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Bonding of resin adhesives to caries-affected dentin - A systematic review

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Key words: Systematic review, bonding, adhesive resins, caries-affected dentin

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Abstract

Background: Minimal invasive dentistry aims at preserving the firm, discoloured caries-affected dentin (CAD), which is remineralizable. Research studies on resin adhesives are usually performed on sound dentin (SD), though CAD is the substrate routinely encountered for bonding in clinical practice.

Aim: To systematically analyze the published literature on resin-dentin bonding to CAD substrate, in order to answer the question: “Does resin adhesive bonding to CAD produce lower bond strength when compared to SD?”

Design: Three electronic databases (Pubmed, Scopus and ISI web of Science) were searched to identify original laboratory studies that evaluated the bond achieved between resin adhesive and natural CAD by measuring their bond strength. Full text articles in English language were only included. Further relevant articles from the reference list of the retrieved studies were accessed through further electronic and manual searches. Only articles that met the specific inclusion criteria were included in the review.

Results: Among the 29 studies included for this review, majority of the studies had tested the simplified etch-and-rinse or self-etch adhesives. 85% of them showed higher bond strength to SD compared to CAD and the remaining 15% of them showed no difference between these two substrates. Among the studies that used 3-step etch-and-rinse adhesives, 40% showed higher and 60% showed no difference, when bond strength was compared between SD and CAD.

Conclusions: Resin adhesives produce lower bond strength to caries-affected dentin than sound dentin.

Clinical significance: Research studies that reported bond strength of resin adhesives to dentin from sound extracted teeth alone cannot not be blindly extrapolated to clinically relevant CAD. Hence, the results from such studies should be dealt with caution.

Introduction

Minimally invasive cavity preparation aims at the removal of softened caries-infected dentin alone, which is non-remineralizable but heavily infected with bacteria. Such a cavity preparation preserves the firm, discoloured caries-affected dentin (CAD) that is remineralizable and has relatively less bacteria. Minimally invasive dentistry is made possible by the current advancement in adhesive technology.

The contemporary resin adhesives have become user friendly and this is achieved by reducing the number of steps required for its successful application in the dental restorative procedures. The dental adhesive system is classified based on: (a) the use of acid etchant or acidic monomer for demineralization of the enamel and dentin and (b) the number of clinical steps involved in their application. Accordingly, the dental adhesive system is broadly classified into either etch-and-rinse adhesive system or self-etch system. The etch-and-rinse adhesive system is further classified into 3-step or 2-step system. The self-etch system is further classified into 2-step or 1-step self-etch system [1,2].

The laboratory studies validating the efficacy of these adhesives are most often performed using normal, sound dentin that is exposed from a freshly cut sound tooth [3,4]. In the routine clinical practice, particularly in this era of minimally invasive dentistry, most often resin adhesives are placed on CAD that is exposed after removal of soft caries-infected dentin. Caries-affected dentin is qualitatively different from normal dentin due to cycles of demineralization and remineralization [5]. It varies from normal sound dentin in several aspects, including physical, chemical biomechanical, which heavily influence the outcomes of resin-dentin bonding [6,7,8]. It only has around half the hardness of normal dentin [9] and the ultimate tensile or cohesive strength of CAD depends on its softness [10]. The intertubular dentin of CAD is partially demineralized due to the caries process [11,12]. The thicker smear layers of CAD being more difficult to remove and etch through, the greater intrinsic water content and reduced calcium in intertubular dentine may not allow the chemical adhesion to be as successful [13,14]. As a result, CAD responded in a different way to bonding procedures and resin adhesives, when compared to normal, sound dentin [15].

Fusayama [16] reported that due to the already existing demineralization of the intertubular dentin in CAD, the acid-etching process would cause greater depths of demineralization in CAD than in sound dentin. Such increased depths of demineralization may not be entirely infiltrated by the resin monomers, leading to exposed, unprotected collagen fibrils at the base of the hybrid layer. The exposed and unprotected collagen fibrils are prone to degradation by endogenous matrix metalloproteinases (MMPs), leading to a decrease in durability of the resin-dentin bond and compromise the longevity of the overlying bonded restoration [17].

Configuration factor or 'C' factor is the ratio of bonded surface area of dentin to unbonded surface area. In clinical conditions (such as in class I cavities) where 'C' factor can be very high, resulting in increased stress at the bonded interfaces [18]. Usually high resin-dentin bond strength is required to withstand such stresses. Hence, it is important to study the immediate (24 h) bond strength of the resin-dentin bonded specimens as low bond strength may lead to failure, because of stresses at the bonded interfaces. It is important to study the bond strength of resin adhesives to the clinically relevant CAD, as it is this substrate to which bonding is commonly performed. Research studies that reports bond strength of resin adhesives to dentin from sound extracted teeth alone should not be blindly extrapolated to bonding of such adhesives to the clinically relevant CAD. Hence, the results from such studies should be dealt with caution.

Dentin-bonded interfaces achieved with contemporary resin adhesives have shown to degrade with time [19,20], due to hydrolytic degradation of adhesive resin as one of the major reasons that results from an increased concentration of hydrophilic monomers [21,22]. As resin-dentin bonded interfaces show degradation with time, it becomes important to achieve a high initial bond strength so that the bonded interfaces could withstand the degradation process over time. This is another reason for why it is necessary to compare the bond strength achieved by resin adhesives between sound and caries-affected dentin. If the initial resin-CAD bond strength is lower than the resin-SD bond strength, then obviously the degradation process will lead to greater reduction in bond strength to CAD eventually. Also, as the dentin carious process involves MMP and cysteine cathepsins activities [23], the degradation could be more pronounced in such a substrate compared to SD.

Minimal invasive dentistry (MID) aims at maximum preservation of tooth tissues; hence contemporary operative management of cavitated lesions of a tooth have moved on from “bonding alone to carious dentine” to “bonding along with an achievement of an optimum seal” at cavo-surface margins of a tooth-restoration interfaces [24]. Achievement of an adequate seal using resin sealant or flowable composite material to a composite restoration that was bonded to CAD is important for several reasons. Firstly, an adequate seal at the cavo-surface margins of tooth-restoration interfaces would prevent the nutritional supply to residual bacteria that remain in CAD. The lack of nutritional supply will prevent recurrent caries in the restored tooth. Secondly, it could facilitate the clinicians to preserve carious dentin tissue in a tooth with deep caries as removal of such tissues could end up in pulpal exposure. Furthermore, when an adequate seal is achieved in a restoration that was placed on CAD in a tooth with symptoms of reversible pulpitis, the signs could get resolved. Henceforth, the remaining tooth tissue at the cavo-surface margins should bond well with the adhesive systems.

From the prognosis and maintenance point of view, preservation of CAD results in a smaller restoration that would be easy to maintain from both a dentist’s and patient’s aspect. More importantly from the patient’s aspect, a smaller restoration would have its cavo-surface margins in a self-cleansable area, which enhances plaque control and prevent the development of recurrent caries [25].

In this current era of evidence-based dentistry, there is a need for high quality evidence to support a therapeutic procedure and the material of choice for such a therapy. Unfortunately, the past and current research work on resin adhesives is almost always based on *in vitro* studies. When one looks for evidence, though laboratory-based research evidence falls last on the hierarchy of "the levels of evidence", it is still considered important, when no other forms of evidence exist. It is imperative to identify well-conducted laboratory studies, so that they could be used as a guide for the development of treatment recommendations (within their intrinsic limitations). The aim of this review was to systematically analyze published literature on bonding of resin adhesives to CAD substrate by comparing their bond strength results. The research question that led to this systematic review was: "Does resin adhesive bonding to CAD produce lower bond strength compared to sound dentin (SD)?"

2. Methods

2.1 Search strategy

Laboratory studies that evaluated the bond achieved between resin adhesive and natural CAD by using bond strength testing was included. This systematic review was performed following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. The electronic databases searched for identifying the relevant studies included PubMed, Scopus, and ISI Web of Science. Only studies with full text article were included. Non-English language articles were not included in this review. Further relevant articles quoted in the reference list of the retrieved studies were accessed through further electronic search and hand search. There was no limit set for the year of publication. The last search was performed on 20th May 2014. MeSH terms were not used. Only the specified keywords mentioned in this review were used for the search. Two authors were involved in the search (ME and CY). 105 articles were identified as duplicates and were excluded. Two authors (ME and CY) screened the title and the abstract. Any disagreement was discussed with the third author (JM) and was decided. One author (ME) completed the full text review. Inclusion was based on consensus of 2 authors (ME and CY). A strict inclusion criteria was set in order to reduce the risk of bias in the included studies.

Key words and their sequence used for searching through electronic databases

#1 dentin bonding

#2 adhesive resin

#3 caries-affected dentin

#4 bond strength

#5 (#1) AND (#2)

#6 (#3) AND (#4)

#7 (#5) AND (#6)

2.2 Criteria for considering studies for this review

This review includes only studies that provided:

(1) A clear objective for conducting the study and/or a note of the hypothesis tested.

(2) Adequate information about the methodology, including the groups studied, sample size per group and the study design for testing the hypothesis.

(3) Adequate information on the materials used in the study and the equipment used for testing.

(4) A test group(s) in which bonding was achieved to CAD substrate and a control group with bonding to the sound dentin substrate.

(5) Teeth with natural dentin caries only. Studies that employed teeth with artificial caries and bovine teeth were excluded from this review.

(6) Sound and CAD substrates from the carious teeth itself. Accordingly, those studies that dealt with sound dentin substrate from other sound teeth for comparison with CAD substrate obtained from the carious teeth were excluded from this review due to the chance for substrate variability.

(7) Adequate information on how CAD was differentiated from sound dentin and the method(s) used to remove CAD.

(8) Used composite resin for restoration/crown build-up, therefore studies in which teeth with restorations/crown build-up done exclusively with glass ionomer cements, resin-modified glass ionomer cements and compomers were not considered.

(9) Adequate information on the outcome measures, in particular the bond strength measurements with a standard testing protocol. The bond strength studied should have had at least a 24 hour lapse of time after the bonding procedure and before bond strength testing was done.

(10) The mean bond strength values for the test(s) and the control groups from testing the bonded teeth using micro-tensile test method after cutting the bonded teeth into multiple specimens of smaller bonded surface areas (approximately 0.8 to 1 mm^2) and test(s) them individually. Studies that used tensile, shear test methods were excluded.

(11) Due to the differences in stresses created at the adhesive interface between microtensile and microshear test methods, only those studies that used microtensile test for bond strength measurements were included.

(12) An appropriate statistical test performed to analyze the bond strength data. Also any studies with inadequate information on the results obtained from the study (with the statistical inference) were not included in the review.

3. Results

The progress through each stage of the review is shown in Fig. 1. The search using the electronic databases with the specified key words retrieved a total of 242 articles. Out of them, 171 articles were excluded after the initial screening, leaving 71 articles for full text evaluation. There were 6 articles that were retrieved from the reference lists and were added to these 71 articles and hence, a total of 77 articles were evaluated by full text. Nevertheless, 48 articles did not meet the inclusion criteria of this review and were excluded. Given this, a final total number of 29 studies that met the inclusion criteria were included for this review.
The list of excluded studies and the reasons for their exclusion are shown in Table 1.

The descriptive statistics of the included studies is shown in Table 2. One study [26] on permanent teeth used the so-called split tooth technique, in which the tooth was hemi-sectioned and the two halves were randomly distributed into test and control groups.

In most of the included studies, the soft caries-infected dentin was identified using a caries detector dye and caries was subsequently excavated using a sharp excavator. Caries-affected dentin was identified by the combined criteria of caries-detector dye, visual examination and hardness to the explorer [27,28,29,30]. Very few included studies used other methods, such as mechanical (bur with a hand piece) [31,32] and chemo-mechanical (Carisolv) [26,31] for removal of caries-infected dentin to expose the caries-affected dentin. Sonoda et al. [26] compared the bonding of two adhesive systems (2-step etch-and-rinse and 1-step self-etch) to

CAD, following two different caries-removal techniques: Carisolv and hand excavation. Results of their study showed that CAD following Carisolv treatment produced significantly higher bond strength with 1-step self-etch adhesive than hand excavation; whilst no significant difference in bond strength was found between the two caries removal techniques with the 2-step etch-and-rinse adhesive. Tachibana et al. [31] showed no significant difference in the bond strength of the 2-step self-etch adhesive to CAD following the four caries removal methods (abrasive paper, slow-speed bur, laser and Cariosolv). Ergücü et al. [32] compared CAD substrate preparation with a round carbon steel bur and laser (Er, Cr:YSGG) to bonding with 3-step etch-and-rinse and 2-step self-etch adhesives and found that laser did not negatively affect bonding of the two adhesive system to CAD.

Most of the included studies tested the bond strength after 24 hours of bonding. Among the adhesive systems, most of the included studies used 2-step etch-and-rinse and 2-step self-etch adhesive systems. Very few studies had tested 3-step etch-and-rinse [32,33,34,35,36] and 1-step self-etch adhesive systems [26,29,35,37,38,39,40,41,42,43].

Table 3. summarizes the studies which compared the bond strengths between sound and CAD achieved with various adhesive systems. When 3-step etch-and-rinse adhesives were used to test the bond strength, 2 [33,36] studies showed significantly higher; while 3 studies [32,34,35] showed no significant difference in bond strength between the two dentin substrates. None of the studies showed higher bond strength of 3-step etch-and-rinse adhesive to CAD than sound dentin. Among the studies that have evaluated the bond strength using 2-step etch-and-rinse adhesives, 13 studies showed significantly higher and 2 studies [23,40] showed no difference in the bond strength between sound dentin compared to CAD.

For the studies that have examined bond strengths of 2-step self-etch adhesives to the two different dentin substrates, 18 studies showed significantly higher bond strength to sound dentin; while 3 studies [29,32,35] showed no difference in bond strength between sound dentin and CAD. None of the studies with 2-step self-etch adhesives showed significantly higher bond strength to CAD than sound dentin. For 1-step self-etch adhesive, 8 studies showed significantly higher bond strength to sound dentin than CAD, 1 study [37] showed no difference and none of the studies showed significantly better bond strength to CAD than sound dentin.

Three [36,44,45] studies included in this review have studied the bond durability. According to these studies, in addition to the group that tested the bonding after 24 hours, there was an additional group that tested the bond strength after aging. One of the studies analyzed the short-term aging of the bonded specimens after 1 week and 1 month [45]. Two other studies had evaluated the durability after 6 months [36,44]. In one of the study [36] that tested the bond strength after 6 months of aging, there was a significant reduction in bond strength in both sound and CAD, when bonding was performed with 2-step etch-and-rinse adhesive systems, either with or without 2% chlorhexidine pretreatment.

4. Discussion

Caries-affected dentin is a very challenging substrate for resin bonding. The structural and biochemical changes that resulted from the caries process make it a truly different substrate for bonding with resin adhesives. Given this, this review was performed to systematically analyze resin bonding to CAD, so that a direct comparison to the sound dentin could be made. This might help the researchers and the clinicians to understand the importance of studying resin-dentin bonding to a clinically relevant substrate and to interpret the findings derived from those studies performed with resin adhesives exclusively on sound dentin with caution.

One of the inclusion criteria in this review was to include only the articles that were published in the English language. Against such a criteria, the chances for language bias in this review is negligible, as the database search and the manual search, retrieved only one non-English article [46], which was in Chinese and was excluded. Three studies [47,48,49] were excluded from the review processes, as there was inadequate information on the sample size. These studies only reported the total number of bonded specimens generated for bond strength testing. The number of teeth used for generating these specimens was not reported. As a result, these studies were excluded from our review, as there is a possibility that only a few teeth have been used in preparing the bonded specimens.

In our review, the studies that have used teeth with simulated dentin caries were also excluded, because such dentin substrate though demineralized, is different from that of sound dentin and therefore cannot be substituted for the natural CAD substrate. Studies that have used sound teeth separately as the control group to study bonding to sound dentin substrate were excluded, as there are chances for substrate variability between the teeth with caries and sound teeth. Hence, only those studies that have reported bonding to sound and CAD substrates, all generated from the same tooth with dentinal caries, were included in this review.

In majority of the included studies, CAD substrate has been identified using the combined criteria of caries-detector dye, visual and tactile examination. Previous studies [50,51] have shown that detection of CAD using caries-detector dyes has wide variability, as this method very much depends on user interpretation. Banerjee et al [52] have stated that caries-detector dyes, in addition to over staining caries-infected dentine, also overstains demineralized CAD substrate that could lead to over estimation and therefore over excavation of the preservable superficial part of CAD substrate.

Chemomechanical caries removal is an alternative method to remove caries-infected dentine and to expose CAD [53]. Banerjee et al [54] studied three caries removal methods and showed that sodium hypochlorite-based “Carisolv” (CarisolvTM gel–OraSolv AB, Gothenburg, Sweden) and pepsin-based “Biosolv” (SFC-V, ‘‘Biosolv’’, 3MESPE AG, Seefeld, Germany) preserved CAD to a greater extent than conventional hand excavation using spoon excavator.

Two studies that were included in this review [31,32] had used laser system in one of the experimental groups, along with other conventional methods in the other groups to excavate the caries-infected dentin and to expose CAD for bonding with resin adhesive. In general, the laser-ablated CAD substrate could be very different, when compared with the CAD substrate using the typical excavation methods. Therefore, the bond strength comparisons of the resin adhesives between SD and laser-ablated CAD were not included in this review.

Micro-tensile bond strength test method was first used in resin-dentin bonding by Sano et al. [55]. This bond strength test method gives more accurate assessment of resin-dentin bond strength as it converts the bonded surfaces into several small specimens with a bonding surface area of less than 1 mm^2 before testing. The bond strength values obtained by this method are more accurate than by conventional tensile or shear test methods [55].

From the results of the bond strength comparisons between sound and CAD with various adhesives, 40% of the studies that used 3-step etch-and-rinse adhesives produced higher bond strength to sound dentin. The remaining 60% of studies showed no difference to sound dentin when compared to CAD. Over 85% of studies that used 2-step etch-and-rinse, 2-step and 1-step self-etch adhesives produced higher bond strength to sound dentin, compared to CAD; while the remaining studies produced similar bond strength values to both the sound and CAD.

The separate etching, priming and adhesive application steps in 3-step etch-and-rinse adhesives could have produced better encapsulation of the demineralized dentin by resin adhesives and hence improved bond strength to CAD substrate. However, there were only 5 studies in this review that used 3-step etch-and-rinse adhesives and therefore, the results should be interpreted with caution. In addition, there were not many studies included in the review with 1-step self-etch adhesives. Further studies are needed with these adhesives to provide a better understanding of their behavior with this clinically relevant substrate.

Among all the included studies in this review, bond durability of resin adhesives to CAD was studied only by three studies [36,44,45]. Komori et al. [36] showed that when 2% chlorhexidine was used along with a 3-step etch-and-rinse adhesive, the bond strengths to both sound and CAD were preserved after 6 months; however, it did not preserve the bond of 2-step etch-and-rinse adhesives to both substrates. There is a need for further studies to study the effect of incorporation of MMP inhibitors in resin-dentin on the durability of resin adhesives to caries-affected dentin.

5. Conclusions

From this review we may conclude that:

(1) Resin adhesives can produce lower bond strength to caries-affected dentin substrate than sound dentin substrate.

(2) Though three-step etch-and-rinse adhesive was only used by a few studies included in this review, it had shown better bonding to caries-affected dentin compared to other resin adhesives systems.

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Figure 1. Flow chart of the articles selection process.

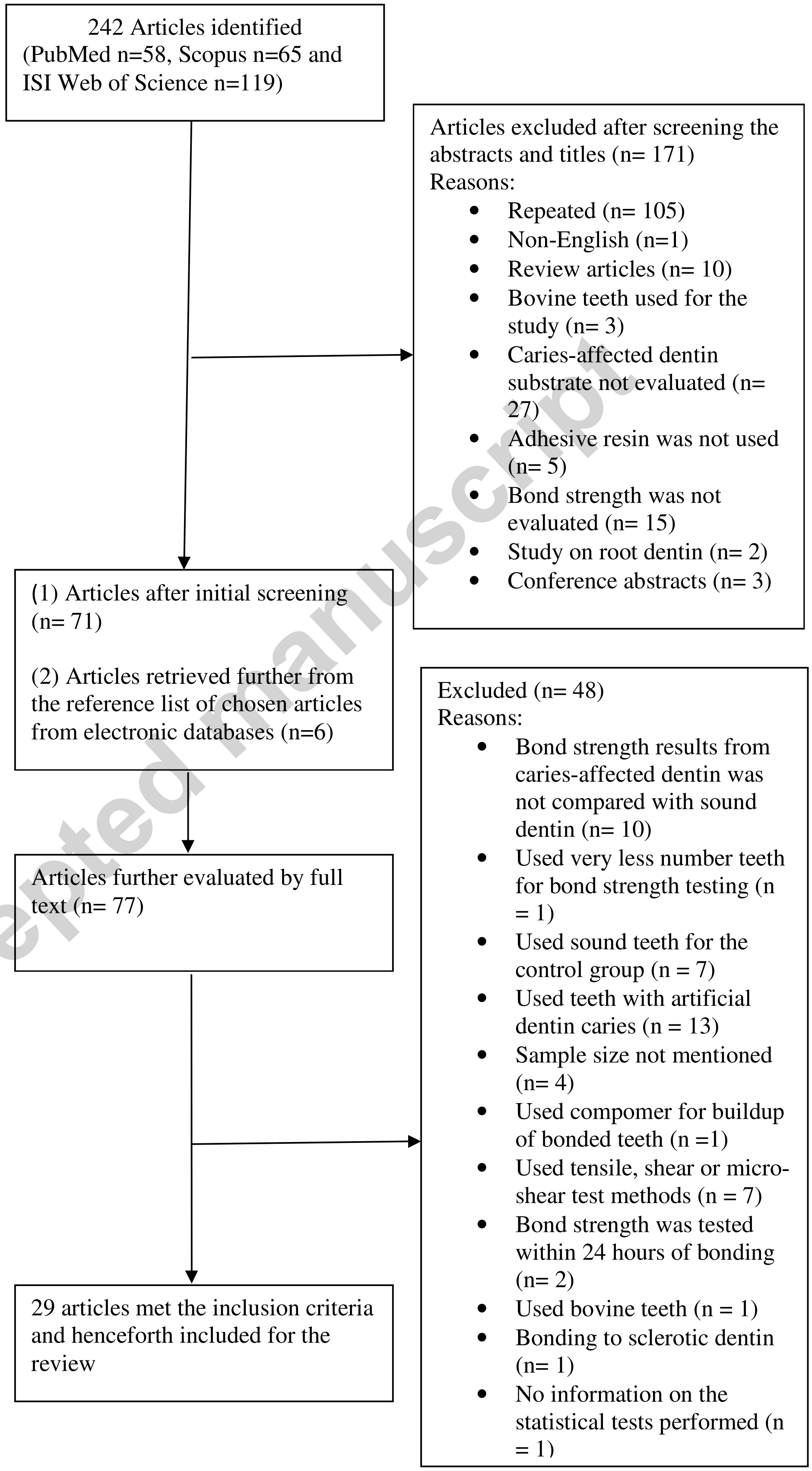

Table 1. Descriptive statistics of the included studies.

Author & Year	**Sample size**	**Technique used for exposing caries – affected dentin substrate for bonding**	**Adhesive system(s) tested**	**Storage time before testing**	**Findings**
Arrais et al 2004 [27]	36	Wet grinding after visual examination & a dental explorer for checking hardness	(1)Clearfil SE Bond *(2-step SE)* (2)Single Bond *(2-step E & R)*	24 h	BS of tested adhesives were significantly higher to SD than CAD
Ceballos et al 2003 [37]	16	Wet grinding after visual examination & staining with 0.5% fuchsin dye	(1)Prime and Bond NT *(2-step E & R)* (2)Scotchbond 1 *(2-step E & R)* (3)Clearfil SE Bond *(2-step SE)* (4)Prompt L-Pop *(1-step SE)*	24 h	E & R adhesives produced higher BS to SD and CAD than self-etch adhesives
Doi et al 2004 [56]	15	Carious lesion was exposed by wet grinding & carious detector dye	(1)Clearfil SE Bond *(2-step SE)* (2)Mac-Bond II *(2-step SE)* (3)Unifil Bond *(2-step SE)*	24 h	BS of tested adhesives were significantly higher to SD than CAD

Ergücü et al 2009 [32]	16	Caries was disclosed by visual and tactile examination along with caries detector dye and was removed by round carbon steel bur	(1)Scotchbond Multi-Purpose *(3-step E& R)* (2)AdheSE *(2-step SE)*	24 h	AdheSE produced significantly lower BS to Scotchbond MP to SD and CAD
Erhardt et al 2008 [44]	144	Wet grinding with 600 grit SiC paper after visual examination, caries detector dye and sharp excavation	(1)Adper Scotchbond 1 (*2-step E & R*) (2) Clearfil Protect Bond (*2-step SE*) (3) AdheSE (*2-step SE*)	24 h and 6 months	(1)BS of tested adhesives were significantly higher to SD than CAD (2) After 6 months, BS of tested adhesives to CAD showed a significant decrease; while BS to SD remained stable
Erhardt et al 2008 [57]	30	Wet grinding with 600 grit SiC paper after visual examination, caries detector dye and sharp excavation	Adper Scotchbond 1 *(2-step E & R)*	24 h	(1) BS of tested adhesives were significantly higher to SD than CAD after etching with H_3PO_4 (2) Use of MMPs inhibitors prior to application of tested adhesive did not affect BS to CAD

Komori et al 2009 [36]	40	Wet grinding with 600 grit SiC paper after visual examination, caries detector dye and sharp excavation	(1)Scotchbond Multi-Purpose *(3-step E & R)* (2)Single Bond 2 *(2-step E & R)*	1 week and 6 months	(1) BS (after 1 week) of tested adhesives was significantly higher to SD than CAD (2) BS of Single Bond 2 to SD and CAD were reduced significantly in both control and 2% CHX pretreatment groups after 6 months of storage
Kunawarote et al 2011 [58]	40	Wet grinding with 600 grit SiC paper after visual examination, caries detector dye and sharp excavation	Clearfil SE Bond *(2-step SE)*	24 h	(1) BS of Clearfil SE Bond was significantly higher to SD than CAD (2)Pretreatment with 0.95 mM HOCl improved BS of Clearfil SE Bond to CAD
Macedo et al 2009 [42]	48	Wet grinding with 600 grit SiC paper after visual examination, caries detector dye and sharp excavation	(1)Adper Single Bond Plus (*2-step E & R*) (2)One Step Plus (*1-step SE*)	24 h	(1) BS of tested adhesives was significantly higher to SD than CAD (2)Application of grape seed extract and glutaraldehyde significantly improved BS to both SD

					and CAD
Nakajima et al 1995 [33]	47	Wet grinding after visual examination & caries detector dye	(1)All Bond 2 *(3-step E & R)* (2)Scotchbond Multi-Purpose (*3-step E & R*) (3)Clearfil Liner Bond 2 *(2-step SE)*	24 h	(1)All Bond 2 and Clearfil Liner Bond 2 produced significantly lower BS to CAD than SD (2) No significant difference in BS between SD and CAD for Scotchbond Multi-Purpose
Nakajima et al 1999 [34]	15	Wet grinding after visual examination & caries detector dye	(1)Scotchbond Multi-Purpose Plus *(3-step E & R)* primer + Adhesive (2)Experimental primer (50% HEMA in water) + Scotchbond Multi-Purpose Plus adhesive	24 h	No significant difference in BS between SD and CAD with moist bonding technique
Nakajima et al 1999 [59]	19	Wet grinding after visual examination & caries detector dye	(1)Clearfil Liner Bond 2 *(2-step SE)* (2)Clearfil Liner Bond 2V *(2-step SE)* (3)A.R.T. Bond *(2-step SE)*	24 h	(1) Clearfil Liner Bond 2 and Clearfil Liner Bond 2V produced significantly lower BS to CAD than SD (2) No significant difference in BS between

					SD and CAD for A.R.T.
Nakajima et al 2000 [30]	24	Wet grinding with 600 grit SiC paper after visual, tactile examination & caries detector dye	(1)OneStep *(2-step E & R)* (2)Single Bond *(2-step E & R)*	24 h	BS of tested adhesives to CAD were significantly reduced by lowering the concentration of PA etchant from 32/35% to 10%
Nakajima et al 2005 [60]	11	Wet grinding with 600 grit SiC paper after visual examination & caries detector dye	Clearfil Protect Bond (*2-step SE*)	24 h	BS of tested adhesive was significantly higher to SD than CAD
Nakajima et al 2006 [45]	18	Wet grinding with 600 grit SiC paper after visual examination & caries detector dye	Clearfil SE Bond *(2-step SE)*	(1)24 h (2)1 week with hydrostatic pressure (3)1 month with hydrostatic pressure	(1) 24 h BS of tested adhesive was significantly higher to SD than CAD (2) BS to SD was significantly lowered by hydrostatic pulpal pressures after 1 month storage, BS to CAD not affected
Omar et al 2007 [35]	30	Occlusal enamel was removed with slow-speed Isomet saw and exposed carious substrate was	(1)Scotchbond Multi-Purpose *(3-step E & R)* (2)Clearfil SE Bond *(2-step SE)* (3)Xeno IV	24 h	(1)Scotchbond Multi-Purpose and Clearfil SE Bond produced similar bond strengths to SD and CAD (2)Bond

		examined visually and using small excavator	*(1-step SE)*		strength of Xeno IV was significantly higher to SD than CAD (3)Thermocycling did not reduce bond strength of tested adhesives to CAD
Pereira et al 2006 [40]	20	Wet grinding with 600 grit SiC paper after visual examination & caries detector dye	(1)Single Bond *(2-step E & R)* (2)Adper Prompt L-Pop *(1-step SE)*	24 h	(1) BS of Adper Prompt L-Pop was significantly higher to SD than CAD (2) No significant difference in BS of Single Bond to SD and CAD
Say et al 2005 [61]	24	Wet grinding with 600 grit SiC paper along with visual examination & caries detector dye	(1)OptiBond Solo Plus *(2-step E & R)* (2)OptiBond Solo Plus self-etch *(2-step SE)* (3)Optibond Solo Plus dual-cure (4) Optibond Solo Plus self-etch dual-cure	24 h	(1)BS of tested adhesives were significantly higher to SD than CAD (2) E & R technique did not show any beneficial effect on CAD compared with SE technique
Scholtanus et al 2010 [29]	15	Hand excavation of soft infected dentin after use of caries detector dye,	(1)Adper Scotchbond 1 XT *(2-step E & R)* (2)Clearfil S^3 Bond *(1-*	24 h	(1)BS of 2-step E & R and 1-step SE adhesive were significantly higher to

		further confirmation was by visual and tactile examination	*step SE)* (3)Clearfil SE Bond *(2-step SE)*		SD than CAD (2)BS of 2-step SE adhesive was not different between SD and CAD
Sonoda et al 2005 [26]	20 (hemisectioned to produce two groups of 20 hemisectioned teeth each)	(1)Hand excavation with sharp spoon excavator (2)Carisolv gel	(1)ABF *(1-step SE)* (2)Prime and Bond NT *(2-step E & R)*	24 h	(1) BS of ABF to SD and chemo-mechanical caries removal groups were both significantly higher than hand-excavated group (2) For Prime and Bond NT, no significant difference in bond strength between SD and CAD
Tachibana et al 2008 [31]	40	(1)Wet grinding with abrasive paper (2)Round steel burs with water cooled slow speed handpiece (3)Carisolv system	Clearfil SE Bond *(2-step SE)*	24 h	(1) BS of tested adhesive was significantly to SD higher than CAD (2)No significant difference in the BS to CAD between the groups
Taniguchi et al 2009 [41]	40	Wet grinding after visual examination and caries detector dye	(1)Clearfil Protect Bond *(2-step SE)* (2)Bond	24 h	(1) BS of tested adhesives was significantly higher to SD

			Force *(1-step SE)*		than CAD (2)NaOCl pretreatment for 15s significantly improved BS to CAD (3)Application of reducing agent, Accel, increased BS to SD and CAD treated with NaOCl for 30s.
Xuan et al 2010 [43]	28	Wet grinding with 600 grit SiC paper after visual examination, caries detector dye and sharp excavation	(1)Adper Single Bond 2 (*2-step E & R*) (2)Clearfil SE Bond (*2-step SE)* (3)Clearfil S^3 Bond (*1-step SE*) (4)iBond GI (1 step SE)	24 h	(1) BS of all tested adhesives was significantly higher to SD than to CAD (2) 2-step E & R adhesive performed better than SE adhesives for CAD
Yazici et al 2004 [62]	12	Initial removal with bur, subsequent removal with wet grinding along with visual examination, sharp excavator and caries detector dye	Clearfil SE Bond *(2-step SE)*	24 h	(1) BS of tested adhesive was significantly higher to SD than CAD (2)Acid etching prior to adhesive application did not improve BS to CAD, but decreased BS to SD

Yoshiyama et al 2000 [63]	12	Wet grinding after visual examination & caries detector dye	(1)Fluoro Bond *(2-step SE)* (2)Single Bond *(2-step E & R)*	24 h	BS of tested adhesives were significantly higher to SD than CAD
Yoshiyama et al 2002 [64]	16	Wet grinding after visual examination, caries detector dye and sharp excavation	(1)Experimental SE adhesive *(2-step SE)* (2)Single Bond *(2-step E & R)*	24 h	BS of experimental SE adhesive and commercial 2-step E &R adhesive were significantly higher to SD than CAD
Yoshiyama et al 2003 [65]	12	Wet grinding after visual examination, caries detector dye and sharp excavation	Clearfil Liner Bond 2V *(2-step SE)*	24 h	BS of tested adhesive was significantly higher to SD than CAD
Yoshiyama et al 2004 [39]	21	Wet grinding after visual examination & caries detector dye	ABF, Protect Bond *(1-step SE)*	24 h	BS of tested adhesive was significantly higher to SD than CAD
Zanchi et al 2010 [28]	19	Wet grinding after visual examination and surface hardness verification with dental explorer	(1)Adper Single Bond *(2-step E & R)* (2)Clearfil SE Bond*(2-step SE)*	24 h	Additional etching increased BS of tested adhesives to CAD, but not enough to reach BS values obtained with SD

Key: BS-bond strength; SD-sound dentin; CAD-caries-affected dentin; E & R: etch & rinse; SE: self-etch

Table 2. Excluded studies from the review that did not fulfill the inclusion criteria

Studies	Reasons for exclusion
Alves et al 2013 [66]	Used teeth with artificial dentin caries in the study
Banerjee et al 2010 [54]	Did not compare BS results between CAD and SD
Botelho Amaral et al 2011 [67]	Used teeth with artificial dentin caries in the study
Burrow et al 2003 [48]	Sample size is not mentioned
Carvalho et al 2013 [68]	Did not compare BS results between CAD and SD
Cehreli et al 2003 [69]	Did not compare BS strength results between CAD and SD
de-Melo et al 2013 [70]	Used teeth with artificial dentin caries in the study
Erhardt et al 2004 [71]	Used bovine teeth in the study
Erhardt et al 2008 [72]	Used sound teeth in control group where SD was bonded for BS comparison with the test groups
Erhardt et al 2014 [73]	Used teeth with artificial dentin caries in the study
Ersin et al 2009 [74]	Used sound teeth in the control group where the sound dentin substrate was bonded for BS comparison with the test groups
Gianini et al 2010 [75]	Did not compare BS results between CAD and SD
Haak et al 2000 [76]	Did not compare BS results between CAD and SD
Hosoya et al 2006 [77]	Used sound teeth in control group where SD was bonded for BS comparison with test groups
Huang et al 2011 [49]	Sample size is not mentioned
Kabbach et al 2014 [78]	Used teeth with artificial dentin caries in the study
Kimochi et al 1999 [79]	Used only 3 teeth for testing the BS
Koyuturk et al 2006 [80]	Shear bond test method was used for BS measurement
Koyuturk et al 2014 [81]	Used compomer for buildup of bonded teeth
Lenzi et al 2012 [82]	Used teeth with artificial dentin caries in the study
Li et al 2011 [83]	Did not compare BS results between CAD and SD
Lopes et al 2003 [84]	Did not study CAD, instead studied sclerotic dentin substrate
Lopes et al 2007 [85]	The study mentioned the number of

	dentin slabs used for testing, but did not mention the number of teeth used for preparing those dentin slabs.
Marquezan et al 2010 [86]	Used teeth with artificial dentin caries in the study
Marquezan et al 2011 [87]	No information about the statistical test(s) used for the analysis of bond strength data
Mobarak 2011 [88]	Micro-shear bond test method was used for BS measurement
Mobarak and El-Badrawy 2012 [38]	Micro-shear bond test method was used for BS measurement
Mobarak et al 2010 [89]	Micro-shear bond test method was used for BS measurement
Nakajima et al 2000 [90]	Used teeth with artificial dentin caries in the study
Nakornchai et al 2005 [91]	Used sound teeth in control group where SD was bonded for BS comparison with test groups
Paranhos et al 2009 [92]	Used teeth with artificial dentin caries in the study
Ricci et al 2010 [93]	Did not compare BS results between CAD and SD
Sacramento et al 2012 [94]	Used teeth with artificial dentin caries in the study
Sattabanasuk et al 2005 [95]	Used teeth with artificial dentin caries in the study
Sattabanasuk et al 2006 [96]	Did not compare BS results between CAD and SD
Sengün et al 2002 [97]	Shear bond test method was used for BS measurement
Sengün et al 2005 [98]	Shear bond test method was used for BS measurement
Silva et al 2006 [99]	Used sound teeth in control group where SD was bonded for BS comparison with test groups
Sirin Karaarslan et al 2012 [100]	Did not compare BS results between CAD and SD
Suzuki et al 2013 [101]	Used sound teeth in control group where SD was bonded for BS comparison with test groups
Toledano et al 2012 [102]	Used sound teeth in control group where SD was bonded for BS comparison with test groups
Tonetto et al 2013 [103]	Used teeth with artificial dentin caries in the study
Tosun et al 2008 [104]	Micro-shear bond test method was used for BS measurement

Urayama et al 2001 [47]	Sample size is not mentioned
Wei et al 2008 [105]	BS of the bonded specimens was tested immediately after an hour of bonding.
Yildiz et al 2013 [106]	Did not compare BS results between CAD and SD
Zanchi et al 2010 [107]	Used teeth with artificial dentin caries in the study
Zawaideh et al 2011 [108]	Bonded specimens were tested for their bond strength within 24 hours of bonding

Table 3. Summary of the adhesive resin bond strength comparison between sound and the caries-affected dentin substrates.

Study	**Adhesives tested**	**Bond strength: Sound dentin (SD) vs. Caries-affected dentin (CAD)**
Arrais et al 2004 [27]	2-step SE 2-step E & R	SD>CAD
Ceballos et al 2003 [37]	2-step E & R 2-step SE 1-step SE	2-step E & R: SD>CAD 2-step SE: SD>CAD 1-step SE: SD=CAD
Doi et al 2004 [56]	2-step SE	SD>CAD
Ergücü et al 2009 [32]	3-step E& R 2-step SE	SD=CAD
Erhardt et al 2008 [44]	2-step E & R 2-step SE	SD>CAD
Erhardt et al 2008 [57]	2-step E & R	SD>CAD
Komori et al 2009 [36]	3-step E & R 2-step E & R	SD>CAD
Kunawarote et al 2011 [58]	2-step SE	SD>CAD
Macedo et al 2009 [42]	2-step E & R 1-step SE	SD>CAD
Nakajima et al 1995 [33]	3-step E & R 2-step SE	SD>CAD
Nakajima et al 1999 [34]	3-step E & R	SD=CAD
Nakajima et al 1999 [59]	2-step SE	SD>CAD
Nakajima et al 2000 [30]	2-step E & R	SD>CAD
Nakajima et al 2005 [60]	2-step SE	SD>CAD
Nakajima et al 2006 [45]	2-step SE	SD>CAD
Omar et al 2007 [35]	3-step E & R 2-step SE 1-step SE	3-step E & R: SD=CAD 2-step SE: SD=CAD 1-step SE: SD>CAD
Pereira et al 2006 [40]	2-step E & R 1-step SE	2-step E & R: SD=CAD 1 step SE: SD>CAD
Say et al 2005 [61]	2-step E & R 2-step SE	SD>CAD

Scholtanus et al 2010 [29]	2-step E & R 1-step SE 2-step SE	SD>CAD SD>CAD SD=CAD
Sonoda et al 2005 [26]	1-step SE 2-step E & R	1-step SE: SD>CAD 2-step E & R: SD=CAD
Tachibana et al 2008 [31]	2-step SE	SD>CAD (Burs, Carisolv)
Taniguchi et al 2009 [41]	2-step SE 1-step SE	SD>CAD
Xuan et al 2010 [43]	2-step E & R 2-step SE 1-step SE	SD>CAD
Yazici et al 2004 [62]	2-step SE	SD>CAD
Yoshiyama et al 2000 [63]	2-step SE 2-step E & R	SD>CAD
Yoshiyama et al 2002 [64]	2-step SE 2-step E & R	SD>CAD
Yoshiyama et al 2003 [65]	2-step SE	SD>CAD
Yoshiyama et al 2004 [39]	1-step SE	SD>CAD
Zanchi et al 2010 [28]	2-step E & R 2-step SE	SD>CAD

Summary:

	Bond strength: Sound dentin (SD) Vs Caries-affected dentin (CAD)		
Adhesives	SD>CAD (n)	SD=CAD (n)	SD<CAD (n)
3-step E & R	2	3	0
2-step E & R	13	2	0
2-step SE	18	3	0
1-step SE	8	1	0

n: number of studies