# Bonding to Sound and Caries-Affected Dentin: A Systematic Review and Meta-Analysis

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**Purpose:** This study systematically reviewed the literature to compare the bonding ability of dental adhesives applied to sound dentin (SoD) vs caries-affected dentin (CAD).

**Materials and Methods:** Three international databases (Medline/PubMed, Scopus, and Web of Science) were searched. Eligible studies which evaluated the bond strength to both SoD and CAD were included. Random effects meta-analyses were conducted to calculate pooled mean difference between substrates, separately for etch-and-rinse and self-etch adhesives. Subgroup analyses were carried out to explore heterogeneity considering the methods used for removal of infected carious dentin. A comparison between etch-and-rinse and self-etch adhesives restricted to CAD was also performed. Statistical heterogeneity was considered using the I2 test. The risk of bias of all included studies was assessed.

**Results:** In total, 2260 articles were found, 65 were selected for full-text reading, and 40 studies were included. The meta-analyses favored SoD over CAD for both etch-and-rinse (effect size: -10.04; 95% confidence interval [CI]: -11.94, -8.14; I2 = 95%) and self-etch adhesives (effect size: -6.76; 95% CI: -8.23, -5.30; I2 = 89%). In the subgroup analyses, SoD was favored irrespective of the method used for caries removal (effect size ≤ -4.86; I2 ≥ 28%): excavation (manual or with burs), grinding with abrasive papers, combination of more than one method, and when the method was not mentioned. The meta-analysis restricted to CAD favored etch-and-rinse over self-etch adhesives (effect size: 3.13; 95% CI: 1.82, 4.44; I2 = 72%). Most included studies were judged as having an unclear risk of bias.

**Conclusion:** Bonding to SoD yields better results compared to CAD. Etch-and-rinse adhesives performed better than self-etch adhesives when applied to CAD.

**Keywords:** adhesion, caries detection, dental tissues, etch-and-rinse adhesives, resin-based restoratives, self-etch adhesives.

*J Adhes Dent 2017; 19: 1–12.*
*doi: ##.####/j.jad.a#####*

*Submitted for publication: 18.08.15; accepted for publication: 14.12.17*

Structural and morphological characteristics of dental substrates involved in the adhesion of composite-based materials play important roles in the performance of dental restorations. Restorative treatment can be clinically successful in the long term when the bonding mechanism of adhesive systems to dental tissues is known and procedures are carried out properly. Current dental adhesive approaches seek to simplify the bonding technique and minimize the difficulties of bonding to dentin,[54] which is still considered the weakest link in dental adhesion.

In vitro testing of dental adhesives usually involves the use of sound dentin (SoD) as the bonding substrate. It is known, however, that caries-affected dentin (CAD) is a more frequent substrate for bonding in clinical practice. Changes caused by the caries process, such as loss of mineral content, increased porosity of intertubular dentin,[44] dissolution of apatite crystals,[5,52] and degradation of unprotected collagen by bacterial and host-mediated enzymes[28,71] may negatively impact the performance of the adhesives applied to CAD. These morphological alterations may result in poorer dentin hybridization[1,50] and reduced mechanical performance of the bonded restorations.[35] Taking into account that the dental substrate usually used in in vitro bonding

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tests is less challenging for adhesion than the substrate found clinically, it might be assumed that the actual performance of dental adhesives is generally overestimated.

Little evidence is available from clinical studies on the performance of dental adhesives when comparing different dentin substrates as the basis for clinical decisions. Clinicians must rely on their own clinical judgement or in vitro data for choosing the best approach to bond to CAD. Pooled in vitro data could aid in drawing more solid conclusions on which strategy is more effective given CAD. A recent systematic review on bonding to CAD[9] showed that from 40% to 85% of studies reported higher bond strengths to SoD, depending on the adhesives tested. However, the authors did not conduct a meta-analysis on bond strength data for comparing the bonding potential between substrates. By means of a systematic review of the literature, this study was designed to evaluate the bond strength of different adhesive approaches (etch-and-rinse and self-etch) applied to SoD vs CAD dentin. The hypothesis tested was that the bond strength to CAD is lower than to SoD.

## MATERIALS AND METHODS

This systematic review was carried out according to the guidelines of the Cochrane Handbook for Systematic Reviews of Interventions[21] and followed the four-phase flow diagram based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement.[39] The present report is based on the PRISMA Statement.

### Study Selection and Search Strategy

In vitro studies that compared the bond strength of adhesive systems to SoD and CAD were selected. The study was required to report at least one comparison between substrates (SoD vs CAD) to be eligible for inclusion, irrespective of the caries detection method, method used for removal of caries-infected dentin, bond strength test, and storage time of specimens before testing. Articles assessing only the bond strength of adhesives to SoD or CAD without comparing the substrates were excluded.

Studies were identified through Medline/PubMed, Scopus, and Web of Science databases. The last search was carried out in March 2015 with no language or date restrictions. References of all included studies were also hand searched. The following search strategy was used in the three databases: dentin* AND (bond* OR adhes*) AND (caries* OR carious OR decay*). Literature search results were de-duplicated using EndNote X7 software (Thomson Reuters; New York, NY, USA). Two independent reviewers (CPI and RSO) initially screened the titles of all identified studies. If the title indicated possible inclusion, the abstract was evaluated. After the abstracts were carefully appraised, manuscripts considered eligible for the review (or in case of doubt) were selected for full-text reading. Discrepancies were resolved by discussion with a third reviewer (RRM).

### Data Collection

A standardized outline was used for data extraction based on the characteristics of studies and groups tested: sample size, carious dentin type (eg, natural, artificially induced), caries detection method (eg, visual examination, hardness, dye staining), method used for removal of carious infected dentin (eg, excavation, grinding), dental substrate used (eg, human molars, bovine incisors), bond strength test, adhesive system type and brand. Dentin bond strength means and standard deviations were also extracted. The authors of the studies were contacted in case of missing or unpublished data; these studies were only included if the authors provided the missing information.

### Assessment of Risk of Bias

The risk of bias was assessed based on previous studies[40,41,58] and the Cochrane Collaboration's tool for assessing the risk of bias.[20] The following parameters were considered: tooth randomization, materials used according to manufacturers' instructions, sample size calculation, blinding of the operator of the testing machine, and caries detection method. The reporting or not of each item was evaluated as high, low, or unclear risk of bias. The parameters used were discussed by the researchers involved and judgment was carried out by a single researcher (RSO). Assessment of risk of bias was conducted using Review Manager 5.3 software (The Nordic Cochrane Centre, The Cochrane Collaboration, 2014; Copenhagen, Denmark).

### Data Analysis

The characteristics of the studies were summarized descriptively. When sufficient data were available, a random effects meta-analysis was conducted to calculate the pooled mean difference between SoD and CAD. Analyses were carried out separately for self-etch and etch-and-rinse adhesives. As a post-hoc decision, a subgroup analysis was carried out to explore the heterogeneity considering the caries removal methods used in the CAD group (excavation, grinding, more than one method, or unknown). An additional comparison between etch-and-rinse and self-etch adhesives restricted to CAD was carried out. In order to avoid overestimation of results, bond strength data included in this additional analysis were restricted to those from studies in which self-etch or etch-and-rinse adhesives were compared under the same conditions (eg, the same method for removal of caries-infected dentin) and when a pairwise comparison was feasible. Statistical heterogeneity was considered using the I2 test (>75% indicates high heterogeneity). The analyses were conducted using Review Manager 5.3 software.

## RESULTS

After screening 2260 unique titles, 121 abstracts, and 65 full-text articles, 40 studies were included in this review. Details of article selection and reasons for exclusions are shown in Fig 1. In total, 26 studies were excluded from the

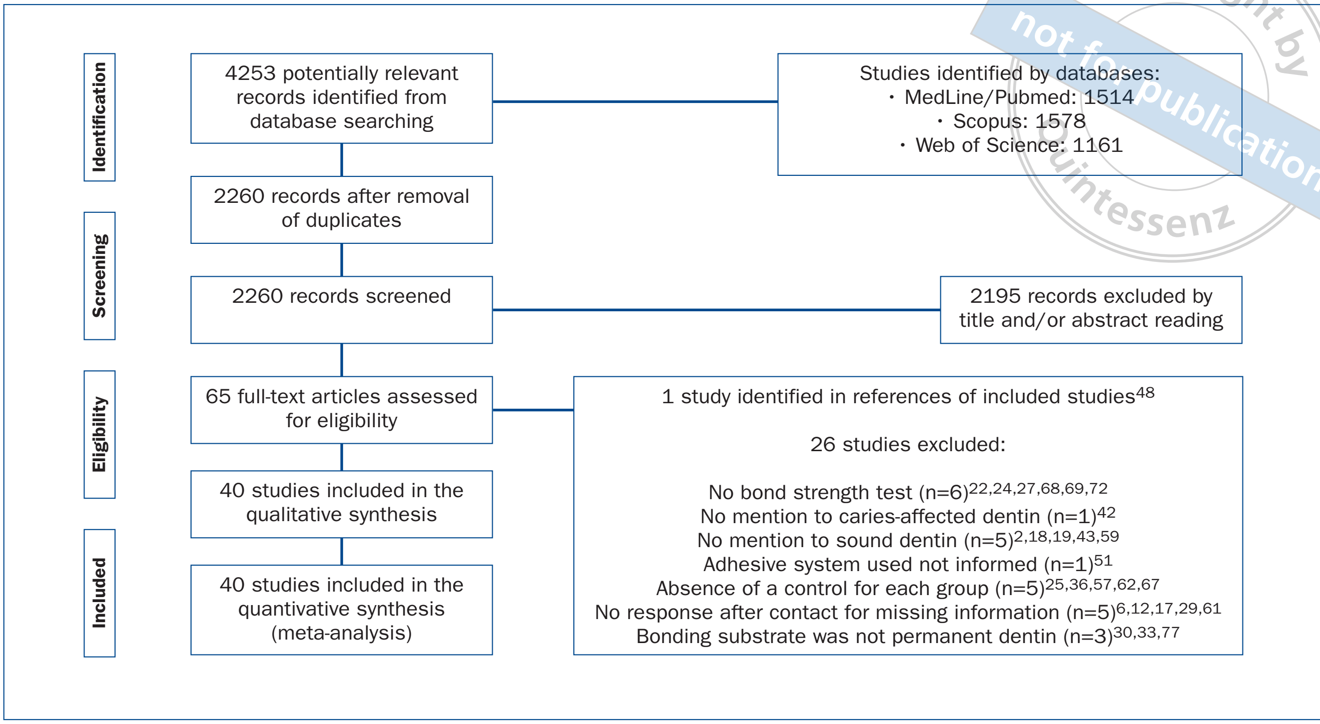





**Fig 1** Flow diagram of the systematic review.

review and one study was included after reading the references of the included articles.[48] The characteristics of the studies included are summarized in Table 1. The adhesives tested and extracted bond strength data are shown in the Appendix.

Of the 40 studies included in the meta-analyses, 39 used human teeth (usually third molars), 36 tested natural caries lesions, and only 4 studies tested artificially induced caries lesions. Regarding the caries detection method, 60% of the studies combined staining with a dye for caries detection and visual examination. Most studies (87.5%) used surface grinding as the method for removal of infected carious dentin, sometimes combining grinding with other methods; excavation alone (manual or with burs) or combined with another method was used in 47.5% of studies. Most studies used microtensile bond strength testing and stored specimens in water at 37°C for 24 h. Regarding the comparison of failure modes between SoD and CAD, although the majority of studies (57.1%) reported no appreciable differences between these substrates, 25% of the studies observed an increased occurrence of cohesive failure within dentin for CAD compared to SoD groups.

The meta-analyses were carried out either using the 40 studies included or excluding the 4 articles[15,55,74,83] which used artificially-induced CAD. Since the results were the same for both analyses, the results including all 40 studies are presented here. Figures 2 and 3 show the results for the meta-analyses and subgroup analyses comparing SoD and CAD. In studies that tested etch-and-rinse adhesives, the meta-analysis favored SoD, with an effect size of -10.04, 95% confidence interval (CI) between -11.94 and -8.14, and I2 = 95% (Fig 2). In the subgroup analysis for studies using excavation to remove infected carious dentin, SoD was favored, with an effect size of -9.34 (95% CI: -12.00, -6.67) and I2 = 94%. When grinding was used as the removal method, the results favored SoD, with an effect size of -10.67 (95% CI: -14.34, -6.99) and I2 = 97%. For studies using more than one method of removal of infected carious dentin, the results favored SoD, with an effect sizes of -4.86 (95% CI: -9.73, 0.00) and I2 = 84%. When analyzing studies that did not mention the removal method, SoD was again favored, with an effect size of -13.77 (95% CI: -16.25, -11.29) and I2 = 70%.

When studies testing self-etch adhesives were considered (Fig 3), the meta-analysis favored SoD, with an effect size of -6.76 (95% CI: -8.23, -5.30) and I2 = 89%. In the subgroup analysis for studies using excavation as the removal method of infected carious dentin, the result favored SoD, with an effect size of -5.61 (95% CI: -7.78, -23.45) and I2 = 89%. For studies using grinding as removal method, SoD was favored, with an effect size of -7.34 (95% CI: -9.97, -4.70) and I2 = 90%. SoD was again favored in studies that used more than one method for removal of infected carious dentin (effect size: -7.45; 95% CI: -9.92, -4.98; I2 = 68%) and in studies that did not report the method (effect size: -13.21; 95% CI: -16.95, -9.46; I2 = 28%).

Figure 4 shows the results for the meta-analysis comparing the bond strength between adhesives restricted to CAD. The results favored etch-and-rinse adhesives over self-etch

doi: ##.####/j.jad.a#####

**Table 1 Characteristics of the studies included**

| Author (year) | Sample size* | Dental substrate and carious dentin type | Caries detection method | Method for removal of caries-infected dentin | Bond strength test | Modes of failure | Conclusion |
|---|---|---|---|---|---|---|---|
| Arrais et al (2004)[1] | 9 teeth | Human third molars with coronal natural caries lesions | Visual examination and surface hardness using a dental explorer | Excavation and grinding (400-, 600-grit SiC papers) | µTBS | NR | SoD had higher bond strength than CAD. Additional and extended acid-etching times improved the bond strength to CAD |
| Burrow et al (2003)[3] | 4-11 specimens | Human molars with natural caries lesions | Biochemical solution | Excavation | µTBS | CAD generally had more cohesive failures in dentin than SoD | Similar bond strengths were observed for SoD and CAD |
| Ceballos et al (2003)[4] | 4 teeth | Human molars with natural coronal caries lesions | Staining and visual examination | Grinding | µTBS | No major differences between substrates | SoD had higher bond strength than CAD depending on the material tested |
| Doi et al (2004)[8] | 5 teeth | Human molars with natural coronal caries lesions | Staining | Grinding (diamond saw and 600-grit SiC paper) | µTBS | Cohesive failures in dentin were observed only for CAD | SoD had higher bond strength than CAD |
| Ekambaram et al (2014)[10] | 16 specimens | Human molars with natural coronal caries lesions | Staining | Excavation (manual) | µTBS | Cohesive failures in dentin were observed only for CAD | SoD generally had higher bond strength than CAD. Use of chlorhexidine preserved the bond strength of hydrophobic adhesive to SoD and CAD |
| Ergüçü et al (2009)[11] | 4 teeth (5 specimens/ tooth) | Human molars with natural coronal caries lesions | Staining and visual and tactile examination | Laser (Er,Cr:YSGG) and excavation (bur) | µTBS | No major differences between substrates | SoD had higher bond strength than CAD |
| Erhardt et al (2008)[13] | 17-19 specimens | Human molars with natural coronal caries lesions | Staining and visual examination | Grinding (180- to 600-grit SiC papers) | µTBS | No major differences between substrates. | SoD had higher bond strength than CAD. Increased exposed collagen zone and decreased hybridization quality were observed in CAD interfaces, which were more prone to hydrolytic degradation than SoD bonds |
| Erhardt et al (2008)[14] | 5 teeth | Human molars with natural coronal caries lesions | Staining | Excavation and grinding (600-grit SiC paper) | µTBS | No major differences between substrates. | SoD had higher bond strength than CAD after acid-etching |
| Erhardt et al (2008)[15] | 6 teeth (4 specimens/ tooth) | Bovine incisors with artificial caries | Microhardness testing | NR | µTBS | No major differences between substrates | SoD had higher bond strength than CAD |
| Huang et al (2011)[23] | 15 specimens | Human molars with natural coronal caries lesions | Staining | Excavation and grinding (600-grit SiC paper) | µTBS | NR | SoD had higher bond strength than CAD |
| Kimochi et al (1999)[26] | 6-8 teeth | Human molars with natural coronal caries lesions | Staining and visual examination | Grinding (600-grit SiC paper) | µTBS | CAD had more cohesive failures in dentin than SoD | SoD had higher bond strength than CAD |
| Koyuturk et al (2006)[31] | 14 teeth | Human molars with natural coronal caries lesions | Staining, visual examination, and surface hardness using a sharp excavator | Grinding (320-grit SiC paper) | SBS | No major differences between substrates | Three adhesives had higher bond strength to SoD and two other adhesives had higher bond strength to CAD |
| Kunawarote et al (2011)[32] | 10 teeth (4-5 specimens/ tooth) | Human molars with natural coronal caries lesions | Staining, radiography and visual examination | Excavation and grinding (600-grit SiC paper) | µTBS | SoD had more cohesive failures within the restorative composite than CAD | SoD had higher bond strength than CAD |
| Macedo et al (2009)[34] | 6 teeth (8 specimens/ tooth) | Human molars with natural occlusal caries lesions | Staining, visual examination, and surface hardness | Grinding (600-grit SiC paper) | µTBS | No major differences between substrates | SoD had higher bond strength than CAD |
| Mobarak et al (2011)[37] | 20 teeth | Human molars with natural occlusal caries lesions | Staining and visual examination | Excavation and grinding (600-grit SiC paper) | µSBS | No major differences between substrates | Similar bond strengths were observed for SoD and CAD. Use of chlorhexidine preserved the bond strength to CAD |
| Mobarak and El-Badrawy (2012)[38] | 20 teeth (2 specimens/ tooth) | Human molars with natural coronal caries lesions | Visual and tactile examination and microhardness testing | Grinding | µSBS | No major differences between substrates | Differences in bond strength between SoD and CAD depended on the adhesive system |
| Nakajima et al (1995)[46] | 10 specimens | Human molars with natural coronal caries lesions | Staining, visual examination and surface hardness using a dental explorer | Grinding (320-, 600-grit SiC papers) | µTBS | No major differences between substrates | SoD generally had higher bond strength than CAD |
| Nakajima et al (1999)[48] | 9-14 specimens | Human molars with natural coronal caries lesions | Staining and visual examination | Grinding (320-, 600-grit SiC papers) | µTBS | NR | Similar bond strengths were observed for SoD and CAD |
| Nakajima et al (2000)45 | 12-19 specimens | Human molars with natural coronal caries lesions | Staining and visual examination | Grinding (180-, 600-grit SiC papers) | µTBS | CAD had more mixed failures than SoD | SoD generally had higher bond strength than CAD |
| Nakajima et al (2000)[47] | 6 teeth (4-5 slices/ tooth) | Human third molars with natural coronal caries lesions | Staining and visual examination | Grinding (600-grit SiC paper) | µTBS | No major differences between substrates | SoD had higher bond strength than CAD |
| Nakajima et al (2005)[44] | 26 specimens | Human molars with natural coronal caries lesions | Staining and visual examination | Grinding (600-grit SiC paper) | µTBS | CAD had more cohesive failures in dentin than SoD | SoD had higher bond strength than CAD. The demineralized zone of the CAD-resin interface (8 µm thick) was thicker than that of SoD (3 µm thick) |

| Author (year) | Sample size* | Dental substrate and carious dentin type | Caries detection method | Method for removal of caries-infected dentin | Bond strength test | Modes of failure | Conclusion |
|---|---|---|---|---|---|---|---|
| Neves et al (2011)[49] | 5 teeth (~35 specimens/ group) | Human molars with natural coronal | Digital radiography | Grinding, laser (Er:YAG), biochemical solution, excavation (bur) | μTBS | CAD had more cohesive failures in dentin than SoD | SoD had higher bond strength than CAD |
| Omar et al (2007)[53] | 5 teeth | Human molars with natural occlusal caries lesions | Visual and microscopy examination | Excavation (bur) and grinding (diamond saw) | μTBS | NR | SoD had higher bond strength than CAD, but not for all adhesives tested |
| Perdigão et al (1994)[55] | 10 teeth | Human molars with artificial lesions induced by acidogenic challenge | Visual examination | NR | SBS | No major differences between substrates | SoD had higher bond strength than hypermineralized and demineralized dentin groups |
| Pereira et al (2006)[56] | 5 teeth (5-8 specimens/ tooth) | Human molars with natural coronal caries lesions | Staining | Grinding (600-grit SiC paper) | μTBS | NR | SoD generally had higher bond strength than CAD |
| Say et al (2005)[60] | 3 teeth (80 specimens / SoD and 40 specimens / CAD) | Human third molars with natural coronal caries lesions | Staining and visual examination | Grinding (600-grit SiC paper) | μTBS | CAD generally had more cohesive failures in dentin than SoD | SoD had higher bond strength than CAD. There were no significant differences between self-etch and etch-and-rinse adhesives in CAD |
| Scholtanus et al (2010)[63] | 10-12 specimens | Human molars with natural occlusal caries lesions | Staining, visual and tactile examination | Excavation | μTBS | No major differences between substrates | SoD generally had higher bond strength than CAD |
| Sengün et al (2002)[65] | 12 teeth | Human molars with natural coronal caries lesions | Staining and visual examination | Excavation and grinding (diamond saw) | SBS | No major differences between substrates | SoD had higher bond strength than CAD, but not for all adhesives tested |
| Sengün et al (2005)[64] | 15 teeth | Human molars with natural coronal caries lesions | Staining and visual examination | Excavation and grinding (320-grit SiC paper) | SBS | No major differences between substrates | Differences in bond strength between SoD and CAD depended on the sensitizer used before bonding |
| Singh et al (2011)[66] | 10 teeth | Human mandibular molars with natural caries lesion | Staining and visual examination | Grinding (220-, 600-grit SiC papers) | μTBS | NR | SoD had higher bond strength than CAD |
| Taniguchi et al (2009)[70] | 12 specimens / group | Human molars with natural coronal caries lesions | Staining and visual examination | Grinding (600-grit SiC paper) | μTBS | No major differences between substrates | SoD generally had higher bond strength than CAD |
| Xie et al (1996)[74] | 11 teeth | Human third molars with artificial lesions induced by acidogenic challenge | Visual examination | NR | μTBS | CAD had more adhesive failures than SoD | Similar bond strengths were observed for SoD and CAD |
| Xuan et al (2010)[75] | 10 beam-shaped specimens/ group | Human third molars with natural coronal caries lesions | Staining and visual examination | Excavation and grinding (600-grit SiC paper) | μTBS | NR | SoD generally had higher bond strength than CAD |
| Yazici et al (2004)[76] | 3 teeth (10-12 specimens/ tooth) | Human mandibular molars with natural coronal caries lesions | Staining and visual examination | Excavation (bur) and grinding (600-grit SiC paper) | μTBS | NR | SoD had higher bond strength than CAD without additional acid-etching. Additional acid-etching did not improve the bond strength to CAD |
| Yoshiyama et al (2000)[81] | 10-12 specimens | Human molars with natural coronal caries lesions | Staining and visual examination | Excavation (bur) and grinding | μTBS | NR | SoD generally had higher bond strength than CAD |
| Yoshiyama et al (2002)[79] | 7-9 specimens | Human molars with natural coronal caries lesions | Staining and visual examination | Excavation (manual) and grinding (600-grit SiC paper) | μTBS | NR | SoD had higher bond strength than CAD. There were no significant differences between self-etch and etch-and-rinse adhesives in CAD |
| Yoshiyama et al (2003)[80] | 15 specimens | Human third molars with natural coronal caries lesions | Staining and visual examination | Excavation (manual) and grinding (600-grit SiC paper) | μTBS | NR | SoD had higher bond strength than CAD |
| Yoshiyama et al (2004)[78] | 7 teeth | Human third molars with natural coronal caries lesions | NR | Grinding | μTBS | NR | SoD had higher bond strength than CAD |
| Zanchi et al (2010)[82] | 30 specimens | Human molars with natural coronal caries lesions | Visual examination and surface hardness using a dental explorer | Excavation and grinding (600-grit SiC paper) | μTBS | CAD generally had more adhesive failures than SoD | SoD generally had higher bond strength than CAD. Additional acid-etching generally improved the bond strength to CAD and reduced to SoD |
| Zanchi et al (2010)[83] | 15 specimens | Human molars with artificial lesions induced by pH cycling | Morphological evaluation | Grinding | μTBS | No major differences between substrates | SoD generally had higher bond strength than CAD |

*Number of teeth or specimens per group; specimens refer to composite-dentin beams for microtensile bond strength (μTBS) or composite cylinders for shear or microshear bond strength (μSBS) tests. NR: not reported.

doi: ##.####/j.jad.a#####

| Study or Subgroup | Carious dentin Mean | Carious dentin SD | Carious dentin Total | Sound dentin Mean | Sound dentin SD | Sound dentin Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **1.4.1 Excavation** | | | | | | | | |
| Arrais et al 2004 | 23.58 | 9.18 | 9 | 50.69 | 10.81 | 9 | 1.4% | -27.11 [-36.38, -17.84] |
| Arrais et al 2004 | 33.97 | 12.18 | 9 | 43.74 | 8.97 | 9 | 1.4% | -9.77 [-19.65, 0.11] |
| Ekambaram et al 2014 | 8.03 | 3.1 | 16 | 18.27 | 4 | 16 | 2.1% | -10.24 [-12.72, -7.76] |
| Ekambaram et al 2014 | 33.61 | 4.2 | 16 | 51.78 | 3.9 | 16 | 2.0% | -18.17 [-20.98, -15.36] |
| Ekambaram et al 2014 | 33.93 | 3.3 | 16 | 52.99 | 4.4 | 16 | 2.0% | -19.06 [-21.75, -16.37] |
| Ekambaram et al 2014 | 19.06 | 3.5 | 16 | 26.56 | 1.9 | 16 | 2.1% | -7.50 [-9.45, -5.55] |
| Ekambaram et al 2014 | 23.45 | 4.8 | 16 | 26.64 | 3.8 | 16 | 2.0% | -3.19 [-6.19, -0.19] |
| Ekambaram et al 2014 | 20.52 | 3.6 | 16 | 25.24 | 4.1 | 16 | 2.0% | -4.72 [-7.39, -2.05] |
| Ekambaram et al 2014 | 28.78 | 3.6 | 16 | 40.83 | 5.7 | 16 | 2.0% | -12.05 [-15.35, -8.75] |
| Ekambaram et al 2014 | 31.76 | 5.2 | 16 | 50.37 | 4.1 | 16 | 2.0% | -18.61 [-21.85, -15.37] |
| Erhardt et al 2008b | 26.2 | 3.5 | 30 | 31.9 | 3.3 | 30 | 2.1% | -5.70 [-7.42, -3.98] |
| Erhardt et al 2008b | 24.9 | 5.8 | 30 | 28.1 | 4.2 | 30 | 2.0% | -3.20 [-5.76, -0.64] |
| Erhardt et al 2008b | 23.8 | 5.5 | 30 | 27.3 | 4.7 | 30 | 2.0% | -3.50 [-6.09, -0.91] |
| Omar et al 2007 | 18.6 | 2.89 | 25 | 22.19 | 4.6 | 25 | 2.1% | -3.59 [-5.72, -1.46] |
| Omar et al 2007 | 16.62 | 6.23 | 25 | 15.7 | 5.5 | 25 | 2.0% | 0.92 [-2.34, 4.18] |
| Scholtanus et al 2010 | 25 | 10 | 10 | 35 | 10.6 | 10 | 1.4% | -10.00 [-19.03, -0.97] |
| Segün et al 2002 | 14.1 | 7.94 | 12 | 10.57 | 4.56 | 12 | 1.8% | 3.53 [-1.65, 8.71] |
| Xuan et al 2010 | 28.98 | 5.44 | 10 | 32.44 | 5.59 | 10 | 1.9% | -3.46 [-8.29, 1.37] |
| Yoshiyama et al 2000 | 18.1 | 2.1 | 10 | 26.4 | 4.8 | 10 | 2.0% | -8.30 [-11.55, -5.05] |
| Yoshiyama et al 2000 | 27.1 | 6.5 | 9 | 46 | 10.5 | 9 | 1.5% | -18.90 [-26.97, -10.83] |
| Yoshiyama et al 2002 | 28.8 | 6.3 | 7 | 50.9 | 3.9 | 7 | 1.8% | -22.10 [-27.59, -16.61] |
| Zanchi et al 2010a | 26.64 | 10.3 | 30 | 47.5 | 11 | 30 | 1.8% | -20.86 [-26.25, -15.47] |
| Zanchi et al 2010a | 35.29 | 12 | 30 | 35.36 | 12.7 | 30 | 1.7% | -0.07 [-6.32, 6.18] |
| Zanchi et al 2010a | 33.43 | 11.9 | 30 | 40.2 | 10.2 | 30 | 1.8% | -6.77 [-12.38, -1.16] |
| **Subtotal (95% CI)** | | | **434** | | | **434** | **45.1%** | **-9.34 [-12.00, -6.67]** |
| Heterogeneity: Tau² = 38.56; Chi² = 357.86, df = 23 (P < 0.00001); I² = 94% | | | | | | | | |
| Test for overall effect: Z = 6.87 (P < 0.00001) | | | | | | | | |
| **1.4.2 Grinding** | | | | | | | | |
| Ceballos et al 2003 | 36.3 | 12.2 | 10 | 43.9 | 11.4 | 10 | 1.3% | -7.60 [-17.95, 2.75] |
| Ceballos et al 2003 | 41.3 | 10.7 | 10 | 56.3 | 11.1 | 10 | 1.4% | -15.00 [-24.56, -5.44] |
| Erhardt et al 2008a | 16.3 | 5.2 | 24 | 25.6 | 6 | 24 | 2.0% | -9.30 [-12.48, -6.12] |
| Erhardt et al 2008a | 16 | 2.3 | 24 | 20.8 | 3.2 | 24 | 2.1% | -4.80 [-6.38, -3.22] |
| Huang et al 2011 | 29.5 | 3.1 | 15 | 68.3 | 4.1 | 15 | 2.0% | -38.80 [-41.40, -36.20] |
| Macedo et al 2009 | 36.75 | 8.5 | 48 | 59.62 | 20 | 48 | 1.7% | -22.87 [-29.02, -16.72] |
| Macedo et al 2009 | 37.38 | 14.8 | 48 | 65.22 | 20.04 | 48 | 1.6% | -27.84 [-34.89, -20.79] |
| Nakajima et al 1995 | 13.01 | 3.64 | 10 | 26.9 | 8.83 | 10 | 1.8% | -13.89 [-19.81, -7.97] |
| Nakajima et al 1995 | 18.49 | 4.04 | 10 | 20.32 | 5.55 | 10 | 1.9% | -1.83 [-6.08, 2.42] |
| Nakajima et al 1999 | 30.2 | 13.4 | 13 | 24.9 | 17.5 | 12 | 1.1% | 5.30 [-6.99, 17.59] |
| Nakajima et al 2000a | 36.9 | 8 | 11 | 47.7 | 6.8 | 10 | 1.7% | -10.80 [-17.13, -4.47] |
| Nakajima et al 2000a | 45 | 7.2 | 9 | 49.7 | 6.1 | 13 | 1.8% | -4.70 [-10.46, 1.06] |
| Nakajima et al 2000a | 41.2 | 0.6 | 9 | 51.7 | 4.3 | 13 | 2.1% | -10.50 [-12.87, -8.13] |
| Nakajima et al 2000a | 40.2 | 11.1 | 16 | 49.5 | 9.3 | 12 | 1.6% | -9.30 [-16.87, -1.73] |
| Nakajima et al 2000b | 48.2 | 3.9 | 9 | 42.4 | 9 | 14 | 1.8% | 5.80 [0.44, 11.16] |
| Pereira et al 2006 | 36.1 | 8.2 | 12 | 43.3 | 14.1 | 12 | 1.4% | -7.20 [-16.43, 2.03] |
| Say et al 2005 | 28.5 | 5 | 10 | 38.7 | 8.9 | 20 | 1.9% | -10.20 [-15.18, -5.22] |
| Say et al 2005 | 10.5 | 3.9 | 10 | 17.2 | 4.7 | 20 | 2.0% | -6.70 [-9.88, -3.52] |
| Singh et al 2011 | 13.19 | 1.24 | 10 | 22.42 | 1.37 | 10 | 2.1% | -9.23 [-10.38, -8.08] |
| Singh et al 2011 | 9.45 | 1.1 | 10 | 18.55 | 0.83 | 10 | 2.1% | -9.10 [-9.95, -8.25] |
| **Subtotal (95% CI)** | | | **318** | | | **345** | **35.5%** | **-10.67 [-14.34, -6.99]** |
| Heterogeneity: Tau² = 61.22; Chi² = 624.62, df = 19 (P < 0.00001); I² = 97% | | | | | | | | |
| Test for overall effect: Z = 5.69 (P < 0.00001) | | | | | | | | |
| **1.4.3 More than one method** | | | | | | | | |
| Erguçu et al 2009 | 17.71 | 3.78 | 20 | 18.25 | 5.5 | 20 | 2.0% | -0.54 [-3.46, 2.38] |
| Erguçu et al 2009 | 16.33 | 6.76 | 20 | 17.32 | 6.1 | 20 | 1.9% | -0.99 [-4.98, 3.00] |
| Erhardt et al 2008c | 34.5 | 6.8 | 18 | 42.6 | 6.2 | 18 | 1.9% | -8.10 [-12.35, -3.85] |
| Erhardt et al 2008c | 27.8 | 7.4 | 18 | 38.4 | 6.9 | 18 | 1.9% | -10.60 [-15.27, -5.93] |
| **Subtotal (95% CI)** | | | **76** | | | **76** | **7.8%** | **-4.86 [-9.73, 0.00]** |
| Heterogeneity: Tau² = 20.51; Chi² = 18.74, df = 3 (P = 0.0003); I² = 84% | | | | | | | | |
| Test for overall effect: Z = 1.96 (P = 0.05) | | | | | | | | |
| **1.4.4 Method not mentioned** | | | | | | | | |
| Perdigão et al 1994 | 1.96 | 2.41 | 10 | 17.47 | 4.59 | 10 | 2.0% | -15.51 [-18.72, -12.30] |
| Perdigão et al 1994 | 4.58 | 2.92 | 10 | 11.4 | 5.45 | 10 | 2.0% | -6.82 [-10.65, -2.99] |
| Perdigão et al 1994 | 2.93 | 1.67 | 10 | 16.84 | 4.06 | 10 | 2.0% | -13.91 [-16.63, -11.19] |
| Perdigão et al 1994 | 1.51 | 1.04 | 10 | 16.14 | 2.21 | 10 | 2.1% | -14.63 [-16.14, -13.12] |
| Zanchi et al 2010b | 23.66 | 5.4 | 15 | 38.63 | 8.6 | 15 | 1.8% | -14.97 [-20.11, -9.83] |
| Zanchi et al 2010b | 15.05 | 5.3 | 15 | 33.73 | 12.6 | 15 | 1.7% | -18.68 [-25.60, -11.76] |
| **Subtotal (95% CI)** | | | **70** | | | **70** | **11.6%** | **-13.77 [-16.25, -11.29]** |
| Heterogeneity: Tau² = 6.03; Chi² = 16.88, df = 5 (P = 0.005); I² = 70% | | | | | | | | |
| Test for overall effect: Z = 10.88 (P < 0.00001) | | | | | | | | |
| **Total (95% CI)** | | | **898** | | | **925** | **100.0%** | **-10.04 [-11.94, -8.14]** |
| Heterogeneity: Tau² = 44.29; Chi² = 1140.72, df = 53 (P < 0.00001); I² = 95% | | | | | | | | |
| Test for overall effect: Z = 10.34 (P < 0.00001) | | | | | | | | |
| Test for subgroup differences: Chi² = 12.39, df = 3 (P = 0.006), I² = 75.8% | | | | | | | | |

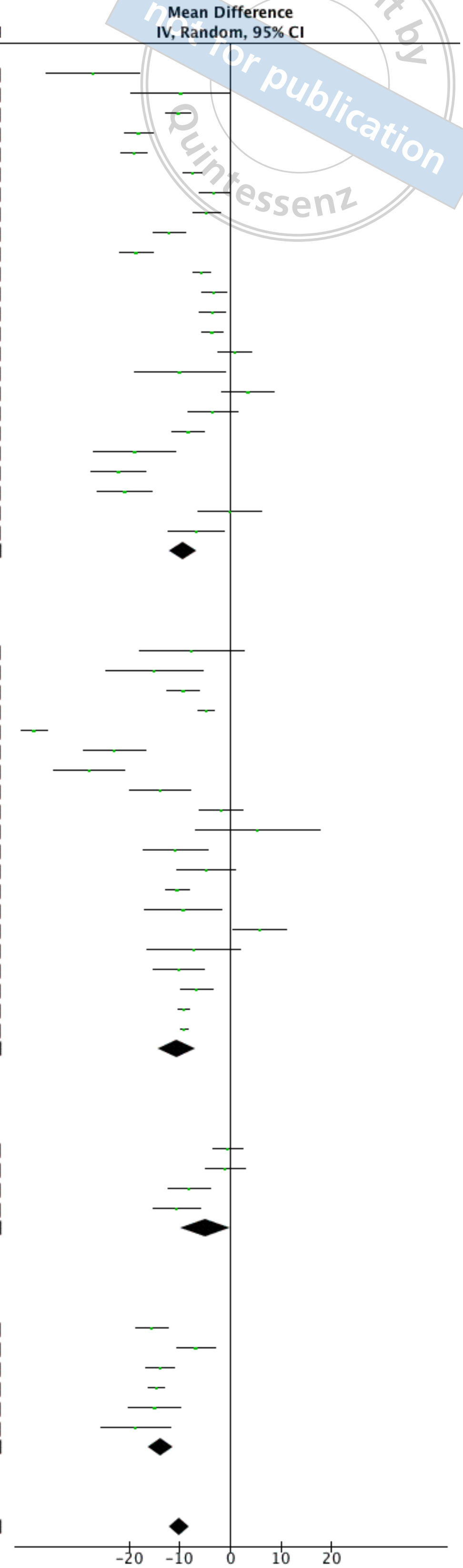
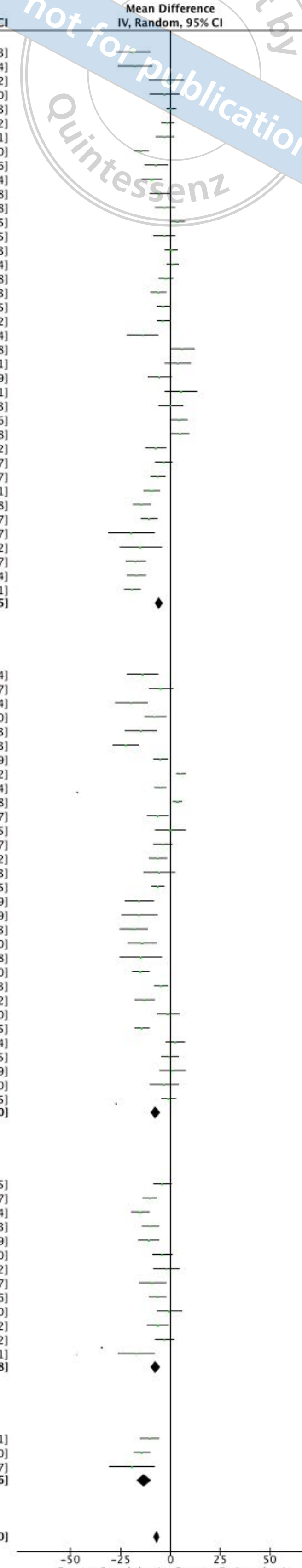



**Fig 2** Summary of findings of the meta-analysis comparing the bond strength of etch-and-rinse adhesives to sound vs caries-affected dentin, according to the methods used for removal of infected carious dentin (subgroup analyses). All analyses showed better results on sound dentin.

**Fig 3** Summary of findings of the meta-analysis comparing the bond strength of self-etch adhesives to sound vs. caries-affected dentin, according to the methods used for removal of infected carious dentin (subgroup analyses). All analyses showed better results sound dentin.

| Study or Subgroup | Carious dentin Mean | Carious dentin SD | Carious dentin Total | Sound dentin Mean | Sound dentin SD | Sound dentin Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **1.3.1 Excavation** | | | | | | | | |
| Arrais et al 2004 | 23.06 | 7.84 | 9 | 41.82 | 10.05 | 9 | 1.0% | -18.76 [-27.09, -10.43] |
| Arrais et al 2004 | 30.76 | 8.16 | 9 | 48.7 | 9.93 | 9 | 1.0% | -17.94 [-26.34, -9.54] |
| Burrow et al 2003 | 27.4 | 6.4 | 11 | 29.4 | 7.9 | 4 | 0.9% | -2.00 [-10.62, 6.62] |
| Burrow et al 2003 | 28.7 | 6.9 | 6 | 31.6 | 7.1 | 8 | 1.0% | -2.90 [-10.30, 4.50] |
| Erguçu et al 2009 | 9.96 | 4.55 | 20 | 9.59 | 2.9 | 20 | 1.3% | 0.37 [-1.99, 2.73] |
| Erguçu et al 2009 | 9.99 | 4.07 | 20 | 11.38 | 5.81 | 20 | 1.3% | -1.39 [-4.50, 1.72] |
| Kunawarote et al 2011 | 39.28 | 5.27 | 11 | 41.93 | 4.93 | 11 | 1.2% | -2.65 [-6.91, 1.61] |
| Kunawarote et al 2011 | 26.77 | 3.47 | 13 | 41.56 | 5.39 | 12 | 1.3% | -14.79 [-18.38, -11.20] |
| Kunawarote et al 2011 | 34.16 | 6.58 | 11 | 41.24 | 7.1 | 11 | 1.2% | -7.08 [-12.80, -1.36] |
| Kunawarote et al 2011 | 31.62 | 6.62 | 12 | 40.87 | 5.33 | 12 | 1.2% | -9.25 [-14.06, -4.44] |
| Mobarak et al 2011 | 20.59 | 5.1 | 10 | 25.94 | 6.4 | 10 | 1.2% | -5.35 [-10.42, -0.28] |
| Mobarak et al 2011 | 21.73 | 6 | 10 | 24.33 | 5.1 | 10 | 1.2% | -2.60 [-7.48, 2.28] |
| Mobarak et al 2011 | 14.67 | 4.5 | 10 | 10.98 | 3.3 | 10 | 1.3% | 3.69 [0.23, 7.15] |
| Mobarak et al 2011 | 20.84 | 6.2 | 10 | 23.79 | 5.9 | 10 | 1.2% | -2.95 [-8.25, 2.35] |
| Mobarak et al 2011 | 9.97 | 3.5 | 10 | 9.46 | 3.4 | 10 | 1.3% | 0.51 [-2.51, 3.53] |
| Mobarak et al 2011 | 9.99 | 3.4 | 10 | 8.74 | 3.2 | 10 | 1.3% | 1.25 [-1.64, 4.14] |
| Omar et al 2007 | 20.23 | 6.1 | 25 | 22.3 | 6.7 | 25 | 1.3% | -2.07 [-5.62, 1.48] |
| Omar et al 2007 | 15.45 | 6.62 | 25 | 21.43 | 7.6 | 25 | 1.3% | -5.98 [-9.93, -2.03] |
| Omar et al 2007 | 20.7 | 5.5 | 25 | 24.25 | 5.7 | 25 | 1.3% | -3.55 [-6.65, -0.45] |
| Omar et al 2007 | 14.8 | 3.89 | 25 | 18.3 | 7.11 | 25 | 1.3% | -3.50 [-6.68, -0.32] |
| Scholtanus et al 2010 | 21 | 11.2 | 12 | 35 | 8.5 | 12 | 1.0% | -14.00 [-21.96, -6.04] |
| Scholtanus et al 2010 | 39 | 5.2 | 12 | 33 | 9.2 | 12 | 1.1% | 6.00 [0.02, 11.98] |
| Segün et al 2002 | 21.19 | 9.17 | 12 | 17.45 | 6.21 | 12 | 1.1% | 3.74 [-2.53, 10.01] |
| Segün et al 2002 | 24.49 | 5.38 | 12 | 29.91 | 8.95 | 12 | 1.1% | -5.42 [-11.33, 0.49] |
| Segün et al 2002 | 17.43 | 9.78 | 12 | 11.99 | 10.15 | 12 | 1.0% | 5.44 [-2.53, 13.41] |
| Segün et al 2002 | 21.49 | 9.15 | 12 | 21.17 | 5.41 | 12 | 1.1% | 0.32 [-5.69, 6.33] |
| Segün et al 2005 | 22.67 | 5.85 | 15 | 18.51 | 5.88 | 15 | 1.3% | 4.16 [-0.04, 8.36] |
| Segün et al 2005 | 25.15 | 5.58 | 15 | 20.44 | 7.11 | 15 | 1.2% | 4.71 [0.14, 9.28] |
| Segün et al 2005 | 21.98 | 7.92 | 15 | 29.25 | 6.4 | 15 | 1.2% | -7.27 [-12.42, -2.12] |
| Segün et al 2005 | 16.95 | 5.78 | 15 | 20.23 | 6.08 | 15 | 1.2% | -3.28 [-7.53, 0.97] |
| Xuan et al 2010 | 14.5 | 3.37 | 10 | 20.77 | 4.73 | 10 | 1.3% | -6.27 [-9.87, -2.67] |
| Xuan et al 2010 | 15.13 | 3.08 | 10 | 24.36 | 5.7 | 10 | 1.3% | -9.23 [-13.25, -5.21] |
| Xuan et al 2010 | 21.18 | 4.96 | 10 | 35.41 | 5.62 | 10 | 1.2% | -14.23 [-18.88, -9.58] |
| Yoshiyama et al 2000 | 17.5 | 2.1 | 10 | 28.2 | 6.1 | 11 | 1.3% | -10.70 [-14.53, -6.87] |
| Yoshiyama et al 2002 | 25.3 | 5 | 7 | 44.9 | 14.6 | 7 | 0.8% | -19.60 [-31.03, -8.17] |
| Yoshiyama et al 2003 | 30 | 10 | 7 | 45 | 10 | 7 | 0.8% | -15.00 [-25.48, -4.52] |
| Zanchi et al 2010a | 29.31 | 9.1 | 30 | 46.59 | 9.9 | 30 | 1.2% | -17.28 [-22.09, -12.47] |
| Zanchi et al 2010a | 34.18 | 10.6 | 30 | 51.28 | 8.5 | 30 | 1.2% | -17.10 [-21.96, -12.24] |
| Zanchi et al 2010a | 23.02 | 7.1 | 30 | 42.24 | 8.3 | 30 | 1.3% | -19.22 [-23.13, -15.31] |
| **Subtotal (95% CI)** | | | **558** | | | **553** | **45.8%** | **-5.61 [-7.78, -3.45]** |
| Heterogeneity: $Tau^2$ = 40.08; $Chi^2$ = 346.90, df = 38 (P < 0.00001); $I^2$ = 89% | | | | | | | | |
| Test for overall effect: Z = 5.08 (P < 0.00001) | | | | | | | | |
| **1.3.2 Grinding** | | | | | | | | |
| Ceballos et al 2003 | 21.5 | 5.5 | 10 | 35.5 | 11.6 | 10 | 1.0% | -14.00 [-21.96, -6.04] |
| Ceballos et al 2003 | 13.4 | 1.9 | 10 | 18.2 | 9.6 | 10 | 1.1% | -4.80 [-10.87, 1.27] |
| Doi et al 2004 | 21.5 | 5.3 | 7 | 41.2 | 10 | 8 | 1.0% | -19.70 [-27.66, -11.74] |
| Doi et al 2004 | 19.6 | 6 | 7 | 27.2 | 3.9 | 7 | 1.2% | -7.60 [-12.90, -2.30] |
| Doi et al 2004 | 20.2 | 5.8 | 7 | 35 | 8.9 | 7 | 1.0% | -14.80 [-22.67, -6.93] |
| Kimochi et al 1999 | 11 | 5.8 | 6 | 33.4 | 6.3 | 8 | 1.1% | -22.40 [-28.77, -16.03] |
| Koyuturk et al 2006 | 29.25 | 4.28 | 14 | 34.09 | 5.49 | 14 | 1.3% | -4.84 [-8.49, -1.19] |
| Koyuturk et al 2006 | 12.28 | 4.03 | 14 | 7.02 | 2.02 | 14 | 1.3% | 5.26 [2.90, 7.62] |
| Koyuturk et al 2006 | 10.91 | 3.09 | 14 | 16.02 | 4.29 | 14 | 1.3% | -5.11 [-7.88, -2.34] |
| Koyuturk et al 2006 | 11.15 | 2.91 | 14 | 7.44 | 3.2 | 14 | 1.3% | 3.71 [1.44, 5.98] |
| Koyuturk et al 2006 | 22.95 | 7.91 | 14 | 29.25 | 6.39 | 14 | 1.2% | -6.30 [-11.63, -0.97] |
| Mobarak et al 2012 | 17.31 | 10.3 | 10 | 17.21 | 6.8 | 10 | 1.0% | 0.10 [-7.55, 7.75] |
| Mobarak et al 2012 | 18.7 | 4.09 | 10 | 22.34 | 6.4 | 10 | 1.2% | -3.64 [-8.35, 1.07] |
| Mobarak et al 2012 | 18.31 | 4.9 | 10 | 24.52 | 4.9 | 10 | 1.2% | -6.21 [-10.50, -1.92] |
| Mobarak et al 2012 | 18.97 | 9.4 | 10 | 24.49 | 8 | 10 | 1.0% | -5.52 [-13.17, 2.13] |
| Mobarak et al 2012 | 7.31 | 2.4 | 10 | 13.67 | 4.4 | 10 | 1.3% | -6.36 [-9.47, -3.25] |
| Nakajima et al 1995 | 13.97 | 4.3 | 10 | 29.52 | 10.9 | 10 | 1.0% | -15.55 [-22.81, -8.29] |
| Nakajima et al 1999 | 29.7 | 10.3 | 12 | 45.2 | 13.9 | 17 | 0.9% | -15.50 [-24.31, -6.69] |
| Nakajima et al 1999 | 39.1 | 8.9 | 12 | 57.4 | 10.4 | 19 | 1.1% | -18.30 [-25.17, -11.43] |
| Nakajima et al 2005 | 29.4 | 7.5 | 12 | 43.5 | 11.1 | 14 | 1.0% | -14.10 [-21.30, -6.90] |
| Pereira et al 2006 | 37.3 | 9.7 | 12 | 52 | 17.5 | 15 | 0.8% | -14.70 [-25.12, -4.28] |
| Say et al 2005 | 29.2 | 4.3 | 10 | 44.2 | 7.7 | 20 | 1.2% | -15.00 [-19.30, -10.70] |
| Say et al 2005 | 13.5 | 3.3 | 10 | 18.3 | 6.1 | 20 | 1.3% | -4.80 [-8.17, -1.43] |
| Taniguchi et al 2009 | 27.9 | 6.2 | 12 | 40.9 | 6 | 12 | 1.2% | -13.00 [-17.88, -8.12] |
| Taniguchi et al 2009 | 35.6 | 9.1 | 12 | 36.8 | 3.9 | 12 | 1.2% | -1.20 [-6.80, 4.40] |
| Taniguchi et al 2009 | 29.8 | 4.6 | 12 | 44 | 4 | 12 | 1.3% | -14.20 [-17.65, -10.75] |
| Taniguchi et al 2009 | 39.9 | 6.7 | 12 | 37.5 | 4.4 | 12 | 1.2% | 2.40 [-2.14, 6.94] |
| Taniguchi et al 2009 | 41.6 | 6.6 | 12 | 42 | 3.6 | 12 | 1.2% | -0.40 [-4.65, 3.85] |
| Taniguchi et al 2009 | 31.4 | 8.5 | 12 | 30.4 | 7.7 | 12 | 1.1% | 1.00 [-5.49, 7.49] |
| Taniguchi et al 2009 | 40.6 | 7.7 | 12 | 43.7 | 9.9 | 12 | 1.1% | -3.10 [-10.20, 4.00] |
| Taniguchi et al 2009 | 33.3 | 5.2 | 12 | 34.4 | 3.5 | 12 | 1.3% | -1.10 [-4.65, 2.45] |
| **Subtotal (95% CI)** | | | **341** | | | **381** | **35.7%** | **-7.34 [-9.97, -4.70]** |
| Heterogeneity: $Tau^2$ = 47.43; $Chi^2$ = 303.88, df = 30 (P < 0.00001); $I^2$ = 90% | | | | | | | | |
| Test for overall effect: Z = 5.46 (P < 0.00001) | | | | | | | | |
| **1.3.3 More than one method** | | | | | | | | |
| Erhardt et al 2008c | 24.2 | 7 | 18 | 28.2 | 6.3 | 18 | 1.2% | -4.00 [-8.35, 0.35] |
| Erhardt et al 2008c | 28.7 | 5 | 18 | 39.2 | 5.2 | 18 | 1.3% | -10.50 [-13.83, -7.17] |
| Erhardt et al 2008c | 24.5 | 5.6 | 18 | 39.5 | 7.6 | 18 | 1.2% | -15.00 [-19.36, -10.64] |
| Erhardt et al 2008c | 17.2 | 5.1 | 18 | 27.2 | 7.7 | 18 | 1.2% | -10.00 [-14.27, -5.73] |
| Neves et al 2011 | 29.8 | 9.9 | 39 | 40.7 | 12.1 | 39 | 1.2% | -10.90 [-15.81, -5.99] |
| Neves et al 2011 | 36.1 | 12.3 | 47 | 40.1 | 12.9 | 47 | 1.2% | -4.00 [-9.10, 1.10] |
| Neves et al 2011 | 37.4 | 13.2 | 31 | 39.3 | 13 | 31 | 1.1% | -1.90 [-8.42, 4.62] |
| Neves et al 2011 | 37.1 | 13.7 | 28 | 46 | 11.5 | 28 | 1.1% | -8.90 [-15.53, -2.27] |
| Neves et al 2011 | 31.7 | 10.1 | 41 | 38 | 9.5 | 41 | 1.2% | -6.30 [-10.54, -2.06] |
| Neves et al 2011 | 41.3 | 13.9 | 31 | 41.7 | 11.7 | 31 | 1.1% | -0.40 [-6.80, 6.00] |
| Neves et al 2011 | 33.7 | 9.2 | 29 | 39.8 | 11.2 | 29 | 1.2% | -6.10 [-11.38, -0.82] |
| Yazici et al 2004 | 16.3 | 5.7 | 10 | 19.2 | 5.8 | 12 | 1.2% | -2.90 [-7.72, 1.92] |
| Yazici et al 2004 | 15.9 | 7 | 10 | 32.9 | 13.7 | 11 | 0.9% | -17.00 [-26.19, -7.81] |
| **Subtotal (95% CI)** | | | **338** | | | **341** | **15.3%** | **-7.45 [-9.92, -4.98]** |
| Heterogeneity: $Tau^2$ = 13.48; $Chi^2$ = 37.70, df = 12 (P = 0.0002); $I^2$ = 68% | | | | | | | | |
| Test for overall effect: Z = 5.91 (P < 0.00001) | | | | | | | | |
| **1.3.4 Method not mentioned** | | | | | | | | |
| Xie et al 1996 | 11.8 | 4.1 | 11 | 22.2 | 6.8 | 11 | 1.2% | -10.40 [-15.09, -5.71] |
| Xie et al 1996 | 8.8 | 3.5 | 11 | 23.1 | 5.8 | 11 | 1.3% | -14.30 [-18.30, -10.30] |
| Yoshiyama et al 2004 | 25.5 | 5 | 7 | 44.9 | 14.6 | 7 | 0.8% | -19.40 [-30.83, -7.97] |
| **Subtotal (95% CI)** | | | **29** | | | **29** | **3.2%** | **-13.21 [-16.95, -9.46]** |
| Heterogeneity: $Tau^2$ = 3.22; $Chi^2$ = 2.78, df = 2 (P = 0.25); $I^2$ = 28% | | | | | | | | |
| Test for overall effect: Z = 6.91 (P < 0.00001) | | | | | | | | |
| **Total (95% CI)** | | | **1266** | | | **1304** | **100.0%** | **-6.76 [-8.23, -5.30]** |
| Heterogeneity: $Tau^2$ = 40.11; $Chi^2$ = 741.92, df = 85 (P < 0.00001); $I^2$ = 89% | | | | | | | | |
| Test for overall effect: Z = 9.04 (P < 0.00001) | | | | | | | | |
| Test for subgroup differences: $Chi^2$ = 11.86, df = 3 (P = 0.008), $I^2$ = 74.7% | | | | | | | | |



| Study or Subgroup | Etch-and-rinse Mean | SD | Total | Self-etch Mean | SD | Total | Weight | Mean Difference IV, Fixed, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Arrais et al 2004 | 33.97 | 12.18 | 9 | 30.76 | 8.16 | 9 | 1.9% | 3.21 [-6.37, 12.79] |
| Arrais et al 2004 | 23.58 | 9.18 | 9 | 23.06 | 7.84 | 9 | 2.8% | 0.52 [-7.37, 8.41] |
| Erguçu et al 2009 | 16.33 | 6.76 | 20 | 9.99 | 4.07 | 20 | 14.4% | 6.34 [2.88, 9.80] |
| Erguçu et al 2009 | 17.71 | 3.78 | 20 | 9.96 | 4.55 | 20 | 25.6% | 7.75 [5.16, 10.34] |
| Erguçu et al 2009 | 28.5 | 5 | 10 | 29.2 | 4.3 | 10 | 10.3% | -0.70 [-4.79, 3.39] |
| Pereira et al 2006 | 36.1 | 8.2 | 12 | 37.3 | 9.7 | 12 | 3.3% | -1.20 [-8.39, 5.99] |
| Say et al 2005 | 10.5 | 3.9 | 10 | 13.5 | 3.3 | 10 | 17.1% | -3.00 [-6.17, 0.17] |
| Yoshiyama et al 2002 | 28.8 | 6.3 | 7 | 25.3 | 5 | 7 | 4.8% | 3.50 [-2.46, 9.46] |
| Zanchi et al 2010a | 35.29 | 12 | 30 | 34.18 | 10.6 | 30 | 5.2% | 1.11 [-4.62, 6.84] |
| Zanchi et al 2010a | 33.43 | 11.9 | 30 | 29.31 | 9.1 | 30 | 6.0% | 4.12 [-1.24, 9.48] |
| Zanchi et al 2010a | 26.64 | 10.3 | 30 | 23.02 | 7.1 | 30 | 8.6% | 3.62 [-0.86, 8.10] |
| **Total (95% CI)** | | | **187** | | | **187** | **100.0%** | **3.13 [1.82, 4.44]** |

Heterogeneity: $Chi^2 = 35.76$, df = 10 ($P < 0.0001$); $I^2 = 72\%$
Test for overall effect: Z = 4.67 ($P < 0.00001$)

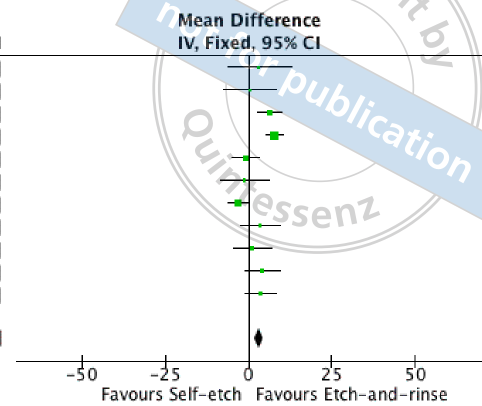



**Fig 4** Meta-analysis comparing the bond strength of etch-and-rinse vs self-etch adhesives applied to caries-affected dentin. The analysis found better results for etch-and-rinse adhesives.

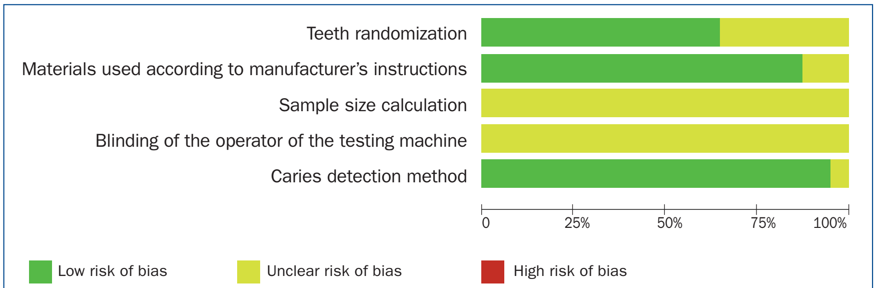



**Fig 5** Risk of bias: proportion of studies with low, unclear, or high risk of bias for each item according to the authors' judgment.

adhesives, with an effect size of 3.13 (95% CI: 1.82, 4.44) and I2 = 72%. Results for the judgment of risk of bias in the studies included in all meta-analyses are presented in Figs 5 and 6. Only 2 studies did not report the method used for caries detection[1,82] and none of the included studies reported sample size calculation or blinding of the operator of the testing machine. Randomization of specimens was reported in more than 50% of the studies assessed. Almost 100% of studies reported that they used adhesive materials according to the manufacturers' instructions.

## DISCUSSION

This review is one of the first to summarize data from in vitro literature on bonding to SoD and CAD. The meta-analyses indicated that bond strength to SoD was always significantly higher than bonding to CAD, irrespective of materials and techniques tested, confirming the hypothesis tested. These results corroborate the observations of a recent review on the same topic.[9] In our systematic review and meta-analyses, 40 studies were included, whereas 29 studies were included in the previous review.[9] The present study covers 79% of papers addressed by Ekambaram et al,[9] whereas their article covers about 57% of the papers included here. These findings highlight the fact that a systematic review is hardly an ultimate, definitive conclusion on a subject or research question; there is usually room for new contributions, particularly when the literature is abundant on a topic and large variability exists between studies. Differences in inclusion and exclusion criteria change between studies, often leading to different sets of included papers, and sometimes perhaps even to different conclusions. For instance, considering the differences between natural and artificially-induced CAD, we conducted analyses either including or not the 4 studies[15,55,74,83] that met the inclusion criteria but used artificial CAD. The results were the same in all analyses; thus, the data reported here considered both carious dentin types.

The present review meta-analyzed the bond strength results to compare SoD and CAD, having an additional focus (subgroup analyses) on the methods used for removal of infected carious dentin before bonding. For instance, different methods for removal of caries could lead to different extents of tissue removal and deeper dentin exposure. Methods such as grinding or bur excavation may be less conservative in removing infected carious dentin, exposing the harder dentin tissue beneath the lesion. In contrast, methods such as laser ablation or biochemical caries removal may lead to altered surface topography. Different surface preparations after caries removal or induction could generate differences in the smear layer left on the surface, in turn affecting the bonding performance. This is particularly relevant for studies using artificial caries lesions without subsequent surface preparation, or when the surface treatment after inducing caries was not reported.[15,55,74] Self-etch adhesives are more sensitive to characteristics of the smear layer than etch-and-rinse adhesives, since the acid-etching step may remove the smear layer. In addition, Neves et al[49] observed that different caries excavation methods may not only influence the dentin bond strengths but also the degree of unprotected collagen left at the bonded interfaces. In this study, irrespective of the methods used for caries removal, SoD was always yielded better results in the analyses for either etch-and-rinse or self-etch adhesives, with different effect sizes only. This might be explained by the fact that at least a minimum of surface flattening is needed for bond strength measurements, regardless of the caries removal method employed. Conditions of the dental surfaces were thus probably relatively similar between studies, since caries removal could not be simply restricted to necrotic tissue.

The meta-analyses were carried out separately for etch-and-rinse and self-etch adhesives, since most of studies did not compare these two adhesive approaches with appropriate controls for each condition. An additional meta-analysis was performed comparing the bond strength of etch-and-rinse vs self-etch adhesives applied to CAD alone. Although not many comparisons were included (11 in total), this additional analysis showed that etch-and-rinse adhesives performed better than self-etch adhesives, meaning that the previous application of phosphoric acid seems beneficial for bonding to CAD in vitro. This result is corroborated by the previous systematic review on bonding to CAD,[9] which indicated that 3-step etch-and-rinse adhesives seemed to perform better in bonding to CAD, although the authors were cautious in interpreting their results because only a few studies had been addressed. The general explanation for the better performance of etch-and-rinse over self-etch adhesives provides two reasons. First, acid etching is more effective in dissolving the superficial tissue for mechanical interlocking with altered CAD[35] than self-etch adhesives, which have a less acidic composition, reducing their potential to demineralize and create microporosities.[54] Second, bonding of self-etch monomers relies on chemical interaction with calcium ions,[16] which are usually in lower concentration in CAD.[5,44,52] It is also important to point out that previous studies[32,34,70] have indicated that bonding to CAD improved with treatments such as deproteinization by oxidizing solutions for self-etch adhesives, or application of collagen cross linkers for etch-and-rinse adhesives. In addition, the higher bond strengths observed for etch-and-rinse adhesives do not necessarily mean that their clinical performance is better than that of self-etch adhesives.

One of the shortcomings of most of the studies included here is that only immediate bond strengths (ie, after 24-h storage in water) were measured. Therefore, only the initial bonding potential of materials and techniques addressed in the papers should be taken into account. The better performance mentioned above of etch-and-rinse adhesives in CAD

| | Teeth randomization | Materials used according to manufacturer's instructions | Sample size calculation | Blinding of the operator of the testing machine | Caries detection method |
|---|---|---|---|---|---|
| Arrais et al 2004 | + | + | ? | ? | ? |
| Burrow et al 2003 | ? | + | ? | ? | + |
| Ceballos et al 2003 | + | + | ? | ? | + |
| Doi et al 2004 | ? | + | ? | ? | + |
| Ekambaram et al 2014 | + | ? | ? | ? | + |
| Ergüçü et al 2009 | + | + | ? | ? | + |
| Erhardt et al 2008a | + | + | ? | ? | + |
| Erhardt et al 2008b | ? | + | ? | ? | + |
| Erhardt et al 2008c | ? | + | ? | ? | + |
| Huang et al 2011 | + | + | ? | ? | + |
| Kimochi et al 1999 | ? | ? | ? | ? | + |
| Koyuturk et al 2006 | + | + | ? | ? | + |
| Kunawarote et al 2011 | + | + | ? | ? | + |
| Macedo et al 2009 | + | + | ? | ? | + |
| Mobarak et al 2011 | + | + | ? | ? | + |
| Mobarak et al 2012 | ? | + | ? | ? | + |
| Nakajima et al 1995 | + | + | ? | ? | + |
| Nakajima et al 1999 | + | + | ? | ? | + |
| Nakajima et al 2000a | + | + | ? | ? | + |
| Nakajima et al 2000b | + | + | ? | ? | + |
| Nakajima et al 2005 | + | + | ? | ? | + |
| Neves et al 2011)49 | + | + | ? | ? | + |
| Omar et al 2007 | + | + | ? | ? | + |
| Perdigão et al 1994 | + | + | ? | ? | + |
| Pereira et al 2006 | ? | + | ? | ? | + |
| Say et al 2005 | + | ? | ? | ? | + |
| Scholtanus et al 2010 | + | + | ? | ? | + |
| Sengün et al 2002 | + | + | ? | ? | + |
| Sengün et al 2005 | + | + | ? | ? | + |
| Singh et al 2011 | ? | + | ? | ? | + |
| Taniguchi et al 2009 | ? | + | ? | ? | + |
| Xie et al 1996 | ? | + | ? | ? | + |
| Xuan et al 2010 | + | + | ? | ? | + |
| Yazici et al 2004 | + | + | ? | ? | + |
| Yoshiyama et al 2000 | ? | + | ? | ? | + |
| Yoshiyama et al 2002 | ? | ? | ? | ? | + |
| Yoshiyama et al 2003 | ? | ? | ? | ? | + |
| Yoshiyama et al 2004 | ? | + | ? | ? | + |
| Zanchi et al 2010a | + | + | ? | ? | ? |
| Zanchi et al 2010b | + | + | ? | ? | + |

**Fig 6** Risk of bias summary: authors' judgment on each item for each included study.

vs self-etch adhesives, for instance, could be different if long-term storage were tested. Another variable to be mentioned is that four studies testing artificially induced CAD were included, in order to broader the investigation and cover one important aspect that is sometimes ignored in bond strength tests: artificial caries lesions tend to be more homogeneous and controlled than natural caries lesions.[36] The use of artificially-induced CAD might allow testing dental adhesives in an altered substrate rather than always focusing on adhesion to sound, unaltered dentin substrate. The number of included studies addressing artificial caries lesions was quite low; it is likely that the effect on the overall meta-analysis was negligible. However, it should be mentioned that artificial CAD is histologically different from natural CAD, particularly due to the possible presence of transparent dentin with occluded dentinal tubules with mineral deposits in natural lesions, which usually take longer to be produced.

Almost all statistical analyses carried out here presented high heterogeneity, and subgroup analyses were performed to identify factors possibly influencing the results. Reasons and variables that influenced the high heterogeneity were hardly identified, since the studies included a high number of covariates. The parameters assessed by the risk of bias tool showed a high prevalence of unclear judgment, indicating possible problems with reporting in the included studies. Unfortunately, reporting problems are commonplace in laboratory studies, especially because there are no consensus guidelines or orientation on how to conduct and report studies in the dental in vitro literature. It is also likely that the present results may have been influenced by publication bias, as studies with poor or negative results may simply not have been published. This last aspect is in fact a concern in all types of literature, not only in vitro. A broad search was used to aid in minimizing this problem, with no restriction to language or publication date.

Current concepts and techniques for caries excavation and adhesion to residual dentin present a number of alternative materials and techniques for application. The dental substrate left after excavation, with remaining caries degradative phenomena, is still a challenge for the bonding of resin-based restorative materials. Results of the present systematic review and meta-analyses corroborate a study[7] which indicated that irrespective of the caries excavation method chosen, it is safer to finish the cavity margins in clean, sound tooth tissue in order to obtain the best performance of dental adhesives. However, this should be done as minimally invasively as possible with regard to caries excavation, and as conservatively as feasible with regard to sound tissue preservation.

Reasons for the observed lower bond strength to CAD have been abundantly addressed in the literature. These include lower mineral content and a deeper demineralized zone in CAD, changes in morphological and other chemical characteristics of mineralized tissues,[13,44,72] changes in the secondary structure of collagen,[72] as well as thicker hybridization in CAD compared to SoD. A study[73] which analyzed the effect of dentin type on bond strength after removing the variance attributable to hardness as a covariate indicated that the condition of dentin had a significant effect on bond strength: even if SoD and CAD had similar intertubular hardness, the bond strength to CAD would still be significantly lower than to SoD. Reduction in the cohesive strength of CAD has been also linked with poor bonding,[79] which corroborates the 25% of the articles included in the systematic review that observed more cohesive failures within CAD than SoD.



## CONCLUSION

Caries-affected dentin is a more challenging substrate for bonding than sound dentin, irrespective of the adhesive approach used. When bonding to caries-affected dentin, the in vitro literature indicates that etch-and-rinse adhesives may yield higher bond strength than self-etch materials. This effect should be taken into account when evaluating dental adhesives in vitro or when developing new bonding agents, which are usually tested only using sound dentin in preclinical tests.

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**Clinical relevance:** Caries-affected dentin is a more challenging substrate for bonding than sound dentin, irrespective of the adhesive approach used. When bonding to caries-affected dentin, the in vitro literature indicates that etch-and-rinse adhesives might lead to higher bond strength than self-etch materials.