Original Article

Clinical effects of different etching modes for universal adhesives: a systematic review and meta-analysis

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Background: To evaluate the clinical performance of universal adhesives in etch-and-rinse or self-etch application modes through meta-analysis.

Methods: A literature search was performed by two reviewers in the PubMed, Cochrane Library, and Embase databases (from January 2000 to March 2020). A total of 2,516 non-replicated records were identified and filtered. Studies that evaluated the clinical performance of universal adhesives using etch-and-rinse or self-etch mode were included. RevMan 5.3.5 (Cochrane, London, UK) was used to perform the meta-analysis.

Results: A total of 13 studies were included in the meta-analysis. The retention rates were higher in etch-and-rinse groups compared with self-etch groups [odds ratio (OR) =0.35, 95% confidence interval (CI): 0.18–0.71, P=0.003]. The etch-and-rinse approach also had better performance in marginal adaptation (OR =0.49, 95% CI: 0.36–0.67, P<0.001) and marginal staining (OR =0.49, 95% CI: 0.36–0.66, P<0.001). The current data showed a very low incidence rate of secondary caries or postoperative sensitivity, and there were no significant differences in the incidence rates between the etch-and-rinse groups and self-etch groups.

Discussion: The current evidence shows that, compared with self-etch approach, the etch-and-rinse approach for universal adhesives provides improved clinical outcomes in terms of retention rates, marginal adaptation, and marginal staining.

Keywords: Adhesive; etch-and-rinse; self-etch; dental bonding; universal adhesives

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Introduction

To restore cavities in teeth, adhesive is used to bond dental resin with teeth. Numerous adhesives have been developed to achieve a simplified adhesion process as well as a satisfying bonding performance (1). The latest generation of dental adhesive is known as universal adhesive (2). Universal adhesives are essentially self-etch adhesives that may be used in etch-and-rinse (with phosphoric acid etching) or self-etch (without phosphoric acid etching) modes (3). Although clinicians are encouraged to apply different bonding strategies depending on the specific clinical situation and their personal preferences (4), the optimal bonding strategy, which will lead to better clinical outcomes, remains questionable.

Several *in vitro* studies have been conducted to evaluate characteristics of universal adhesives (5-8). Etching mode and thermomechanical loading significantly influenced the marginal integrity of universal adhesives. Kaczor *et al.* found that significant better marginal integrity was observed in etch-and-rinse groups compared with self-etch groups in enamel. In dentin, the greatest percentage of continuous margin was achieved for Adhese Universal in the ER group (100%) before TML and for both universal adhesives in the SE groups (61%) after TML. Thermomechanical loading did not influence the margin integrity in the enamel, while it did influence the margin integrity in dentin (6). Diniz *et al.* found that etch-and-rinse approach lead to higher bond strength of enamel compared with self-etch approach (9). Stape *et al.* reported that different etching methods, etching time, and the pH of universal adhesives are factors which are susceptible to the fatigue strength and dentin bonding properties of universal adhesives (10). Hirokane *et al.* found that double layer application techniques increase early enamel bond strength of universal adhesives. The effect may resulted from enhancing the bond durability of universal adhesives in terms of fatigue stress (11). Surmelioglu *et al.* found that total-etching with either flattening and/or phototherapy have a higher shear bond strength compared with self-etching after immediate bleaching (12). Shafiei *et al.* reported that in the groups with no pretreatment, the expert group did not showed positive effect on the bonding effectiveness of resin cement compared with the student group. But in the groups with a 2-step adhesive pretreatment, the expert group obtained better results compared with the student group (13).

Based on these studies, several meta-analysis studies have also published. Rosa *et al.* found that the etch-and-rinse strategy improved the enamel bond strength of universal adhesives (14). However, for dentin bond strength, an ultra-mild universal adhesive was improved by the etch-and-rinse strategy, while no significant difference was observed between groups of mild universal adhesives (14). Similar results were confirmed by Cuevas-Suárez *et al.* and Elkaffas *et al.* (15,16). Kaczor *et al.* performed a meta-analysis on nanoleakage of universal adhesives (1), and found that the results were contradictory among different universal adhesives. The etch-and-rinse strategy reduced nanoleakage of G-Bond Plus and Peak Universal adhesives (Ultradent, UT, USA), while the self-etch strategy reduced nanoleakage of All-Bond Universal (Bisco, IL, USA). For Prime&Bond Elect (Dentsply Caulk, DE, USA) or Scotchbond Universal (3M, MN, USA), no significant difference in nanoleakage was found between the two etching strategies (1). The results from these studies are valuable, however, results from *in vivo* study also are needed.

Some randomized clinical trials have demonstrated better clinical outcomes of the etch-and-rinse mode compared to self-etch mode. Oz *et al.* found that universal adhesives exhibited better results in retention using the etch-and-rinse mode (17). Atalay *et al.* reported that a less satisfying performance of marginal adaptation and marginal staining was observed when using the self-etch mode (18). Perdigão *et al.* showed improved clinical performance of universal adhesives when using the etch-and-rinse strategy, regardless of whether the three-step or two-step etch-and-rinse strategy was employed (19). Nevertheless, some studies showed no statistically significant differences in clinical performance between the etch-and-rinse and self-etch modes (20-22). Although these studies helped us to better understand the operation strategy of using universal adhesives, a consensus has not yet been achieved. Thus, a systematic review and meta-analysis is urgently needed to assemble the data and offer a clear conclusion.

In this study, we systematically reviewed the randomized clinical trial literature regarding the clinical performance of universal adhesives using the etch-and-rinse or self-etch modes. The hypothesis tested was that there is no difference in the clinical performance when using universal adhesives with either the etch-and-rinse or self-etch strategy. The results showed that, compared with the self-etch approach, the etch-and-rinse approach for universal adhesives improved clinical outcomes in terms of retention rates, marginal adaptation, and marginal staining. We present the following article in accordance with the PRISMA reporting checklist (available at http://dx.doi.org/10.21037/apm-21-890).

Methods

This meta-analysis was conducted in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement (23). The research question was as follows: do different etch modes (etch-and-rinse *vs.* self-etch) affect the clinical performance of universal adhesives? This review was not registered. The review protocol was not prepared. If more information needed, please contact the corresponding author.

Search strategy

Two independent reviewers performed the literature search for articles from January 1st, 2000 to March 6th, 2020, in the PubMed (https://pubmed.ncbi.nlm.nih.gov/), Embase (https://www.embase.com/), and Cochrane Library (https://www.cochranelibrary.com/) databases. The search strategy is shown in *Table 1*. The references of the included literature were also screened to identify additional potential

Table 1 Search strategy used in PubMed

Steps	Search terms
#1	((((((Root Caries[MeSH Terms]) OR (Dental Caries[MeSH Terms])) OR (Noncarious Cervical Lesions[Title/Abstract])) OR (non-carious cervical lesions[Title/Abstract])) OR (NCCLs[Title/Abstract])) OR (caries[Title/Abstract])) OR (cavities[Title/Abstract])
#2	((((((((adhesive[MeSH Terms]) OR (adhesive[Title/Abstract])) OR (Single Bond[Title/Abstract])) OR (bonding agent[Title/Abstract])) OR (self-etching[Title/Abstract])) OR (self-etch[Title/Abstract])) OR (etch[Title/Abstract] AND rinse[Title/Abstract])) OR (etch-and-rinse[Title/Abstract])) OR (acid etching[Title/Abstract])
#3	((((((randomized controlled trial[Publication Type]) OR (randomized controlled trial[Title/Abstract])) OR (clinical trial[Title/Abstract])) OR (randomized[Title/Abstract])) OR (randomly[Title/Abstract])) OR (trial[Title/Abstract])) OR (Groups[Title/Abstract])
#4	#1 AND #2 AND #3

studies. All of the studies were imported into NoteExpress 3.0.2.6390 software (Beijing, China) to manage the references sufficiently.

Study selection

Duplicate studies obtained from different databases were removed using the NoteExpress software. The titles and abstracts of the studies were assessed by two reviewers. Studies fulfilling all of the following criteria were included: (I) the study was a randomized clinical trial; (II) at least one universal adhesive was used in the study; (III) both the etch-and-rinse and self-etch modes were used in different groups; (IV) the United States Public Health Service (USPHS) or World Dental Federation (FDI) criteria was used for clinical evaluation; and (V) the study was published in English. The exclusion criteria were as follows: (I) *in vitro* studies; (II) studies that did not include all experimental groups; (III) detailed data was not available; (IV) studies involving multiple reports of the same cohort; and (V) pilot studies, study protocols, case reports, meta-analysis, and reviews. The full text of potential studies was read if the title and abstract did not contain sufficient data to make a clear decision. Disagreements between the two reviewers were resolved through discussion and consensus with a third reviewer.

Data extraction

Data was extracted from the included studies and tabulated with the help of WPS Office 2019 (Kingsoft office, Beijing, China). The following data were collected: the family name of the first author, year of publication, lesions of the teeth, criteria used for clinical evaluation, the last assessment time, and the clinical evaluation results of each group (including retention, marginal adaptation, marginal staining, recurrence of caries, and postoperative sensitivity). If multiple clinical results of different evaluation times were provided, we extracted the most recent results and used them in the meta-analysis. If the data of interest was not available from the article, we contacted the corresponding author via e-mail. If the author did not respond within 1 month, the missing information was not included.

Risk of bias assessment

Risk of bias of the included studies was assessed according to the guidelines of the PRISMA statement (23). The Cochrane Collaboration's tool for assessing the risk of bias in randomized trials was used to assess the risk of bias in the included studies. Seven items of each study were assessed, including random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other bias. Two reviewers independently performed the assessment, and disagreements were resolved through discussion and consensus with a third reviewer.

Risk of bias also was evaluated at the study level. Studies with six or seven low risks of bias items were considered as low risk of bias. Studies with four or five low risk of bias items were classified as medium risk of bias. Otherwise, the study was denoted as high risk of bias.

Statistical analysis

Meta-analysis was performed using Review Manager 5.3 (The Cochrane Collaboration, Copenhagen, Denmark). Retention, marginal adaptation, marginal staining,

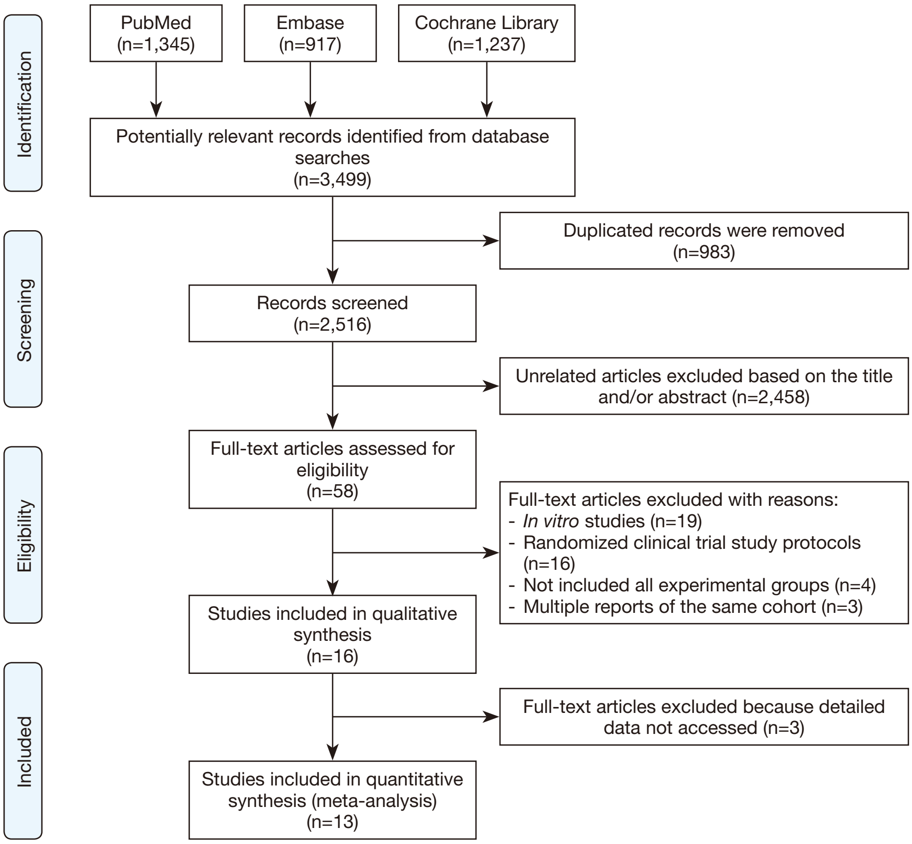

Figure 1 Flowchart of the literature search and study selection process.

recurrence of caries, and postoperative sensitivity were compared between the etch-and-rinse and self-etch modes. Because the data obtained from clinical evaluation results by USPHS or FDI criteria is ordinal categorical variable, we defined the evaluation result "A" as a good outcome, while the others (B, C, D, and E) as bad outcome (unfavourable events). The data was turned into dichotomous data, and was analyzed using the Mantel-Haenszel test in a random effects model ($P<0.05$ was considered to indicate statistical significance). Pooled-effect estimates of odds ratios (ORs) were obtained with a 95% confidence interval (CI). Heterogeneity of the included studies was assessed using Cochran's Q test ($P<0.1$ indicates heterogeneity exist) and I^2 statistics ($I^2 \geq 25\%$, $I^2 \geq 50\%$, and $I^2 \geq 75\%$ indicate low, moderate, and high heterogeneity, respectively).

Results

Study selection

Figure 1 is a flowchart showing the selection process according to the PRISMA statement. A total of 3,499 publications were retrieved from the three databases. After removing 983 duplicates, 2,516 publications were screened. We excluded 2,458 unrelated articles based on the title and/or abstract. Among the 58 remaining candidates, 42 publications were excluded (19 *in vitro* studies, 16 randomized clinical trial study protocols, four did not include all experimental groups, and three multiple reports of the same cohort). The remaining 16 studies were included in the qualitative synthesis. Of these, 13 publications were included in the quantitative synthesis (meta-analysis), while the other three publications were excluded as detailed data could not be accessed.

Descriptive analysis

The characteristics of the 16 included studies are shown in *Table 2*. The following information was extracted: first author, year of publication, lesions of the teeth, criteria used in clinical evaluation, the last assessment time, the universal

Table 2 Summary of the included studies in the systematic review

Author	Year	Lesions	Criteria	Assessment time	Universal adhesive	Design	Meta-analysis	References
Atalay	2020	NCCLs	USPHS	36 months	Single Bond Universal	Randomized controlled trial	Yes	(18)
Carvalho	2019	Class I and II carious lesions	USPHS and FDI	12 to 20 (15.8±2.7) months	Scotchbond Universal	Randomized controlled trial	Yes	(24)
Kemaloğlu	2020	NCCLs	USPHS	24 months	Single Bond Universal	Randomized controlled trial	Yes	(22)
Lawson	2015	NCCLs	USPHS	24 months	Scotchbond Universal	Randomized controlled trial	Yes	(25)
Loguercio	2015	NCCLs	USPHS and FDI	36 months	Scotchbond Universal	Randomized controlled trial	Yes	(21)
Loguercio	2018	NCCLs	USPHS and FDI	18 months	Tetric N-Bond Universal	Randomized controlled trial	Yes	(26)
Lopes	2016	NCCLs	USPHS and FDI	6 months	Xeno Select universal adhesive	Randomized controlled trial	Yes	(27)
Matos	2019	NCCLs	USPHS and FDI	18 months	Universal adhesive with or without copper nanoparticles	Randomized controlled trial	Yes	(28)
Oz	2019	NCCLs	USPHS	24 months	GLUMA Universal, All-Bond Universal	Randomized controlled trial	Yes	(17)
Perdigão	2020	NCCLs	USPHS	36 months	Scotchbond Universal	Randomized controlled trial	Yes	(19)
Ruschel	2019	NCCLs	USPHS	36 months	Scotchbond Universal, Prime & Bond Elect Universal	Randomized controlled trial	Yes	(29)
Zanatta	2019	NCCLs	FDI	24 months	Scotchbond Universal	Randomized controlled trial	Yes	(20)
Çakır	2019	Class I carious lesions	USPHS and FDI	24 months	Gluma Bond Universal, Clearfil Universal, Prime & Bond Elect Universal, All bond Universal, and Single Bond Universal	Randomized controlled trial	Yes	(30)
Lenzi	2017	Moderately deep dentin carious lesions on occlusal or occluso-proximal surfaces	USPHS	18 months	Scotchbond Universal	Randomized controlled trial	No	(31)
Burke	2017	Posterior teeth which required two restorations	USPHS	3 years	Scotchbond Universal	Split-mouth	No	(32)
Haak	2018	NCCLs	FDI	6 months	Scotchbond Universal	Randomized controlled trial	No	(33)

NCCL, non-carious cervical lesion; USPHS, United States Public Health Service; FDI, Fédération Dentaire Internationale/World Dental Federation.

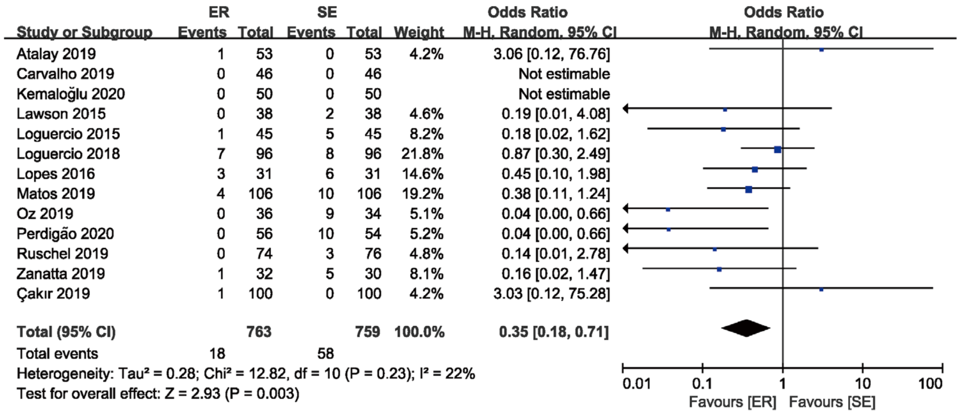

Figure 2 Forest plot for retention showed that there were fewer unfavourable events in the etch-and-rinse groups compared with the self-etch groups.

adhesive used, and the study design. The included studies were published between 2015 and 2020, and 44% (7/16) of them were published in 2019. Seventy-five percent (12/16) of the studies used non-carious cervical lesions in the trial, while the remaining 25% used carious lesions. Fifty percent (8/16) of the studies used the USPHS criteria for clinical evaluation, 12.5% (2/16) of them used the FDI criteria, and the remaining 37.5 (6/16) of them used both the USPHS and FDI criteria. The last clinical assessment time ranged from 6 months to 36 months, and 62.5 (10/16) of the assessment periods were at least 24 months. Scotchbond Universal (3M, MN, USA) was the most commonly used (56%, 9/16) universal adhesive, followed by Single Bond Universal (3M, MN, USA) (19%, 3/16). 94% (15/16) of the studies were randomized controlled trials, while the remaining 6% (1/16) were split-mouth design studies.

Meta-analysis

Thirteen studies were included in the meta-analysis (17-22,24-30). All of the studies provided original clinical outcome evaluation data for retention, marginal adaptation, marginal staining, and secondary caries. Ten studies provided clinical data for postoperative sensitivity. Compared with self-etch approach, the etch-and-rinse approach for universal adhesives had a better clinical outcome in terms of retention, marginal adaptation, and marginal staining. Both of the etching approaches showed a very low incidence rate of secondary caries or postoperative sensitivity, and there were no significant differences in the incidence rates between them.

Figure 2 shows the meta-analysis results for retention. There were fewer unfavourable events in the etch-and-rinse groups (2.4%, 18/763) compared with the self-etch groups (7.6%, 58/759). Also, the retention rates were higher in the etch-and-rinse groups compared with the self-etch groups (OR =0.35, 95% CI: 0.18–0.71, P=0.003). Cochran's Q test did not show heterogeneity among the included studies (P=0.23), and the I^2 statistics indicated no heterogeneity among the included studies (I^2=22%).

For marginal adaptation, the unfavourable events rates in the etch-and-rinse and self-etch groups were 12.9% (96/745) and 21.1% (149/707), respectively (*Figure 3*). The etch-and-rinse approach lead to better marginal adaptation than the self-etch approach (OR =0.49, 95% CI: 0.36–0.67, P<0.001). Cochran's Q test (P=0.55) and the I^2 statistics (I^2=0%) did not show heterogeneity among the included studies.

For marginal staining, the etch-and-rinse groups had a lower rate of unfavourable events (12.2%, 91/744) than the self-etch groups (20.1%, 142/706) (*Figure 4*). The etch-and-rinse approach exhibited better performance in marginal staining (OR =0.49, 95% CI: 0.36–0.66, P<0.001). No heterogeneity among included studies was found by Cochran's Q test (P=0.90) and the I^2 statistics (I^2=0%).

The incidence rates of recurrent caries were low in both the etch-and-rinse (0.27%, 2/748) and self-etch (0.70%, 5/713) groups (*Figure 5*). The current data did not show a significant difference in the incidence rates between the groups (P=0.40).

Three studies did not report the clinical evaluation results for postoperative sensitivity (17-22,24-30). Data

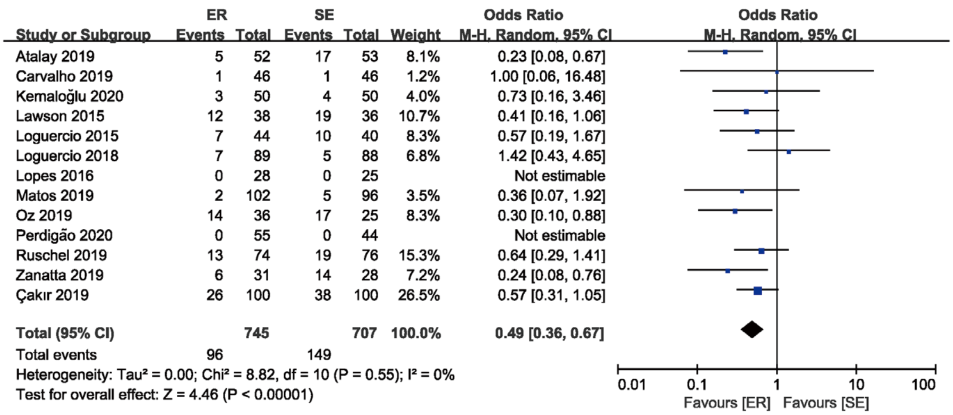

Figure 3 Forest plot for marginal adaptation showed that the etch-and-rinse approach resulted in better marginal adaptation than the self-etch approach.

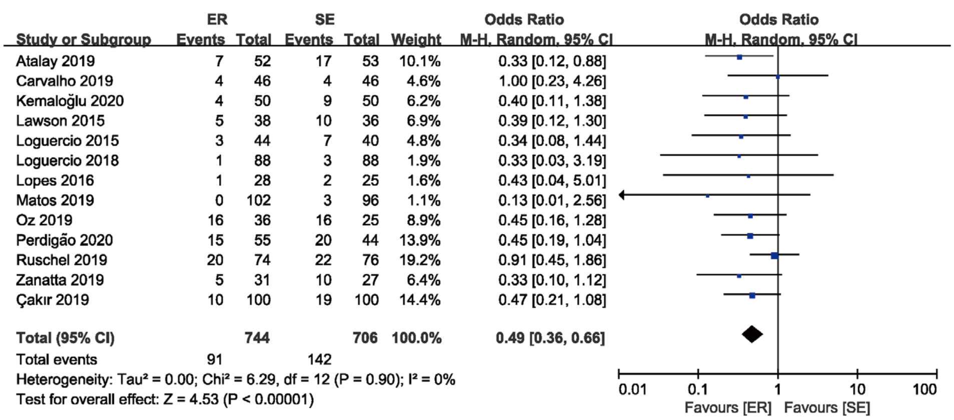

Figure 4 Forest plot for marginal staining showed a lower rate of unfavourable events in the etch-and-rinse groups compared to the self-etch groups.

from the other 10 articles was analyzed. Few patients suffered postoperative sensitivity in both the etch-and-rinse groups (0.69%, 4/583) and the self-etch groups (1.1%, 6/545) (*Figure 6*). No significant difference was observed between the groups (P=0.51).

Risk of bias

Seven items of each study were assessed and summarized in *Figure 7*. At the study level, nine of the 13 studies (69%) were classified as low risk of bias. The remaining four studies (31%) were considered as medium risk of bias. None of the included studies was denoted as high risk of bias. For individual items (*Figure 8*), 85% of the included studies were assessed as low risk of bias in both "random sequence generation" and "blinding of participants and personnel". There were 69%, 77%, and 46% of the studies that were assessed as low risk of bias in items "allocation concealment", "blinding of outcome assessment", and "incomplete outcome data", respectively. All of the included studies were assessed as low risk of bias in selective reporting and other bias.

Discussion

This meta-analysis revealed that, compared with self-etch approach, the application of the etch-and-rinse approach for universal adhesives improved clinical outcomes in

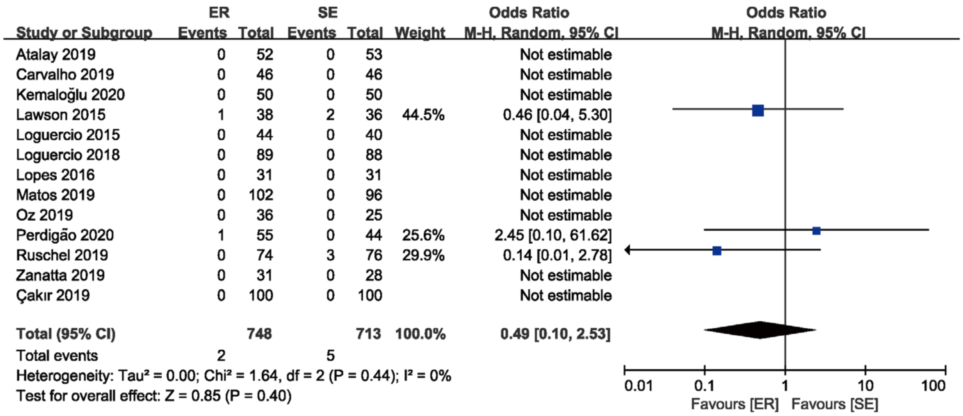

Figure 5 Forest plot for recurrence of caries did not show a significant difference in the incidence rates between the etch-and-rinse and self-etch groups.

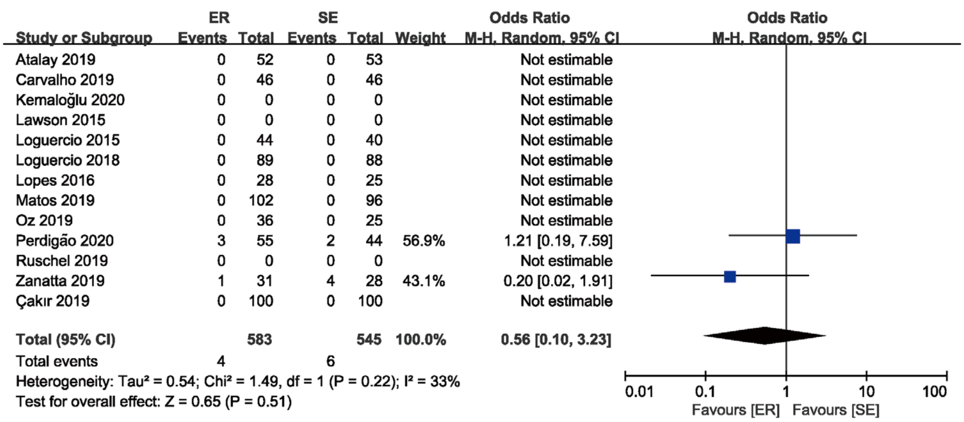

Figure 6 Forest plot for postoperative sensitivity did not show significant differences between the etch-and-rinse groups and the self-etch groups.

terms of retention rates, marginal adaptation, and marginal staining. No significant differences in the incidence rates of secondary caries or postoperative sensitivity were observed between the etch-and-rinse and self-etch groups. To the best of the authors' knowledge, this is the first meta-analysis reporting on the clinical benefits of the different etching approaches for universal adhesives.

Before universal adhesives, there were etch-and-rinse adhesives and self-etch adhesives (2). In the past, etch-and-rinse adhesives were considered to offer better clinical performance compared to self-etch adhesives (34,35). However, in some aspects, such as micro tensile bond strength (μTBs) or postoperative sensitivity, recent meta-analyses have shown that the differences between the different adhesives were statistically insignificant (36,37). Universal adhesives can be used in conjunction with different etching strategies. However, the optimal strategy for universal adhesives remains contentious. In this study, the results showed that the etch-and-rinse approach is significantly superior to the self-etch approach. Based on these results, we suggest that the etch-and-rinse approach should be preferentially used for universal adhesives in order to achieve a better clinical result.

Etching is an important step to improve the bonding strength of adhesives. In the etch-and-rinse strategy, etching with phosphoric acid dissolves hydroxyapatite and produces macro- and micro-porosities on the surface of the enamel (38). This process increases the total surface area of

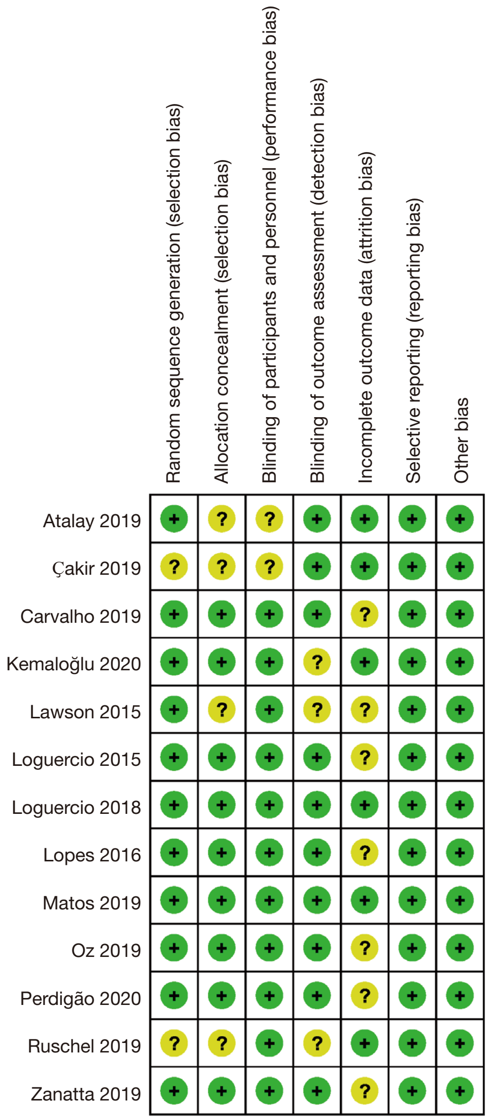

Figure 7 Risk of bias of seven items of each study.

the substrate, and allows resin monomers to infiltrate into the enamel and form "prism-like" resin tags (15). In the self-etch strategy, the dental substrates are conditioned and primed simultaneously (39). Self-etch strategies cannot etch enamel to the same depth as phosphoric acid (40). This may explain why the etch-and-rinse strategy used for universal adhesives leads to better clinical outcomes, compared with the self-etch strategy.

Despite the continuous improvement of adhesives, nanoleakage may occur between the surface of the dentin and the hybrid layer (41). Nanoleakage enables bacterial acidic products and enzymes get into and degrade the dentin-adhesive interface (42). Time-dependent hydrolytic degradation caused by water is another factor in the degradation process (36). Degradation of the dentin-adhesive interface may lead to several problems, such as the loss of retention, marginal staining, and secondary caries (43). Kaczor *et al.* reported that the etching mode significantly influences the nanoleakage of universal adhesives (1). In this study, the results showed that the etch-and-rinse groups had higher retention rates, as well as lower marginal adaptation and marginal staining rates, compared to the self-etch groups. Thus, we infer that phosphoric acid etching may reduce nanoleakage and slow the degradation

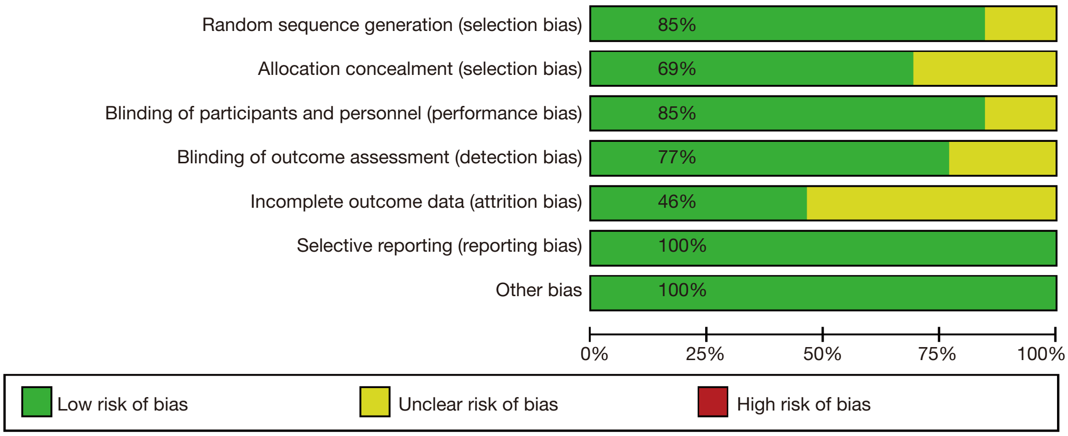

Figure 8 Summary of each risk of bias item.

process of the dentin-adhesive interface.

Conclusions

The current evidence shows that, compared with self-etch approach, the etch-and-rinse approach for universal adhesives provides improved clinical outcomes in terms of retention rates, marginal adaptation, and marginal staining.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at http://dx.doi.org/10.21037/apm-21-890

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/apm-21-890). All authors report funding from the Xiamen Science and Technology People-Benefit Project (No.3502Z20174088).

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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