 2018) (cont.)*

Electronic Database	Strategy Used
SCOPUS (n=3771)	#1 TITLE-ABS-KEY ("tooth erosion") OR TITLE-ABS-KEY ("tooth abrasion") OR TITLE-ABS-KEY ("tooth wear") OR TITLE-ABS-KEY ("dental restoration, permanent") OR TITLE-ABS-KEY (erosion*, AND tooth) OR TITLE-ABS-KEY (tooth AND erosion*) OR TITLE-ABS-KEY ("abrasion, dental") OR TITLE-ABS-KEY ("abrasion, tooth") OR TITLE-ABS-KEY ("teeth abrasions") OR TITLE-ABS-KEY (tooth AND abrasion*) OR TITLE-ABS-KEY ("teeth abrasion") OR TITLE-ABS-KEY (wear*, AND dental) OR TITLE-ABS-KEY ("dental wear") OR TITLE-ABS-KEY (wear*, AND tooth) OR TITLE-ABS-KEY (tooth AND wear*) OR TITLE-ABS-KEY (teeth AND abfraction*) OR TITLE-ABS-KEY ("restoration, permanent dental") OR TITLE-ABS-KEY ("dental restoration, permanent") OR TITLE-ABS-KEY ("restorations, permanent dental") OR TITLE-ABS-KEY ("dental restorations, permanent") OR TITLE-ABS-KEY ("permanent filling, dental") OR TITLE-ABS-KEY ("permanent fillings, dental") OR TITLE-ABS-KEY ("dental filling, permanent") OR TITLE-ABS-KEY ("dental fillings, permanent") OR TITLE-ABS-KEY ("permanent dental fillings") OR TITLE-ABS-KEY (dental AND permanent AND filling*) OR TITLE-ABS-KEY (cervical AND lesion*) OR TITLE-ABS-KEY ("class v") OR TITLE-ABS-KEY (nccl*) OR TITLE-ABS-KEY ("cervical filling") OR TITLE-ABS-KEY (non-carious AND cervical AND lesion*) OR TITLE-ABS-KEY (noncarious AND cervical AND lesion*) OR TITLE-ABS-KEY ("cervical restoration") OR TITLE-ABS-KEY (class AND v AND lesion*) OR TITLE-ABS-KEY ("cervical fillings") #2 TITLE-ABS-KEY("Bis-GMA, BPDM, HEMA dental-bonding resin") OR TITLE-ABS-KEY("Dental bonding") OR TITLE-ABS-KEY("Dentin-Bonding Agents") OR TITLE-ABS-KEY("hydroxyethyl methacrylate") OR TITLE-ABS-KEY("Bisphenol A-Glycidyl Methacrylate") OR TITLE-ABS-KEY("Dental Cements") OR TITLE-ABS-KEY("Solvents") OR TITLE-ABS-KEY("Ethanol") OR TITLE-ABS-KEY("Acetone") OR TITLE-ABS-KEY("Bonding, Dental") OR TITLE-ABS-KEY("Dental Cements Curing") OR TITLE-ABS-KEY(Dental Cement* Curing) OR TITLE-ABS-KEY(Agent*, Dentin Bonding) OR TITLE-ABS-KEY(Curing, Dental Cement*) OR TITLE-ABS-KEY("Dental Cement Curing") OR TITLE-ABS-KEY("Bonding Agents, Dentin") OR TITLE-ABS-KEY(Bonding Agent*, Dentin) OR TITLE-ABS-KEY("Bonding Agent, Dentin") OR TITLE-ABS-KEY("Bis-GMA") OR TITLE-ABS-KEY(Adhesive system*) OR TITLE-ABS-KEY(Dentin bonding system*) OR TITLE-ABS-KEY("HEMA") OR TITLE-ABS-KEY("hydroxyethyl methacrylate") OR TITLE-ABS-KEY("2-hydroxyethyl methacrylate") OR TITLE-ABS-KEY("glycol methacrylate") OR TITLE-ABS-KEY("Bisphenol A-Glycidyl Methacrylate") OR TITLE-ABS-KEY(Solvent*) OR TITLE-ABS-KEY("Methacrylate, Bisphenol A-Glycidyl") OR TITLE-ABS-KEY("BisGMA") OR TITLE-ABS-KEY("Bisphenol A Glycidyl Methacrylate Polymer") OR TITLE-ABS-KEY("Dentin bonding") OR TITLE-ABS-KEY("Ethanol") OR TITLE-ABS-KEY("Alcohol, Ethyl") OR TITLE-ABS-KEY("Alcohol, Absolute") OR TITLE-ABS-KEY("Alcohol, Grain") OR TITLE-ABS-KEY("Absolute Alcohol") OR TITLE-ABS-KEY(Acetone*) OR TITLE-ABS-KEY(Cement*, Dental) OR TITLE-ABS-KEY("Cement, Dental") OR TITLE-ABS-KEY(Adhesive*, Dental) OR TITLE-ABS-KEY(Self-etch adhesive*) OR TITLE-ABS-KEY(Self-etching adhesive*) OR TITLE-ABS-KEY("Etch-and-rinse adhesive") OR TITLE-ABS-KEY(Adhesive material*) OR TITLE-ABS-KEY(Universal adhesive*) OR TITLE-ABS-KEY(Total-etch adhesive*) OR TITLE-ABS-KEY(All-in-one adhesive*) OR TITLE-ABS-KEY(One-bottle adhesive*) OR TITLE-ABS-KEY("Etch-and-rinse bonding agents") OR TITLE-ABS-KEY("total-etch bonding agents") OR TITLE-ABS-KEY(Self etching bonding agent*) OR TITLE-ABS-KEY(Multimode adhesive*) OR TITLE-ABS-KEY(Self-etch bonding agent*) OR TITLE-ABS-KEY(Universal bonding agent*) OR TITLE-ABS-KEY(One-bottle bonding agent*) OR TITLE-ABS-KEY("All-in-one bonding agent") OR TITLE-ABS-KEY("Total-etch bonding agent") OR TITLE-ABS-KEY("all in one bonding agents") OR TITLE-ABS-KEY("all in one bonding agent") #3 TITLE-ABS-KEY("Clinical") OR TITLE-ABS-KEY("Randomized") OR TITLE-ABS-KEY("Intervention Study") OR TITLE-ABS-KEY("Intervention Studies") OR TITLE-ABS-KEY(Controlled Trial*) OR TITLE-ABS-KEY("Prospective") OR TITLE-ABS-KEY(Follow-up*) OR TITLE-ABS-KEY("follow up") OR TITLE-ABS-KEY(Trial*) OR TITLE-ABS-KEY("Longitudinal") OR TITLE-ABS-KEY("Quasi-Experimental") OR TITLE-ABS-KEY("Non-Randomized") OR TITLE-ABS-KEY("Nonrandomized") #1 AND #2 AND #3

"universal" (2E&R or 1SE). Also, pH assessment is described for self-etch systems (eight mild/intermediately strong and one strong).

Risk of Bias Assessment

Four of the 27 selected studies were rated as unclear for random sequence generation.[13,35,36,45] Two studies were unclear,[39,45] whereas one study[13] did not perform the allocation concealment. Twenty-two papers were rated as unclear regarding the blinding of participants and personnel.[13-15,19,20,30-46] However, this third domain was not regarded as a key domain in the risk of bias assessment. Eight studies were classified as unclear,[19,35,37-39,43-45] and one did not blind the evaluators.[13] Ten studies presented high risk of bias for the incomplete outcome data domain for the following reasons: the clinical criteria used to assess the results were not described[13,45]; only alpha scores were reported[36-38,41-44]; or only bravo scores were reported.[12] Five studies showed high risk of bias for selective reporting,[12,13,15,20,45] and six studies presented other bias.[20,38-40,42,46]

Four papers were classified as low risk of bias.[26-29] Nevertheless, six other papers were also included as low risk of bias,[14,30-34] regardless of being checked as unclear for the blinding of participants and personnel, because this domain was not considered a key

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Table 1: *Electronic Databases Searched and Strategies Used (up to August 9, 2018) (cont.)*

Electronic Database	Strategy Used
Web of Science (n=1371)	#1 TS=(Tooth erosion OR Tooth abrasion OR Tooth wear OR Dental restoration, permanent OR Erosion*, tooth OR Tooth erosion* OR Abrasion, dental OR Abrasion, tooth OR Teeth abrasions OR Tooth abrasion* OR Teeth abrasion OR Wear*, dental OR Dental wear OR Wear*, tooth OR Tooth wear* OR Teeth abfraction* OR Restoration, permanent dental OR Dental restoration, permanent OR Restorations, permanent dental OR Dental restorations, permanent OR Permanent Filling, Dental OR Permanent Fillings, Dental OR Dental Filling, Permanent OR Dental Fillings, Permanent OR Permanent dental fillings OR Dental permanent filling* OR Cervical lesion* OR Class V OR NCCL* OR Cervical filling OR Non-carious cervical lesion* OR Noncarious cervical lesion* OR Cervical restoration OR Class V lesion* OR Cervical fillings) #2 TS=(Bis-GMA, BPDM, HEMA dental-bonding resin OR Dental bonding OR Dentin-Bonding Agents OR hydroxyethyl methacrylate OR Bisphenol A-Glycidyl Methacrylate OR Dental Cements OR Solvents OR Ethanol OR Acetone OR Bonding, Dental OR Dental Cements Curing OR Dental Cement* Curing OR Agent*, Dentin Bonding OR Curing, Dental Cement* OR Dental Cement Curing OR Bonding Agents, Dentin OR Bonding Agent*, Dentin OR Bonding Agent, Dentin OR Bis-GMA OR Adhesive system* OR Dentin bonding system* OR HEMA OR hydroxyethyl methacrylate OR 2-hydroxyethyl methacrylate OR glycol methacrylate OR "Bisphenol A-Glycidyl Methacrylate" OR Solvent* OR Methacrylate, Bisphenol A-Glycidyl OR BisGMA OR "Bisphenol A Glycidyl Methacrylate Polymer" OR Dentin bonding OR Ethanol OR Alcohol, Ethyl OR Alcohol, Absolute OR Alcohol, Grain OR Absolute Alcohol OR Acetone* OR Cement*, Dental OR Cement, Dental OR Adhesive*, Dental OR Self-etch adhesive* OR Self-etching adhesive* OR Etch-and-rinse adhesive OR Adhesive material* OR Universal adhesive* OR Total-etch adhesive* OR All-in-one adhesive* OR One-bottle adhesive* OR Etch-and-rinse bonding agents OR Total-etch bonding agents OR Self etching bonding agent* OR Multimode adhesive* OR Self-etch bonding agent* OR Universal bonding agent* OR One-bottle bonding agent* OR "All-in-one bonding agent" OR Total-etch bonding agent OR "all in one bonding agents" OR "all in one bonding agent") #3 TS=(Clinical OR Randomized OR Intervention Study OR Intervention Studies OR Controlled Trial* OR Prospective OR Follow-up* OR follow up OR Trial* OR Longitudinal OR Quasi-Experimental OR Non-Randomized OR Nonrandomized) #1 AND #2 AND #3
REBEC (n=0)	Dental adhesives and non-carious cervical lesions
Gray literature (n=0)	Dental adhesives AND non-carious cervical lesions
Clinical trials (n=12)	Dental adhesives OR dentin bonding agents OR ethanol OR acetone non-carious cervical lesions OR noncarious cervical lesions

domain. The summary of risk of bias assessment is presented in Figure 2.

Meta-analyses

The meta-analysis included only papers with a low risk of bias, and the available data for each clinical parameter and overall survival rates were taken into account. Two meta-analyses were carried out for 10 of the selected studies[14,26-34]: one for the clinical evaluation parameters and another one for the overall survival rates at different follow-up periods. Considering not all studies used the same clinical evaluation criteria, and the selected studies presented different follow-up periods, different numbers of studies were included in the meta-analyses for different clinical parameters. Although the study by Häfer and others[26] was classified as low risk of bias, it could not be used for the meta-analysis regarding clinical evaluation parameters, because this clinical trial used customized clinical evaluation criteria, which made it impossible to compare its results with the remaining studies. However, as survival rates could still be extracted from this paper, it was included in the second meta-analysis, resulting in different numbers of studies for each one of the two meta-analyses.

In the first meta-analysis (Figure 3), which included nine studies, two studies did not provide data for marginal adaptation,[32,33] seven studies did not provide data for surface texture and color,[14,27,29,30,32-34] three studies did not provide data for postoperative sensitivity,[14,27,31] one study did not provide data for secondary caries,[27] seven studies did not provide data for anatomic form,[14,27,28,30,32-34] and one study supplied sufficient data only for the pulp vitality parameter.[30]

In the second meta-analysis (Figure 4), which included 10 studies, two studies did not provide information for survival rates at six months,[27,30] two studies did not provide data at 12 months,[27,29] eight studies did not provide data at 18 months,[14,26,27,30-34] three studies did not provide data at 24 months,[27-29] six studies did not provide data at 36 months,[14,27-29,31,34] and only two studies provided data at 60[33] and 72 months.[27]

The overall heterogeneity between studies was not significant ($I^2 = 0.00\%$) for both meta-analyses. The heterogeneity values for each clinical evaluation

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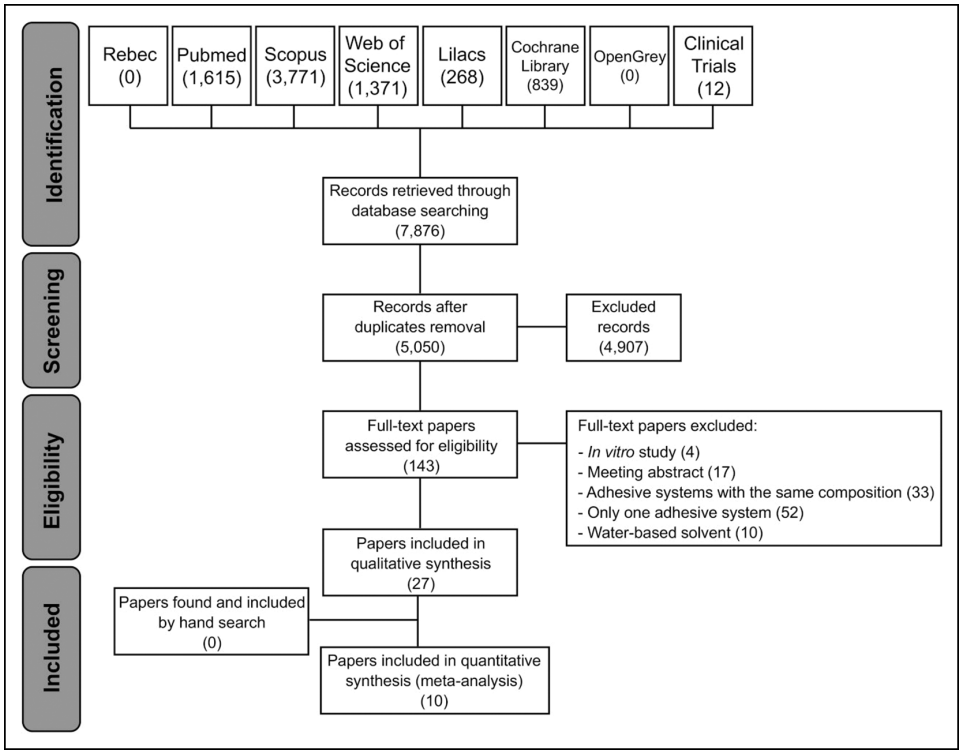

Figure 1. *Flow diagram of the identified, eligible, and included studies of this systematic review and meta-analysis.*

parameter were also not significant, ranging from 0% to 38% (38% for sensitivity, 34% for retention, and 0% for the remaining criteria). The heterogeneity for survival rates at each follow-up period was not significant either, except for the 12- and 18-month follow-ups, ranging from 0% to 88% (88% for 18 months, 62% for 12 months, 46% for 24 months, 0% for all the other follow-up periods).

The overall risk difference of each clinical evaluation parameter was 0.00 [–0.01, 0.00] (p=0.57), whereas it was –0.01 [–0.04, 0.02] (p=0.46) for retention, 0.00 [–0.02, 0.01] (p=0.82) for marginal adaptation, 0.00 [–0.01, 0.01] (p=0.63) for marginal discoloration, 0.00 [–0.04, 0.04] (p=1.00) for surface texture, 0.00 [–0.04, 0.04] (p=1.00) for color, –0.01 [–0.04, 0.02] (p=0.65) for sensitivity, 0.00 [–0.01, 0.01] (p=1.00) for secondary caries, 0.00 [–0.03, 0.03] (p=1.00) for anatomic form, and 0.00 [–0.04, 0.04] (p=1.00) for pulp vitality.

The overall risk of difference for survival rates was 0.00 [–0.01, 0.01] (p=0.91), whereas it was 0.00 [–0.01, 0.01] (p=0.99) for six months, 0.00 [–0.02, 0.02] (p=0.88) for 12 months, –0.14 [–0.39, 0.11] (p=0.27) for 18 months, 0.01 [–0.02, 0.04] (p=0.52) for 24 months, 0.00 [–0.04, 0.03] (p=0.91) for 36 months, –0.01 [–0.08, 0.06] (p=0.82) for 60 months, and –0.04 [–0.20, 0.12] (p=0.65) for 72 months (Figures 3 and 4).

High quality of evidence by the GRADE approach was evidenced for both meta-analyses (Tables 4 and 5), with very strong association of at least 919 events per 1000. Visual inspection of the funnel plot revealed a symmetric distribution, which suggests there were no publication biases for survival rates (Figure 5). The authors would also like to highlight that a meta-analysis including all studies, regardless of their risk of bias, was performed previously to the meta-analysis hereby presented, and the significance of their results, as well as the certainty of evidence, were similar to the statistical analysis included in the present study (that considered only studies with low risk of bias). Therefore, the authors opted to include only the last meta-analysis, without high risk of bias studies.

DISCUSSION

Several systematic reviews and meta-analyses regarding the differences in clinical performance between SE and E&R bonding agents can be found in the scientific literature.[3,47-50] However, to the knowledge of the authors of this article, there is no review dealing with the potential influence of different solvents contained in bonding agents on the clinical outcomes of direct composite restorations in NCCLs. Therefore, the aim of this systematic review and meta-analysis was to compare the

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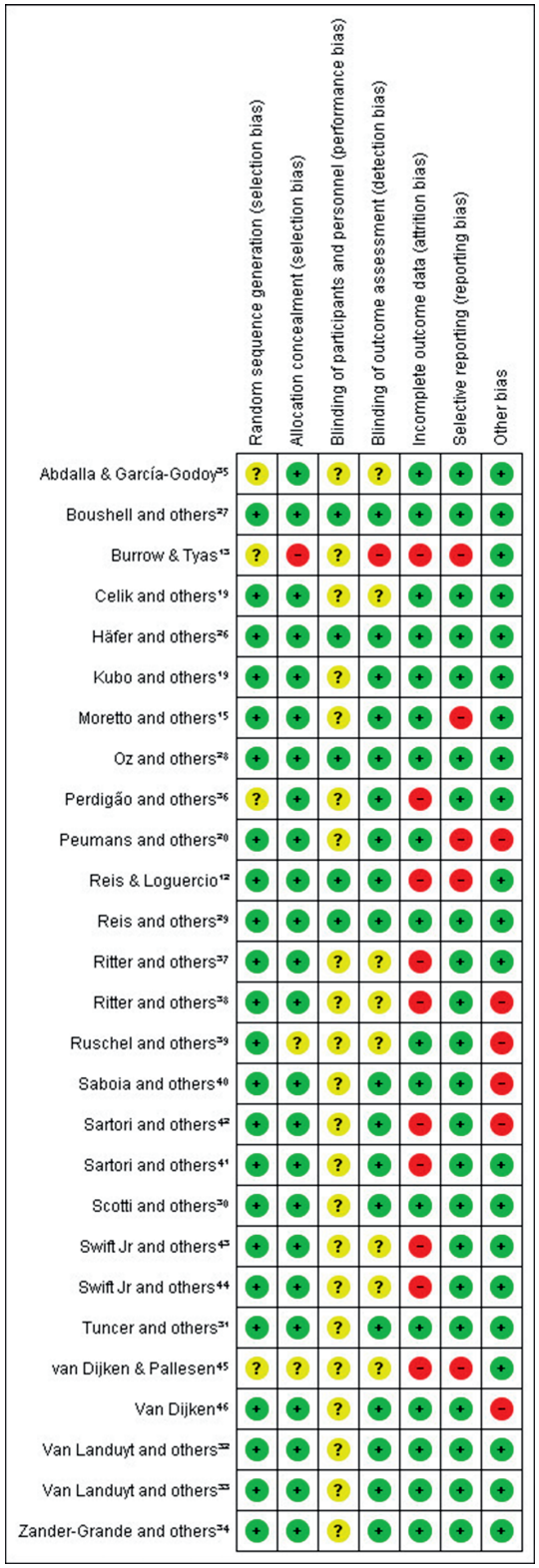

Figure 2. *Risk of bias assessment for the studies included in this systematic review and meta-analysis: (+) low; (?) unclear; or (–) high risk of bias.*

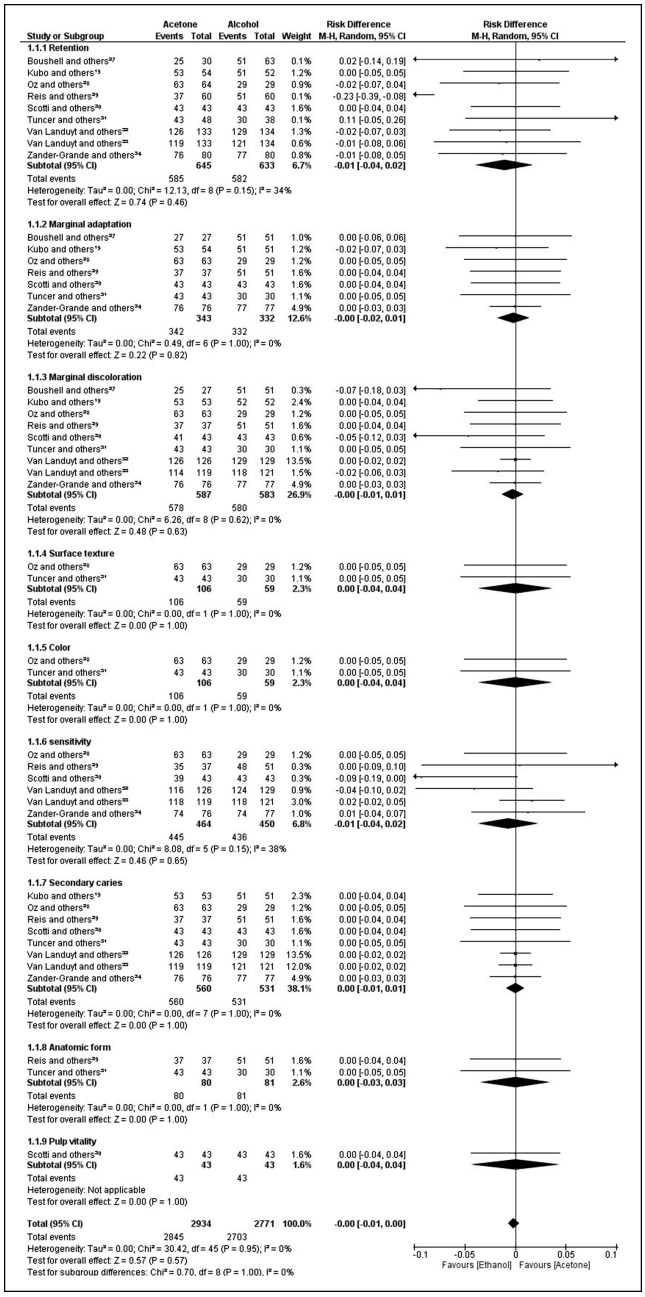

Figure 3. *Forest plot of clinical evaluation parameters of acetone- × alcohol-based bonding agents with all studies included in this systematic review and meta-analysis.*

clinical evaluation parameters and survival rates of composite restorations placed in NCCLs using acetone- or alcohol-based dental adhesives that have been reported in randomized controlled clinical trials.

In the present paper, all risk of bias assessment criteria were considered key domains, except for the blinding of participants and personnel. Random

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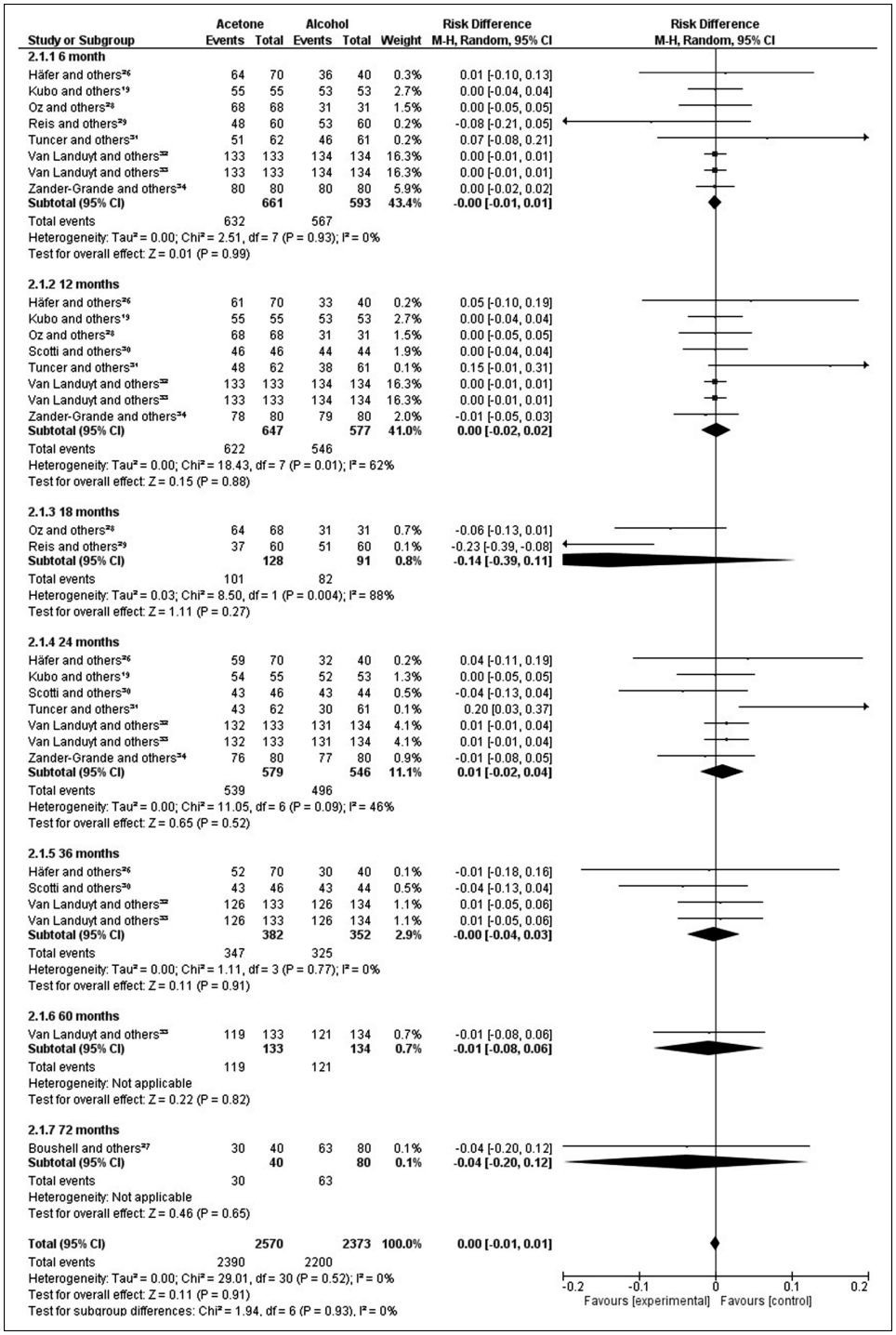

Figure 4. *Forest plot of survival rates at different follow-up periods of acetone- × alcohol-based bonding agents with all studies included in this systematic review and meta-analysis.*

sequence generation and allocation concealment were the first two criteria analyzed for each of the selected papers. Random sequence generation describes the method used for randomization, and allocation concealment ensures no intervention allocations could have been foreseen before or during patient enrollment.[51] Randomization is essential in clinical trials to guarantee that participants of both intervention and comparison groups present similar known and unknown prognostic factors.[51] Another critical domain to avoid the selection of biased RCTs is the blinding of outcomes assessors, as it reduces the risk of detection bias (eg, observer, ascertainment, or assessment bias), and it also has a strong

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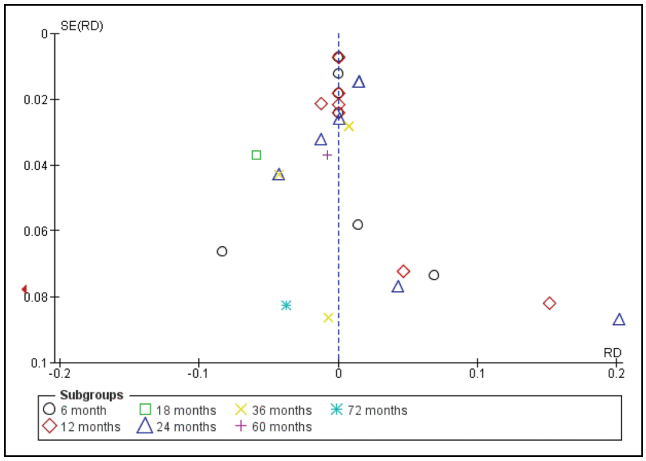

Figure 5. *Funnel plot of publication bias related to survival rates. RD, risk difference; SE, standard error.*

effect for trials that involve subjective evaluation parameters, like the ones selected for this review and meta-analysis.[52,53]

Incomplete outcome data and selective reporting were also regarded as exclusion criteria for studies that did not meet these domains. Key information is often not reported in therapeutic assessment studies, which means that the supposed methodologic quality of published trials might not reveal their actual quality.[54] Moreover, selective reporting is likely to lead to an overestimation of the effect of the experimental treatment.[55] Six of the selected papers were not included in the meta-analysis because of other bias criteria, which were determined by the two independent evaluators of this review. Other bias included the following: 1) mismatch between the composition of adhesives described in the study and the composition described in the manufacturer's safety data sheet[20]; 2) study designed around the assumption that the tested bonding agents would not present statistical differences[38]; 3) data reported the probability of maintenance of alpha scores over time instead of success rates[39]; 4) data reported only alpha scores for marginal staining, whereas bravo scores were not shown[40]; 5) lack of clarity in the description of the evaluated parameters[42]; and 6) inclusion of patients with caries activity, periodontal disease, or parafunctional habits in the study.[46]

The only domain that was not critical for a paper to be classified as low risk of bias was the blinding of participants and personnel. In other words, the RCTs that did not report or did not blind patients and/or operators were nevertheless included for the meta-analyses. Blinding of participants is not paramount for clinical studies of dental adhesives, because these products do not present a systemic effect, and most of the time, patients are unaware of the intricacies of restorative procedures, leading to very little to almost no influence in the final outcomes. As for the blinding of personnel (operators), it is not possible for studies involving adhesive procedures because bonding agents present distinct compositions, which means that each product requires a unique application protocol. Therefore, operators must know which product they are about to use, so the patient can receive the correct treatment.

Retention, marginal integrity, and marginal discoloration are the main parameters used to assess the clinical effectiveness of dental adhesives.[6] Fracture and loss of retention are clinically significant events that require intervention from clinicians, such as the restoration of cavities or repair of composite restorations.[56] Conversely, marginal integrity and discoloration are rather subjective parameters compared with retention, and these criteria are not predictive of failures, as the presence of marginal defects without an indisputable carious lesion cannot be interpreted as a sign of the potential development of secondary caries.[57] However, marginal gaps and/or discoloration are confounding factors that can lead to the misdiagnosis of secondary caries while also affecting the esthetic appearance of composite restorations.[57,58]

The present meta-analysis used published data, which is a fact worth noting, because raw data should preferably be used. However, the raw data of the included manuscripts was not publicly available, and none of the contacted authors shared them with us. Furthermore, the published results of the papers included in the meta-analysis were sufficient to determine the scientific evidence (or lack thereof) regarding the different bonding agents with distinct organic solvents.

According to Figure 3, a similar clinical behavior regarding key prognostic parameters (retention, marginal adaptation, and marginal discoloration) can be expected for composite restorations placed using dental adhesives containing acetone compared with those based on alcohol, regardless of adhesive resin composition or bonding strategies (E&R vs SE). According to a systematic review performed by Peumans and others,[6] the type of composite used is not a main factor related to the restoration outcome, because NCCLs present a relatively small C-factor. Also, three-step E&R and mild two-step SE bonding agents were shown to produce efficient bonding, whereas two-step E&R and SE adhesives with a pH

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< 1.5 had an inferior performance in comparison.[6] Nonetheless, the mode of action of the adhesives evaluated in this systematic review and meta-analysis seemed to have played a minor role on their performance related to solvent content, which might have happened because both groups (alcohol- and acetone-based) presented even numbers of E&R and SE adhesive systems (four E&R, four SE, and one "universal" for alcohol-based; and four E&R, three SE, and one "universal" for the acetone-based).

Moreover, the role of solvent type might be more important for E&R adhesives, because they involve a prior dentin-etching step, and the collagen network might collapse during air drying,[5,59] making these products more sensitive to operator mistakes. SE adhesives, on the other hand, need the addition of a solvent to their composition only to ensure ionization of functional monomers,[5] but dentin demineralization and resin infiltration occur simultaneously, likely without a huge influence of solvent type. However, another more in-depth systematic review and meta-analysis would be necessary to correlate solvent type and mode of action of dental adhesive systems, as well as to analyze all subclasses of bonding agents, which is beyond the scope of the present paper.

Thus, the first null hypothesis was accepted. Different solvents have been suggested to affect the clinical performance of dental adhesives, because their type and concentration might impact the adhesive tolerance to dentin moisture.[28] Based on previous *in vitro* publications, one could expect the clinical performance of composite restorations placed using acetone-based bonding agents to be worse than alcohol-based bonding agents, considering acetone-containing products are believed to form thinner adhesive layers that are more prone to polymerization inhibition by oxygen and polymer degradation.[12] Also, increasing concentrations of acetone have been shown to negatively affect the microtensile bond strength of adhesive formulations.[60]

Both high-vapor pressure solvents (acetone and alcohol) can wet the dentin surface and promote effective bonding, as evidenced by the results of the present systematic review and meta-analysis. The most likely influence of solvents on adhesive systems might be related to their application method[16,59]: bonding agents with acetone are more sensitive to the air-drying of etched dentin, as this solvent cannot re-expand the shrunken collagen network.[17] Acetone also tends to quickly dehydrate the etched dentin surface, because it has higher vapor pressure than ethanol and water. However, most of the trials included in the meta-analyses reported trained and/or experienced operators performed the composite restorations in a controlled clinical situation,[14,26,29,30,32-34] which might have led to similar results for both solvents, because the effects of operator mistakes were dramatically reduced due to operators strictly following the manufacturers' instructions.

Other aspects occasionally reported in RCTs involving dental adhesives are surface texture, color, and anatomic form of composite restorations. Although the meta-analysis revealed no differences between restorations performed with acetone- or alcohol-containing bonding agents, these parameters are much more related to the performance of dental composites than to bonding agents themselves, as they describe surface characteristics instead of dentin bonding parameters. Moreover, postoperative sensitivity is another important clinical evaluation parameter, because it is believed to be caused by a modification in the hydrodynamics of dentinal fluids due to incomplete adhesive penetration or inadequate hybridization.[47] The meta-analysis showed a similar performance for postoperative sensitivity between adhesive systems containing distinct solvents, and no secondary carious lesions were reported for any of the types of bonding agents. The results for these two parameters demonstrate that acetone- and alcohol-based adhesives present adequate bonding and comparable dentin sealing ability, providing long-lasting composite restorations.

A second meta-analysis was performed to compare survival rates of composite restorations placed using acetone- or alcohol-based adhesive systems over different follow-up periods (Figure 4). Survival rates can be described as the percentage of composite restorations that did not fail (loss or need of replacement/repair) at a certain evaluation time.[56,61] Once again, there was no statistical difference between the two solvents, showing that composite restorations placed using both types of adhesives performed favorably in clinical trials with follow-ups ranging from 6 to 72 months. Hence, the second null hypothesis was also accepted. However, some of these results should be interpreted with caution. The follow-ups of 12 and 18 months presented high heterogeneity among studies (62% and 88%, respectively), which means the extracted data from the selected set of clinical trials varied from one to another,[22] leading to more favorable survival rates (although not statistically significant) for restorations placed using alcohol-based bonding agents, especially at 18 months. Also, only one publication reported data for the 60-month follow-up,[33] and the

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Table 4. *Evidence Profile: Clinical Performance of NCCL Restorations With Acetone- and Alcohol-Based Dentin Bonding Agents*

	Certainty Assessment					
No. of Participants (Studies)	**Risk of Bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other Considerations**	**Overall Certainty of Evidence**
Retention						
1278 (9 RCTs)	Not serious	Not serious	Not serious	Not serious	Very strong association	HIGH
Marginal adaptation						
675 (7 RCTs)	Not serious	Not serious	Not serious	Not serious	Very strong association	HIGH
Marginal discoloration						
1170 (9 RCTs)	Not serious	Not serious	Not serious	Not serious	Very strong association	HIGH
Surface texture						
165 (2 RCTs)	Not serious	Not serious	Not serious	Serious [a]	Very strong association	HIGH
Color						
165 (2 RCTs)	Not serious	Not serious	Not serious	Serious [a]	Very strong association	HIGH
Sensitivity						
914 (6 RCTs)	Not serious	Serious [b]	Not serious	Not serious	Very strong association	HIGH
Secondary caries						
1091 (8 RCTs)	Not serious	Not serious	Not serious	Not serious	Very strong association	HIGH
Anatomic form						
161 (2 RCTs)	Not serious	Not serious	Not serious	Serious [a]	Very strong association	HIGH
Pulp vitality						
86 (1 RCT)	Not serious	Not serious	Not serious	Serious [a]	Very strong association	HIGH
Clinical performance overall						
5705 (9 RCTs)	Not serious	Not serious	Not serious	Not serious	Very strong association	HIGH

Abbreviation: CI, confidence interval.
[a] *Number of events is lower than 300.*
[b] *Little variation in the effect estimates across studies.*

72-month follow-up analysis also consisted of data extracted from a single study.[27] Thus, more long-term clinical trials are necessary to allow for a reliable prediction of the performance of composite restorations placed using acetone- or alcohol-based bonding agents over time.

Methodologic variability is a limitation that must be considered in the present meta-analyses. Beveling

Table 5: *Evidence Profile: Survival Rate of NCCL Restorations With Acetone- and Alcohol-Based Dentin Bonding Agents*

	Certainty Assessment					
No. of Participants (Studies)	**Risk of Bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other Considerations**	**Overall Certainty of Evidence**
Survival Rate Overall						
4943 (10 RCTs)	Not serious	Serious[a]	Not serious	Not serious	Very strong association	HIGH

Abbreviation: CI, confidence interval.
[a] *Little variation in the effect estimates across studies.*

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Table 4. *Evidence Profile: Clinical Performance of NCCL Restorations With Acetone- and Alcohol-Based Dentin Bonding Agents (ext.)*

Certainty Assessment	Summary of Findings				
No. of Participants (Studies)	Study Event Rates, No./Total (%)		Relative Effect (95% CI)	Anticipated Absolute Effects	
	With Alcohol	With Acetone		Risk With Alcohol	Risk Difference With Acetone
Retention					
1278 (9 RCTs)	582/633 (91.9)	585/645 (90.7)	Not estimable	919 per 1000	919 fewer per 1000 (919 fewer to 919 fewer)
Marginal adaptionation					
675 (7 RCTs)	332/332 (100.0)	342/343 (99.7)	Not estimable	1000 per 1000	1000 fewer per 1000 (1000 fewer to 1000 fewer)
Marginal discoloration					
1170 (9 RCTs)	580/583 (99.5)	578/587 (98.5)	Not estimable	995 per 1000	995 fewer per 1000 (995 fewer to 995 fewer)
Surface texture					
165 (2 RCTs)	59/59 (100.0)	106/106 (100.0)	Not estimable	1000 per 1000	1000 fewer per 1000 (1000 fewer to 1000 fewer)
Color					
165 (2 RCTs)	59/59 (100.0)	106/106 (100.0)	Not estimable	1000 per 1000	1000 fewer per 1000 (1000 fewer to 1000 fewer)
Sensitivity					
914 (6 RCTs)	436/450 (96.9)	445/464 (95.9)	Not estimable	969 per 1000	969 fewer per 1000 (969 fewer to 969 fewer)
Secondary caries					
1091 (8 RCTs)	531/531 (100.0)	560/560 (100.0)	Not estimable	1000 per 1000	1000 fewer per 1000 (1000 fewer to 1000 fewer)
Anatomic form					
161 (2 RCTs)	81/81 (100.0)	80/80 (100.0)	Not estimable	1000 per 1000	1000 fewer per 1000 (1000 fewer to 1000 fewer)
Pulp vitality					
86 (1 RCT)	43/43 (100.0)	43/43 (100.0)	Not estimable	1000 per 1000	1000 fewer per 1000 (1000 fewer to 1000 fewer)
Clinical performance overall					
5705 (9 RCTs)	2703/2771 (97.5)	2845/2934 (97.0)	Not estimable	975 per 1000	975 fewer per 1000 (975 fewer to 975 fewer)

of the enamel margins was carried out before restorative procedures in some of the selected studies,[14,26,30,32,33] whereas other studies did not do it.[27-29,31,34] Roughening of the superficial, hypermineralized dentin surface was performed in most of the selected clinical trials,[14,26,27,30,32,33] but some of them did not provide information regarding this aspect.[28,29,31,34] Some papers included teeth with different levels of dentin sclerosis,[27,29-34] and all studies had cavities of varied shapes and dimensions. All these clinical aspects can influence microretention, which might have affected the results of

Table 5: *Evidence Profile: Survival Rate of NCCL Restorations With Acetone- and Alcohol-Based Dentin Bonding Agents (ext.)*

Certainty Assessment	Summary of Findings				
No. of Participants (Studies)	Study Event Rates, No./Total (%)		Relative Effect (95% CI)	Anticipated Absolute Effects	
	With Ethanol	With Acetone		Risk With Ethanol	Risk Difference With Acetone
Survival Rate Overall					
4943 (10 RCTs)	2200/2373 (92.7)	2390/2570 (93.0)	Not estimable	927 per 1000	927 fewer per 1000 (927 fewer to 927 fewer)

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the meta-analyses performed in this review. Furthermore, all the selected papers[14,26-34] compared adhesives with not only different solvents, but also with distinct monomer compositions. Therefore, even if some adhesive systems contained a solvent type that could have affected the clinical performance of composite restorations unfavorably, their monomer chemistry might have compensated this disadvantage, improving their clinical results.

CONCLUSION

Based on the results of this systematic review and meta-analysis, there is no significant difference in the clinical performance of dental adhesives based on solvent type (alcohol- or acetone-based), regardless of adhesive mode of action or application.

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Conflict of Interest

The authors of this manuscript certify that they have no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that is presented in this article.

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