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Literature Review

Is Conventional Resin Cement Adhesive Performance to Dentin Better Than Self-adhesive? A Systematic Review and Meta-Analysis of Laboratory Studies

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Clinical Relevance

Conventional multistep resin cements presented higher adhesive performance to dentin than simplified self-adhesive cements, which is an important criterion for indirect restoration prognosis.

SUMMARY

This study aimed to conduct a systematic review of the literature on laboratory studies assessing bonding performance to dentin of conventional and self-adhesive resin cements, in cementing indirect restorations. This review was reported according to the PRISMA Statement. Of a total of 518 studies, 36 were screened full text and reviewed according to exclusion criteria. Nineteen papers were included in the systematic review and meta-analyses, according to the following inclusion criteria: studies that evaluated the bond strength to dentin of indirect restorations cemented with dual conventional or self-adhesive resin cements and those that presented bond strength data in MPa as an outcome. Statistical analyses were conducted using RevMan 5.1. Comparisons were performed with random effects models at 5% significance level. A global analysis comparing conventional and self-adhesive cements and three subgroup analyses comparing immediate and long-term

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results were performed. Global analysis showed a difference between groups, with conventional resin cements presenting higher bond strength results than self-adhesive resin cements, in immediate and long-term time periods (both p=0.03). Immediate and long-term bond strength results were different for self-adhesive cements, favoring immediate bond strength (p=0.03), but immediate and long-term bond strength results for conventional resin cements were not different (p=0.06). Medium or high risk of bias was found in all studies. Conventional multistep resin cements showed superior overall adhesive performance compared with simplified self-adhesive resin cements when used to cement indirect restorations to dentin.

INTRODUCTION

Adhesive dentistry has developed to the point of allowing restorative procedures to be performed with minimal tooth preparation, thereby contributing toward preserving the dental substrate. This is an important factor affecting restoration longevity.[1] Resinous luting agents have improved indirect restorative treatments, by promoting better retention and lower solubility, thereby reinforcing restoration and tooth structure.[2,3] The first dual resin cements, called "conventional resin cements" or "regular cements,"[4] were developed as systems, containing the resinous luting agent and a specific adhesive system or primer, used as an adhesion agent. The adhesive strategy for these conventional resin cements can use etch-and-rinse or self-etch approaches, depending on the adhesion agent.

The concept of self-adhesive luting agents was conceived in the early 2000s as a new class of resin cement capable of combining adhesive and cement in a single application, without requiring pretreatment of the dental substrate and the restoration surface.[5] By mixing adhesive and cement in a single formulation, these cements promote simultaneous demineralization and substrate penetration. The simplified technique results in fewer operator-sensitive steps during the procedure compared with the traditional, conventional multistep resin cements.[6] The luting agent class is considered a heterogeneous group of resin cements, with substantial differences in terms of composition, setting reaction, pH, and bonding performance.[7]

Dentin adhesion remains a concern regarding long-term retention. The adhesive interface can be considered the weakest link of the adhesion chain and may jeopardize restorative longevity.[8] Studies assessing dual resin cement adhesion to dentin are controversial. Some laboratory investigations assert that conventional multistep resinous luting agents promote higher and more stable adhesion to dentin,[2,8-10] whereas others indicate that self-adhesive resin cements provide adequate bonding performance.[11-13] Hitz and others[14] also stated that not all self-adhesive resin cements could be considered valid alternatives to conventional multistep resin cements, because chemical formulation is crucial to their performance.

Considering that opinions may diverge, the present study aimed to make a systematic review of the available scientific literature for laboratory studies that assessed the bonding performance of conventional and self-adhesive resin cements to unaltered dentin, when cementing indirect restorations. The null hypothesis was that there would be no difference in bonding strength between the two classes of resin cements tested, even regarding long-term bond strength.

METHODS

The present systematic review was conducted according to the Cochrane Handbook for systematic reviews of interventions[15] and reported according to the PRISMA statement.[16] A research question was defined to guide the literature search strategy and establish the variables analyzed in the meta-analysis: "Does the dual resinous cement type (conventional or self-adhesive) influence immediate and long-term bond strength to dentin when used to cement an indirect restoration to dentin?"

Search Strategy

The following electronic databases were used to search and identify studies that could be included in the present systematic review: MEDLINE (National Library of Medicine) via PubMed, Scopus, and ISI Web of Science (Core Collection). A computer search of databases and reference lists of the studies to be included were the search strategies used in this review. All the studies included were published before January 9, 2018. No publication year or language limit was applied.

The MEDLINE search via PubMed was performed with MeSH terms and keywords, as follows: "((((((((dentin[MeSH Terms]) OR dentin) OR dentins) OR dentine) OR dentines)) AND (((((bond strength*) OR microtensile bond strength) OR microshear bond strength) OR microtensile) OR microshear)) AND ((adhesive cementation) OR resin luting agent*) OR conventional resin luting cement*) OR self-adhesive luting cement*) OR adhesive cementation strategies) OR adhesive*) OR dental cement*) OR dental cements[MeSH Terms]) OR dental adhesives) OR adhesive, dental) OR adhesives, dental) OR dental adhesive) OR cement, dental) OR luting agent*) OR cements, dental) OR dental bonding[MeSH Terms]) OR dental bonding) OR bonding, dental) OR curing, dental cement) OR dental cement curing) OR bonding strategy) OR bonding strategies) OR cementation strategy) OR cementation strategies) OR adhesive bond*) OR etching protocol) OR universal adhesive*) OR multimode adhesive*) OR multi-mode adhesive*) OR self-adhesive resin cement*) OR bonding method*) OR dual-polymerizing resin cement*) OR adhesion) OR cementation) OR adhesive cement[-MeSH Terms]) OR adhesive cement) OR resin cements[MeSH Terms]) OR resin cements) OR cements, resin) OR resin cement) OR cement, resin) OR cementation[MeSH Terms]) OR cementation)) AND ((((((((((ceramic* indirect restoration) OR indirect composite resin) OR indirect resin composite) OR indirect resin) OR indirect composite restorations) OR dental porcelain[MeSH Terms]) OR dental porcelain) OR porcelain*) OR porcelain, dental) OR dental porcelains) OR porcelains, dental).” The following search terms were used for the Scopus and ISI Web of Science search: “(bond AND strength) AND (resin AND cement) AND (dentin) AND (indirect AND restoration).”

The titles and abstracts of the studies assessed were reviewed independently by two authors (LLM and ACF) and selected for further review if they met the following inclusion criteria: laboratory studies that assessed bond strength, where an indirect restorative material (composite resin or ceramic) was cemented to unaltered dentin, and at least one self-adhesive resin cement was tested. Immediate or long-term bond strength values were considered. The abstracts were selected if both reviewers reached a consensus; otherwise, the abstract was set aside for later evaluation.

The final decision on the inclusion of an eligible study was made based on the assessment of full-text papers of potentially relevant studies, made by two authors (LLM and ACF), according to the exclusion criteria: at least one group of the study had to follow the resin cement manufacturer’s cementation protocol; the study had to test at least one conventional resin cement (control group for the meta-analysis); resin cements had to be dual (chemical and photo-activation simultaneously); and the adhesion substrate had to be coronary and composed of sound dentin, with no enamel for cementation. Only phosphoric acid etching was accepted for surface substrate modification. Any other type of dentin substrate modification was not accepted. Studies with no test group for sound dentin were excluded. The bond strength test had to have used a micro scale (microtensile [μTBS] or microshear [μSBS]), and the values had to be presented in MPa, with mean and SD data.

Last, the reference lists of all the included studies were reviewed manually, and the full texts of studies that could potentially fulfill the inclusion criteria were examined.

When needed, contact was made with the corresponding author by email, requesting data missing from the paper. Studies that did not provide all the required data, despite several attempts to contact the author for the data, were also excluded. Disagreements about study eligibility were solved by discussion and consensus with a third reviewer (AFM).

Data Extraction

Data extraction was defined and performed by one author (LLM) and revised by a second author (AFM), using a standardized protocol. The data were extracted from the full-text articles selected for inclusion, using a standardized form in a computer program (Office Excel 2013 Software, Microsoft Corporation, Redmond, WA, USA). Similar information was categorized according to the main outcomes considered in this review. The following data were extracted from each study: publication year, sample size, resin cements assessed, inclusion of an aging protocol, and bond strength test used. Bond strength mean (MPa) and SD values were also extracted in this step to conduct future meta-analyses.

Risk of Bias Assessment

Risk of bias of the included studies was evaluated independently by two authors (LLM and ACF), based on a score adapted for laboratory studies, reported in previous systematic reviews.[17,18] The following parameters were used to determine the score: randomization of teeth for experimental groups, teeth free of caries or previous restoration, materials used according the manufacturer’s instructions, teeth with similar dimensions, adhesive procedures performed by a single operator, sample size calculation, and blinded operator of the testing

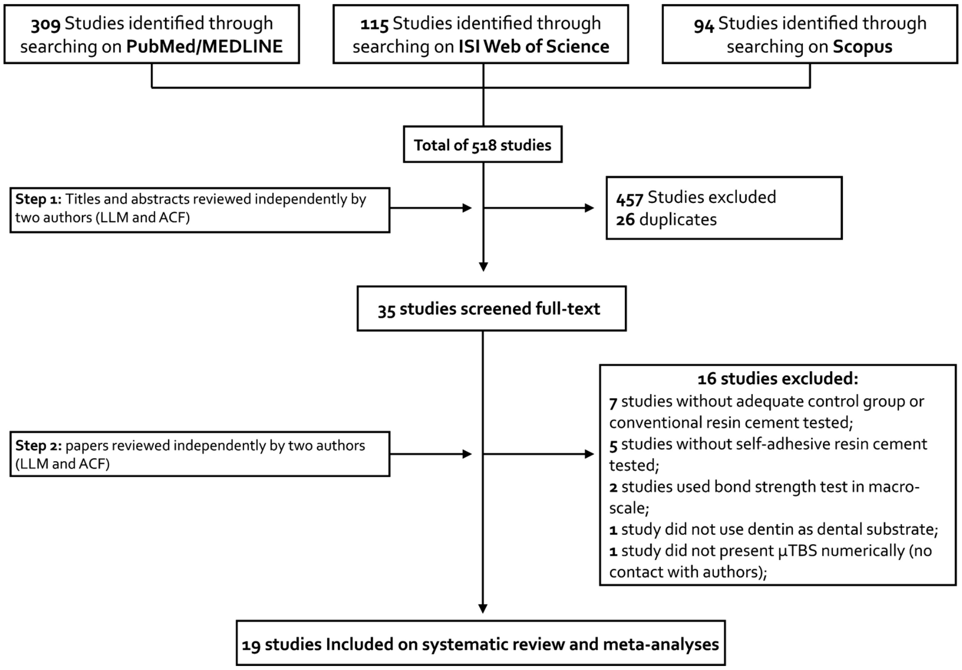


Figure 1. *Flowchart of study selection according to PRISMA statement.*

machine. Each parameter received the following score, based on its description in the article: 1, if the parameter was correctly described in the text; 0, if the information was not described in the text. The risk of bias classification was calculated according to the sum of 1 received by the study: 1-2 = high risk, 3-5= medium risk, and 6-7= low risk of bias.

Data Analysis

The pooled effect estimates for the meta-analysis were obtained by comparing the bond strength means with the conventional and the self-adhesive resin cements in the global analysis and in the three different subgroup analyses, according to use of an aging method before the bond strength test (immediate or long term). Each cement tested according to inclusion and exclusion criteria was considered an independent test group. Studies that reported immediate and long-term results were analyzed in all the three subgroups. No aging methods or time points were considered; the only consideration was if the specimens were submitted to an aging process. When called for, specific formulas were applied to combine multiple values into single sample sizes, mean values, and SDs for groups within a given study.[15]

Statistical heterogeneity between studies was evaluated by the Cochran Q test, with a threshold p value of 0.1 and inconsistency of I^2, where values >50% were considered indicative of high heterogeneity.[15] All analyses were performed with the Review Manager (RevMan version 5.3 software 2014, Cochrane Collaboration, Copenhagen, Denmark), using the random effects method. The number of specimens was considered as the number of experimental units; $p \leq 0.05$ was considered statistically significant (Z-test). Forest plots were constructed to illustrate the meta-analysis calculation.

RESULTS

Search and Selection

Figure 1 shows a flowchart describing the study selection process, according to the PRISMA statement.[16] The search strategy resulted in 518 potentially eligible studies, with 309 papers in MEDLINE via PubMed, 94 papers in Scopus, and 115 papers in ISI Web of Science. Of these, 457 were excluded for not meeting the inclusion criteria, and 26 were duplicates. The first screening resulted in 35 studies singled out for further full-text evaluation. According to the exclusion criteria, 16 studies were excluded: two presented a bond strength test on a macro scale[19,20]; seven did not present an adequate control group or did not test a conventional resin cement[21-27]; five studies did not assess a self-adhesive resin cement[28-32]; one study did not mention the dentin substrate[33]; and one study did not present the microtensile bond strength (µTBS) numerically.[34] After applying the exclusion criteria, 19 studies were included for systematic review and meta-analysis.

The meta-analysis included studies that were published between 2009 and 2016. Most papers used human molars. Only two studies used bovine incisors,[4,13] and another two studies used premolars with inlay preparations.[9,35] In the collection of included articles, the most frequently assessed conventional resin cements were RelyX ARC etch-and-rinse[4,8-10,12,36-41] and Panavia F2.0 self-etch.[7,11,35,38-44] The most commonly assessed self-adhesive resin cements were RelyX Unicem,[7,10-13,35,36,38,41-44] followed by RelyX U100[4,8,9,37,45] and G-cem.[10,11,41,43,44]

The methodologic test used in all the 19 selected studies was μTBS, with nontrimming beams. Most studies presented long-term bond strength results,[7-9,11,12,35-40,42] with different aging methods: five studies[9,35-37,40] performed mechanical cycling, with a number of cycles ranging from 50,000[36] up to 2,000,000,[37] loading from 50[40] to 100 N,[37] and frequency from 1[36] to 4 Hz[9,37]; two studies stored specimens in artificial saliva[8,36] and two stored them in distilled water,[12,38] with a storage time ranging from 1[12] to 24 months[36]; three studies performed thermocycling,[7,11,42] all with the same parameters (5000 cycles, 5°C-55°C); and two studies used a simulated pulpal pressure aging design[39,40] for periods of 7 days[40] and 3 months.[39] Two papers[36,40] performed more than one aging method, but the specimens in both studies were submitted to only one aging method. The complete descriptive data per study in this collection is presented in Table 1.

Meta-analyses

The data from the 19 included studies were submitted to a meta-analysis calculation. The meta-analyses were conducted considering a global analysis (conventional vs self-adhesive resin cements; Figure 2) and three subgroup analyses: 1, conventional vs self-adhesive cements, considering only the after-aging results (Figure 3); 2, immediate vs aging bond strength of self-adhesive cements (Figure 4); and 3, immediate vs aging bond strength of conventional resin cements (Figure 5).

The global meta-analysis results are presented in Figure 2. In this analysis, heterogeneity (I^2 test) was 99%, and Cochran Q and Z (p=0.03) tests were <0.05, thus corroborating the control group results (conventional resin cements). Considering the immediate and after-aging results pooled, the conventional resin cements showed better bond strength results than those of the self-adhesive resin cements. The first subgroup analysis (conventional vs self-adhesive after aging) presented Cochran Q and Z (p=0.03) tests <0.05, with I^2=99%, showing that conventional resin cements had better bond strength results than self-adhesive resin cements (Figure 3). Subgroup analyses 2 and 3, which analyzed both resin cement types separately, showed different results. Subgroup analysis 3 (Figure 4) showed a difference between immediate and long-term bond strength results for self-adhesive cements, favoring immediate bond strength, which showed higher bond strength values than the aged group (p=0.03, I^2=99%). On the other hand, the subgroup analysis for conventional resin cements (Figure 5) indicated the Cochrane Q test as <0.05. However, the Z test was >0.05 (p=0.06), thus indicating no difference between the immediate and the aged groups (I^2=98%).

Risk of Bias

Medium or high risk of bias was found in all the studies included (Table 2). In the present collection of articles, three took tooth dimensions into consideration,[4,35,37] one had the same operator for the adhesive technique,[7] two calculated the sample size,[35,38] and two had a blinded operator for the adhesive test.[4,7]

DISCUSSION

The present systematic review and meta-analysis established the pooled effect of data from laboratory studies that assessed the adhesion performance to dentin of two different resin cement types: conventional and self-adhesive. This study provides the first step to guide the decision-making process for selecting the most reliable adhesive strategy for cementing indirect coronal restorations. The overall results showed that the conventional adhesive approach, whereby the resin cement is applied in combination with an adhesive system or primer agent, tends to promote higher immediate- and long-term bond strength to dentin. The null hypothesis of the present study was rejected, because conventional multistep resin cements presented higher overall and long-term bond strength results.

The conventional class of resin cements was the first adhesive resinous luting agent to use an intermediate adhesion agent (adhesive system or specific primer) between the restorative material and the dental substrate. In the present collection of studies, the two most frequently assessed conventional resin cements were RelyX ARC (3M-ESPE, St Paul, MN, USA) and Panavia F2.0 (Kuraray Medical Inc, Okayama, Japan), etch-and-rinse and self-etch resin cements, respectively. Both systems were

Table 1: *Descriptive Data From Studies Included in Meta-analyses*

Paper	Type of Teeth	Restorative Material	Aging Method	Conventional Cements	Self-adhesive Cements
D'Arcangelo and others 2009[42]	Human	Resin composite/ ceramic	Thermocycling (5000 cycles, 5-55°C)	CoreXFlow (Dentsply DeTey, York, PA, USA) Enacem HF (Micerium, Aveno, GE, Italy) Panavia F2.0 (Kuraray, Chiyoda, Tokyo, Japan)	RelyX Unicem (3M ESPE, St. Paul, MN, USA)
Aguiar and others 2010[43]	Human	Resin composite	No aging	Panavia F2.0 (Kuraray)	RelyX Unicem (3M ESPE) BisCem (Bisco Schaumburg, IL, USA) G-CEM (GC, Tokyo, Japan)
Sarr and others 2010[44]	Human	Ceramic	No aging	Panavia F2.0 (Kuraray) Clearfil Esthetic cement (Kuraray) Calibra (Dentsply) Variolink II (Ivoclar Vivadent, Schaan, Liechtenstein)	RelyX Unicem (3M ESPE) MaxCem (Kerr, Brea, CA, USA) MonoCem (Shofu, Kyoto, Japan)G-CEM (GC, Tokyo, Japan) Multilink Sprint (Ivoclar Vivadent)
Guarda and others 2010[13]	Bovine	Ceramic	No aging	Variolink II (Ivoclar Vivadent)	RelyX Unicem (3M ESPE)
De Angelis and others 2011[7]	Human	Resin composite/ ceramic	Thermocycling (5000 cycles, 5-55°C)	Enacem HF (Micerium, Aveno) Panavia F2.0 (Kuraray)	RelyX Unicem (3M ESPE) MaxCem Elite (Kerr) iCEM Self-adhesive (Heareus Kulzer, Hanau, Germany)
Inukai and others 2012[35]	Human	Resin Composite	Mechanical cycling (250,000 cycles, 100 N, 4 Hz)	Panavia F2.0 (Kuraray)	RelyX Unicem (3M ESPE) Clearfil SA cement (Kuraray)
Fuentes and others 2013[41]	Human	Resin composite	No aging	RelyX ARC (3M ESPE)	RelyX Unicem (3M ESPE) G-CEM (GC) MaxCem Elite (Kerr)
Suzuki and others 2013[38]	Human	Resin composite	6-mo water storage	RelyX ARC (3M ESPE) Panavia F (Kuraray)	RelyX Unicem (3M ESPE)
Aguiar and others 2014[361]	Human	Resin composite	Mechanical cycling (50,000 cycles, 80 N, 1 Hz) 12- and 24-mo storage in artificial saliva	RelyX ARC (3M ESPE) Clearfil esthetic cement (Kuraray)	RelyX Unicem (3M ESPE) Clearfil SA Cement (Kuraray)
Feitosa and others 2014[37]	Human	Ceramic	Mechanical cycling (2,000,000 cycles, 100 N, 4 Hz)	RelyX ARC (3M ESPE)	RelyX U100 (3M ESPE)
Rigolin and others 2014[45]	Human	Ceramic	No aging	Variolink II (Ivoclar Vivadent) Multilink (Ivoclar Vivadent)	RelyX U100 (3M ESPE)
Prochnow and others 2014[9]	Human	Resin composite	Mechanical cycling (1,000,000 cycles, 88 N, 4 Hz)	RelyX ARC (3M ESPE)	RelyX U100 (3M ESPE)
Vaz and others 2012[12]	Human	Resin Composite	1-mo storage in artificial saliva	RelyX ARC (3M ESPE) C&B cement (Bisco)	RelyX Unicem (3M ESPE)
Stape and others 2014[8]	Human	Resin composite	24-mo storage in artificial saliva	RelyX ARC (3M ESPE)	RelyX U100 (3M ESPE)
Giannini and others 2015[11]	Human	Resin composite	Thermocycling (5000 cycles, 5-55°C)	Panavia F2.0 (Kuraray)	RelyX Unicem (3M ESPE) RelyX Unicem 2 (3M ESPE) Clearfil SA Cement (Kuraray) G-CEM (GC)
Skupien and others 2015[4]	Bovine	Resin composite	No aging	RelyX ARC (3M ESPE)	RelyX U100 (3M ESPE)

Table 1: Continued.

Paper	Type of Teeth	Restorative Material	Aging Method	Conventional Cements	Self-adhesive Cements
Bacchi and others 2015[39]	Human	Resin composite	3-mo simulated pulpal pressure	RelyX ARC (3M ESPE) Panavia F2.0 (Kuraray)	RelyX U200 (3M ESPE)
Bacchi and others 2015[40a]	Human	Resin composite	7-day simulated pulpal pressure Mechanical cycling (200,000 cycles, 50 N, 2 Hz) Thermocycling (5000 cycles, 5-55°C)	RelyX ARC (3M ESPE) Panavia F2.0 (Kuraray)	RelyX U200 (3M ESPE)
Fuentes and others 2016[10]	Human	Resin composite	No aging	RelyX ARC (3M ESPE)	RelyX Unicem (3M ESPE) G-CEM (GC) Speedcem (Ivoclar Vivadent) MaxCem Elite (Kerr) Smartcem2 (Dentsply)

All studies used microtensile bond strength (μTBS) as the bond strength test.
[a] These studies used more than one aging method in the same specimens.

tested with different adhesion agents, as follows: RelyX ARC was used together with Adper Singlebond[4,8-10,12,36-41] (3M-ESPE) and Panavia 2.0 was used with ED primer (Kuraray Medical Inc), a self-etch primer included in the Panavia F2.0 system.[7,11,35,38-40,42-44] Our review findings are corroborated by studies like that of Prochnow and others[10] and Fuentes and others,[41] in which RelyX ARC was the conventional resin cement, and that of Aguiar and others[43] and Sarr and others,[44] in which Panavia F2.0 was tested. Despite the adhesive strategy, etch-and-rinse and self-etch conventional multistep dual resin cements seem to promote higher immediate- and long-term dentin bond strength than simplified self-adhesive cements.[9,10,39,43,44]

The results for immediate- and long-term bond strength revealed that conventional multistep resin

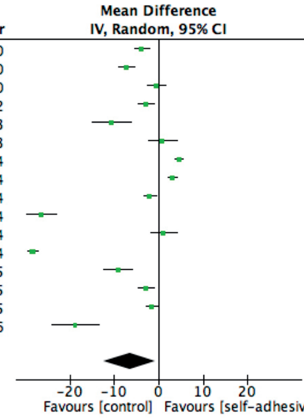
Table 2: *Risk of Bias Assessment of the Studies Included*

Study	Random	Caries	Materials	Teeth	Adhesive	Sample	Blinding	Risk
D'Arcangelo and others 2009[42]	Y	Y	N	N	N*	N	N*	High
Aguiar and others 2010[43]	Y	Y	Y	N	N*	N	N*	Medium
Sarr and others 2010[44]	N	Y	Y	N	N*	N	N*	High
Guarda and others 2010[13]	Y	Y	Y	N	N*	N	N*	Medium
De Angelis and others 2011[7]	N	Y	N	N	Y	N	Y	Medium
Inukai and others 2012[35]	Y	Y	N	Y	N*	Y	N*	Medium
Fuentes and others 2013[41]	Y	Y	Y	N	N*	N	N*	Medium
Suzuki and others 2013[38]	N	Y	N	N	N*	Y	N*	High
Aguiar and others 2014[36]	N	Y	Y	N	N*	N	N*	High
Feitosa and others 2014[37]	Y	Y	N	Y	N*	N	N*	Medium
Rigolin and others 2014[45]	Y	Y	Y	N	N*	N	N*	Medium
Prochnow and others 2014[9]	Y	Y	Y	N	N*	N	N*	Medium
Vaz and others 2012[12]	N	Y	Y	N	N*	N	N*	High
Stape and others 2014[8]	Y	Y	N	N	N*	N	N*	High
Giannini and others 2015[11]	N	Y	Y	N	N*	N	N*	High
Skupien and others 2015[4]	Y	Y	Y	Y	N*	N	Y	Medium
Bacchi and others 2015[39]	Y	Y	Y	N	N*	N	N*	Medium
Bacchi and others 2015[40]	Y	Y	Y	N	N*	N	N*	Medium
Fuentes and others 2016[10]	Y	Y	Y	N	N*	N	N*	Medium

Abbreviations: N, no; Y, yes
* not mentioned by authors

Study or Subgroup	Self-adhesive Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year	Risk of Bias A	B	C	D	E	F	G
Aguiar et al, 2010	11.7	7.9	168	15.5	4.3	56	6.3%	−3.80 [−5.44, −2.16]	2010	+	+	+	−	−	−	−
Sarr et al, 2010	12.8	8.4	198	20.1	9.3	192	6.3%	−7.30 [−9.06, −5.54]	2010	+	+	+	−	−	−	−
Guarda et al, 2010	18.5	3.2	30	19	5	30	6.3%	−0.50 [−2.62, 1.62]	2010	+	+	+	−	−	−	−
Inukai et al, 2012	17.2	4.3	64	20	4.1	32	6.3%	−2.80 [−4.57, −1.03]	2012	+	+	−	+	−	−	−
Fuentes et al, 2013	13.5	6.9	37	24.1	7.2	14	6.1%	−10.60 [−14.98, −6.22]	2013	+	+	+	−	−	−	−
Suzuki et al, 2013	17.2	6.5	32	16.3	9.8	64	6.2%	0.90 [−2.39, 4.19]	2013	−	+	−	−	−	+	−
Aguiar et al, 2014	19.1	2.3	80	14.5	3.5	80	6.3%	4.60 [3.68, 5.52]	2014	−	+	+	−	−	−	−
Feitosa et al, 2014	6.5	2.6	48	3.4	3.1	48	6.3%	3.10 [1.96, 4.24]	2014	+	+	−	+	−	−	−
Rigolin et al, 2014	10.3	3.9	52	12.3	5	115	6.3%	−2.00 [−3.40, −0.60]	2014	+	+	+	−	−	−	−
Prochnow et al, 2014	8.7	6	28	35.1	9.1	48	6.2%	−26.40 [−29.80, −23.00]	2014	+	+	+	−	−	−	−
Vaz et al, 2014	31.3	7.4	60	30.2	12.9	120	6.2%	1.10 [−1.87, 4.07]	2014	−	+	+	−	−	−	−
Stape et al, 2014	13.1	3.4	80	41.5	3.3	80	6.3%	−28.40 [−29.44, −27.36]	2014	+	+	−	−	−	−	−
Skupien et al, 2015	9.7	5.3	43	18.9	12.8	84	6.2%	−9.20 [−12.36, −6.04]	2015	+	+	+	+	−	−	+
Bacchi et al, 2015a	21.2	3.1	60	24	9.1	120	6.3%	−2.80 [−4.61, −0.99]	2015	+	+	+	−	−	−	−
Bacchi et al, 2015b	21.2	3.1	60	22.7	7.7	180	6.3%	−1.50 [−2.87, −0.13]	2015	+	+	+	−	−	−	−
Fuentes et al, 2016	14.4	8.3	80	33.2	11.8	22	6.0%	−18.80 [−24.06, −13.54]	2016	+	+	+	−	−	−	−
Total (95% CI)			**1120**			**1285**	**100.0%**	**−6.47 [−12.32, −0.63]**								

Heterogeneity: Tau² = 140.44; Chi² = 2864.11, df = 15 (P < 0.00001); I² = 99%
Test for overall effect: Z = 2.17 (P = 0.03)



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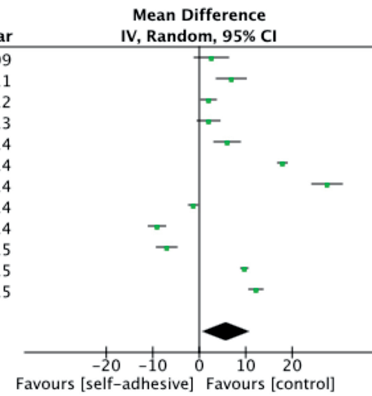
Study or Subgroup	Control Mean	SD	Total	Self-adhesive Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
D'Arcangelo et al, 2009	15.8	14.3	120	13.2	8.5	40	8.1%	2.60 [−1.07, 6.27]	2009
De Angelis et al, 2011	16.6	10.5	48	9.7	5.1	72	8.2%	6.90 [3.70, 10.10]	2011
Inukai et al, 2012	15.8	3.9	32	13.8	3.9	64	8.4%	2.00 [0.35, 3.65]	2012
Suzuki et al, 2013	16.6	8.5	64	14.6	3.9	36	8.3%	2.00 [−0.44, 4.44]	2013
Vaz et al, 2014	34.3	12.1	120	28.3	7.1	60	8.3%	6.00 [3.19, 8.81]	2014
Stape et al, 2014	27.8	3.6	80	9.9	2.9	80	8.4%	17.90 [16.89, 18.91]	2014
Prochnow et al, 2014	32.7	10.7	56	5.2	4.6	30	8.2%	27.50 [24.25, 30.75]	2014
Feitosa et al, 2014	3.4	2.8	48	4.7	2	48	8.4%	−1.30 [−2.27, −0.33]	2014
Aguiar et al, 2014	11.5	6.5	80	20.6	5.3	80	8.4%	−9.10 [−10.94, −7.26]	2014
Giannini et al, 2015	33.2	5.8	45	40.2	9.6	180	8.3%	−7.00 [−9.20, −4.80]	2015
Bacchi et al, 2015a	17.5	5	180	7.8	0.9	60	8.5%	9.70 [8.93, 10.47]	2015
Bacchi et al, 2015b	18.4	8.2	120	6.2	1.1	60	8.4%	12.20 [10.71, 13.69]	2015
Total (95% CI)			**993**			**810**	**100.0%**	**5.76 [0.58, 10.94]**	

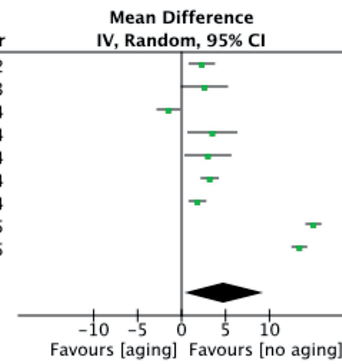
Heterogeneity: Tau² = 82.47; Chi² = 1478.91, df = 11 (P < 0.00001); I² = 99%
Test for overall effect: Z = 2.18 (P = 0.03)



3

Study or Subgroup	No Aging Mean	SD	Total	Aging Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Inukai et al, 2012	16.1	4.3	64	13.8	3.9	64	11.2%	2.30 [0.88, 3.72]	2012
Suzuki et al, 2013	17.2	6.5	32	14.6	3.8	32	10.9%	2.60 [−0.01, 5.21]	2013
Aguiar et al, 2014	19.1	2.3	80	20.6	5.3	80	11.2%	−1.50 [−2.77, −0.23]	2014
Prochnow et al, 2014	8.7	6	28	5.2	4.6	30	10.8%	3.50 [0.73, 6.27]	2014
Vaz et al, 2014	31.3	7.4	60	28.3	7.1	60	10.9%	3.00 [0.41, 5.59]	2014
Stape et al, 2014	13.1	3.3	80	9.9	2.9	80	11.2%	3.20 [2.24, 4.16]	2014
Feitosa et al, 2014	6.5	2.6	48	4.7	2	48	11.2%	1.80 [0.87, 2.73]	2014
Bacchi et al, 2015b	21.2	3.1	60	6.2	1.1	60	11.3%	15.00 [14.17, 15.83]	2015
Bacchi et al, 2015a	21.2	3.1	60	7.8	0.9	60	11.3%	13.40 [12.58, 14.22]	2015
Total (95% CI)			**512**			**514**	**100.0%**	**4.84 [0.34, 9.33]**	

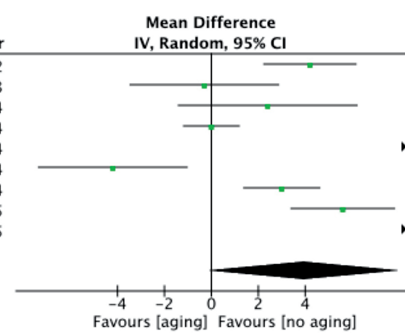
Heterogeneity: Tau² = 46.57; Chi² = 1010.94, df = 8 (P < 0.00001); I² = 99%
Test for overall effect: Z = 2.11 (P = 0.03)



4

Study or Subgroup	No aging Mean	SD	Total	Aging Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Inukai et al, 2012	20	4.1	32	15.8	3.9	32	11.2%	4.20 [2.24, 6.16]	2012
Suzuki et al, 2013	16.3	9.8	64	16.6	8.4	64	10.8%	−0.30 [−3.46, 2.86]	2013
Prochnow et al, 2014	35.1	9.1	48	32.7	10.7	56	10.5%	2.40 [−1.41, 6.21]	2014
Feitosa et al, 2014	3.4	3.1	48	3.4	2.8	48	11.4%	0.00 [−1.18, 1.18]	2014
Stape et al, 2014	41.5	3.2	80	27.7	3.6	80	11.4%	13.80 [12.74, 14.86]	2014
Vaz et al, 2014	30.1	12.9	120	34.3	12.1	120	10.8%	−4.20 [−7.36, −1.04]	2014
Aguiar et al, 2014	14.5	3.5	80	11.5	6.5	80	11.3%	3.00 [1.38, 4.62]	2014
Bacchi et al, 2015a	24	9.1	120	18.4	8.3	120	11.2%	5.60 [3.40, 7.80]	2015
Bacchi et al, 2015b	27.7	7.7	180	17.5	5	180	11.4%	10.20 [8.86, 11.54]	2015
Total (95% CI)			**772**			**780**	**100.0%**	**3.94 [−0.24, 8.12]**	

Heterogeneity: Tau² = 39.56; Chi² = 419.22, df = 8 (P < 0.00001); I² = 98%
Test for overall effect: Z = 1.85 (P = 0.06)



5

Figure 2. *Global analysis comparing conventional (control) vs self-adhesive resin cements.*

Figure 3. *First subgroup analysis: conventional (control) vs self-adhesive resin cements after aging.*

Figure 4. *Second subgroup analysis: self-adhesive cement performance comparing immediate vs long-term results.*

Figure 5. *Third subgroup analysis: conventional resin cement performance comparing immediate vs long-term results.*

cements did not show any significant difference between immediate and aged bond strength data, considering that the latter indicates a more stable long-term adhesion. Exposed dentinal collagen fibrils are subject to degradation mechanisms, like hydrolysis by water, mechanical fatigue, denaturation, or even a collagenolytic process derived from matrix metalloproteinases and cathepsins, inherently present in dentin.[46] The ability to envelop exposed collagen fibrils is directly dependent on priming steps, wetting characteristics of the bonding agent, and its chemical composition.[12] Although conventional resin cements are more technique sensitive, because they need a specific bond agent, these cements are more capable of interpenetrating the demineralized dentin substrate.

The mechanism of adhesion to dentin is an important issue that should be understood to explain the poorer performing self-adhesive cement in the present study collection. De Munck and others[5] published one of the first studies assessing self-adhesive cements, described at the time as a new class of resin cement. The concept dealt with a resin-based cement that combines cement and adhesive in a single application, not requiring pretreatment of dental substrate or restorative materials.[5] Its adhesive properties were said to be similar to those of self-etch adhesives, because these cements were based on acidic monomers capable of demineralizing and promoting micro-mechanical retention, and some of them were capable of chemical interaction with hydroxyapatite.[5] Dentin hybridization requires hybrid layer formation by superficial demineralization, followed by resin monomer infiltration and polymerization, creating micro-mechanical retention. Without the etch-and-rinse process, the self-etch process does not remove the smear layer, but rather, dissolves and incorporates it into the hybrid layer.

Acidic monomers are responsible for priming and conditioning dental substrates simultaneously, and adhesion depends on them.[47] The demineralization capacity of self-etching systems is considered limited, specifically compared with etching acids like phosphoric acid.[48] De Munck and others[5] assessed the interaction to dentin of RelyX Unicem (the most widely tested self-adhesive resin cement in the present meta-analyses) with ultra-structural transmission electron microscopy (TEM) and field-emission scanning electron microscopy (Fe-SEM). They observed that Unicem interacted only superficially with underlying dentin and did promote hybrid layer or tag formation. Furthermore, the authors observed an irregular interaction zone. When the cement was applied over a fractured dentin piece with no smear layer, they observed hardly any cement-dentin interaction. The cement interaction with intratubular dentin was similar to that of intertubular dentin. The self-etch cement tested in the same study (Panavia F) formed what the authors called a "true hybrid layer."[5] Another issue concerning a self-adhesive resin cement is its pH-neutralization behavior. These cements have a low pH when mixed and manipulated, an important factor in the adhesion process. Cements with insufficient pH neutralization after self-curing can lead to a reduction in their mechanical properties, thus jeopardizing long-term adhesion.[49,50] This behavior is considered material dependent, because it is directly related to cement composition and may diverge among different commercial brands.[50] In fact, the lack of interaction with the dental substrate, combined with reduced etching and demineralization capacity of acidic monomers and the lack of pH neutralization of some cements, could be the factors mainly responsible for the lower dentin bond strength values presented by the self-adhesives.

The results of this systematic review with meta-analyses do not refute the validity of using self-adhesive resin cements. When considering root canal glass-fiber post cementation, self-adhesive resin cements performed better than the conventional ones.[17,51] Another point to be deliberated concerns self-adhesive cement interaction with restorative materials. Published laboratory studies assessing the interaction of self-adhesive cements with indirect restorative materials showed adequate bond strength to these substrates, with a brand-dependent distinction regarding chemical composition.[50,52] Adhesion to dentin remains an issue of scientific assessment, because it is considered the weak link in the adhesion process. As for self-adhesive resin cements, further attention is needed by researchers and manufacturers to develop better material and clinical protocols.

Heterogeneity was considered high and statistically significant in all the meta-analyses researched (I^2=98-99%). Methodologic discrepancies, mainly regarding the different aging methods, could represent the key factor responsible for this heterogeneity. Because of this methodologic variety, the studies could not be categorized according to aging methods, unless at least one aging method was used. Furthermore, greater methodologic rigor is needed to counter the neglected risk of bias parameters seen in this review. Risk of bias assessment showed that most of the studies included had medium or high risk. This indicates the likelihood that these laboratory studies did not control all the variables that could influence the results, and this somewhat explains the high heterogeneity.

An important limitation of the present review is that it included only laboratory studies, with controlled environment and variables. The extracted data reveal only the adhesion to dentin factor in the retention of an indirect restoration to dentin, without considering other important parameters, like tooth preparation design and retention, restoration type and extension, tooth position technique sensitivity, and the operator,[53] who may influence ultimate survival of the restoration.

CONCLUSION

Despite the high heterogeneity and limitations of the present review of laboratory studies with meta-analyses, conventional multistep resin cements showed better overall adhesive performance to dentin compared with simplified self-adhesive resin cements. Laboratory results are an important factor to be considered in restoration longevity prognosis; however, other clinical aspects must be considered in assessing clinical success.

Conflict of Interest

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

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