META-ANALYSIS / *MÉTA-ANALYSE*

Restorative Dentistry / *Dentisterie Restauratrice*

ASSESSMENT OF CLINICAL PERFORMANCE OF UNIVERSAL ADHESIVES VERSUS OTHER ADHESIVE SYSTEMS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF CLINICAL TRIALS

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Abstract: Universal adhesives (UAs) often exhibit comparable or even superior bond strength to traditional adhesive systems, ensuring reliable and long-lasting adhesion between the resin composite and the tooth structure.
Therefore, this study aimed to assess the clinical performance of UAs compared to other adhesive systems in direct resin composite restorations through a systematic review and meta-analysis.
Two reviewers executed a literature search in five electronic databases: PubMed, EMBASE, Scopus, Web of Science, and Scielo. Clinical trials comparing the clinical evaluation of resin composite restorations in Class I, Class II, or Class V cavities placed with an universal adhesive (UA) system against resin composite restorations placed with another non-UA system were included in the review.
An analysis was carried out using Review Manager software version 5.3.5 (London, England, United Kingdom). Standardized effect sizes with 95% confidence intervals were calculated to allow comparisons between different interventions and different outcomes. The methodological quality of each study was assessed using the Cochrane RoB2 tool for randomized clinical trials.
A total of 2331 potentially relevant studies were identified. After title and abstract examination, 14 studies remained in the systematic review. From these, a total of 11 studies were included in the meta-analysis. The retention rates of resin composite restorations after 6 months showed no significant difference between total-etch (TE, $p=0.83$), or self-etch (SE, $p=0.78$) adhesives and UAs applied in TE and SE modes ($p>0.05$). However, UAs applied in selective-enamel etching (SEE) mode demonstrated superior clinical performance compared to other adhesives ($p=0.01$), particularly TE adhesives ($p=0.02$). Similarly, after >12 months of follow-up, there were no significant differences in retention rates among different adhesive modes ($p>0.05$). Additionally, the incidence of secondary caries did not significantly differ across adhesive modes at both 6-month and >12-month evaluations ($p>0.05$).
This systematic review and meta-analysis suggested that UAs demonstrate comparable clinical performance to TE and SE adhesive systems in direct resin composite restorations, particularly in terms of restoration retention rates and the incidence of secondary caries. UAs applied in SEE mode exhibited superior clinical outcomes compared to other adhesive systems. These findings indicate that UAs can be considered a viable alternative to traditional adhesive systems in clinical practice, offering flexibility in application while maintaining comparable long-term outcomes.

Keywords: Adhesives; Composite Resins; Etch-and-Rinse; Randomized Clinical Trial; Self-Etch; Universal Adhesive.

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Conflicts of interest:
The authors declare no conflicts of interest.

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ÉVALUATION DES PERFORMANCES CLINIQUES DES ADHÉSIFS UNIVERSELS PAR RAPPORT À D'AUTRES SYSTÈMES ADHÉSIFS : UNE REVUE SYSTÉMATIQUE ET UNE MÉTA-ANALYSE DES ESSAIS CLINIQUES

Résumé: Les adhésifs universels (UA) présentent souvent une force d'adhérence comparable, voire supérieure, aux systèmes adhésifs traditionnels, garantissant une adhérence fiable et durable entre la résine composite et la structure dentaire. Par conséquent, cette étude visait à évaluer les performances cliniques des UA par rapport à d'autres systèmes adhésifs dans les restaurations directes en composite de résine grâce à une revue systématique et une méta-analyse. Deux évaluateurs ont effectué une recherche documentaire dans cinq bases de données électroniques : PubMed, EMBASE, Scopus, Web of Science et Scielo. Des essais cliniques comparant l'évaluation clinique des restaurations en résine composite dans des cavités de classe I, de classe II ou de classe V placées avec un système adhésif universel (UA) par rapport aux restaurations en résine composite placées avec un autre système non-UA ont été incluses dans la revue. Une analyse a été réalisée à l'aide du logiciel Review Manager version 5.3.5 (Londres, Angleterre, Royaume-Uni). Des tailles d'effet standardisées avec des intervalles de confiance à 95 % ont été calculées pour permettre des comparaisons entre différentes interventions et différents résultats. La qualité méthodologique de chaque étude a été évaluée à l'aide de l'outil Cochrane RoB2 pour les essais cliniques randomisés.

Au total, 2 331 études potentiellement pertinentes ont été identifiées. Après examen des titres et des résumés, 14 études sont restées dans la revue systématique. Parmi celles-ci, un total de 11 études ont été incluses dans la méta-analyse. Les taux de rétention des restaurations en résine composite après 6 mois n'ont montré aucune différence significative entre les adhésifs à mordançage total (TE, $p = 0{,}83$) ou auto-mordançants (SE, $p = 0{,}78$) et les UA appliqués en modes TE et SE ($p > 0{,}05$).). Cependant, les UA appliqués en mode gravure sélective de l'émail (SEE) ont démontré des performances cliniques supérieures par rapport aux autres adhésifs ($p = 0{,}01$), en particulier les adhésifs TE ($p = 0{,}02$). De même, après plus de 12 mois de suivi, il n'y avait aucune différence significative dans les taux de rétention entre les différents modes d'adhésion ($p > 0{,}05$). De plus, l'incidence des caries secondaires ne différait pas significativement selon les modes d'adhésion lors des évaluations à 6 mois et à plus de 12 mois ($p > 0{,}05$). Cette revue systématique et méta-analyse suggèrent que les UA démontrent des performances cliniques comparables à celles des systèmes adhésifs TE et SE dans les restaurations directes en composite de résine, notamment en termes de taux de rétention des restaurations et d'incidence des caries secondaires. Les UA appliqués en mode SEE ont présenté des résultats cliniques supérieurs par rapport aux autres systèmes adhésifs. Ces résultats indiquent que les UA peuvent être considérés comme une alternative viable aux systèmes adhésifs traditionnels dans la pratique clinique, offrant une flexibilité d'application tout en conservant des résultats comparables à long terme.

Mots clés: Adhésifs ; Résines composites ; gravure et rinçage ; Essai clinique randomisé ; Auto-mordançage ; Adhésif universel.

Introduction

Dentin adhesives are unique in the sense that they may be one of the few biomaterials employed in science that change commercial names frequently, making it extremely difficult for clinicians to stay updated or to decide which adhesive to use in their daily clinical practices [1]. Randomized controlled trials are regarded as the elite design for assessing diverse methods in healthcare involvements [2], as well as the most trustworthy evidence-based research in dentistry [3]. Laboratory researches are popular as they produce faster discoveries, but they do not account for the complicated oral environment [4]. The present focus of adhesive dentistry research is on enhancing the quality of resin-dentin bonding and understanding their breakdown processes [5]. Numerous ways have been proposed to improve the lifespan of the union of dental restorative materials to the tooth structure [6-8], but few have been examined clinically [9-12].

Contemporary adhesive systems are categorized as total-etch (TE) or self-etch (SE) adhesives based on their adhesion method and the treatment given to the smear layer [13]. After the dentin and the enamel substrates have been totally etched with phosphoric acid, TE adhesives are applied, and thus the smear layer was removed [14]. On the contrary, the acid etching phase is removed with SE adhesives since they include monomers with acidic functional groups that concurrently etch and prepare the dental substrate [15]. Therefore, the smear layer was modified and incorporated in the hybridized complex [16].

Currently, clinicians are interested in taking advantage of more adaptable adhesive approaches. A new generation of bonding systems designated as "universal" or "multimode" adhesives has been initiated on the market [17]. The term "universal" refers to the addition of resinous monomers to offer chemical bonding to dental hard tissue and metals [18]; and to the versatility of these adhesives, as dentists can select between TE, SE, or selective etching of enamel margins (SEE), based on the specific clinical circumstances and the preferences of the operators [19]. Besides, when employed in the TE mode, universal adhesives (UAs) may be applied to moist or dry dentin [20]. Moreover, one of the key difficulties with the previous generation of one-step SE or "all-in-one" adhesives was the increase of nanoleakage (NL) after any form of aging protocol and the delimited bond stability. The existence of diverse combinations of hydrophilic and hydrophobic constituents within a single bottle contributed to its inadequate long-term performance [13]. Since UAs are an example of one-step SE adhesive, the stability and longevity of bonded surfaces formed by these novel adhesives remain in doubt [21].

Meaningfully higher failure rates per year have been described for strong one-step SE adhesives (5.4%) when compared to mild one-step SE adhesives (3.6%) [22]. Since the pH of the majority of UAs is equal to or greater than 2.0, the enhanced retention rates for mild one-step SE adhesive systems may be a strong predictor of clinical effectiveness of new UAs if employed as SE adhesives on dentin. A previous clinical investigation confirmed the superior clinical performance of mild one-step SE adhesives over strong one-step SE adhesives [23].

Additionally, there is some disagreement over whether UAs should be used in an TE mode on both enamel and dentin. Mechanically, bond strength (BS) to dentin of the TE and SE methods are comparable after 24 h aging [24,25]. Etching, on the other hand, eliminates calcium (Ca) from dentin, leaving a thin network of collagen fibers surrounded by water. Ca removal from the adhesive interface might prevent any potential ionic interaction between Ca and the adhesive's phosphate and/or carboxylate groups. Indeed, when UAs are employed as TE adhesives to dentin substrate, their dentin-sealing capacity deteriorates. When universal adhesive (UA) is applied to dentin in SE mode in a previous report, it resulted in the lowest immediate NL [26], as well as after one year of water storage [27].

Mild SE adhesives, while effective on dentin, are ineffective in etching enamel [13]. Scotchbond Universal adhesive, for example, has enamel bond strengths (BSs) of 28.7 MPa in SE mode and 40.1 MPa in TE mode [28]. Marginal discoloration and marginal leakage are two consequences of inadequate enamel etching. Thus, comparable to the most SE adhesives, UA relies on enamel etching for persistent bonding to enamel [29].

Concisely, UAs have a substantial benefit over earlier generations of adhesive systems in that they are approved for a broader range of restoration treatments and adhesion tactics [29]. Furthermore, when employed in SE mode, these novel adhesives chemically bond to hydroxyapatite (HAp) in dentin [6]. Bonding to enamel substrate, though, still necessitates phosphoric acid etching to generate a strong micromechanical connection that may enhance the chemical bonding to HAp supplied by their acidic monomers [30]. As a result, SEE is suggested as an adhesive method for the majority of clinical uses of UAs [31].

A preceding finding denoted that depending on the number of cavity walls, resin composite may adhere differently to the dentin, and there may be more breaks through the adhesive in the gingival wall than in the axial wall. Thus, clinical trials using UAs in different configuration cavities are required [32].

In this circumstance, clinical assessment of dental restorations entails the use of criteria defined for specific aspects thought to be important in the clinical performance of restorative materials. The evaluation can be estimated using a variety of criterion, including the

United States Public Health Service (USPHS) criteria and the Fédération Dentaire Internationale (FDI), the latter of which is divided into aesthetic, functional, and biological parameters of the restorations [33]. On one hand, for the USPHS criteria, the restorations can be divided to 3 scores: Alpha, Bravo, and Charlie [34]. On the other hand, for the FDI criteria, the restorations can be classed to 5 scores: clinically very good for score 1, clinically good for score 2, clinically sufficient for score 3, clinically unsatisfactory for score 4, and clinically bad for score 5 [33]. Studies evaluating the clinical behavior of different bonding techniques by means of modified FDI and USPHS criteria found that FDI criteria is more susceptible to small variations in clinical results than the modified USPHS criteria [9, 10, 12].

Presently, there are only a few studies that evaluate the clinical evaluation of resin composite restorations in different cavities placed with an UA [9-12]. Therefore, the aim of this systematic review and meta-analysis was to evaluate the clinical performance of UAs when compared to other adhesive systems in a direct resin composite restoration. Accordingly, the null hypothesis tested was that there would be no difference in clinical performance to dental substrates when using UAs or other adhesive systems for resin composite restorations in different cavities.

Materials and Methods

Data Sources

This study protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO acknowledgement of receipt: CRD42017079479). It followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Statement [35]. The following research question was posed based on the PICO acronym (P - adults featuring permanent teeth, with Class I, Class II or Class V cavities, I – resin composite restorations placed with UAs, C – resin composite restorations placed with TE or SE strategies, and O – clinical performance): "What are the retention rates and secondary caries rates of composite resin restorations placed with UAs when compared with other adhesive systems?"

Search strategy

A search strategy for MEDLINE via PubMed based on the concepts of participant and intervention of the focused PICO question was elaborated. The strategy was adapted to other electronic databases (EMBASE, Scopus, Web of Science, and Scielo) (Table 1). There was no restriction based on publication date and/or language. Additionally, grey literature was investigated by searching the first one hundred results of Google Scholar database. Moreover, the reference lists of all primary and eligible studies of this systematic review were hand searched for additional relevant publications.

Eligibility criteria

The title and abstract of each identified article were assessed by two independent reviewers (CECS and RB) to determine if the article should be considered. Manuscripts for full-text review were selected according to the following eligibility criteria: (1) clinical trials reporting the clinical evaluation of resin composite restorations in Class I, Class II, or Class V cavities placed with an UA system; (2) included a control group where the resin composite restorations were placed with a TE or SE adhesive; (3) evaluated the clinical performance of the resin composite restorations with at least 6 months of follow-up. Case reports, case series, pilot studies, expert opinions, conference abstracts, and reviews were excluded. In case of disagreements at the time of the selection of the studies for the full-text review, they were resolved by discussion and consensus by a third reviewer (LH).

Data extraction

The Microsoft Office Excel 2016 (Microsoft Corporation, Redmond, Washington, USA) was used to extract the data of interest from the included manuscripts. These were placed on a standardized form. Two reviewers (RB and LH), who received training in this software, independently performed the anal-

Table 1. Search strategy used in MEDLINE via PubMed.

Number	Terms used
# 1	molar OR bicuspid OR premolar OR dentition, permanent OR permanent dentition OR posterior teeth OR posterior tooth OR dental caries OR dental decay OR class i OR class ii OR class v OR non-carious cervical lesions OR non carious cervical lesions OR non-carious, cervical lesion OR non-carious cervical lesions
# 2	Universal adhesive OR adhesive, universal OR universal adhesives OR adhesives, universal OR Multimode adhesive OR multimode adhesive OR multimode adhesives OR multi-mode adhesives OR Universal bond OR Universal bonding agent OR multi-mode bond OR multimode bond OR multimode bonding agent OR multimode bonding agent
# 3	clinical efficacy OR clinical evaluation OR clinical study OR randomized clinical trial OR clinical trial OR controlled clinical trial

ysis. The data recovered from each manuscript were study and year, type of clinical trial, registration, number of participants and number of teeth restored, class restoration and substrate, UA and adhesive strategy used; TE or SE adhesive used as control, resin composite placed, restoration evaluation criteria used, and follow-up.

Quality assessment

Risk of bias of the selected articles was evaluated and classified according to the Cochrane RoB2 tool for randomized clinical trials [36]. They were evaluated by two reviewers (RB and NK) according to the following items: selection bias (sequence generation, allocation concealment), performance and detection bias (blinding of operators or participants and personnel), bias due to incomplete data, reporting bias (selective reporting, unclear withdrawals, missing outcomes), and other bias (protocol record in CONSORT). Each domain was classified as having a low risk, unclear risk, or high risk of bias.

Statistical analysis

The main outcomes evaluated were retention rate and secondary caries, and the meta-analysis was performed using the Review Manager software version 5.3.5 (London, England, United Kingdom). Analyses were carried out by using the fixed-effect model, and pooled-effect estimates were obtained by comparing the retention ratios of the UAs with those from other commercial types of adhesives. Data from studies were summarized into the subsequent follow-ups: 6-12 months and <12 months. In case duplication was found in the data of a study within the range described above, data from the longest follow-up period were used. Data from each study were dichotomized as acceptable or unacceptable. The acceptable restorations were those that received the Alpha and Bravo scores. The unacceptable restorations were those that received the Charlie and Delta score in at least one of the characteristics.

Standardized effect sizes with 95% confidence intervals (95% CI) were calculated to allow comparisons between different interventions and different outcomes. The prevalence of unacceptable (events) and the total number of restorations per group were used to calculate the risk difference using a random effects model. In order to quantify the effects of different outcomes, a separate meta-analysis was executed for the different application modes of the UA (TE, SE, and SEE). Subgroup analyses were implemented according to the adhesive system used for comparison (TE or SE). Also, different analyses were performed for short-term (6 months) and long-term (>12 months) outcomes. Statistical heterogeneity of the treatment effect among studies was assessed using the Cochran's Q test and the inconsistency I2 test.

Results

A total of 2331 publications were retrieved in all databases. A flowchart that summarizes the study selection process according to the PRISMA Statement is shown in Figure 1. The literature review retrieved 1531 manuscripts for the initial examination after the duplicates were removed. Of these, 1508 studies were excluded after reviewing the titles and abstracts. In total, 23 studies were assessed by full-text reading. After the full-text was examined, 9 studies were excluded: in 5 studies, a control group was not used; in 2 studies, UAs were not applied; 1 study was found to be retracted on request of the Editor in Chief; and finally, the full-text of 1 article could not be retrieved. Then, a total of 14 studies were included in the qualitative analysis [37-50]. Of these, three articles lacked of absolute values for performing the meta-analysis, and they were excluded for the quantitative analysis [40, 42, 48].

The qualitative analysis of the studies incorporated in this systematic review is outlined in Table 2. The majority of the studies analyzed the clinical performance of resin composites in Class V restorations, 2 in Class II and 1 study in Class I. All the studies evaluated the clinical performance in permanent teeth. Several UAs were identified in this review, including Scotchbond™Universal (3M Deutschland GmbH, Seefeld, Germany), Prime and Bond Universal (Dentsply Sirona, Konstanz, Germany), All-Bond Universal (Bisco; Schaumburg, IL, USA), Futurabond DC (Voco America), Clearfil Universal Bond Quick (Kuraray Noritake; Tokyo, Japan), Tetric N-Bond Universal (Ivoclar Vivadent. Schaan, Liechtenstein), Futurabond U (Voco, Cuxhaven, Germany), Adhese Universal (Ivoclar Vivadent AG, Liechtenstein), Gluma Universal (Kulzer GmgH, Hanau, Germany), iBond Universal (Kulzer GmgH, Hanau, Germany), and Peak Universal (Ultradent, South Jordan, UT, USA). UAs were applied in TE, SE, and SEE modes, and were compared against several brands and types of other adhesive systems, including three-step and two-step TE adhesives, and one-step and two-step SE adhesives. Among the criteria used for the evaluation of the restorations, the FDI criteria, the Modified Cvar and Ryge criteria, the modified USPHS criteria, and the USPHS criteria were found. The maximum follow-up recorded was 4 years.

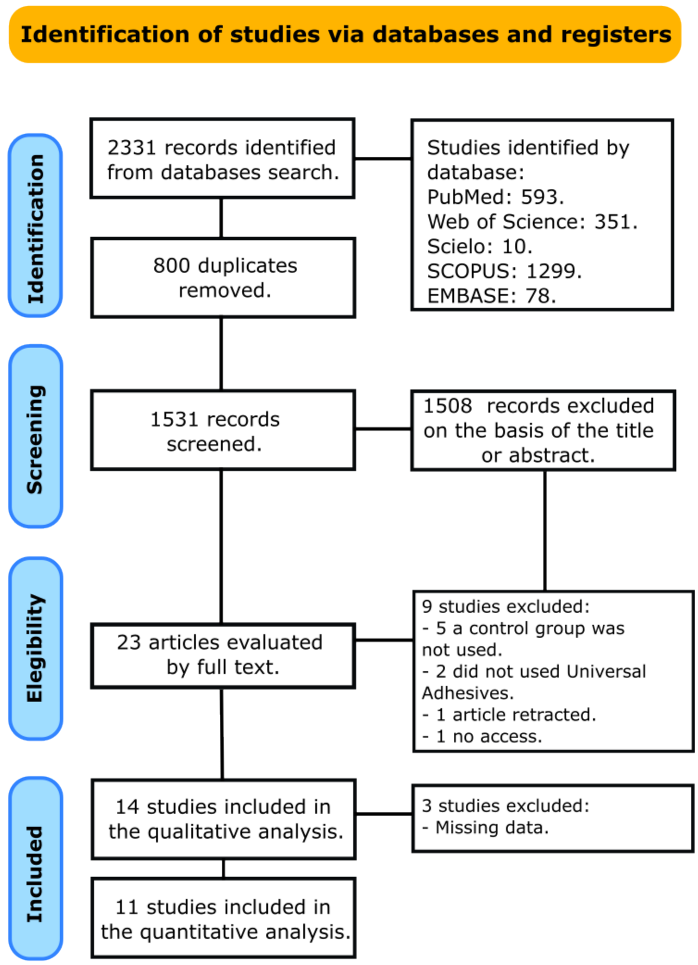

Figure 1. Flowchart summarizing the selection of the studies

Table 2. Characteristics of the clinical trials included.

Study and year	Type of clinical trial	Registration	Number of participants (number of teeth)	Class restoration and substrate	Universal adhesive and adhesive strategy	Adhesive control and strategy	Resin composite	Restoration evaluation criteria used	Follow-up
Haak, 2018	Randomized controlled trial	German Clinical Trials Register # DRKS00011084 (http://www.drks.de/DRKS00011084)	22 patients with 4 non-carious cervical lesions (NCCLs)	Class V, permanent teeth	Universal adhesive Scotchbond™ Universal (3M Deutschland GmbH, Seefeld, Germany)/ 3 etching protocols: self-etch (SE), selective-enamel-etch (SEE) and total-etch (TE).	Optibond™ FL (Kerr GmbH, Rastatt, Germany)/ Three-step TE adhesive	Filtek Supreme™ XTE (3 M Deutschland GmbH, Seefeld, Germany)	Fédération Dentaire Internationale (FDI) criteria	14 days and 6 months

Lawson, 2015	Single-center, randomized, comparator-controlled, and parallel-designed study with blinding of patients and clinical evaluators	Non mentioned	37 adults' patients with 3 or 6 NCCLs	Class V, permanent teeth	Scotchbond Universal (3M ESPE, St. Paul, USA)/ TE and SE modes	Scotchbond Multi-purpose (3M ESPE, St. Paul, USA)/ Three-step TE adhesive	Filtek Supreme Ultra universal (3M ESPE, St. Paul, USA)	Modified Cvar and Ryge criteria	6, 12, and 24 months
de Oliveira, 2023	Randomized controlled trial, double-blind, split-mouth study	Non mentioned	26 volunteers (60 restorations)	Class V, permanent teeth	Prime and Bond Universal (Dentsply Sirona, Konstanz, Germany)/ SE mode	Optibond All-in-One (Kerr, New South Wales, Australia)/ One-step SE adhesive Clearfil SE (Kuraray Medical Inc., Tokyo, Japan)/ Two-step SE adhesive	Filtek Z350 XT (3M ESPE, Sumaré, SP, Brazil)	The modified United States Public Health Services (USPHS) criteria	1 and 2-year.
van Dijken, 2017	Randomized controlled trial	Non mentioned	57 patients (120 restorations)	Class II, permanent teeth	All-Bond Universal (Bisco; Schaumburg, IL, USA)/ SEE mode	Optibond XTR (Kerr; Orange, CA, USA)/ Two-step SE adhesive	Aelite LS (Bisco; Schaumburg, IL, USA)	The modified USPHS criteria	During the 3-year follow-up
Haak, 2019	Randomized double-blinded clinical trial	Clinical Trials Register #DRKS00011084	55 patients (165 restorations)	Class V, permanent teeth	Scotchbond™ Universal (3M Oral Care, St Paul, MN, USA)/ SE and SEE modes	Optibond™ FL (Kerr GmbH, Rastatt, Germany)/ Three-step TE adhesive	Filtek Supreme XTE (3M Oral Care, Seefeld, Germany)	FDI criteria	14 days, 6 months, and 12 months

Handa, 2023	Clinical trial	Non mentioned	30 patients (120 restorations)	Class V, permanent teeth	Single Bond Universal (3M ESPE, St. Paul, USA)/ SE mode Futurabond DC (Voco America)/ SE mode	Adper™ Single Bond 2 (3M ESPE, St. Paul, USA): Two-step TE adhesive Futurabond NR (Voco America): Two-step SE adhesive	Filtek Z350XT (3M ESPE, St. Paul, USA)	The modified USPHS criteria	3,6,12, and 24 months
Oz, 2022	Randomized controlled clinical trial	Clinical Trials Number: NCT04481087	34 patients (234 restorations)	Class V, permanent teeth	Clearfil Universal Bond Quick (Kuraray Noritake; Tokyo, Japan)/ SE, TE, and SEE modes Tetric N-Bond Universal (Ivoclar Vivadent. Schaan, Liechtenstein)/ TE mode	Clearfil SE (Kuraray Medical Inc., Tokyo, Japan)/ Two-step SE adhesive	Tetric N-Ceram (Ivoclar Vivadent. Schaan, Liechtenstein)	The modified USPHS criteria	6,12, and 24 months
Manarte-Monteiro, 2021	Prospective, double-blind, six-arm (two control groups) randomized controlled clinical trial	ClinicalTrials.gov (NCT02698371).	38 patients (210 restorations)	Class V, permanent teeth	Futurabond U (Voco, Cuxhaven, Germany)/ SE and TE modes Adhese Universal (Ivoclar Vivadent AG,Liechtenstein)/ SE and TE modes	Futurabond DC (Voco, Cuxhaven, Germany): one-step SE adhesive	Admira Fusion (Voco, Cuxhaven, Germany)	FDI criteria	1 and 2-year
de Souza, 2019	Double-blind randomized controlled clinical trial	Clinical trials registry database REBEC (http://www.ensaiosclinicos.gov. br) under protocol RBR-5hncr3	67 patients (148 restorations)	Class V, permanent teeth	Scotchbond Universal (3M ESPE, St. Paul, USA)/ TE mode	Scotchbond Multi-Purpose (3M ESPE, St. Paul, USA): Three-step TE adhesive	Filtek Z350 XT (3M ESPE, Sumaré, Brazil)	The modified USPHS criteria	6 months

Zanatta, 2019	Randomized, double-blind clinical study	Clinical Trials Registry (ReBEC - www.ensaiosclinicos.gov.br) under the identification number RBR-4rw55d	34 patients (152 restorations)	Class V, permanent teeth	Scotchbond Universal Adhesive (3M ESPE, St Paul, MN, USA)/ TE and SE modes	Adper Single Bond 2 (3M ESPE, St Paul, MN, USA)/ Two-step TE adhesive Clearfil SE Bond (Kuraray, Kurashiki, Okayama, Japan) Two-step SE adhesive	Filtek Supreme (3M ESPE, St Paul, MN, USA)	FDI criteria	6,12, and 24 months
Oz, 2019	Randomized, controlled, prospective clinical trial	Non mentioned	20 patients (155 restorations)	Class V, permanent teeth	All Bond Universal (Bisco; Schaumburg, IL, USA), Gluma Universal (Kulzer GmgH, Hanau, Germany) / TE, SE, and SEE modes	Single Bond 2 (3M ESPE, St Paul, MN, USA)/ Two-step TE adhesive	Tetric N-Ceram (Ivoclar Vivadent, Liechtenstein)	USPHS criteria	6,12, and 24 months
Haak, 2023	Randomized controlled clinical	Clinical Trials Register (DRKS) DRKS00011064 (http://apps.who.int/trialsearch, accessed on 30 July 2015)	50 patients (179 restorations)	Class V, permanent teeth	iBond Universal (Kulzer GmgH, Hanau, Germany)/ TE, SE, and SEE modes	Optibond™ FL (Kerr GmbH, Rastatt, Germany)/ Three-step TE adhesive	Venus Diamond Flow (Kulzer GmbH, Hanau, Germany)	FDI criteria	6, 12, 24 and 36 months

Dukić, 2021	Double-blinded, clinical study	UPI 034-04/17-6/1; 251-60-4/115-17-3	103 patients (299 restorations)	Class I, permanent teeth	Scotchbond Universal (3M/Espe, St. Paul, MN, USA)/TE	Prime&Bond NT (Dentsply Sirona, York, PA, USA)	Grandio Flow (Voco, Cuxhaven, Germany) Voco Solobond M (Voco, Cuxhaven, Germany) Tetric Evoflow (Vivadent, Schaan, Liechtenstein) Excite (Vivadent, Schaan, Liechtenstein Xflow (Dentsply Sirona, York, PA, USA) Prime&Bond NT (Dentsply Sirona, York, PA, USA) Filtek Supreme XT Flow (3M/Espe, St. Paul, MN, USA) Scotchbond Universal (3M/Espe, St. Paul, MN, USA)	The modified USPHS criteria	12, 24 and 36 months

Hoshino, 2022	Randomized, prospective, and split-mouth study	#RBR-3gg3mg	53 patients (159 restorations)	Class II, permanent teeth	Peak Universal (Ultradent, South Jordan, UT, USA): SE mode	Adper Single Bond 2 (3M ESPE, St Paul, MN, USA)/ Two-step TE adhesive XP Bond2 (DENTSPLY Caulk Milford, DE, USA)/ Two-step TE adhesive	Amelogen Plus (Ultradent, South Jordan, UT, USA) Filtek Bulk Fill Flow 3M ESPE Dental Products TM, St. Paul, MN, USA Filtek Z350XT 3M ESPE Dental Products TM, St. Paul, MN, USA SureFil SDR (DENTSPLY Caulk Milford, DE, USA) TPH3 (DENTSPLY Caulk Milford, DE, USA)	The modified USPHS criteria	6 months, 1-year, 3 -year, and 4-year

The results from the meta-analysis of the retention rate are presented in Figures 2-7. The retention of resin composite restorations after 6 months of follow-up was similar between TE and SE adhesives against UAs applied in TE (p=0.83), and SE (p=0.78) modes. On the other hand, the clinical performance of UAs applied in the SEE mode (p=0.01) was superior compared to other adhesives. The last result was more evident when the UAs were compared with TE adhesives (p=0.02).

Study or Subgroup	Universal adhesives Events	Universal adhesives Total	Other adhesives Events	Other adhesives Total	Weight	Risk Difference M-H, Fixed, 95% CI
1.1.1 Self-etch adhesives						
de Oliveira, 2023	0	20	0	20	6.2%	0.00 [-0.09, 0.09]
de Oliveira, 2023	0	20	0	20	6.2%	0.00 [-0.09, 0.09]
Oz, 2022	2	38	1	40	12.1%	0.03 [-0.06, 0.11]
Zanatta, 2019	0	38	1	38	11.8%	-0.03 [-0.10, 0.04]
Subtotal (95% CI)		**116**		**118**	**36.4%**	**0.00 [-0.04, 0.04]**
Total events	2		2			
Heterogeneity: Chi^2 = 0.95, df = 3 (P = 0.81); I^2 = 0%						
Test for overall effect: Z = 0.03 (P = 0.98)						
1.1.2 Total-etch adhesives						
Haak, 2018	0	22	1	22	6.9%	-0.05 [-0.16, 0.07]
Haak, 2019	0	55	9	55	17.1%	-0.16 [-0.26, -0.06]
Lawson, 2015	2	41	1	41	12.8%	0.02 [-0.06, 0.11]
Oz, 2019	5	21	0	29	7.6%	0.24 [0.05, 0.42]
Oz, 2019	4	20	0	29	7.4%	0.20 [0.02, 0.38]
Zanatta, 2019	0	38	0	38	11.8%	0.00 [-0.05, 0.05]
Subtotal (95% CI)		**197**		**214**	**63.6%**	**0.01 [-0.04, 0.06]**
Total events	11		11			
Heterogeneity: Chi^2 = 22.18, df = 5 (P = 0.0005); I^2 = 77%						
Test for overall effect: Z = 0.31 (P = 0.76)						
Total (95% CI)		**313**		**332**	**100.0%**	**0.01 [-0.03, 0.04]**
Total events	13		13			
Heterogeneity: Chi^2 = 23.10, df = 9 (P = 0.006); I^2 = 61%						
Test for overall effect: Z = 0.28 (P = 0.78)						
Test for subgroup differences: Chi^2 = 0.04, df = 1 (P = 0.84), I^2 = 0%						

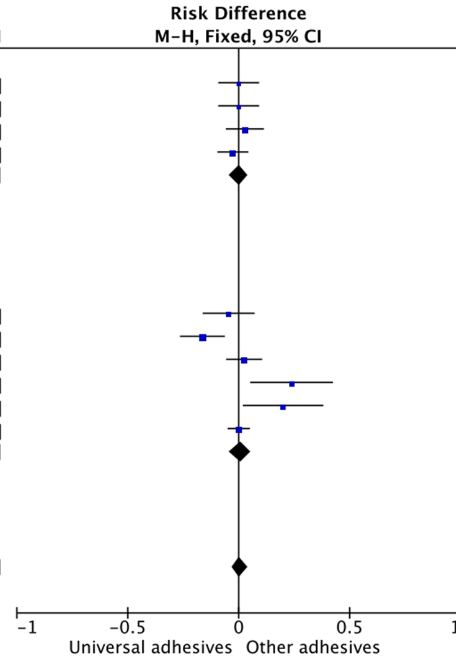

Figure 2. Retention of resin composite restorations placed with universal adhesives using the self-etch mode after 6 months of follow-up.

Study or Subgroup	Universal adhesives Events	Universal adhesives Total	Other adhesives Events	Other adhesives Total	Weight	Risk Difference M-H, Fixed, 95% CI
1.3.1 Self-etch adhesives						
Oz, 2022	0	42	1	40	24.8%	-0.03 [-0.09, 0.04]
Subtotal (95% CI)		**42**		**40**	**24.8%**	**-0.03 [-0.09, 0.04]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.74 (P = 0.46)						
1.3.2 Total-etch adhesives						
Haak, 2018	0	22	1	22	13.3%	-0.05 [-0.16, 0.07]
Haak, 2019	0	55	9	55	33.3%	-0.16 [-0.26, -0.06]
Oz, 2018	0	20	0	29	14.3%	0.00 [-0.08, 0.08]
Oz, 2018	1	20	0	29	14.3%	0.05 [-0.07, 0.17]
Subtotal (95% CI)		**117**		**135**	**75.2%**	**-0.07 [-0.13, -0.01]**
Total events	1		10			
Heterogeneity: Chi^2 = 10.38, df = 3 (P = 0.02); I^2 = 71%						
Test for overall effect: Z = 2.40 (P = 0.02)						
Total (95% CI)		**159**		**175**	**100.0%**	**-0.06 [-0.11, -0.01]**
Total events	1		11			
Heterogeneity: Chi^2 = 10.55, df = 4 (P = 0.03); I^2 = 62%						
Test for overall effect: Z = 2.50 (P = 0.01)						
Test for subgroup differences: Chi^2 = 1.05, df = 1 (P = 0.31), I^2 = 4.9%						

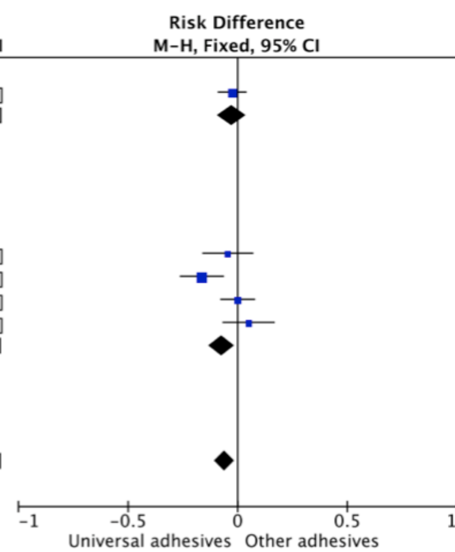

Figure 3. Retention of resin composite restorations placed with universal adhesives using the total-etch mode after 6 months of follow-up.

Study or Subgroup	Universal adhesives Events	Universal adhesives Total	Other adhesives Events	Other adhesives Total	Weight	Risk Difference M-H, Fixed, 95% CI
1.2.1 Self-etch adhesives						
Oz, 2022	0	42	1	40	9.9%	-0.03 [-0.09, 0.04]
Oz, 2022	2	38	1	40	9.5%	0.03 [-0.06, 0.11]
Zanatta, 2019	0	38	1	38	9.2%	-0.03 [-0.10, 0.04]
Subtotal (95% CI)		**118**		**118**	**28.6%**	**-0.01 [-0.05, 0.04]**
Total events	2		3			
Heterogeneity: $Chi^2 = 1.18$, df = 2 (P = 0.55); $I^2 = 0\%$						
Test for overall effect: Z = 0.36 (P = 0.72)						
1.2.2 Total-etch adhesives						
de Souza, 2019	1	37	1	37	9.0%	0.00 [-0.07, 0.07]
Haak, 2018	0	22	1	22	5.3%	-0.05 [-0.16, 0.07]
Hoshino, 2022	1	53	0	53	12.9%	0.02 [-0.03, 0.07]
Hoshino, 2022	1	53	0	53	12.9%	0.02 [-0.03, 0.07]
Lawson, 2015	0	41	1	41	10.0%	-0.02 [-0.09, 0.04]
Oz, 2018	0	22	0	29	6.1%	0.00 [-0.08, 0.08]
Oz, 2018	0	22	0	29	6.1%	0.00 [-0.08, 0.08]
Zanatta, 2019	0	38	0	38	9.2%	0.00 [-0.05, 0.05]
Subtotal (95% CI)		**288**		**302**	**71.4%**	**0.00 [-0.02, 0.02]**
Total events	3		3			
Heterogeneity: $Chi^2 = 2.18$, df = 7 (P = 0.95); $I^2 = 0\%$						
Test for overall effect: Z = 0.00 (P = 1.00)						
Total (95% CI)		**406**		**420**	**100.0%**	**-0.00 [-0.02, 0.02]**
Total events	5		6			
Heterogeneity: $Chi^2 = 3.70$, df = 10 (P = 0.96); $I^2 = 0\%$						
Test for overall effect: Z = 0.21 (P = 0.83)						
Test for subgroup differences: $Chi^2 = 0.10$, df = 1 (P = 0.75), $I^2 = 0\%$						

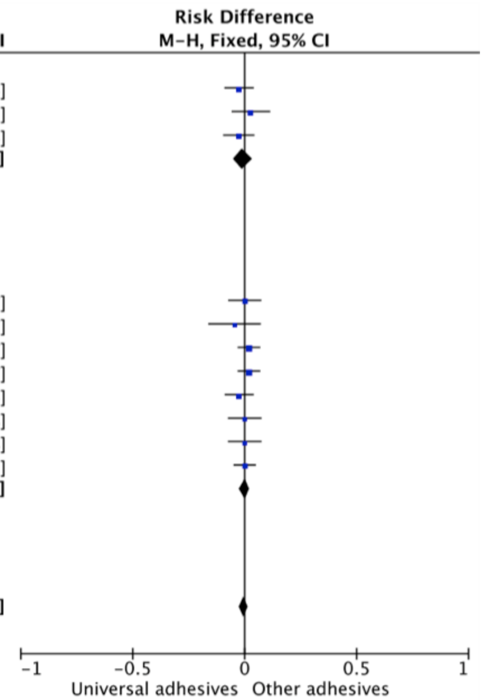

Figure 4. Retention of resin composite restorations placed with universal adhesives using the selective enamel etch mode after 6 months of follow-up.

On the other hand, the retention of resin composite restorations after >12 months of follow-up was similar between TE and SE adhesives against UAs applied in SE (p=0.68), TE (p=0.22), and SEE (p=0.91) modes.

Study or Subgroup	Universal adhesives Events	Universal adhesives Total	Other adhesives Events	Other adhesives Total	Weight	Risk Difference M-H, Fixed, 95% CI
2.2.1 Self-etch adhesives						
Manarte-Monteiro, 2021	2	30	1	29	7.3%	0.03 [-0.08, 0.14]
Manarte-Monteiro, 2021	0	32	1	29	7.6%	-0.03 [-0.12, 0.05]
Oz, 2022	0	42	2	35	9.5%	-0.06 [-0.15, 0.03]
Oz, 2022	0	37	2	35	8.9%	-0.06 [-0.15, 0.03]
Zanatta, 2019	2	30	3	30	7.5%	-0.03 [-0.17, 0.11]
Subtotal (95% CI)		**171**		**158**	**40.8%**	**-0.03 [-0.08, 0.01]**
Total events	4		9			
Heterogeneity: $Chi^2 = 1.88$, df = 4 (P = 0.76); $I^2 = 0\%$						
Test for overall effect: Z = 1.36 (P = 0.17)						
2.2.2 Total-etch adhesives						
Dukic, 2021	5	42	2	43	10.6%	0.07 [-0.04, 0.19]
Dukic, 2021	5	42	5	42	10.4%	0.00 [-0.14, 0.14]
Dukic, 2021	5	42	1	41	10.3%	0.09 [-0.01, 0.20]
Lawson, 2015	0	38	3	38	9.5%	-0.08 [-0.18, 0.02]
Oz, 2018	0	18	0	24	5.1%	0.00 [-0.09, 0.09]
Oz, 2018	0	18	0	24	5.1%	0.00 [-0.09, 0.09]
Zanatta, 2019	2	30	4	36	8.1%	-0.04 [-0.18, 0.09]
Subtotal (95% CI)		**230**		**248**	**59.2%**	**0.01 [-0.04, 0.06]**
Total events	17		15			
Heterogeneity: $Chi^2 = 7.46$, df = 6 (P = 0.28); $I^2 = 20\%$						
Test for overall effect: Z = 0.46 (P = 0.65)						
Total (95% CI)		**401**		**406**	**100.0%**	**-0.01 [-0.04, 0.03]**
Total events	21		24			
Heterogeneity: $Chi^2 = 11.02$, df = 11 (P = 0.44); $I^2 = 0\%$						
Test for overall effect: Z = 0.41 (P = 0.68)						
Test for subgroup differences: $Chi^2 = 1.66$, df = 1 (P = 0.20), $I^2 = 39.8\%$						

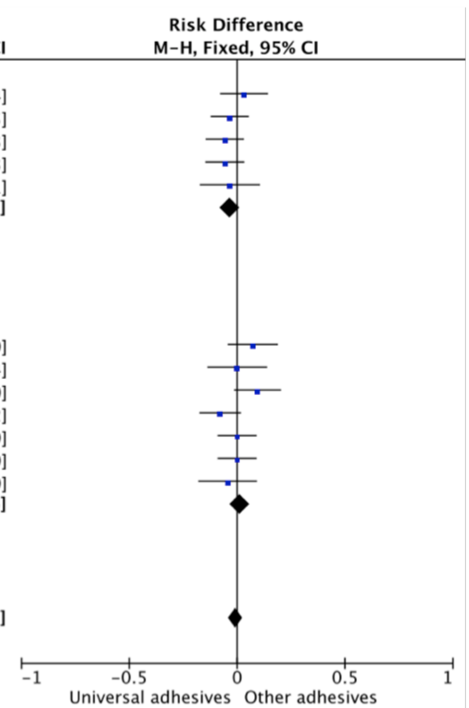

Figure 5. Retention of resin composite restorations placed with universal adhesives using the self-etch mode after >12 months of follow-up.

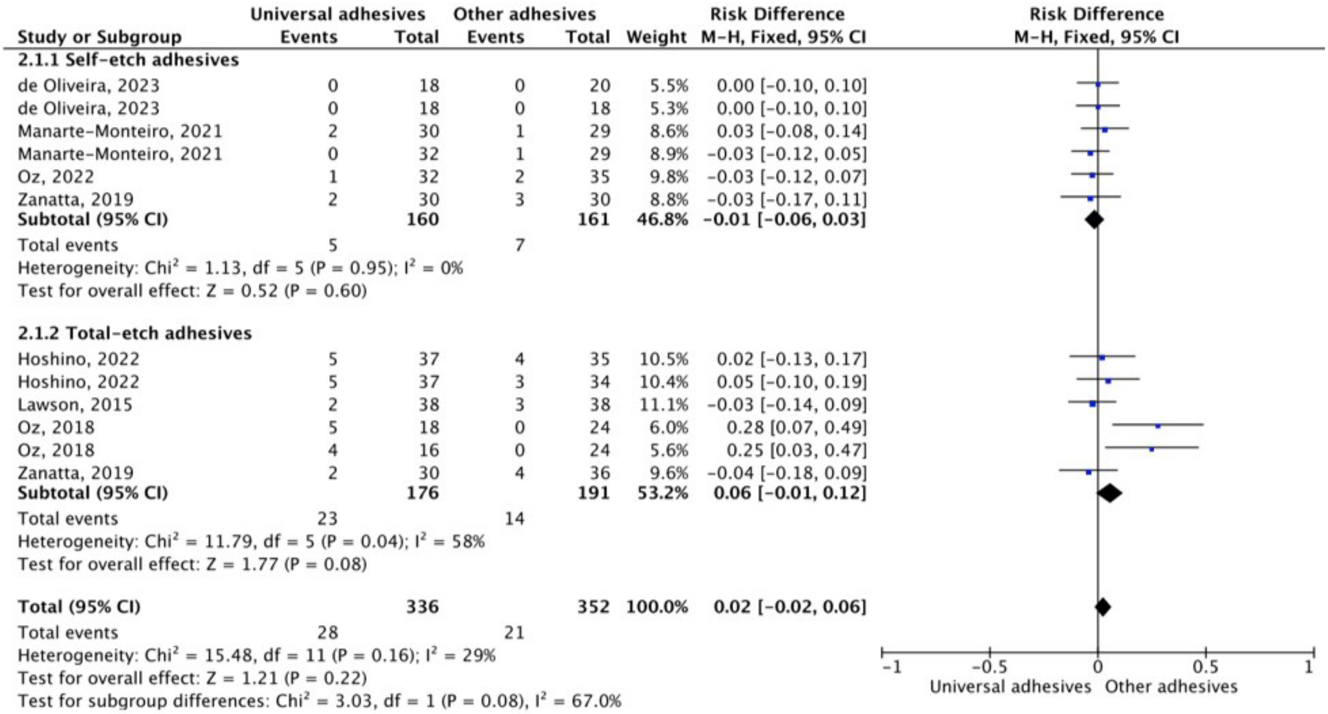

Figure 6. Retention of resin composite restorations placed with universal adhesives using the total-etch mode after >12 months of follow-up.

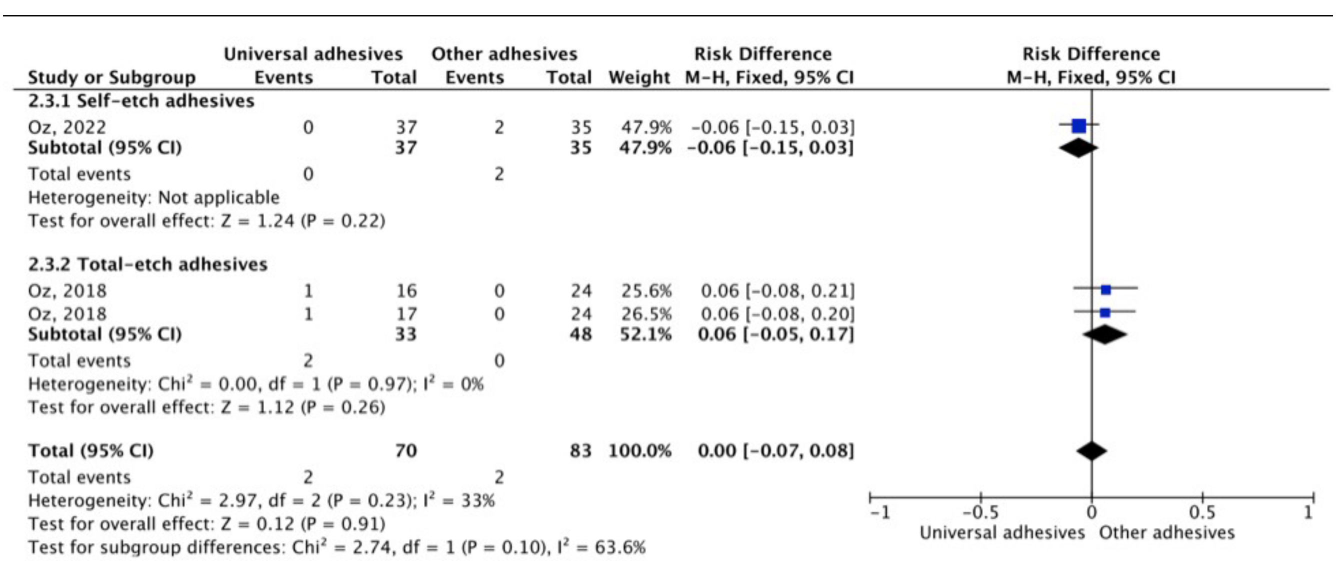

Figure 7. Retention of resin composite restorations placed with universal adhesives using the selective enamel etch mode after >12 months of follow-up.

The results from the meta-analysis of the secondary caries are presented in Figures 8-13. At 6-month evaluation, there were no statistically significant differences between TE or SE adhesives against UAs applied in the SE (p=1.00), TE (p=1.00), and SEE (p=1.00) modes.

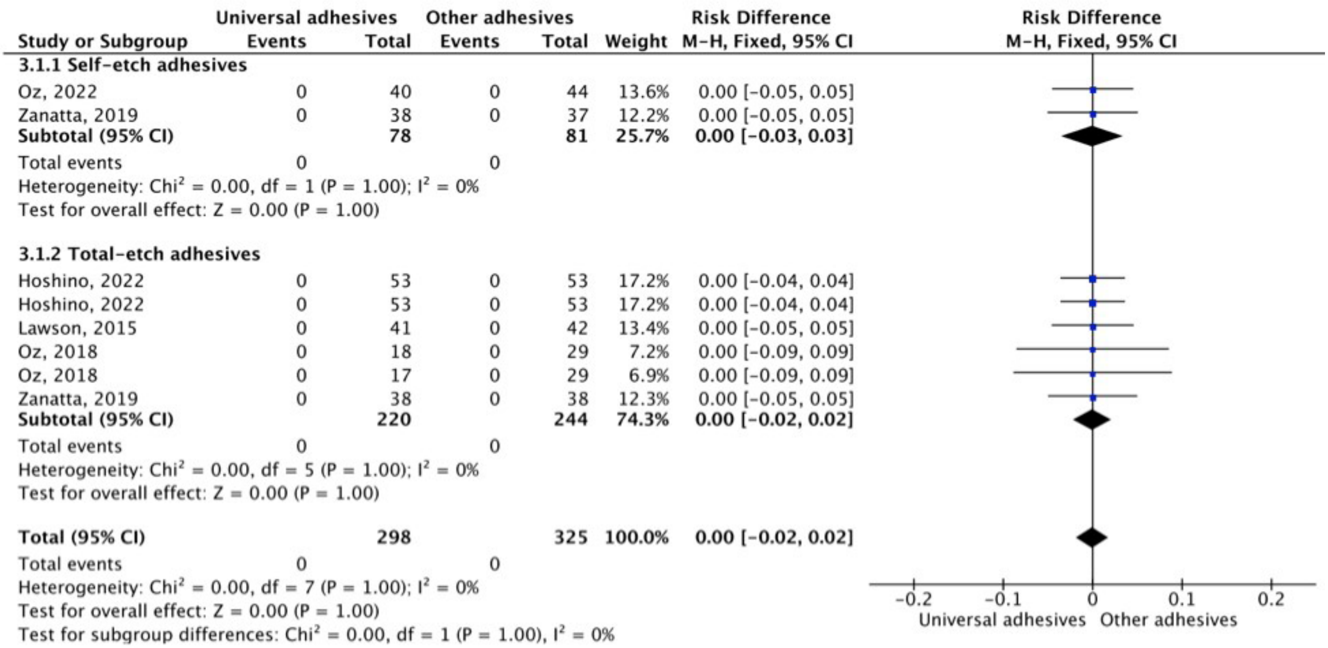

Figure 8. Secondary caries of resin composite restorations placed with universal adhesives using the self-etch approach at 6 months of follow-up.

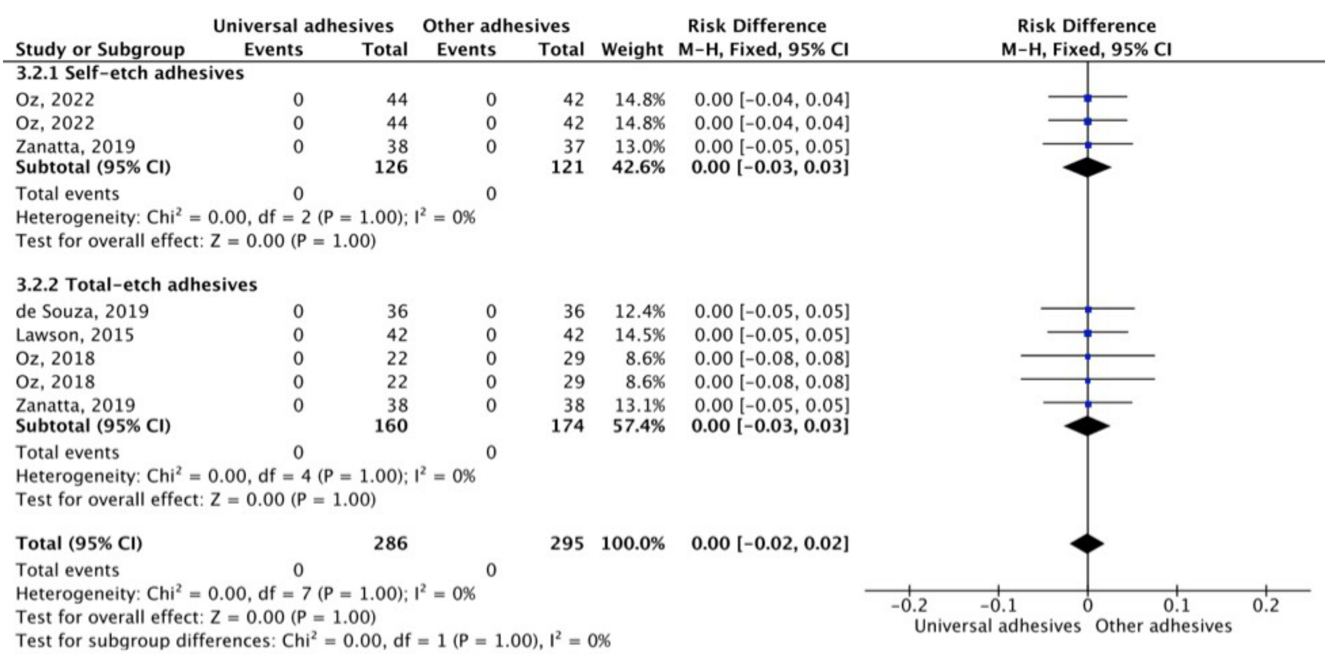

Figure 9. Secondary caries of resin composite restorations placed with universal adhesives using the total-etch approach at 6 months of follow-up.

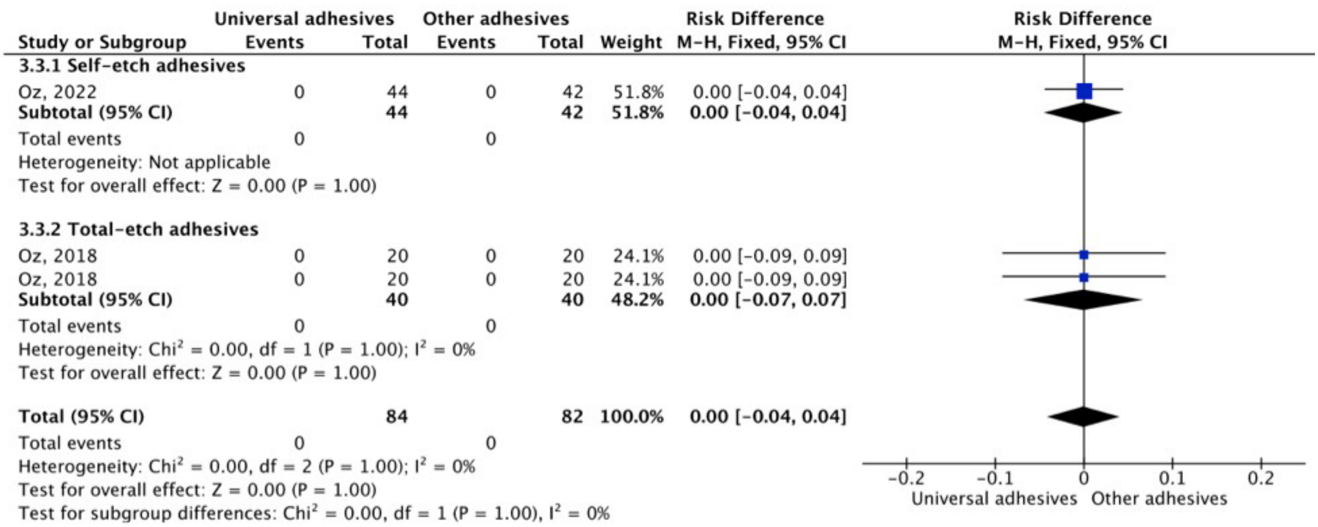

Figure 10. Secondary caries of resin composite restorations placed with universal adhesives using the selective enamel etching approach at 6 months of follow-up.

For the comparison performed at more than 12 months of follow-up, there were no statistically significant differences between TE or SE adhesives against UAs applied in the SE (p=0.82), TE (p=0.98), and SEE (p=1.00) modes.

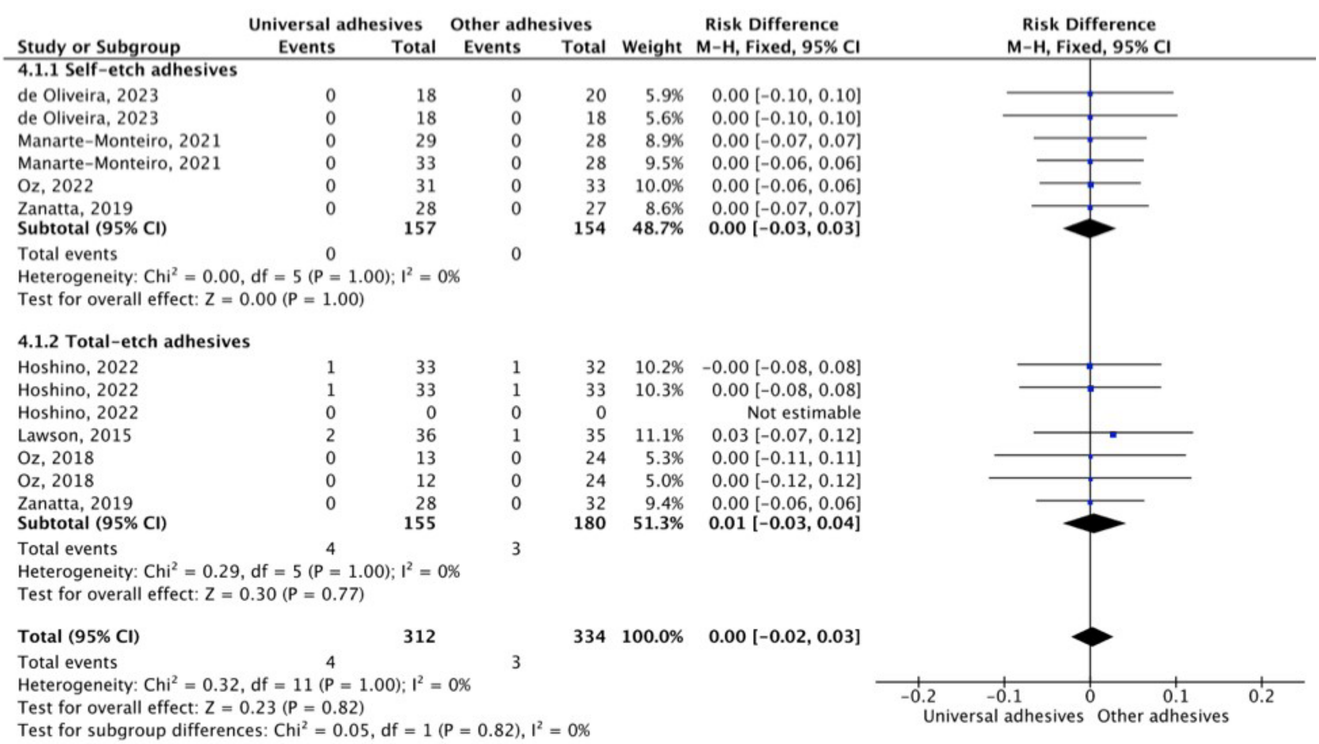

Figure 11. Secondary caries of resin composite restorations placed with universal adhesives using the self-etch approach at >12 months of follow-up.

Study or Subgroup	Universal adhesives Events	Universal adhesives Total	Other adhesives Events	Other adhesives Total	Weight	Risk Difference M-H, Fixed, 95% CI
4.2.1 Self-etch adhesives						
Manarte-Monteiro, 2021	0	29	0	28	7.3%	0.00 [-0.07, 0.07]
Manarte-Monteiro, 2021	0	31	0	28	7.5%	0.00 [-0.06, 0.06]
Oz, 2022	0	37	0	33	8.9%	0.00 [-0.05, 0.05]
Oz, 2022	0	37	0	33	8.9%	0.00 [-0.05, 0.05]
Zanatta, 2019	0	31	0	27	7.4%	0.00 [-0.07, 0.07]
Subtotal (95% CI)		**165**		**149**	**40.0%**	**0.00 [-0.03, 0.03]**
Total events	0		0			
Heterogeneity: $Chi^2 = 0.00$, df = 4 (P = 1.00); $I^2 = 0\%$						
Test for overall effect: Z = 0.00 (P = 1.00)						
4.2.2 Total-etch adhesives						
Dukic, 2021	0	42	0	43	10.9%	0.00 [-0.04, 0.04]
Dukic, 2021	0	42	0	42	10.7%	0.00 [-0.05, 0.05]
Dukic, 2021	0	42	0	41	10.6%	0.00 [-0.05, 0.05]
Lawson, 2015	1	38	1	35	9.3%	-0.00 [-0.08, 0.07]
Oz, 2018	0	18	0	24	5.3%	0.00 [-0.09, 0.09]
Oz, 2018	0	18	0	24	5.3%	0.00 [-0.09, 0.09]
Zanatta, 2019	0	31	0	32	8.0%	0.00 [-0.06, 0.06]
Subtotal (95% CI)		**231**		**241**	**60.0%**	**-0.00 [-0.02, 0.02]**
Total events	1		1			
Heterogeneity: $Chi^2 = 0.00$, df = 6 (P = 1.00); $I^2 = 0\%$						
Test for overall effect: Z = 0.03 (P = 0.98)						
Total (95% CI)		**396**		**390**	**100.0%**	**-0.00 [-0.02, 0.02]**
Total events	1		1			
Heterogeneity: $Chi^2 = 0.00$, df = 11 (P = 1.00); $I^2 = 0\%$						
Test for overall effect: Z = 0.02 (P = 0.98)						
Test for subgroup differences: $Chi^2 = 0.00$, df = 1 (P = 0.98), $I^2 = 0\%$						

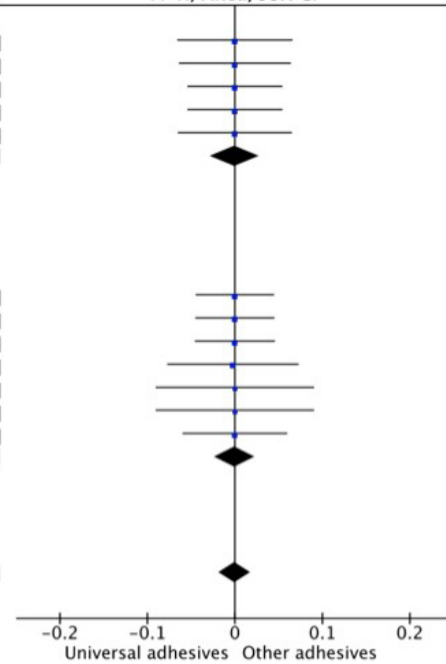

Figure 12. Secondary caries of resin composite restorations placed with universal adhesives using the total-etch approach at >12 months of follow-up.

Study or Subgroup	Universal adhesives Events	Universal adhesives Total	Other adhesives Events	Other adhesives Total	Weight	Risk Difference M-H, Fixed, 95% CI
4.3.1 Self-etch adhesives						
Oz, 2022	0	37	0	33	48.1%	0.00 [-0.05, 0.05]
Subtotal (95% CI)		**37**		**33**	**48.1%**	**0.00 [-0.05, 0.05]**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						
4.3.2 Total-etch adhesives						
Oz, 2018	0	15	0	24	25.4%	0.00 [-0.10, 0.10]
Oz, 2018	0	16	0	24	26.5%	0.00 [-0.10, 0.10]
Subtotal (95% CI)		**31**		**48**	**51.9%**	**0.00 [-0.07, 0.07]**
Total events	0		0			
Heterogeneity: $Chi^2 = 0.00$, df = 1 (P = 1.00); $I^2 = 0\%$						
Test for overall effect: Z = 0.00 (P = 1.00)						
Total (95% CI)		**68**		**81**	**100.0%**	**0.00 [-0.05, 0.05]**
Total events	0		0			
Heterogeneity: $Chi^2 = 0.00$, df = 2 (P = 1.00); $I^2 = 0\%$						
Test for overall effect: Z = 0.00 (P = 1.00)						
Test for subgroup differences: $Chi^2 = 0.00$, df = 1 (P = 1.00), $I^2 = 0\%$						

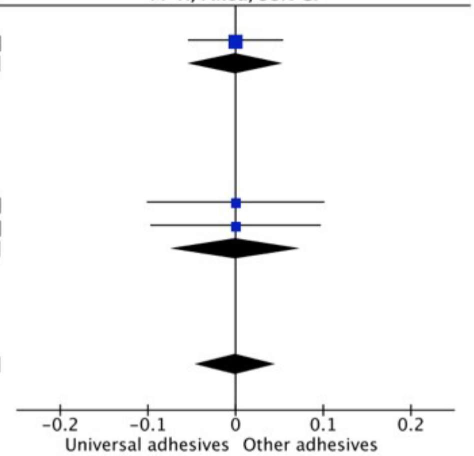

Figure 13. Secondary caries of resin composite restorations placed with universal adhesives using the selective enamel etching approach at >12 months of follow-up.

Regarding the methodological quality assessment parameters, most of the articles were categorized as having a low risk of bias since most of them reported the risk selected (Table 3).

Table 3: Qualitative synthesis (risk of bias assessment) for clinical trials.

Study	Selection bias	Performance and detection bias	Bias due to incomplete data	Reporting bias	Other bias
Haak, 2018 [37]	Low risk	Low risk	Low risk	Low risk	Low risk
Lawson, 2015 [38]	Low risk	Low risk	Low risk	Low risk	High risk
de Oliveria ,2023 [39]	Low risk	Low risk	Low risk	Low risk	High risk
van Dijken, 2017 [40]	Low risk	High risk	High risk	Low risk	High risk
Haak, 2019 [41]	Low risk	Low risk	Low risk	Low risk	Low risk
Handa, 2023 [42]	Low risk	High risk	High risk	Low risk	High risk
Oz, 2022 [43]	Low risk	Low risk	Low risk	Low risk	Low risk
Manarte-Monteiro, 2021 [44]	Low risk	Low risk	Low risk	Low risk	Low risk
de Souza, 2019 [45]	Low risk	Low risk	Low risk	Low risk	Low risk
Zanatta, 2019 [46]	Low risk	Low risk	Low risk	Low risk	Low risk
Oz, 2019 [47]	Low risk	Low risk	Low risk	Low risk	High risk
Haak, 2023 [48]	Low risk	Low risk	High risk	Low risk	Low risk
Dukić, 2021 [49]	Low risk	Low risk	Low risk	Low risk	Low risk
Hoshino, 2022 [50]	Low risk	Low risk	Low risk	Low risk	Low risk

Discussion

This systematic review and meta-analysis was directed to focus on the clinical performance of UAs compared to other adhesive systems for direct cavity restorations. As a result, the null hypothesis tested was partially accepted since a significant difference was found only in the retention rate for one mode (UAs in a SEE mode) after 6 months follow-up.

Randomized clinical trials are regarded as the gold standard approach for evaluating the dental treatment and are used as a reference by experts in their choices [38,39,51,52]. Research attempts to simplify multistep dental adhesives resulted in the invention of "universal" adhesives. UAs have gained popularity in dentistry due to their low toxicity, ability to be used in both SE and TE treatments, flexibility, and the number of application steps required [53]. Biomaterials' adhesion to enamel and dentin may become impaired with time, resulting in bond breakdown and NL [54].

The clinical evaluation of UAs in resin composite restorations across different cavity configurations is necessary to validate their effectiveness and reliability in real-world practice. Comprehensive clinical studies assessing parameters such as retention rates, marginal integrity, and secondary caries incidence are essential to establish the long-term performance of UAs in resin composite restorations. Such evaluations will provide valuable insights into the clinical efficacy and suitability of UAs as alternatives to traditional adhesive systems in modern restorative dentistry [27,55].

Prior investigations on many UAs assessed their BS in both TE and SE modes. For enamel, numerous authors [56,57] stated that the BS of a UA was considerably improved in the TE mode, however, for dentin, other findings [24,25,27] reported no difference in the immediate BS of pre-etched and self-etched dentin using various UAs. A UA with a pH of 2.7 exhibited higher BS when applied in the SE mode, both immediately and after one year of aqueous storage. Conversely, another UA with a pH of 3.2, demonstrated enhanced BS following dentin pre-etching. The UA systems evaluated in the present study have variable pH. Overall, while pre-etching enamel enhances the BS of UAs, consensus is lacking regarding the effect of pre-etching dentin [38].

It is strongly advised to perform an additional selective phosphoric-acid etching of the enamel cavity margins in order to provide an adequately retentive etching pattern [13,58,59]. When a SE adhesive was applied after enamel etching, higher enamel BS was shown experimentally and clinically with an enhanced marginal integrity and a lack of marginal discoloration [60,61].

For the retention rate of resin composite restorations after 6 months, the meta-analysis found no difference between TE and SE against UAs applied in TE (p=0.83) and SE (p=0.78) modes. On the other hand, the clinical performance of UAs applied in the SEE mode (p=0.01) was superior in comparison with other adhesives. The last result was more evident when the UAs were compared with TE adhesives (p=0.02).

When UAs were employed in the SEE mode, wherein only the enamel is etched while the dentin remains unetched, the retention rate displayed was notably higher compared to other adhesive systems. This could be linked to the selective etching process which improves adherence between the adhesive and the enamel substrate. This procedure removes the outer enamel layer, revealing the prismatic enamel structure, and forming a micromechanical interlocking surface for improved bonding [62,63].

The use of phosphoric acid etching on enamel surfaces offers several benefits in dental bonding procedures. Firstly, it improves surface wettability, which refers to the ability of a liquid, such as adhesive resin, to spread evenly across the enamel surface, ensuring better contact and adhesion [64]. Additionally, phosphoric acid etching increases surface roughness, creating microscopic irregularities on the enamel surface. These irregularities provide more surface area for the adhesive to bond to, improving the overall BS [65]. Moreover, phosphoric acid elevates the surface free energy of the enamel, which encourages better interaction and adhesion between the adhesive and the enamel [66]. Despite these benefits, it is critical to emphasize that phosphoric acid etching may lead to a slight decrease in enamel surface hardness. Yet, this reduction in hardness is generally considered acceptable in exchange for the improved bonding achieved through enhanced surface characteristics [67].

In contrast, applying phosphoric acid to the dentin structure reduces wettability and enhances hydrophobicity due to the intense demineralization of the smear layer and the superficial layer of dentin [68]. Further, aside from the adverse attributes of the substrate for adhesion, it was observed that the hydrophobic nature of demineralized dentin induces the migration of water from deeper dentin layers, resulting in weaker bonding leading to osmotic blisters and the hydrolysis of the adhesive itself [69]. Moreover, the use of phosphoric acid for etching dentin activates endogenous collagenolytic proteases, which are associated with the degradation of the interface between the adhesive and the dentin. Therefore, clinicians electing to employ UAs in a TE mode might notice shortcomings owing to the etchant's influence on both enamel and dentin, despite its several advantages for enamel bonding [70].

Hence, prior studies have illustrated that the selection of a UA in the SEE mode serves as an adaptation of the SE approach, presenting a more clinically relevant application than employing a UA in the TE mode for an advanced SE adhesive [22]. Although clinical retention remains largely unaffected by this process, incorporating additional enamel etching might enhance marginal adaptation and reduce marginal staining in cervical composite restorations [58]. These observations are supported both clinically and by optical coherence tomography, which revealed a significant reduction in adhesive defects following enamel etching, evident immediately after restoration placement. Prior to applying the mild SE-UA with a pH of 2.7, SEE emerges as an advocated approach to enhance enamel BS [18].

When UAs were applied in either TE or SE modes, involving simultaneous etching of both enamel and dentin or etching of dentin only, respectively, there were no significant differences in retention rates compared to TE or SE adhesives. While these techniques also create micromechanical retention through etching, they may not provide the same level of enamel surface preparation and bonding stability as SEE [21]. Enamel etching in TE and SE modes may be less controlled, potentially leading to variations in bonding effectiveness and retention rates over time [71].

Dentin, a more complex and diverse substrate than enamel, presents obstacles for adhesive bonding [72]. In TE mode, where both enamel and dentin are etched, the interaction of the adhesive with dentin may influence the overall BS and durability of the restoration [29]. Likewise, in SE mode, the self-etching adhesive system interacts directly with dentin, which can affect the quality of the formed bonds [73]. Discrepancies in dentin composition, moisture content, and dentinal tubule density may also lead to changes in bonding effectiveness between different adhesive systems and application methodologies [74].

The observed differences in retention rates between adhesive systems and application modes may reflect their long-term stability and clinical performance. While short-term studies regularly focus on immediate BS, long-term retention is crucial for the longevity and success of resin composite restorations. The superior retention rate of UAs in SEE mode implies that this application technique may offer enhanced resistance to degradation, marginal discoloration, and secondary caries formation with time [47]. This suggests that the mode of application may affect the adhesive's interaction with the tooth structure and its subsequent performance over time [75].

Overall, the findings shed light on the importance of considering the application mode of UAs in clinical practice using the SEE mode, as it can affect the long-term success (6 months here in this study) of resin composite restorations.

A previous systematic review of clinical trials highlights the noteworthy performance of two-bottle TE and SE materials over "simplified" one-bottle counterparts in meeting American Dental Association provisional acceptance criteria at 6 months [76]. These simplified adhesives, incorporating hydrophilic primers like 2-Hydroxyethyl methacrylate (HEMA), risk dentinal bond integrity due to their permeable adhesive layer, making them susceptible to hydrolytic degradation [77]. Nevertheless, certain UAs, although containing HEMA, demonstrate increased hydrophobicity due to the presence of 10-Methacryloyloxydecyl dihydrogen phosphate (10-MDP), which may account for their favorable performance compared to two-bottle TE materials [18,19,78,79]. Knowing that in the presence of HEMA, even in a low concentration, the mechanical integrity of the nano-layers (10-MDP and Ca) inside the adhesive, which were observed between MDP and mineralized tissue, is reduced [74]. Indeed, the incorporation of 10-MDP and other co-polymers in UAs promotes enhanced bonding to Ca, facilitating the cross-linking of collagen fibers and contributing to long-term clinical success [78,79].

This monomer (10-MDP) includes a phosphate radical as part of its molecule that, along with the carboxylate radical originating from the polyalkenoate copolymer in the UA, undergoes a reaction with the Ca from HAp to generate stable bonds known as ''HAp nano-layering'' [18,19,29]. This nano-layering is a crucial part of bonding to enamel and to dentin as well [46], and might provide an explanation for the satisfactory performance of this adhesive on the enamel, even when selective etching is not employed, as observed by the results obtained for the retention rates. Interestingly, the retention of resin composite restorations after more than 12 months of follow-up showed no significant difference between traditional TE and SE adhesives against UAs, regardless of the application mode [SE ($p=0.68$), TE ($p=0.22$), SEE ($p=0.91$)]. This insinuates that despite variances in adhesive composition and application technique, the long-term retention of composite restorations is analogous across various adhesive systems and modes of application.

The persistent integrity of the adhesive interfaces over time can be linked to a variety of factors which include the process of maturation of the adhesive layer and the formation of a resilient bond between the dental restorative material and the tooth structure [80]. As time passes, the dental restorations are exposed to chemical and mechanical stresses by the oral environment, which redistributes the forces within the restoration. This process is a main contributor of the development of a more consistent interface. In addition, the adaptation of surrounding tissues to the dental restoration also affects its long-term retention [81]. The quality of the seal between the restoration and the tooth surface, commonly known as the marginal integrity, is essential for avoiding microleakage and subsequent bacterial entry, which can reduce the longevity of the restoration [82].

Moreover, the choice of the adhesive mode might influence the stress distribution within the restoration and its interaction with the tooth structure [8]. TE adhesives usually involve eliminating the smear layer and demineralizing the enamel and the dentin surfaces to deepen the penetration of the adhesive resin [83]. In contrast, SE adhesives are designed to concurrently etch and prime the tooth surface, which might not only lead to a more conservative approach, but may also result in variations in BS and long-term stability [6].

Furthermore, patient compliance with oral hygiene practices and dietary habits are examples of external factors that can significantly impact the longevity of resin composite restorations [84,85]. Insufficient oral hygiene and an excess of occlusal forces may amplify the risk of restoration failure due to frequent caries or fracture [86]. The long-term clinical performance can also be rooted to the operator's technique and the material handling during restoration placement. Ensuring proper isolation, adequate polymerization, and meticulous adaptation of the restoration to the tooth structure are imperative steps for achieving durable bonding [87].

To summarize, while the adhesive mode choice might affect the initial BS and short-term outcomes, a number of complex factors can determine the long-term success of resin composite restorations. Understanding these factors and optimizing adhesive protocols accordingly are paramount for enhancing the clinical performance and longevity of dental restorations. The long-term stability of adhesive interfaces may result in convergence in retention rates across different adhesive modes as the initial BS stabilizes over time, limiting further degradation or improvement [88]. While short-term studies prioritize BS, the success of resin composite restorations centers around factors like marginal integrity and resistance to microleakage and secondary caries [89]. Traditional TE and SE adhesive systems used in this review exhibit satisfactory long-term performance, indicating their effectiveness in providing durable bonds compared to UAs after >12 months.

Additionally, biological responses of the pulp-dentin complex and periodontal tissues may influence retention rates with time [90]. This was in disagreement with the findings of this meta-analysis. Despite variations in the adhesive method, similar retention rates between TE and SE adhesives against UAs after >12 months imply that both traditional and contemporary techniques offer lasting bonding solutions. Further research is merited to optimize adhesive protocols for enhanced clinical performance and restoration longevity.

Concerning the secondary caries, there were no statistically significant differences between TE or SE adhesives against UAs applied in the SE (p=1.00), TE (p=1.00), and SEE (p=1.00) modes after 6 months follow-up. The same finding was found for the comparison performed at more than 12 months of follow-up, there were no statistically significant differences between TE or SE adhesives against UAs applied in the SE (p=0.82), TE (p=0.98), and SEE (p=1.00) modes.

The absence of statistically significant differences in the incidence of secondary caries among restorations bonded with TE or SE adhesives compared to those bonded with UAs can be linked to multiple prospects. Variance exists in some clinical variables across time, resulting in different materials with varying clinical performance. Initially, it specifies that the adhesive method used may not be the main factor influencing the formation of secondary caries in resin composite restorations. Other determinants, like those that are specific to patients (oral hygiene habits and dietary choices), restoration-related factors (marginal adaptation and material composition), and clinical protocols (operator technique and post-operative care), could play a more major role in influencing the development of secondary caries [86,91,92].

Further, the absence of significant differences in the incidence of secondary caries across different adhesive modes insinuates that the adhesive interface created by TE, SE, and UAs may provide a comparable protection against the infiltration of bacteria and consequent caries formation. This finding highlights the importance of attaining a well-sealed restoration interface regardless of the adhesive method [86,91].

Yet, it is essential to carefully analyze these results. Factors like the duration of the follow-up, the criteria used in diagnosis of secondary caries, and the sample size could affect the outcomes of the study [92,93]. Also, variations in material handling may present a confounding variable that could impact the incidence of secondary caries. Overall, while these findings deliver important data related to the influence of adhesive method on secondary caries formation, further research with larger sample sizes and longer follow-up durations is vital to confirm these results and clarify the complex interactions between adhesive techniques and the growth of secondary caries in resin composite restorations [10,23].

This meta-analysis of clinical trials has provided valuable insights into the longitudinal visualization of primary indicators of adhesive breakdown across the entire interface between the tooth and the restoration. But, acknowledging the limitations of this study is crucial for future revisions and studies related to this subject. Firstly, the duration of the follow-up in the included trials were different, and longer-term studies could offer more comprehensive observations and a deeper understanding of adhesive performance over time. In addition, the range of cavity configurations involved in this analysis was limited, and further investigations should incorporate a broader spectrum of clinical scenarios to improve the generalizability of the outcomes. Furthermore, while the focus of this meta-analysis was on specific adhesive systems, the field of adhesive dentistry is continually evolving, and upcoming research should explore the performance of a wider range of adhesive formulations to capture the full spectrum of clinical applications and challenges.

Conclusions

In conclusion, this systematic review and meta-analysis suggested that UAs demonstrate comparable clinical performance to TE and SE adhesive systems in direct resin composite restorations, particularly in terms of restoration retention rates and incidence of secondary caries. Notably, no significant differences were observed in retention rates after 6 months and >12 months of follow-up across the various adhesive modes evaluated. However, UAs applied in SEE mode exhibited superior clinical outcomes compared to other adhesive systems. These findings indicate that UAs can be considered a viable alternative to traditional adhesive systems in clinical practice, offering flexibility in application while maintaining comparable long-term outcomes. Further research may be warranted to explore the potential benefits and limitations of UAs in specific clinical scenarios and patient populations.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

References

1. Thalacker C. Dental adhesion with resin composites: a review and clinical tips for best practice. British Dental Journal. 2022 May 13;232(9):615-9.
2. Opdam NJ, Collares K, Hickel R, Bayne SC, Loomans BA, Cenci MS, Lynch CD, Correa MB, Demarco F, Schwendicke F, Wilson NH. Clinical studies in restorative dentistry: new directions and new demands. Dental Materials. 2018 Jan 1;34(1):1-2.
3. Reis A, De Geus JL, Wambier L, Schroeder M, Loguercio AD. Compliance of randomized clinical trials in noncarious cervical lesions with the CONSORT statement: a systematic review of methodology. Operative dentistry. 2018 May 1;43(3):E129-51.
4. Van Meerbeek B, Peumans M, Poitevin A, Mine A, Van Ende A, Neves A, De Munck J. Relationship between bond-strength tests and clinical outcomes. Dental materials. 2010 Feb 1;26(2):e100-21.
5. Hardan L, Bourgi R, Cuevas-Suárez CE, Zarow M, Kharouf N, Mancino D, Villares CF, Skaba D, Lukomska-Szymanska M. The bond strength and antibacterial activity of the universal dentin bonding system: A systematic review and meta-analysis. Microorganisms. 2021 Jun 6;9(6):1230.
6. Bourgi R, Daood U, Bijle MN, Fawzy A, Ghaleb M, Hardan L. Reinforced Universal Adhesive by Ribose Crosslinker: A Novel Strategy in Adhesive Dentistry. Polymers 2021, 13, 704.
7. Kharouf N, Eid A, Hardan L, Bourgi R, Arntz Y, Jmal H, Foschi F, Sauro S, Ball V, Haikel Y, Mancino D. Antibacterial and bonding properties of universal adhesive dental polymers doped with pyrogallol. Polymers. 2021 May 11;13(10):1538.
8. Hardan L, Bourgi R, Cuevas-Suárez CE, Devoto W, Zarow M, Monteiro P, Jakubowicz N, Zoghbi AE, Skaba D, Mancino D, Kharouf N. Effect of different application modalities on the bonding performance of adhesive systems to dentin: a systematic review and meta-analysis. Cells. 2023 Jan 3;12(1):190.
9. Reis A, Carrilho M, Breschi L, Loguercio AD. Overview of clinical alternatives to minimize the degradation of the resin-dentin bonds. Operative dentistry. 2013 Jun 1;38(4):E103-27.
10. Mena-Serrano A, Kose C, De Paula EA, Tay LY, Reis A, Loguercio AD, Perdigão J. A new universal simplified adhesive: 6-month clinical evaluation. Journal of Esthetic and Restorative Dentistry. 2013 Feb;25(1):55-69.
11. Perdigão J, Kose C, Mena-Serrano AP, De Paula EA, Tay LY, Reis AL, Loguercio AD. A new universal simplified adhesive: 18-month clinical evaluation. Operative dentistry. 2014 Mar 1;39(2):113-27.
12. Lopes LD, Calazans FS, Hidalgo R, Buitrago LL, Gutierrez F, Reis A, Loguercio AD, Barceleiro MO. Six-month follow-up of cervical composite restorations placed with a new universal adhesive system: a randomized clinical trial. Operative dentistry. 2016 Sep 1;41(5):465-80.
13. Van Meerbeek B, Yoshihara K, Yoshida Y, Mine AJ, De Munck J, Van Landuyt KL. State of the art of self-etch adhesives. Dental materials. 2011 Jan 1;27(1):17-28.
14. Pashley DH, Tay FR, Breschi L, Tjäderhane L, Carvalho RM, Carrilho M, Tezvergil-Mutluay A. State of the art etch-and-rinse adhesives. Dental materials. 2011 Jan 1;27(1):1-6.
15. Moszner N, Hirt T. New polymer‐chemical developments in clinical dental polymer materials: Enamel–dentin adhesives and restorative composites. Journal of Polymer Science Part A: Polymer Chemistry. 2012 Nov 1;50(21):4369-402.
16. Bourgi R, Kharouf N, Cuevas-Suárez CE, Lukomska-Szymańska M, Devoto W, Kassis C, Hasbini O, Mancino D, Haikel Y, Hardan L. Effect of Modified Triple-Layer Application on the Bond Strength of Different Dental Adhesive Systems to Dentin. Journal of Functional Biomaterials. 2023 Oct 17;14(10):522.
17. Hardan L, Orsini G, Bourgi R, Cuevas-Suárez CE, Nicastro M, Lazarescu F, Filtchev D, Cornejo-Ríos E, Zamarripa-Calderón JE, Sokolowski K, Lukomska-Szymanska M. Effect of active bonding application after selective dentin etching on the immediate and long-term bond strength of two universal adhesives to dentin. Polymers. 2022 Mar 11;14(6):1129.
18. Perdigão J, Loguercio AD. Universal or multi-mode adhesives: why and how?. The journal of adhesive dentistry. 2014 Apr;16(2):193-4.
19. Alex G. Universal adhesives: the next evolution in adhesive dentistry. Compend Contin Educ Dent. 2015 Jan 1;36(1):15-26.
20. Nagarkar S, Theis-Mahon N, Perdigão J. Universal dental adhesives: Current status, laboratory testing, and clinical performance. Journal of Biomedical Materials Research Part B: Applied Biomaterials. 2019 Aug;107(6):2121-31.
21. Cuevas-Suarez CE, de Oliveira da Rosa WL, Lund RG, da Silva AF, Piva E. Bonding performance of universal adhesives: an updated systematic review and meta-analysis. Journal of Adhesive Dentistry. 2019 Jan 1;21(1).

22. Peumans M, De Munck J, Mine A, Van Meerbeek B. Clinical effectiveness of contemporary adhesives for the restoration of non-carious cervical lesions. A systematic review. Dental Materials. 2014 Oct 1;30(10):1089-103.

23. Loguercio AD, De Paula EA, Hass V, Luque-Martinez I, Reis A, Perdigão J. A new universal simplified adhesive: 36-Month randomized double-blind clinical trial. Journal of dentistry. 2015 Sep 1;43(9):1083-92.

24. Perdigão J, Sezinando A, Monteiro PC. Laboratory bonding ability of a multi-purpose dentin adhesive. American journal of dentistry. 2012 Jun 1;25(3):153.

25. Wagner A, Wendler M, Petschelt A, Belli R, Lohbauer U. Bonding performance of universal adhesives in different etching modes. Journal of dentistry. 2014 Jul 1;42(7):800-7.

26. Sezinando A, Perdigao J. Interfacial characterization of a new universal dentin adhesive. J Dent Res. 2012;91(Special Issue A).

27. Marchesi G, Frassetto A, Mazzoni A, Apolonio F, Diolosà M, Cadenaro M, Di Lenarda R, Pashley DH, Tay F, Breschi L. Adhesive performance of a multi-mode adhesive system: 1-year in vitro study. Journal of dentistry. 2014 May 1;42(5):603-12.

28. Perdigao J, Sezinando A, Monteiro P. Evaluation of a new universal adhesive using different bonding strategies. J Dent Res. 2012 Mar 21;91(Special issue A).

29. Hardan L, Bourgi R, Kharouf N, Mancino D, Zarow M, Jakubowicz N, Haikel Y, Cuevas-Suárez CE. Bond strength of universal adhesives to dentin: A systematic review and meta-analysis. Polymers. 2021 Mar 7;13(5):814.

30. Josic U, Mazzitelli C, Maravic T, Radovic I, Jacimovic J, Mancuso E, Florenzano F, Breschi L, Mazzoni A. The influence of selective enamel etch and self-etch mode of universal adhesives' application on clinical behavior of composite restorations placed on non-carious cervical lesions: A systematic review and meta-analysis. Dental Materials. 2022 Mar 1;38(3):472-88.

31. Perdigão J, Swift Jr EJ. Universal adhesives. Journal of Esthetic and Restorative Dentistry. 2015 Nov;27(6):331-4.

32. Purk JH, Dusevich V, Glaros A, Eick JD. Adhesive analysis of voids in class II composite resin restorations at the axial and gingival cavity walls restored under in vivo versus in vitro conditions. Dental Materials. 2007 Jul 1;23(7):871-7.

33. Hickel R, Peschke A, Tyas M, Mjör I, Bayne S, Peters M, Hiller KA, Randall R, Vanherle G, Heintze SD. FDI World Dental Federation: clinical criteria for the evaluation of direct and indirect restorations—update and clinical examples. Clinical oral investigations. 2010 Aug;14:349-66.

34. Cvar JF, Ryge G. Reprint of criteria for the clinical evaluation of dental restorative materials. 1971. Clinical oral investigations. 2005 Dec;9(4):215-32.

35. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Bmj. 2021 Mar 29;372.

36. Minozzi S, Cinquini M, Gianola S, Gonzalez-Lorenzo M, Banzi R. The revised Cochrane risk of bias tool for randomized trials (RoB 2) showed low interrater reliability and challenges in its application. Journal of clinical epidemiology. 2020 Oct 1;126:37-44.

37. Haak R, Schmidt P, Park KJ, Häfer M, Krause F, Ziebolz D, Schneider H. OCT for early quality evaluation of tooth–composite bond in clinical trials. Journal of dentistry. 2018 Sep 1;76:46-51.

38. Lawson NC, Robles A, Fu CC, Lin CP, Sawlani K, Burgess JO. Two-year clinical trial of a universal adhesive in total-etch and self-etch mode in non-carious cervical lesions. Journal of dentistry. 2015 Oct 1;43(10):1229-34.

39. de Oliveira RP, de Paula BL, de Melo Alencar C, Alves EB, Silva CM. A randomized clinical study of the performance of self-etching adhesives containing HEMA and 10-MDP on non-carious cervical lesions: A 2-year follow-up study. Journal of Dentistry. 2023 Mar 1;130:104407.

40. van Dijken JW, Pallesen U. Three-year Randomized Clinical Study of a One-step Universal Adhesive and a Two-step Self-etch Adhesive in Class II Composite Restorations. Journal of Adhesive Dentistry. 2017 Jul 1;19(4).

41. Haak R, Hähnel M, Schneider H, Rosolowski M, Park KJ, Ziebolz D, Häfer M. Clinical and OCT outcomes of a universal adhesive in a randomized clinical trial after 12 months. Journal of dentistry. 2019 Nov 1;90:103200.

42. Handa A, Bhullar KK, Batra D, Brar RS, Khanna M, Malhotra S. Clinical performance of various bonding agents in noncarious cervical defects. Journal of Conservative Dentistry and Endodontics. 2023 May 1;26(3):271-4.

43. Oz FD, Dursun MN, Ergin E. Clinical Performance of a" No Wait" Universal Adhesive in Noncarious Cervical Lesions: A Two-year Randomized Controlled Clinical Trial. The Journal of Adhesive Dentistry. 2022 Aug 1;24(1):313-23.

44. Manarte-Monteiro P, Domingues J, Teixeira L, Gavinha S, Manso MC. Universal adhesives and adhesion modes in non-carious cervical restorations: 2-year randomised clinical trial. Polymers. 2021 Dec 22;14(1):33.

45. Souza MY, Jurema AL, Caneppele TM, Bresciani E. Six-month performance of restorations produced with the ethanol-wet-bonding technique: a randomized trial. Brazilian oral research. 2019 Jul 1;33:e052.

46. Zanatta RF, Silva TM, Esper MA, Bresciani E, Goncalves SE, Caneppele TM. Bonding performance of simplified adhesive systems in noncarious cervical lesions at 2-year follow-up: a double-blind randomized clinical trial. Operative dentistry. 2019 Sep 1;44(5):476-87.

47. Oz FD, Ergin E, Canatan S. Twenty-four-month clinical performance of different universal adhesives in etch-and-rinse, selective etching and self-etch application modes in NCCL–a randomized controlled clinical trial. Journal of applied oral science. 2019 Apr 11;27:e20180358.

48. Haak R, Stache G, Schneider H, Häfer M, Schmalz G, Schulz-Kornas E. Effect of the Adhesive Strategy on Clinical Performance and Marginal Integrity of a Universal Adhesive in Non-Carious Cervical Lesions in a Randomized 36-Month Study. Journal of Clinical Medicine. 2023 Sep 5;12(18):5776.

49. Dukić W, Majić M, Prica N, Oreški I. Clinical evaluation of flowable composite materials in permanent molars small class I restorations: 3-year double blind clinical study. Materials. 2021 Jul 31;14(15):4283.

50. Endo Hoshino IA, Fraga Briso AL, Bueno Esteves LM, Dos Santos PH, Meira Borghi Frascino S, Fagundes TC. Randomized prospective clinical trial of class II restorations using flowable bulk-fill resin composites: 4-year follow-up. Clinical Oral Investigations. 2022 Sep;26(9):5697-710.

51. Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials. The lancet. 2001 Apr 14;357(9263):1191-4.

52. Moher D, Jones A, Lepage L, Consort Group, CONSORT Group. Use of the CONSORT statement and quality of reports of randomized trials: a comparative before-and-after evaluation. Jama. 2001 Apr 18;285(15):1992-5.

53. Jang JH, Lee MG, Woo SU, Lee CO, Yi JK, Kim DS. Comparative study of the dentin bond strength of a new universal adhesive. Dental materials journal. 2016 Jul 29;35(4):606-12.

54. Brkanović S, Sever EK, Vukelja J, Ivica A, Miletić I, Krmek SJ. Comparison of Different Universal Adhesive Systems on Dentin Bond Strength. Materials. 2023 Feb 12;16(4):1530.

55. Loguercio AD, Reis A, Bortoli G, Patzlaft R, Kenshima S, Filho LR, Accorinte MD, Van Dijken JW. Influence of adhesive systems on interfacial dentin gap formation in vitro. Operative Dentistry. 2006 Jul 1;31(4):431-41.

56. Fernando de Goes M, Sanae Shinohara M, Santiago Freitas M. Performance of a new one-step multi-mode adhesive on etched vs non-etched enamel on bond strength and interfacial morphology. Journal of Adhesive Dentistry. 2014 May 1;16(3).

57. Takamizawa T, Barkmeier WW, Tsujimoto A, Scheidel DD, Erickson RL, Latta MA, Miyazaki M. Effect of phosphoric acid pre-etching on fatigue limits of self-etching adhesives. Operative dentistry. 2015 Jun 1;40(4):379-95.

58. Schroeder M, Correa IC, Bauer J, Loguercio AD, Reis A. Influence of adhesive strategy on clinical parameters in cervical restorations: A systematic review and meta-analysis. Journal of dentistry. 2017 Jul 1;62:36-53.

59. Frankenberger R, Lohbauer U, Roggendorf MJ, Naumann M, Taschner M. Selective enamel etching reconsidered: better than etch-and-rinse and self-etch?. Journal of Adhesive Dentistry. 2008 Sep 1;10(5).

60. Peumans M, De Munck J, Van Landuyt KL, Poitevin A, Lambrechts P, Van Meerbeek B. Eight-year clinical evaluation of a 2-step self-etch adhesive with and without selective enamel etching. Dental Materials. 2010 Dec 1;26(12):1176-84.

61. Qin W, Lei L, Huang QT, Wang L, Lin ZM. Clinical effectiveness of self-etching adhesives with or without selective enamel etching in noncarious cervical lesions: A systematic review. Journal of Dental Sciences. 2014 Dec 1;9(4):303-12.

62. Cardenas AM, Siqueira F, Rocha J, Szesz AL, Anwar M, El-Askary F, Reis A, Loguercio A. Influence of conditioning time of universal adhesives on adhesive properties and enamel-etching pattern. Operative dentistry. 2016 Sep 1;41(5):481-90

63. Wong J, Tsujimoto A, Fischer NG, Baruth AG, Barkmeier WW, Johnson EA, Samuel SM, Takamizawa T, Latta MA, Miyazaki M. Enamel etching for universal adhesives: Examination of enamel etching protocols for optimization of bonding effectiveness. Operative dentistry. 2020 Jan 1;45(1):80-91.

64. Retief DH, Middleton JC, Jamison HC. Optimal concentration of phosphoric acid as an etching agent. Part III: Enamel wettability studies. The Journal of Prosthetic Dentistry. 1985 Jan 1;53(1):42 6.

65. Barkmeier WW, Erickson RL, Kimmes NS, Latta MA, Wilwerding TM. Effect of enamel etching time on roughness and bond strength. Operative dentistry. 2009 Mar 1;34(2):217-22.

66. Tsujimoto A, Iwasa M, Shimamura Y, Murayama R, Takamizawa T, Miyazaki M. Enamel bonding of single-step self-etch adhesives: influence of surface energy characteristics. Journal of dentistry. 2010 Feb 1;38(2):123-30.

67. Zafar MS, Ahmed N. The effects of acid etching time on surface mechanical properties of dental hard tissues. Dental Materials Journal. 2015 May 29;34(3):315-20.

68. Yamauchi K, Tsujimoto A, Jurado CA, Shimatani Y, Nagura Y, Takamizawa T, Barkmeier WW, Latta MA, Miyazaki M. Etch-and-rinse vs self-etch mode for dentin bonding effectiveness of universal adhesives. Journal of oral science. 2019;61(4):549-53.

69. Tay FR, Pashley DH. Have dentin adhesives become too hydrophilic?. Journal-Canadian Dental Association. 2003 Dec 1;69(11):726-32.

70. Breschi L, Mazzoni A, Ruggeri A, Cadenaro M, Di Lenarda R, Dorigo ED. Dental adhesion review: aging and stability of the bonded interface. Dental materials. 2008 Jan 1;24(1):90-101.

71. Da Rosa WL, Piva E, da Silva AF. Bond strength of universal adhesives: A systematic review and meta-analysis. Journal of dentistry. 2015 Jul 1;43(7):765-76.

72. Bourgi R, Hardan L, Rivera-Gonzaga A, Cuevas-Suárez CE. Effect of warm-air stream for solvent evaporation on bond strength of adhesive systems: A systematic review and meta-analysis of in vitro studies. International Journal of Adhesion and Adhesives. 2021 Mar 1;105:102794.

73. Fabiao AD, Fronza BM, André CB, Cavalli V, Giannini M. Microtensile dentin bond strength and interface morphology of different self-etching adhesives and universal adhesives applied in self-etching mode. Journal of Adhesion Science and Technology. 2021 Apr 3;35(7):723-32.

74. Bourgi R, Hardan L, Cuevas-Suárez CE, Devoto W, Kassis C, Kharma K, Harouny R, Ashi T, Mancino D, Kharouf N, Haikel Y. Effectiveness of Different Application Modalities on the Bond Performance of Four Polymeric Adhesive Systems to Dentin. Polymers. 2023 Sep 28;15(19):3924.

75. Perdigão J, Araujo E, Ramos RQ, Gomes G, Pizzolotto L. Adhesive dentistry: Current concepts and clinical considerations. Journal of Esthetic and restorative Dentistry. 2021 Jan;33(1):51-68.

76. Rêgo HM, Alves TS, Bresciani E, Niu LN, Tay FR, Pucci CR. Can long-term dentine bonding created in real life be forecasted by parameters established in the laboratory?. Scientific reports. 2016 Nov 25;6(1):37799.

77. Häfer M, Schneider H, Rupf S, Busch I, Fuchß A, Merte I, Jentsch H, Haak R, Merte K. Experimental and clinical evaluation of a self-etching and an etch-and-rinse adhesive system. J Adhes Dent. 2013 May 1;15(3):275-86.

78. Häfer M, Jentsch H, Haak R, Schneider H. A three-year clinical evaluation of a one-step self-etch and a two-step etch-and-rinse adhesive in non-carious cervical lesions. Journal of dentistry. 2015 Mar 1;43(3):350-61.

79. Heintze SD, Rousson V, Mahn E. Bond strength tests of dental adhesive systems and their correlation with clinical results–a meta-analysis. Dental materials. 2015 Apr 1;31(4):423-34.

80. Carvalho RM, Manso AP, Geraldeli S, Tay FR, Pashley DH. Durability of bonds and clinical success of adhesive restorations. Dental materials. 2012 Jan 1;28(1):72-86.

81. Ikeda M, Kurokawa H, Sunada N, Tamura Y, Takimoto M, Murayama R, Ando S, Miyazaki M. Influence of previous acid etching on dentin bond strength of self-etch adhesives. Journal of oral science. 2009;51(4):527-34.

82. Heintze SD, Ruffieux C, Rousson V. Clinical performance of cervical restorations—a meta-analysis. dental materials. 2010 Oct 1;26(10):993-1000.

83. Takamizawa T, Barkmeier WW, Tsujimoto A, Berry TP, Watanabe H, Erickson RL, Latta MA, Miyazaki M. Influence of different etching modes on bond strength and fatigue strength to dentin using universal adhesive systems. Dental Materials. 2016 Feb 1;32(2):e9-21.

84. Powers JM, Wataha JC. Dental Materials-E-Book: Foundations and Applications. Elsevier Health Sciences; 2015 Dec 27.

85. Brunthaler A, König F, Lucas T, Sperr W, Schedle A. Longevity of direct resin composite restorations in posterior teeth: a review. Clinical oral investigations. 2003 Jun;7:63-70.

86. Ferracane JL. Resin composite—state of the art. Dental materials. 2011 Jan 1;27(1):29-38.

87. Ferracane JL. Hygroscopic and hydrolytic effects in dental polymer networks. Dental Materials. 2006 Mar 1;22(3):211-22.

88. Van Meerbeek B, De Munck J, Yoshida Y, Inoue S, Vargas M, Vijay P, Van Landuyt K, Lambrechts P, Vanherle G. Adhesion to enamel and dentin: current status and future challenges. Operative Dentistry-University of Washington-. 2003 Oct;28(3):215-35.

89. Loguercio AD, Bittencourt DD, Baratieri LN, Reis A. A 36-month evaluation of self-etch and etch-and-rinse adhesives in noncarious cervical lesions. The Journal of the American Dental Association. 2007 Apr 1;138(4):507-14.

90. Heintze SD. Clinical relevance of tests on bond strength, microleakage and marginal adaptation. Dental Materials. 2013 Jan 1;29(1):59-84.

91. Mjör IA, Moorhead JE, Dahl JE. Reasons for replacement of restorations in permanent teeth in general dental practice. International dental journal. 2000 Dec 1;50(6):361-6.

92. Opdam NJ, Bronkhorst EM, Loomans BA, Huysmans MC. 12-year survival of composite vs. amalgam restorations. Journal of dental research. 2010 Oct;89(10):1063-7.

93. Inoue S, Vargas MA, Abe Y, Yoshida Y, Lambrechts P, Vanherle G, Sano H, Van Meerbeek B. Microtensile bond strength of eleven contemporary adhesives to dentin. Journal of Adhesive Dentistry. 2001 Sep 1;3(3).