Journal of the Mechanical Behavior of Biomedical Materials 80 (2018) 258–268

Contents lists available at ScienceDirect

Journal of the Mechanical Behavior of Biomedical Materials

journal homepage: www.elsevier.com/locate/jmbbm

Bonding of composite cements to zirconia: A systematic review and meta-analysis of in vitro studies

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ARTICLE INFO

Keywords:
Zirconia
Dental cement
Composite resin
Bond strength
Systematic review
Meta-analysis

ABSTRACT

Objectives: The aim of this study was to systematically review the literature and statistically analyze bond strength data to identify the influence that composite cements, type of test methodology, chemical and mechanical pre-treatments have on the bond strength of composite cements to zirconia in three different artificial aging conditions.

Methods: The literature was electronically searched in MEDLINE, PUBMED, EMBASE, and SCOPUS to select relevant articles that evaluated the bond strength between zirconia and composite cements. A manual search was performed by scanning the reference lists of included studies. All articles were published online before December 2016 and in English. From electronic database and manual searches, 444 studies were identified; 161 articles with 1632 test results met the inclusion criteria. Test results were assigned into 3 aging conditions: non-aged, intermediate-aged and aged groups. Generalized estimating equations (GEE) were used to explore actual mean bond strengths. As the bond strength is a non-negative value, lognormal distribution was used.

Results: In non-aged condition, data showed statistically significant interactions between cement type and type of test. There was no statistically significant interaction between mechanical and chemical pre-treatments.

In intermediate-aged and aged conditions, data showed no statistically significant interactions between mechanical and chemical pre-treatments and between cement type and type of test.

Conclusions: This meta-analysis appeared to indicate that mechanical pre-treatments, and in particular ceramic coating, combined with methacryloyloxydecyl dihydrogen phosphate (MDP) containing primers yielded the highest long-term bond strength (aged-condition). However, data are limited and caution should be exercised before applying these results to clinical situations.

1. Introduction

Zirconia is widely used in dentistry as a material of choice for indirect ceramic restorations due to its mechanical, biocompatible and esthetic properties. Bonding strength of zirconia to composite cements has been improved by conditioning the zirconia surface with mechanical and chemical pre-treatment techniques (Inokoshi et al., 2014; Özcan and Bernasconi, 2015). Researchers have shown that mechanical pre-treatments such as alumina air abrasion, tribochemical silica coating, laser irradiation, chemical etching and ceramic coating can improve the bond strength of zirconia to composite cements due to an increase of surface roughness and micro-mechanical interlocking (Akin et al., 2012; Casucci et al., 2011; Kern et al., 2009; Senyilmaz et al., 2007; Ural et al., 2010). Additionally, functional monomers containing primers have been applied to the surface of zirconia as chemical pre-treatments. Methacryloyloxydecyl dihydrogen phosphate (MDP), phosphonic acid acrylate, or anhydride containing primers promote chemical bond to zirconia and potentially create a durable bond (Cura et al., 2012; Inokoshi et al., 2013; Nakayama et al., 2010; Tsuo et al., 2006; Yoshida et al., 2004).

Bonding to zirconia was systematically reviewed by Papia et al. (2014) and Tzanakakis et al. (2016). Tzanakakis et al. (2016) concluded that alumina air abrasion and tribochemical silica coating combined with adhesive monomers could enhance bonding effectiveness of zirconia. The results were consistent with Papia et al. (2014) who found that abrasive surface treatment and/or silica coating combined with a

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https://doi.org/10.1016/j.jmbbm.2018.02.008
Received 10 December 2017; Received in revised form 6 February 2018; Accepted 7 February 2018
Available online 08 February 2018
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primer could achieve sufficient bond strength for bonding composite cements to oxide ceramics. However, these review papers did not perform statistical analysis of the bond strength data between zirconia and composite cements.

Meta-analyses of bonding to zirconia were previously carried out by Inokoshi et al. (2014) and Özcan and Bernasconi (2015). These studies also concluded that the combination of mechanical and chemical pretreatment techniques increased the bond strength between zirconia and composite cements (Inokoshi et al., 2014; Özcan and Bernasconi, 2015). In addition, the authors identified the following five factors which influence the quality of the bond of composite cements to zirconia: (i) mechanical preparation of the zirconia surface, (ii) chemical preparation of the zirconia surface, (iii) the type of cement, (iv) artificial aging, (v) test methodology (Inokoshi et al., 2014; Özcan and Bernasconi, 2015). However, some of the statements suggesting the selection of specific protocols and cement type in the previous two meta-analytical papers were controversial (Inokoshi et al., 2014; Özcan and Bernasconi, 2015). Furthermore, with the previous two meta-analytical studies, it was difficult to indicate which specific mechanical and/or chemical pre-treatments and which type of cement would provide the highest long-term bonding to zirconia and should therefore be selected by clinicians.

Inokoshi et al. (2014) collected papers for their meta-analysis up to December 2013. Özcan and Bernasconi (2015) systematically searched relevant publications from 1995 to June 2011. More research has been completed since the publication of these reviews making another analysis of bonding of composite cements to zirconia compelling.

This study analyzed the data of bond strength of zirconia cemented with composite cements in three aging conditions: non-aged, intermediate-aged and aged. The aim of this study was to systematically review the literature and statistically analyze bond strength data to identify the influence that composite cements, type of test methodology, chemical and mechanical pre-treatments have on the bond strength of composite cements to zirconia in three different aging conditions.

2. Materials and methods

2.1. Search sources and strategy

The literature was electronically searched in PUBMED, MEDLINE, EMBASE, and SCOPUS. A manual search was also performed by selecting papers from the reference lists of included studies, which were not detected by the electronic search. The following terms were searched: “zirconia”; OR “zirconium oxide$”; OR “ZrO2”; OR “zirconia ceramic$”; OR “YTZP”, “Y-TZP”; OR “YTZP ceramic$”, “Y-TZP ceramic $”; OR “YTZP zirconia”, “Y-TZP zirconia”; OR “YPSZ”, “Y-PSZ”; OR “YPSZ ceramic$”, “Y-PSZ ceramic$”; OR “YPSZ zirconia”, “Y-PSZ zirconia” AND “dental cement$”; OR “dental adhesive cement$”; OR “dental luting cement$”; OR “composite cement$”; OR “resin cement$”; OR “resin composite cement$”; OR “dental bonding”; OR “dental luting”; OR “dental adhesion”; OR “dental retention”; OR “dental cementation”; OR “adhesive retention”; OR “adhesive luting resin$”; OR “resin bonding” AND “bond strength”; OR “shear bond strength”; OR “microshear bond strength”, “micro-shear bond strength”; OR “tensile bond strength” OR “microtensile bond strength”, “micro-tensile bond strength”. Both free-text and Medical Subject Headings (MeSH) could have either been included in the title or the abstract.

2.2. Selection criteria

Articles included in the meta-analysis followed the inclusion criteria: (i) published as a full paper and in English, (ii) published online before December 2016, (iii) evaluated the bond strength of composite cements to zirconia with 3 antagonists: zirconia, composite resin or composite cement, (iv) included data on shear, micro-shear, tensile, and micro-tensile bond tests (MPa).

Articles or test results meeting one or more of the following criteria were excluded: (i) literature reviews, systematic reviews and meta-analyses, (ii) articles which had not been included quantitative data of mean and standard deviation of bond strength, (iii) articles that repeated the same bond strength data in another publication (iv) articles or test results based on glass-infiltrated zirconia, hot isostatic pressed zirconia, zirconia posts and zirconia implants, (v) the bond strength of composite resins to zirconia copings, (vi) the bond strength of veneering porcelain to zirconia frameworks.

Partially missing data from included papers, were retrieved by contacting the corresponding authors. Papers, which provided incomplete data, were excluded if the corresponding author was unable to provide the requested information.

2.3. Data extraction and collection

All articles were screened and selected by two authors. Disagreements about the included studies were resolved by involving a third researcher.

Excel spreadsheets (Microsoft Corp., Washington, USA) were used to collect the following data: (i) mean and standard deviation of the bond strength, (ii) type of bond strength test, (iii) number of specimens, (iv) mechanical and chemical pre-treatment techniques, (v) type of cement and curing mode, (vi) storage condition and duration (days or months) and/or number of thermocycling procedures, (vii) size area and shape of the tested interface, (viii) type of antagonist, (ix) significance level. Information regarding the included papers and test results were collected in Appendix Table A.1 and Table B.1.

Pre-treatment techniques were classified into 2 main groups: mechanical and chemical. Mechanical pre-treatments were classified into 6 groups: (i) no mechanical pre-treatment (also including polishing with silicon carbide and grinding), (ii) alumina air abrasion, (iii) tribochemical silica coating, (iv) laser irradiation, (v) chemical etching, (vi) ceramic coating (Inokoshi et al., 2014). Chemical pre-treatments were classified into 4 groups: (i) no chemical pre-treatment, (ii) MDP-containing primers, (iii) functional primers (without MDP in composition), (iv) silanes.

Composite cements were divided into 3 groups: (i) MDP-containing cements, (ii) MDP-free functional monomer-containing cements, (iii) functional monomer-free cements (Inokoshi et al., 2014).

All test groups were divided into 3 aging conditions: (i) non-aged condition applied to specimens stored for equal or less than 1 day in air or water or a desiccator or an incubator with 98–100% humidity and/or subjected to thermocycling for less than 500 cycles prior to the bond strength test, (ii) intermediate-aged condition applied to specimens stored from 2 days to 6 months in air or water or a desiccator or an incubator with 98–100% humidity and/or subjected to thermocycling for 500–5000 cycles, (iii) aged condition applied to specimens stored for more than 6 months in air or water or a desiccator or an incubator with 98–100% humidity and/or subjected to thermocycling for more than 5000 cycles. Data sets achieved from the 3 aging conditions (“Non-aged”, “Intermediate-aged” and “Aged”) were analyzed separately to assess bond strength.

2.4. Statistical analysis

Non-parametric method, Kruskal-Wallis test was used to compare the actual mean bond strength between tests. Because of the nested structure of the data, there was high correlation among test results taken from each article. To alleviate this issue, generalized estimating equations (GEE) were used to explore actual mean bond strength in each aging condition. The GEE includes an additional variance component to accommodate correlated data and to allow for differences among articles. As mean bond strength is a non-negative value and rightly skewed, lognormal distribution was used. Assuming no specific order between observations of the same study, the compound-

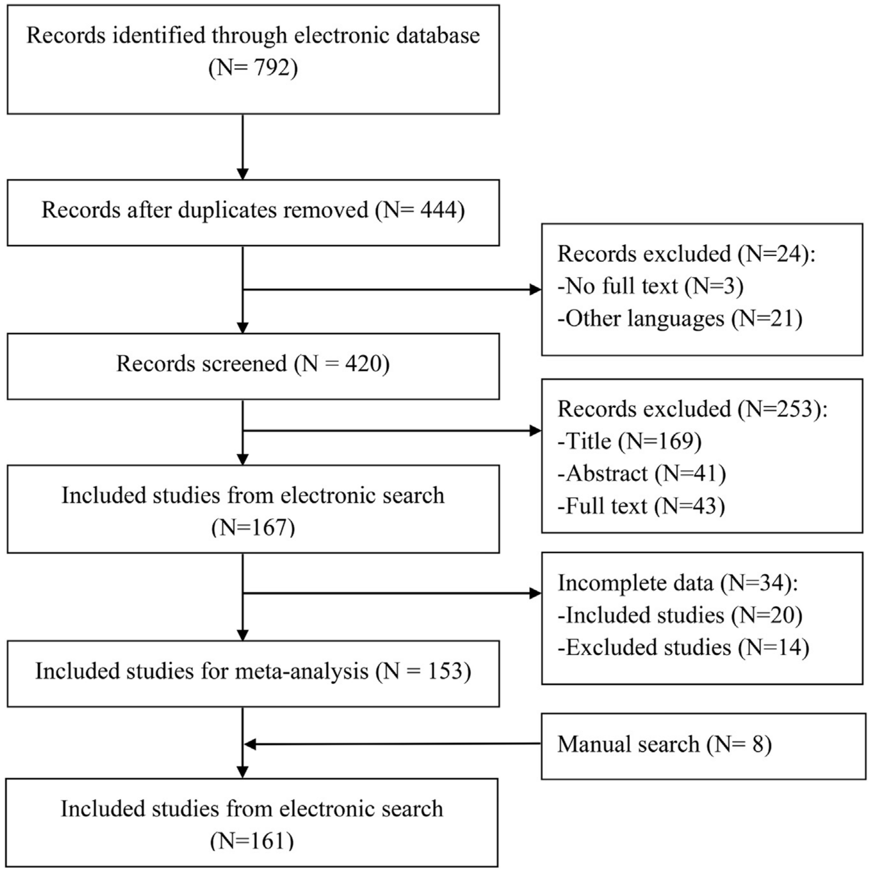

Fig. 1. Flow chart of literature searches, N = the number of articles.

symmetric correlation structure was applied. One-way interactions between "mechanical and chemical pre-treatments", and "cement type and type of test" were explored in each aging condition. Antagonists were accounted for in all models. Actual mean bond strength (i.e. marginal means) and associated 95% confidence intervals, and the p-value were reported ($\alpha = 0.05$). All analyses were conducted in SAS v9.2 (SAS Institute Inc., Cary, NC, USA).

3. Results

Four hundred and forty-four articles were identified from electronic search, which 167 remained after applying exclusion criteria. Thirty-four articles, out of the 167 which satisfied the inclusion criteria, had incomplete data and the corresponding authors were contacted for the missing information. Fourteen articles were excluded due to incomplete data resulting in a total of 153 articles included. Eight additional articles were collected from manual search, giving a total of 161 articles (Supplement 1) and 1632 test results for inclusion in the meta-analysis (Fig. 1).

Macro-shear bond test was the most commonly used test (115 studies, 1121 test results), followed by micro-shear bond test (20 studies, 151 test results), micro-tensile (19 studies, 186 test results) and macro-tensile bond test (12 studies, 174 test results) respectively.

The range of the mean bond strength in this meta-analysis was between 0 and 82.2 MPa (Appendix Table C.1). Kruskal-Wallis tests showed that there was no statistically significant difference among the bond strength tests except the macro-shear bond strength test with the lowest median bond strength (Appendix Table C.1 and Table C.2). Similarly results were also found in generated data from GEE, where the actual mean bond strength of the macro-shear bond test was significantly lower than the other tests (Appendix Table C.1).

The number of test results showing data on the frequency of type of cement, type of chemical and mechanical pre-treatments was reported in Appendix Table D.1.

Of a total number of 1632 test results; 1359 groups used light or dual-cured composite cements; 261 groups used self-cured composite cements; in the remaining 12 groups the curing technique was unknown.

Composite cement was commonly used as an antagonist with 781 (47.9%) test results while cemented composite resin and zirconia were used in 679 (41.6%) and 172 (10.5%) test results, respectively.

Most studies applied a round interface specimen design (1455 test results) compared to a square interface (177 test results) for both (micro/macro) tensile and shear bond tests.

3.1. Non-aged conditions

One hundred and nine studies with 658 test results were included in the non-aged group. Data analysis did not show significant interactions between mechanical and chemical pre-treatments but showed significant interactions between cement type and type of test (shear/tensile bond tests) (Table 1).

3.1.1. Effect of chemical pre-treatment by mechanical pre-treatment

When one of the following mechanical pre-treatment protocols was used; (i) no mechanical pre-treatment, (ii) alumina air abrasion and (iii) laser irradiation, MDP-containing primers it resulted with the highest actual mean bond strength to zirconia among the chemical pre-treatment groups (all $p < 0.05$). However in tribochemical silica coated groups, there was no significant difference between the use of MDP-containing primers and silane application groups ($p = 0.28$). In chemically etched groups, functional primers achieved significantly higher

Table 1
One-way statistical analysis of different interactions affecting the bond strength in each artificial aging condition.

Interaction	p-value (p)		
	Non-aged	Intermediate	Aged
Mechanical x chemical pre-treatments	0.116	0.246	0.146
Cement type x type of test (shear/ tensile)	0.049*	0.790	0.714

* Significant difference ($p < 0.05$).

actual mean bond strength than MDP-containing primers ($p = 0.01$). For ceramic-coated groups, no significant difference in the actual mean bond strength among the pre-treatment groups was found (all $p > 0.05$). Results are summarized in Fig. 2A.

3.1.2. Effect of mechanical pre-treatment by chemical pre-treatment

When the chemical pre-treatment protocol was used only the group labeled (i) no chemical pre-treatment, no mechanical pre-treatment yielded the lowest actual mean bond strength among the mechanical pre-treatment groups (all $p < 0.05$). For MDP-containing primers, alumina air abraded groups achieved significantly higher actual mean bond strength than chemically etched groups ($p = 0.02$). For functional primers, chemically etched groups yielded significantly higher actual mean bond strength than no mechanical pre-treatment, alumina air abrasion, and laser irradiation (all $p < 0.05$). In the case of silane application groups, there were no significant differences in the actual mean bond strength among alumina air abrasion, tribochemical silica coating, and ceramic coating (all $p > 0.05$). Results are summarized in Fig. 2B.

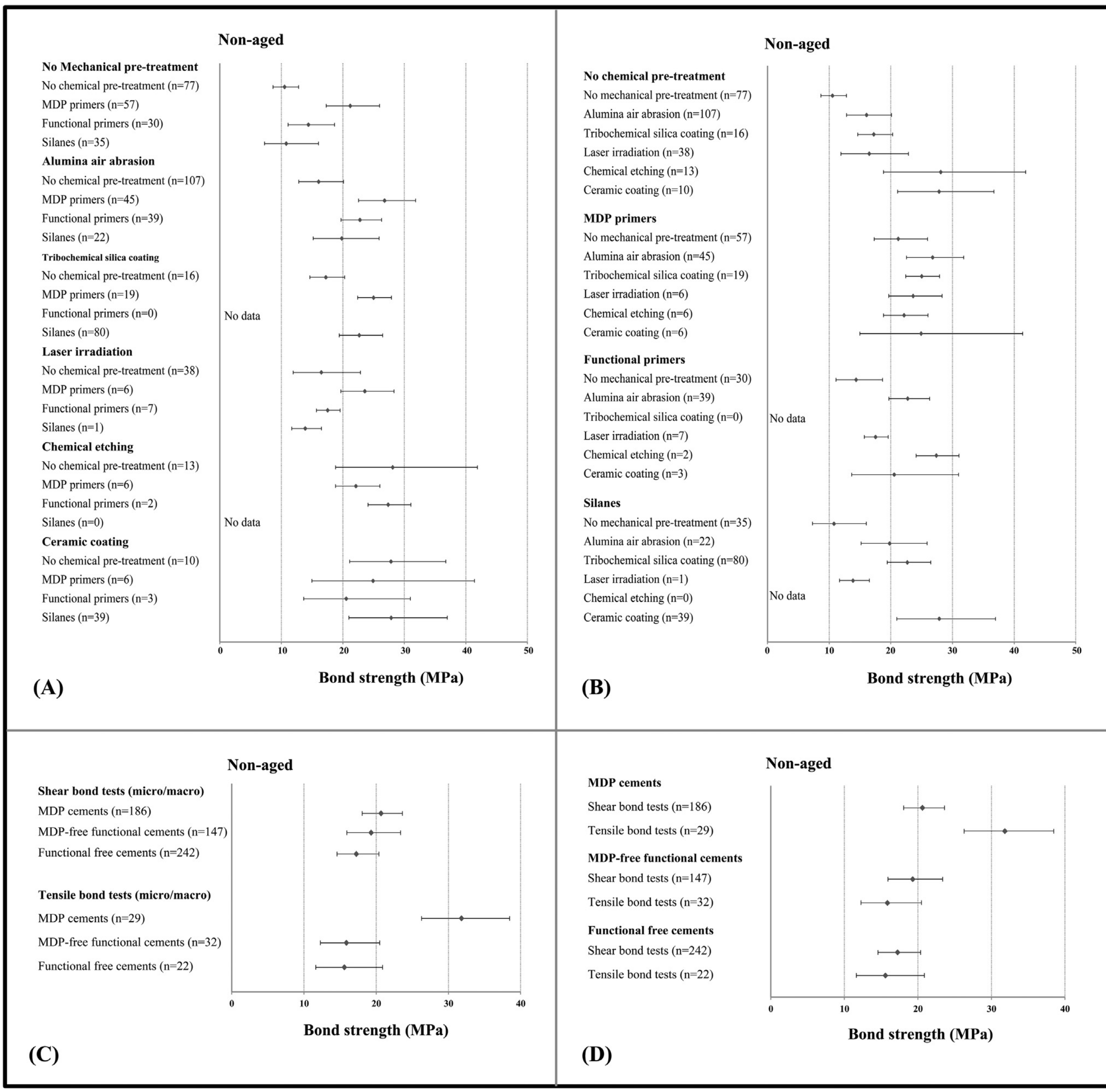

Fig. 2. Summary of GEE models in the non-aged group: (A) The effect of chemical pre-treatment by mechanical pre-treatment, (B) The effect of mechanical pre-treatment by chemical pre-treatment, (C) The effect of cement type by type of test, and (D) The effect of type of test by cement type on the actual mean bond strength (MPa). Error bars represent 95% confidence intervals, n = the number of test results.

3.1.3. Effect of cement type by type of test

Groups with shear bond tests, no significant differences were observed in the actual mean bond strength between MDP-containing cements and MDP-free functional monomer-containing cements ($p = 0.41$); whilst in the case of tensile bond tests, MDP-containing cements had significantly higher actual mean bond strength than MDP-free functional monomer-containing cements and functional monomer-free cements (both $p < 0.05$). Results are summarized in Fig. 2C.

3.1.4. Effect of type of test by cement type

Groups with MDP-containing cements, the tensile bond tests had significantly higher actual mean bond strength than shear bond tests ($p < 0.0001$); while in the case of MDP-free functional monomer-containing cements and functional monomer-free cements, no significant differences between the types of test were found ($p = 0.17$ and $p = 0.54$, respectively). Results are summarized in Fig. 2D.

3.2. Intermediate-aged conditions

Sixty-eight studies with 512 test results were included in the intermediate-aged group. Data analysis did not show significant interactions between mechanical and chemical pre-treatments and between cement type and type of test (Table 1).

3.2.1. Effect of chemical pre-treatment by mechanical pre-treatment

When the mechanical pre-treatment protocol was used only the group labeled (i) no mechanical pre-treatment with MDP-containing primers or functional primers achieved significantly higher actual mean bond strength than no chemical pre-treatment ($p = 0.01$ and $p = 0.03$, respectively). In alumina air abraded groups, MDP-containing primers yielded significantly higher actual mean bond strength than no chemical pre-treatment and silane application groups ($p = 0.002$ and $p < 0.0001$, respectively). For tribochemical silica coated groups, no significant difference in the actual mean bond strength between MDP-containing primers and functional primers was found ($p = 0.55$). In case of laser-irradiated groups, no chemical pre-treatment or MDP-containing primers obtained significantly higher actual mean bond strength than silane application groups ($p = 0.003$ and $p = 0.046$, respectively). In chemically etched groups, there was no significant difference in the actual mean bond strength between no chemical pre-treatment and MDP-containing primers ($p = 0.24$). Where ceramic-coated groups were applied, functional primers yielded the lowest actual mean bond strength of all chemical pre-treatment groups (all $p < 0.05$). Results are summarized in Fig. 3A.

3.2.2. Effect of mechanical pre-treatment by chemical pre-treatment

When the chemical pre-treatment protocol was used only the group labeled (i) no chemical pre-treatment, ceramic-coated groups achieved significantly higher actual mean bond strength than no mechanical pre-treatment, alumina air abrasion, and tribochemical silica coating (all $p < 0.05$). However, in MDP-containing primers, alumina air abraded or tribochemical silica coated groups yielded significantly higher actual mean bond strength than no mechanical pre-treatment, laser irradiation, chemical etching and ceramic coating (all $p < 0.05$). For functional primers, tribochemical silica coated groups achieved the highest actual mean bond strength among the mechanical pre-treatment groups (all $p < 0.05$). In the case of silane application groups, tribochemical silica coated or ceramic-coated groups achieved significantly higher actual mean bond strength than the other mechanical pre-treatments (all $p < 0.05$). Results are summarized in Fig. 3B.

3.2.3. Effect of cement type by type of test

Groups with shear bond tests, MDP-containing cements yielded significantly higher actual mean bond strength than functional monomer-free cements ($p = 0.03$); whilst in the case of tensile bond tests; there were no significant differences in the actual mean bond strength among all cement types (all $p > 0.05$). Results are summarized in Fig. 3C.

3.2.4. Effect of type of test by cement type

All groups of cement types, the tensile bond tests had significantly higher actual mean bond strength than the shear bond tests (all $p < 0.05$). Results are summarized in Fig. 3D.

3.3. Aged conditions

Sixty-five studies with 462 test results were included in the aged group. Data analysis did not show significant interactions between mechanical and chemical pre-treatments and between cement type and type of test (Table 1).

3.3.1. Effect of chemical pre-treatment by mechanical pre-treatment

When one of the following mechanical pre-treatment protocols was used: (i) no mechanical pre-treatment, (ii) laser irradiation and (iii) chemical etching, MDP-containing primers achieved significantly higher actual mean bond strength than no chemical pre-treatment (all $p < 0.05$). Where alumina air abrasion or ceramic coating was applied, MDP-containing primers yielded significantly higher actual mean bond strength than no chemical pre-treatment and silane application groups (all $p < 0.05$). In case of tribochemical silica coating groups, MDP-containing primers or functional primers yielded significantly higher actual mean bond strength than no chemical pre-treatment ($p = 0.01$ and $p = 0.0003$, respectively). Results are summarized in Fig. 4A.

3.3.2. Effect of mechanical pre-treatment by chemical pre-treatment

When the chemical pre-treatment protocol was used only the group labeled (i) no chemical pre-treatment, presented no significant difference in the actual mean bond strength among alumina air abrasion, tribochemical silica coating and ceramic coating (all $p > 0.05$). In the case of MDP-containing primers, ceramic-coated groups achieved the highest actual mean bond strength among the various mechanical pre-treatments (all $p < 0.05$). For functional primers, tribochemical silica coated groups yielded significantly higher actual mean bond strength than the other mechanical pre-treatments (both $p < 0.05$). In silane application groups, no significant difference in the actual mean bond strength was found between tribochemical silica coating and ceramic coating ($p = 0.51$). Results are summarized in Fig. 4B.

3.3.3. Effect of cement type by type of test

All groups of bond tests (shear/tensile), there was no significant difference in the actual mean bond strength among all cement types (all $p > 0.05$). Results are summarized in Fig. 4C.

3.3.4. Effect of type of test by cement type

All groups of cement types, no significant difference in the actual mean bond strength was found between the types of test (all $p > 0.05$). Results are summarized in Fig. 4D.

4. Discussion

From 2014 to 2016, two systematic reviews and two meta-analyses were published on the topic of bonding to zirconia (Inokoshi et al., 2014; Özcan and Bernasconi, 2015; Papia et al., 2014; Tzanakakis et al., 2016). The latest literature considered in these publications for statistical analysis was however dated December 2013 (Inokoshi et al., 2014). In the present study the authors collected and analyzed bond strength data from publications up to December 2016. A meta-analysis was carried out to identify the variables influencing the bond strength between composite cements and zirconia. The following factors were identified: mechanical pre-treatment, chemical pre-treatment, cement type, type of test, artificial aging, and type of antagonist to the bond strength between composite cements and zirconia.

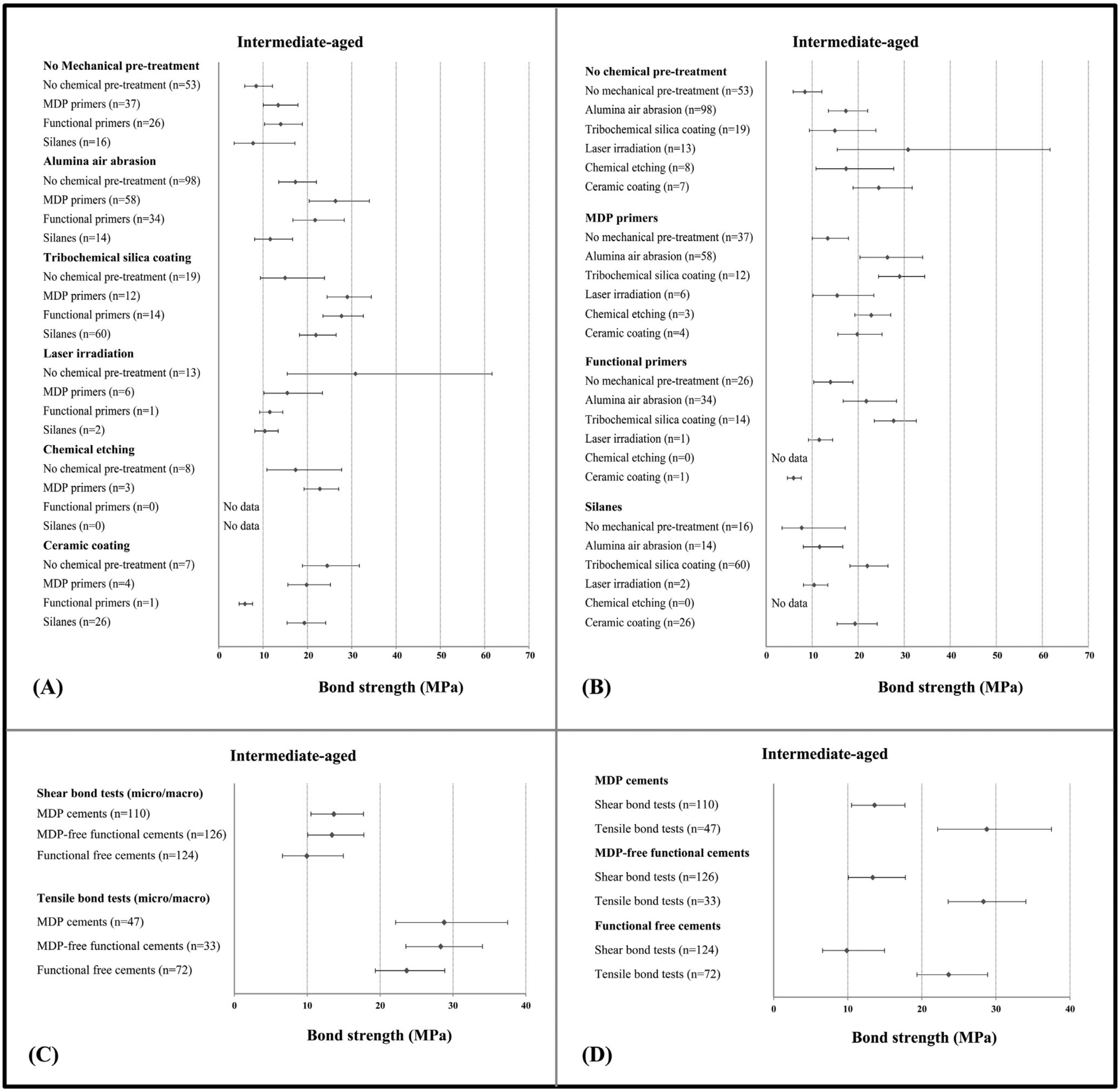

Fig. 3. Summary of GEE models in the intermediate-aged group: (A) The effect of chemical pre-treatment by mechanical pre-treatment, (B) The effect of mechanical pre-treatment by chemical pre-treatment, (C) The effect of cement type by type of test, and (D) The effect of type of test by cement type on the actual mean bond strength (MPa). Error bars represent 95% confidence intervals, n = the number of test results.

In this study, one-way statistical analysis stratifying the data following interactions between "mechanical and chemical pre-treatments", and "cement type and type of test" were developed in all artificial aging conditions. The interaction between mechanical and chemical pre-treatments in all artificial aging conditions and the interaction between cement type and type of test in intermediated-aged and aged conditions were not statistically significant (Table 1). This was done in the attempt to define trends comparing "mechanical pre-treatments and chemical pre-treatments", and "cement type and type of test" in each aging condition. To examine which mechanical and chemical pre-treatments tended to provide the highest actual mean bond strength of zirconia and composite cements in each artificial aging condition, we analyzed which chemical pre-treatment showed statistically significant higher actual mean bond strength in each mechanical pre-treatment and which mechanical pre-treatment presented statistically significant higher actual mean bond strength in each chemical pre-treatment. The results of this study appear to indicate that the highest bond strength in each artificial aging condition is linked to the effects of chemical pre-treatment by mechanical pre-treatment and the effect of mechanical pre-treatment by chemical pre-treatment. From this perspective, alumina air abrasion combined with MDP-containing primers provided the highest actual mean bond strength in non-aged conditions. In intermediate-aged condition, alumina air abrasion combined with MDP-containing primers and tribochemical silica coating also combined with MDP-containing primers yielded the highest actual mean bond strength. Ceramic coating combined with MDP-containing primers provided the highest actual mean bond strength in aged condition. These results are partly consistent with Inokoshi et al. (2014) and Özcan and Bernasconi (2015) who concluded that conditioning the zirconia surface with both mechanical and chemical pre-treatments

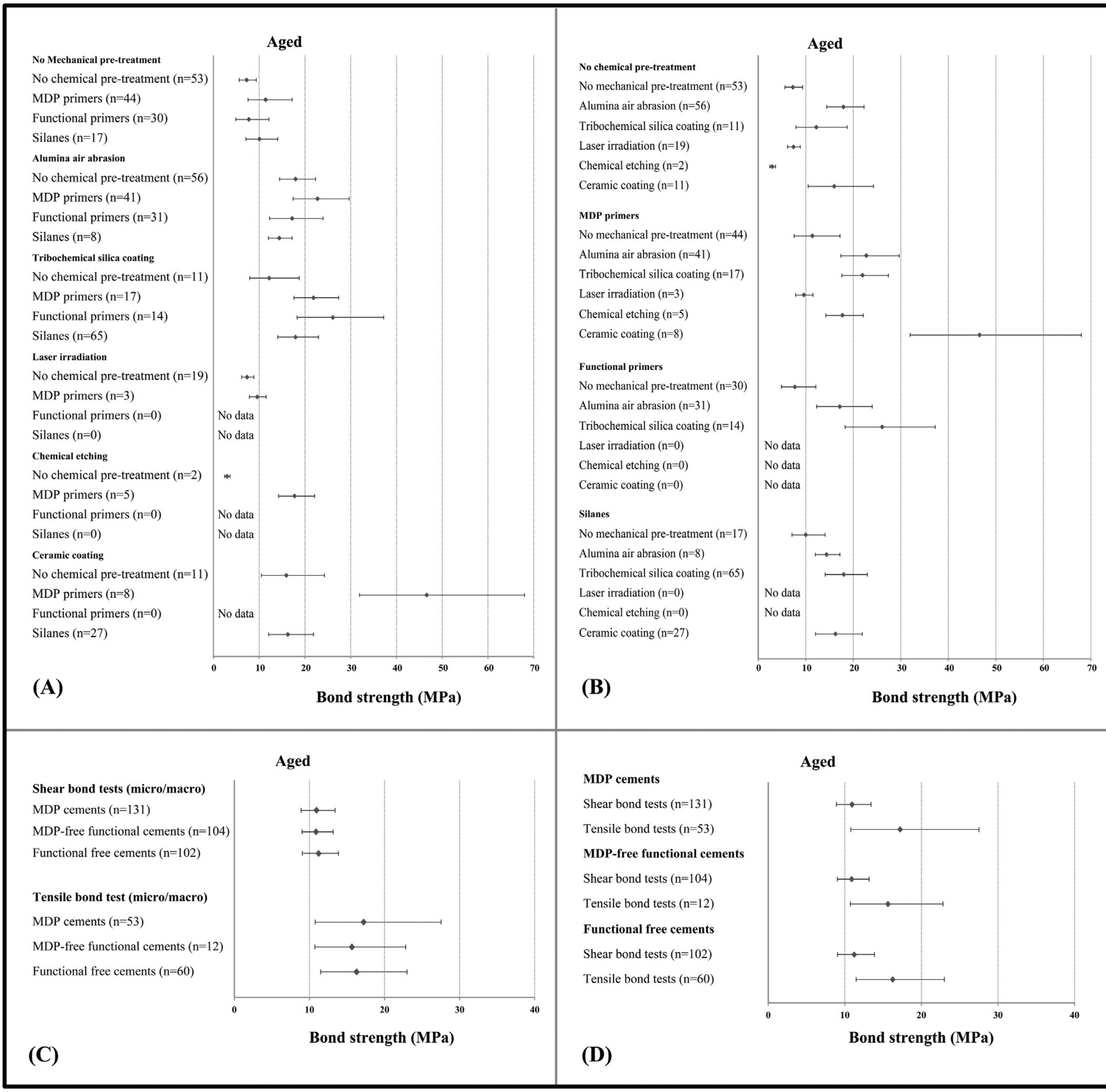

Fig. 4. Summary of GEE models in the aged group: (A) The effect of chemical pre-treatment by mechanical pre-treatment, (B) The effect of mechanical pre-treatment by chemical pre-treatment, (C) The effect of cement type by type of test, and (D) The effect of type of test by cement type on the actual mean bond strength (MPa). Error bars represent 95% confidence intervals, n = the number of test results.

enhanced the bond strength.

As far as the mechanical pre-treatments are concerned, the present study tends to show that ceramic coating provides the highest actual mean bond strength values in aged conditions. This result is consistent with the findings from previous studies (Aboushelib, 2011; Cheung and Botelho, 2015; Vanderlei et al., 2014). The highest actual mean bond strength of this pre-treatment may be attributed to the silica composition of the coated layer on zirconia surface via different techniques e.g. selective infiltration etching (Aboushelib, 2011), glazing techniques (Vanderlei et al., 2014), ceramic liner (Cheung and Botelho, 2015). The silica layers allow for hydrofluoric acid etching which leads to the creation of rougher surface on the coating layer, this in turn provides micro-mechanical interlocking to composite cements (Aboushelib et al., 2007). In addition, the silica layer fused on zirconia surface can bond chemically to silane containing primers (Valentino et al., 2012). The silane also creates cross linkages with methacrylate groups in composite cements increasing the bond strength (Özcan et al., 2011; Plueddemann, 1970). On the other hand, the use of ceramic coating may negatively impact on the accuracy and fitting of the restorations (Cheung and Botelho, 2015; Cura et al., 2012; Everson et al., 2012; Vanderlei et al., 2014). Further investigations of the use of ceramic coating on the inner surface of indirect restorations should be carried out to evaluate the clinical feasibility of these procedures.

In general, the meta-analysis carried out in the present study tends to show that MDP-containing primers provided the highest actual mean bond strength values regardless of the aging conditions. These results are in accordance with previous experimental studies supporting the use of MDP to increase the bonding effectiveness to zirconia (da Silva et al., 2014; Kim et al., 2015; Nakayama et al., 2010). Nagaoka et al. (2013) proved the chemical nature of the bond between MDP and zirconia surface. Reactions may be formed between the di-valent phosphoryl groups of MDP monomer and hydroxyl groups on the zirconia surface (Koizumi et al., 2012). However, other studies highlighted that mechanical pre-treatment of the zirconia surface is required to minimize long-term strength degradation of the bond between zirconia and composite cements (Kern et al., 2009; May et al., 2010).

Types of cement were classified in three groups: (i) MDP-containing cements, (ii) MDP-free functional monomer-containing cements, (iii) functional monomer-free cements. Data on bond strength analyzed in this meta-analysis confirmed that MDP-containing cements tend to provide the highest actual mean bond strength values in any aging condition. These results are consistent with a previous meta-analysis by Özcan and Bernasconi (2015) who indicated that MDP-containing cements were essential for bonding to zirconia even after artificial aging. However, in the aged condition, this meta-analysis found that the cement type was irrelevant, as long as composite cement was used. This finding was in agreement with Inokoshi et al. (2014) who showed that cement types did not affect the bond strength between composite cements and zirconia in aged dataset.

Nominal bond strength tests such as macro-shear, micro-shear, macro-tensile and micro-tensile bond strength test are widely used to calculate the bond strength by dividing the maximum force by the bonding area. The lack of an international standard for testing the bond between composite cements and zirconia explains the variety of tests used by researchers and the difficulties in comparing data achieved under different experimental conditions. Despite the lack of consensus on which test is the most appropriate, the macro-shear bond test resulted with the most frequent methodology used for measuring the bond strength between composite cements and zirconia (Inokoshi et al., 2014). This is likely due to the fact that specimen preparation and the test itself are relatively simple (Pashley et al., 1995; Sudsangiam and van Noort, 1999). On the other hand, macro-tensile bond test is not extensively used as shear bond test perhaps due to the difficulty in aligning the specimens in the testing machine and the detrimental effect that poor alignment may have on stress distribution and hence on the consistency of the results (Oilo, 1993; Sudsangiam and van Noort, 1999). Finite element analysis showed that the stress distribution at the bonded interface of both macro-shear and macro-tensile specimens is non-uniform (Van Noort et al., 1989). Van Noort et al. (1989) proved that elastic modulus mismatch of bonded materials, the mode and point of load application and specimen geometry influenced the stress distribution along the bonded interface. These factors may lead to uneven stress distribution at the bonded surface and consequently cause a greater incidence of cohesive failure of the substrate (Sudsangiam and van Noort, 1999). Cohesive failure of the material on either side of interface is indicative of the mechanical properties of the tested materials rather than the strength of the bond (Della Bona and van Noort, 1995). The micro-tensile bond test was developed to minimize the issues associated to cohesive failure in the substrate (Sano et al., 1994). Smaller specimen size leads to better stress distributions, fewer cohesive failure and reduction in flaw density. Specimens tested under these experimental conditions are more likely to show a greater incidence of adhesive failure and are thought to be a more reliable expression of the actual adhesive bond strength (Pashley et al., 1995; Sano et al., 1994; Schreiner et al., 1998). However, the micro-tensile bond test is technically demanding, labor intensive and strength values may be difficult to measure when bond strength is less than 5 MPa (Pashley et al., 1995). Similarly to the macro-shear and macro-tensile bond tests, the micro-shear bond test is affected by uneven stress distribution along the bond interface and hence data may not be representative of the actual bond strength (Placido et al., 2007). Strain energy release rate test is based on measuring the energy released as a result of the controlled propagation of a crack along the bonded interface in specimens loaded with a 4-point bending configuration (Charalambides et al., 1989). This test is thought to provide a more accurate evaluation of the actual bond strength than nominal bond strength test (Charalambides et al., 1989; DeHoff et al., 1995; Elsaka, 2013; Suansuwan and Swain, 1999). However, there are limited studies evaluating the bond strength by strain energy release rate and further research about this test methodology are needed.

Stiffness of the antagonist (zirconia, composite resin or composite cement) is an important factor affecting the bond strength. This meta-analysis showed that the actual mean bond strength of zirconia cemented to zirconia is significantly higher than zirconia cemented to composite resin or composite cement respectively (Appendix Table E.1). Finite element analysis showed that higher elastic modulus mismatch between substrate and antagonist resulted in higher stress concentration at the interface and in turn lowered the bond strength (Van Noort et al., 1989). Therefore, the antagonist was treated as a confounder and taken into account in all models of the present meta-analysis.

Artificial aging was divided into 3 groups: non-aged, intermediate-aged and aged conditions. Most of the included studies performed artificial aging via water storage and/or a thermocycling procedures in order to simulate intraoral conditions. In this meta-analysis, the comparison between the actual mean bond strength of intermediate-aged and non-aged conditions did not show significant difference. However, the actual mean bond strength in the aged condition decreased significantly in comparison with non-aged and intermediate-aged conditions (Appendix Table F.1). The significant decrease of the actual mean bond strength in aged condition could be due to prolonged water penetration into the interface of bonded materials, which resulted in hydrolytic degradation of polymer matrix of the interface components (Santerre et al., 2001). Additionally, temperature changes in the thermocycling process may amplify the coefficient of thermal expansion mismatch of the bonded materials, which generates mechanical stresses at the bonded interface resulting in strength degradation (Gale and Darvell, 1999). Furthermore, the combination of long-term water storage and thermocycling can considerably decreased the bond strength between composite cement and zirconia as reported by Heikkinen et al. (2013). Bond strength values obtained after prolonged aging are likely to be a more accurate indication of the actual long-term clinical performance of a cementation system.

The meta-analysis carried out in this study showed some limitations. Firstly, the mode of failure of bonded materials could not be analyzed owing to the variety of definitions of failure mode reported in included studies. Secondly, studies reporting the bond strength between zirconia and tooth structure were excluded due to the scatter of data associated to the morphological and physical variations of the bonded substrates. Finally, even though the results of this meta-analysis showed that ceramic coating combined with MDP-containing primers would provide the highest long-term bond strength of zirconia to composite cements among the other mechanical and chemical pre-treatments, the number of test groups supporting these results was limited. We should therefore interpret these results with caution before applying them to clinical situations. Further laboratory and clinical research regarding the use of ceramic coating is required to confirm the long-term bond strength and allow the formulation of clinical guidelines.

5. Conclusions

Within the limitations of this study, the following conclusions were drawn:

1. In a non-aged condition, in general alumina air abrasion combined with MDP-containing primer groups tended to yield the highest actual mean bond strength compared to the other mechanical and chemical pre-treatments, particularly when MDP-containing cements were used.
2. In an intermediate-aged condition, in general tribochemical silica coating or alumina air abrasion combined with MDP-containing primer groups tended to yield the highest actual mean bond strength

compared to the other mechanical and chemical pre-treatments, particularly when MDP-containing cements was used.

3. In an aged condition, in general ceramic coating combined with MDP-containing primer groups tended to yield the highest actual mean bond strength compared to the other mechanical and chemical pre-treatments, when composite cement was used. However, due to the low number of test groups tested in the aged condition, one should exercise caution before applying the results of this meta-analysis to the clinical situation.

Acknowledgements

This work was supported by Postgraduate Research Support Scheme, The University of Sydney. The authors express their thanks to A/Prof. Ky-Anh Nguyen and Dr. Linda Quach for editing the manuscript. Dr. Putsadeeporn Thammajaruk gratefully acknowledges the Office of Higher Education Commission, Thailand, for Strategic Scholarships Fellowships Frontier Research Network (Specific for Southern region).

Appendix A

See Table A.1

Table A.1
Parameters kept in the database for each paper.

Parameter	Example
Title	Bonding quality of contemporary dental.
Corresponding author	K.M. Abdelaziz
Journal	J. Investig. Clin. Dent. 2012 3(2) 142–147
Doi	10.1111/j.2041-1626.2011.00106.x
Source of article	MEDLINE
Objective	To evaluate the shear bond strength…
ID of study in the database	ID_00101
Zirconia substrate name used	Cercon Zirconia
Mechanical pre-treatment	Alumina air abrasion with 50, 110, 250 µm
Chemical pre-treatment	Metal/zirconia primer or none
Composite cement name used	Multilink or SpeedCem
Type of curing method	Chemical-cured (Multilink) Light-cured (SpeedCem)
Thermocycling procedure (cycles)	No
Storage duration (in day(s)/month (s))	1 day
Test area (micro/macro)	Macro
Test mode	Shear
Shape of the tested interface	Round
Bonding area (mm^2)	12.57

Appendix B

See Table B.1

Table B.1
Parameters kept in the database for each test result.

Parameter	Example
ID of study in the database	ID 00101
ID of test result	ID 0010101
Zirconia substrate name used/ type	Cercon Zirconia/ Yttria stabilized zirconia
Mechanical pre-treatment	Alumina air abrasion
Chemical pre-treatment	Functional primer
Additional treatment	Steam cleaned and thoroughly air dried, ultrasonic cleaning for 1 min
Composite cement name used	Multilink
Type of composite cement	Functional monomer-free cement
Type of curing method	Self-cured
Antagonist	Composite cement
Test area (micro/macro)	Macro
Test mode (shear/tensile)	Shear
Type of test	Macro-shear
Shape of tested interface	Round
Storage condition and duration	Distilled water at 37 °C for 1 day
Thermocycling procedure (cycles)	No
Mean bond strength (MPa)	15.7
Standard deviation	3.3
Significant level	0.05
Number of specimens in test result	10
Number of pretesting failure in test result	0

Appendix C

See Table C.1 and C.2

Table C.1
The medians, ranges, actual mean bond strength and 95% of confidence intervals (CIs) of the bond strength (MPa) by bond strength tests.

Bond strength test	Number of studies	Medians	Ranges	Actual mean bond strength[a]	95% CIs
Micro-shear bond strength test	20	18.7	0–55.7	21.90	18.51–25.91
Micro-tensile bond strength test	19	18.19	0–53.4	20.44	17.69–23.63
Macro-shear bond strength	115	9.01	0–82.2	12.12	10.73–13.69
Macro-tensile bond strength	12	23.7	0–53	22.88	18.24–28.70

[a] Generated from GEE model, adjusted for the antagonist.

Table C.2
The p-value comparing between the bond strength tests by Kruskal-Wallis test.

Bond strength test	Micro-shear bond strength test	Micro-tensile bond strength test	Macro-shear bond strength test	Macro-tensile bond strength test
Micro-shear bond strength test	–	0.512	< 0.0001*	0.775
Micro-tensile bond strength test	–	–	< 0.0001*	0.412
Macro-shear bond strength	–	–	–	< 0.0001*
Macro-tensile bond strength	–	–	–	–

* Significant difference ($p < 0.05$).

Appendix D

See Table D.1

Table D.1
The frequency of mechanical and chemical pre-treatments and composite cements.

		Number of test results
Mechanical pre-treatment	No mechanical pre-treatment	475
	Alumina air abrasion	553
	Tribochemical silica coating	327
	Laser irradiation	96
	Chemical etching	39
	Ceramic coating	142
Chemical pre-treatment	No chemical pre-treatment	611
	MDP-containing primers	377
	Functional primers	232
	Silanes	412
Composite cement	MDP-containing cements	556
	MDP-free functional monomer-containing cements	454
	Functional monomer-free cements	622

Appendix E

See Table E.1

Table E.1
The actual mean bond strength and 95% CIs by antagonists.

Antagonist	The actual mean bond strength (MPa)	95% CIs
Zirconia	25.22	19.90–31.95
Composite resin	16.34	14.56–18.33
Composite cement	12.28	10.55–14.29

Appendix F

See Table F.1

Table F.1
The actual mean bond strength and 95% CIs by aging conditions.

Aging condition	The actual mean bond strength (MPa)	95% CIs
Non-aged	16.92	15.07–18.99
Intermediate-aged	16.40	14.03–19.17
Aged	9.77	7.87–12.14

Appendix G. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.jmbbm.2018.02.008.

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