Clin Oral Invest (2012) 16:1–14
DOI 10.1007/s00784-011-0626-8

REVIEW

Retention of orthodontic brackets bonded with resin-modified GIC versus composite resin adhesives—a quantitative systematic review of clinical trials

Steffen Mickenautsch · Veerasamy Yengopal · Avijit Banerjee

Received: 12 February 2011 / Accepted: 5 October 2011 / Published online: 18 October 2011

Abstract The aim of this systematic review was to establish whether the clinical debonding (failure) rates of orthodontic brackets bonded either with resin-modified glass ionomer (RM-GIC) or with composite resin adhesive are the same. Five databases were searched for articles up to 18 November 2010. Inclusion criteria were titles/abstracts relevant to the review question and two or more arm clinical trial. Exclusion criteria were the following: no computable data recorded and subjects of both groups not followed up in the same way. From the accepted trials, datasets were analysed concerning clinical precision and internal validity. Eleven trials were accepted. From these, 15 dichotomous datasets were extracted. Relative risk with 95% confidence interval of nine datasets showed no statistically significant differences in outcome between the treatment and control group after 6 months–1.32 years. Five showed a statistically significant difference ($p<0.05$), favouring resin composite bonding after 12 and 18 months. One favoured RM-GIC after 10 months. Meta-analysis found no difference in the failure rate between the two treatment groups after 12 months (RR, 1.11; 95% CI, 0.87–1.42; $p=0.40$) and found in favour of composite resin adhesive after >14 months (RR, 2.25; 95% CI, 1.60–3.17; $p<0.00001$). All trials had poor internal validity due to selection and detection/performance bias risk. The current evidence suggests no difference between the types of materials after 12 months but favours composite resin adhesives after a >14-month period. However, its risk of selection and detection/performance bias are high, and all results need to be regarded with caution. Further high quality randomised control trials addressing this topic are needed. The clinical relevance of this study is that RM-GIC may have the same clinical debonding (failure) rate as composite resin adhesives after 1 year when used for bonding of orthodontic brackets.

Keywords Resin-modified glass ionomer cement · Composite resin · Orthodontic treatment · Systematic review · Orthodontic brackets

S. Mickenautsch (✉) · V. Yengopal
Division of Public Oral Health, Faculty of Health Science,
University of the Witwatersrand,
7 York Rd., Parktown,
Johannesburg 2193, South Africa
e-mail: neem@global.co.za

A. Banerjee
Unit of Conservative Dentistry, King's College London Dental Institute, KCL, Guy's Dental Hospital,
London Bridge,
London SE1 9RT, UK

Introduction

Modern-day orthodontic brackets are cemented to labial or lingual enamel tooth surfaces acting as a medium for delivery of forces applied by the arch wire and auxiliaries on the teeth. The factors implicated in the successful transfer of orthodontic forces include the surface preparation of the bonded enamel surface, the type of cement used and the shape/material/surface finish of the bracket [1–4]. The ideal cement used for orthodontic bracket bonding should exhibit enough retention to resist displacement during normal oral function. It should also transmit the required orthodontic forces to the tooth itself and be readily removable once treatment is complete, without causing damage to the tooth surface and, ideally, without leaving on the tooth a copious surface residue, which needs to be removed by drill or air abrasion [5].

The two conventional adhesives commonly used to bond brackets to teeth are resin methacrylates and glass ionomer cement (GIC) derivatives [6–8]. These have different mechanisms for adhesion: composite resins use micro-mechanical retention of an acid-etched enamel surface±the use of a suitable primer/bonding agent to help couple the two surfaces, whereas the conventional GIC-based materials (C-GIC) form a chemical bond between the conditioned enamel surface (calcium ions) and the bracket. In the last two decades, the beneficial properties of the two have been combined in the development of resin-modified GICs (RM-GICs), where the acid-based chemical reaction of the GIC has been admixed with the light-activated additional polymerisation of hydroxyethyl methacrylate [9].

Studies exist in the literature comparing the efficacy of the type of adhesive used on the retention of orthodontic brackets both in vitro and in vivo, often with conflicting conclusions [10, 11]. This variation in outcomes may be ascribed to the degree of control of the variables mentioned above, the actual orthodontic forces placed on the teeth and the relative longevity of the follow-up period.

One systematic review, following the Cochrane-recommended methodology, has covered several orthodontic adhesives; such as chemical versus light cure composite, chemical cure composite versus C-GIC and compomers, with regard to successful bracket bonding and decalcification of enamel around brackets [12]. Although this systematic review followed the Cochrane recommended methodology, quality assessment of included trials on the basis of their internal validity was limited, and bias risk was not investigated in depth. In addition, this systematic review adopted a qualitative synthesis of trial results and did not include RM-GIC. The cut-off date for the systematic literature search was the year 2000.

Against such background, the aim of this systematic review was quantitative, in-depth appraisal of the current existing clinical evidence and its risk of bias/systematic error regarding the efficacy for orthodontic bracket bonding, of RM-GIC in comparison to that of composite resins—the current gold standard. The objective was to answer the review question as to whether in orthodontic patients with bonded brackets RM-GIC and composite resin adhesive used for bonding the orthodontic brackets have equal clinical debonding (failure) rates.

Materials and methods

Systematic search strategy

No review protocol was officially registered. PubMed was systematically searched for articles reporting on clinical trials up to 18 November 2010. The string of MeSH and text search terms, with Boolean operators: *(*"Glass ionomer cements"[Mesh] AND "composite resins"[Mesh]) AND "orthodontic brackets"[Mesh] was stepwise developed after completion of the following electronic searches:

1. ("Glass ionomer cements"[Mesh]=5,224 articles found
2. ("Glass ionomer cements"[Mesh] AND "composite resins"[Mesh]) = 2584 articles found
3. ("Glass ionomer cements"[Mesh] AND "composite resins"[Mesh]) AND "orthodontic brackets"[Mesh]= 132 articles found

After completion, a subsequent search in the databases (Biomed Central, Cochrane Library, Directory of Open Access Journals and Science-Direct) as well as a reference check of the included articles, was conducted.

Articles from the search results were selected for review on the basis of their compliance with the broad inclusion criteria:

1. Two- or more arm clinical trial
2. Relevant to the review question: comparison of RM-GIC versus composite resin/debonding (trials investigating conventional GIC were not included)

No limitations were made as to the publication language of articles. Where only a relevant title without a listed abstract was available, a full copy of the article was assessed for inclusion.

Article review

Only articles that complied with the inclusion criteria were reviewed further. Full copies of articles were reviewed independently by two reviewers (VY and SM). Articles were excluded if:

1. No computable data were reported.
2. Subjects of both groups were not followed up in the same way.

Disagreements between reviewers were resolved through discussion and consensus.

Data extraction from accepted trials

The outcome measure was bonding failure (debonding). Two reviewers (VY and SM) independently extracted data from the accepted trials. Individual dichotomous datasets (DS), consisting of the number of evaluated units (N) and the number of units (brackets and/or patients) with bonding failure (n), were extracted for both types of materials in the control and the test group. Where possible, missing data were calculated from information given in the text or tables. Disagreements between reviewers during data extraction were resolved through discussion and consensus.

Statistical analysis

RevMan Version 4.2 statistical software from The Nordic Cochrane Centre, The Cochrane Collaboration (Copenhagen, 2003) was used to analyse the individual datasets. Differences in treatment groups were computed on the basis of relative risk (RR), with 95% confidence intervals (CIs).

Meta-analysis, using a fixed effects model, was considered for datasets only if they complied with criteria for clinical homogeneity. Datasets were considered clinically homogeneous if the datasets covered the same study length and unit of investigation (bonded teeth or patients with orthodontic treatment). In addition, to the requirements for clinical homogeneity, heterogeneity of datasets was graphically investigated using a Galbraith plot (MIX Version 1.7). The percentage of total variations across datasets (I^2) was used in assessing statistical heterogeneity (RevMan Version 4.2). [17]. Statistical significance for assessing statistical heterogeneity between datasets (DS) was set as α=0.10. Pooled datasets were assigned a Mantel–Haenszel weight directly proportional to their sample size. Sensitivity analysis of meta-analysis results, derived using a fixed effects model and expressed as RR with 95% confidence intervals, was conducted. RevMan Version 4.2 was used to investigate whether the overall meta-analysis results (in RR) would change if analysed as odds ratio (OR) or when using a random effects model.

Quality of studies and assessment of potential bias risk

Criteria for quality assessment of trials are listed in Table 1. Quality assessment of accepted trials was undertaken on the basis of availability of evidence indicating successful prevention of selection and detection/performance bias from the start to end of each trial. If a trial merely reported that randomisation was conducted, reported only the name of the randomisation method used or included a detailed description of the randomisation process without providing any evidence that randomisation was indeed effective throughout the trial, this was regarded as inadequate [13, 14].

Sensitivity analysis was done using the RevMan Version 4.2 statistical software of The Nordic Cochrane Centre, The Cochrane Collaboration (Copenhagen, 2003), in order to investigate potential attrition bias risk in trials.

To investigate publication bias, a funnel plot was generated using the datasets from the included clinical trials. The standard error (SE) of the mean differences was plotted on the *y*-axis, and the ln of the RR on the *x*-axis, using MIX Version 1.7 meta-analysis software [15]. In addition, Egger's linear regression method [16] was used to calculate an intercept with a 95% C), with statistical significance set at α=0.05.

Results

Literature search

Figure 1 provides information on the number of articles identified through the search strategy. Nine articles were identified through the PubMed search [18–26] and four during the reference check [27–30]. From the 13 articles considered for possible inclusion, two were excluded [25, 26]. The reasons for exclusion were lack of computable data: follow-up period per investigated subgroups not reported [25], number of evaluated teeth (*N*) and number of failures (*n*) not reported [26]. Thus, the results presented were obtained from 11 trials [18–24, 27–30]. Table 2 describes the characteristics of the included trials and the datasets derived from the results presented in each of them.

Dataset extraction and analysis

Fifteen dichotomous datasets were extracted from the 11 accepted trials. Nine of the 15 showed no difference between the two materials after periods lasting from 6 to 18 months (Table 3). Five dichotomous datasets (DS 06, 09, 11, 12 and 14) extracted from five trials [20, 23, 27, 28, 30] showed statistically significant results (p<0.05) in favour of composite resin after 12, 14 and 18 months. One dataset (DS 13) extracted from one trial [29] showed in favour of RM-GIC after 10 months.

Meta-analysis

Each of two groups of datasets was considered to have met the criteria for clinical homogeneity: (a) group 1, DS 04, 05, 07, 08, 10 and 15 after 12 months and (b) group 2, DS 01, 06 and 12 after >14 months. Investigation using a Galbraith plot (Fig. 2) indicated homogeneity for the first group of datasets but not for the second group. Subsequent investigation of statistical heterogeneity showed that both groups of datasets were suitable for meta-analysis with a fixed effects model: group 1, I^2=0%, p=0.83 and group 2, I^2=41.5%, p=0.18).

The meta-analysis results of both groups were generated in the form of two forest plots (Figs. 3 and 4). Figure 3 shows a pooled relative risk of 1.11 (95% CI,0.87–1.42; p=0.40) after 12 months. Figure 4 shows a pooled relative risk of 2.25 (95% CI, 1.60–3.17; p<0.00001).

Sensitivity analysis indicated robustness of these results, regardless of whether they were analysed as RR or OR, or when a fixed or random effects model was used (Table 4).

Table 1 Quality assessment criteria of trials

Score	Criteria	Impact on bias risk
Randomisation and concealment		
A	Randomisation: details of any adequate type of allocation method that generates random sequences with the patient as unit of randomisation are reported[a] Concealment: trial provides evidence[b] that concealment was indeed effective and that the random sequence could not have been observed or predicted throughout the duration of the trial	Doubts may still exist whether the trial results are influenced by selection bias but no indication can be found from the trial report to support such doubt.
B	Randomisation: details of any adequate type of allocation method that generates random sequences with the patient as unit of randomisation are reported[a] Concealment: trial reports on any adequate method to prevent direct observation[c] and prediction[d] of the allocation sequence and sequence generation rules	Despite the implementation of method considered to be able to prevent unmasking of the concealed allocation sequence through direct observation and prediction, there are reasons to expect that the concealed allocation sequence may have been unmasked during the cause of the trial.
C	Randomisation: details of any adequate type of allocation method that generates random sequences with the patient as unit of randomisation are reported[a] Concealment: trial reports on any adequate method to prevent direct operator observation of allocation sequence and sequence generation rules[c]. However, the allocation sequence and sequence generation may have been sufficiently predicted	Despite the implementation of method considered to be able to prevent unmasking of the concealed allocation sequence through direct observation, there are reasons to expect that operators could have predicted the concealed allocation sequence.
D	Randomisation: details of any adequate type of allocation method that generates random sequences with the patient as unit of randomisation are reported[a] Concealment: the trial report does not include information on how the allocation of random sequence was concealed. The allocation could have been directly observed and/or predicted	Despite the theoretical chance for each patient to be allocated to either treatment group, operator knowledge of the allocation sequence may have lead to patient allocation that favoured the outcome of one type of treatment above the other
0	Trial does not comply with criteria A–D	No guaranty of equal chance for patients to be allocated to either treatment group, thus allocation may have favoured the outcome of one type of treatment above the other
Baseline data for randomised trials		
A	Baseline data collected before randomisation and reported for both treatment groups/Data shows no significant differences between both groups	Evidence is given that randomisation has lead to equal groups suggesting little risk of selection bias
B	Baseline data collected before randomisation and reported for both treatment groups/Data shows significant differences between both groups but has been statistically adjusted appropriately	Differences have been adjusted, thus the influence of possible selection bias appears to be reduced
C	Baseline data collected before randomisation and reported for both treatment groups/Data shows significant differences between both groups without being statistically adjusted	Reported differences may be due to ineffective randomisation, thus indicate risk of selection bias
0	Trial does not comply with criteria A–C	No evidence is given whether randomisation has indeed lead to equal groups with differences beyond chance, thus differences may exists indicating selection bias
Blinding/masking		
Score	Criteria	Impact on bias risk
A	Trial reports on any type of method that is known to prevent patient AND operator AND evaluator to discern whether patients are allocated to the test- or the control group (blinding/masking) Trial reports a process with which the effect of blinding/masking was evaluated, as well as the results of such evaluation	Evidence is given that the trial results may not have been influenced by detection/performance bias that may have favoured the outcome of one type of treatment above the other
B	Trial reports on any type of method that is known to prevent patient AND operator AND evaluator to discern whether patients are allocated to the test- or the control group (blinding/masking) Trial report does not give reason for doubt that the patient allocation to either the test- or the control group has been unmasked throughout the duration of the trial	Doubts may still exist whether the trial results are influenced by detection/performance bias but no indication can be found from the trial report to support such doubt. However, no evaluation of the Blinding/Masking effect has been included in the trial, thus no evidence for lack of bias is given
C	Trial reports on any type of method that is known to prevent patient AND operator AND evaluator to discern whether patients are allocated to the test- or the control group (blinding/masking) Trial report gives reason for doubt that the patient allocation to	Despite the implementation of method considered to be able to prevent unmasking, there are reasons to expect that operators/ patients could have discovered the allocation.

	either the test- or the control group has been unmasked throughout the duration of the trial	
0	No process reported or implemented able to blind/mask patients AND operators whether patients were allocated to either the test- or the control group (it is insufficient to report that blinding/masking was done without reporting the details of the process)	Knowledge about the patient allocation may have caused patients/operator to act in a way that may have favoured the outcome of one type of treatment above the other
Loss to follow-up		
Score	Criteria	Impact on bias risk
A	Available case analysis, loss-to-follow up reported per treatment group/Subsequent sensitivity analysis does not indicate a possible risk of bias effect	The trial allows to extract evidence that the loss-to-follow up may has not favoured the outcome of one type of treatment above the other
B	Available case analysis, loss-to-follow up reported per treatment group/Subsequent sensitivity analysis indicates a possible risk of bias effect	The trial allows to assess the risk that the loss-to-follow up may have favoured the outcome of one type of treatment above the other
0	Trial does not report number of included participants per treatment group at baseline or give any indication that would allow to ascertain the loss-to-follow up rate per treatment group	The trial carries an unknown risk that the loss-to-follow up may have favoured the outcome of one type of treatment above the other
Trial outcome		
0	The trial reports on secondary of surrogate outcomes as endpoints	Even if the surrogate results would highly correlate with primary (i.e. clinical outcomes) they cannot serve as valid replacements and need to be regarded for hypothesis development, only
A	The trial reports on primary outcomes as endpoints	Primary outcomes may provide evidence for hypothesis testing

[a] Excluded are types of allocation methods that are considered as inadequate: cluster randomisation, fixed block randomisation with block size two, minimization, alternation, randomisation of teeth, use of date of birth or patient record number, "quasi"-randomisation, splitmouth

[b] For example by reporting results of the Berger–Exner test or any other statistical tests that show that covariates of compared groups were similar at baseline

[c] For example by opening of opaque envelope, obtaining allocation from tables, computer generated or form other sources

[d] For example central randomisation, sequence allocation by other than operator; excluding varied block randomisation

Quality assessment of trials and risk of bias

Selection, detection/performance bias risk

All trials reported on primary clinical outcomes and thus were rated with 'score A' in this assessment category.

None of the accepted trials reported sufficient details of any randomisation process, which had given each patient the same chance of being allocated to either the RM-GIC or the composite resin group and ensured that direct observation and prediction of the allocation sequences was successfully prevented. Moreover, none of the accepted trials statistically compared the baseline data between groups, and none fulfilled the criteria (Table 1) related to successful blinding/masking of patients, operators and trial evaluators. For that reasons, all trials were rated in these assessment categories with 'score 0'.

Attrition bias risk

Sensitivity analysis was used in computing datasets, under the assumption that either:

1. All teeth lost to follow-up developed carious lesions.
2. None of the teeth lost to follow-up developed carious lesions.

Loss-to-follow up was reported for two datasets (DS 04 and 05). The numbers of teeth lost to follow-up per dataset are shown in Table 2. The results of neither situation (1 and 2) changed the outcome of both datasets from their original findings to any statistically significant results:

(a) DS 04: 1. RR 0.96 (95% CI, 0.29–3.21) $p=0.95$; 2. RR 4.82 (0.24–98.96) $p=0.31$
(b) DS 05: 1. RR 0.72 (95% CI, 0.24–2.19) $p=0.957$; 2. RR 1.01 (0.15–7.02) $p=0.99$

Against this background, all trials were rated with 'score A'.

Publication bias risk

Publication bias was investigated using one funnel plot. The funnel plot showed an even distribution that did not suggest publication bias (Fig. 5). Egger's linear regression method for the same datasets showed an intercept of 0.54 (95% CI, −1.84; 2.92) and $p=0.63$.

Discussions

Quantitative systematic reviews are more valuable than qualitative synthesis, in that they provide opportunities for detecting statistically significant ($p<0.05$) treatment effects

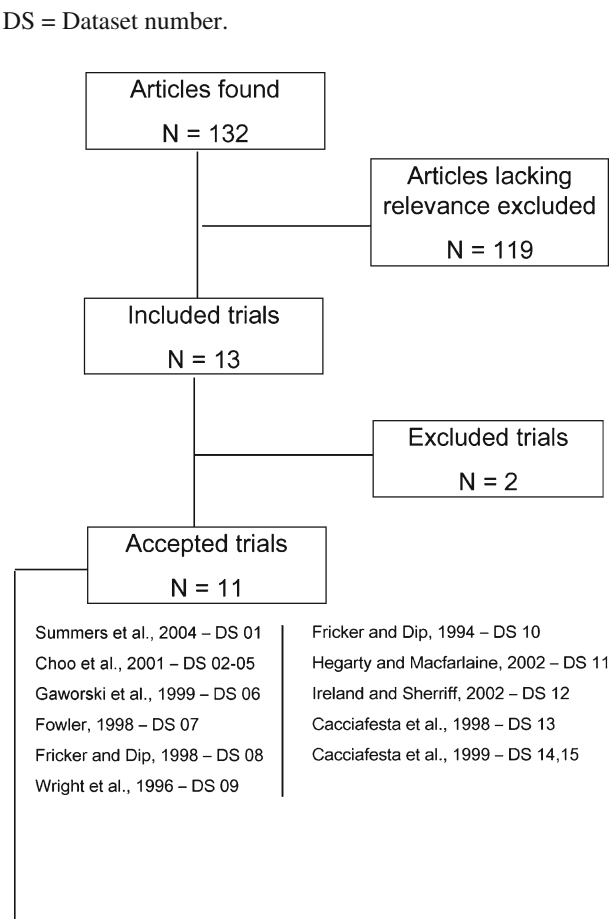


Fig. 1 Flow diagram of trial selection. *N* Number of trials, *DS* dataset number

and for improving precision of effect estimation by quantifying their outcomes [31]. Quantitative collation of clinical information from separate trials covering a particular treatment approach and comparison of materials used provides a more objective assessment of the currently available evidence. In this case, the clinical debonding (failure) rates of orthodontic brackets bonded either with RM-GIC or with composite resin adhesive were compared.

Systematic literature search

This systematic review employed a broad search strategy with very unrestrictive inclusion and exclusion criteria for trials. The result was the acceptance of any investigation that compared the clinical efficacy of RM-GIC with that of composite resin adhesives. Unlike common recommendations for the conduct of systematic reviews [31], no restrictions for acceptance were based on criteria related to the internal validity of trials. In that way, the exclusion of trials from review was highly minimised, thus allowing the widest possible range of available information covering this topic. Despite these considerations, only 8.3% (N=11) of all articles found could be accepted (Fig. 1). This indicates that there is a general lack of available trials covering this topic and that the adoption of a broad search strategy with very unrestrictive inclusion and exclusion criteria for trials was appropriate. The adopted search strategy facilitated a comprehensive overview of the evidence currently available and the subjecting of such evidence to:

1. A detailed analysis of available trial results
2. An in-depth evaluation of its validity in light of potential risk of bias

This two-point approach made it possible to report on the present status quo, as derived from the currently available data, and to use the conclusions as a basis for recommendations concerning the need for further research regarding this topic.

Trial results and analysis

Of the 15 extracted dichotomous datasets, nine showed no difference between the two types of materials, five favoured composite resin and one favoured RM-GIC (Table 3). The trial by Cacciafesta et al. [30] indicated that no difference was observed in the failure rate when brackets were bonded on teeth soaked with saliva (DS 15) and that composite resin adhesive proved to be superior to RM-GIC when

Table 2 Details of accepted trials

Article	Study design	DS	Age	Patients	Type of bracket bonded	Type of wire	RM-GIC treatment group					Composite resin treatment group					Follow-up period
							Type of material	BSL	*N*	*n*	LTF	Type of material	BSL	*N*	*n*	LTF	
Summers et al. [18]	SM	01	–	–	–	–	Fuji Ortho LC	199	199	13	0	Light bond	199	199	10	0	1.32 years
Choo et al. [19]	SM	02	–	Full upper and lower appliance patients	GAC micro-arch universal orthodontic premolar bracket (GAC International, Bohemia, New York) with a base dimension of 3.12 _ 3.40 mm	0.010-in stainless steel ligature wires around 1st molars, premolars, canines/ nickel titanium arch wires 0.012-inch were tied in	Fuji Ortho LC	84	84	3	0	Trans-bond	81	81	5	0	6 months
		03					3 M Multi-Cure	85	85	3	0		86	86	5	0	
		04					Fuji Ortho LC	84	81	2	3		81	76	0	5	12 months
		05					3 M Multi-Cure	85	82	2	3		86	81	2	5	
Gaworski et al. [20]	SM	06	–	Maxillary and mandibulary premolar, canine, and incisor teeth were bonded allowing up to 20 teeth per patient	–	–	Fuji Ortho LC	149	149	37	0	Light bond	149	149	11	0	14 months
Fowler [21]	PG	07	–	Full upper and lower appliance patients	Optimesh 0.022 slot	0.016 NiTi aligning archwires	Fuji Ortho LC	1747	1747	107	0	Concise	1,674	1,674	90	0	12 months
Fricker and Dip [22]	SM	08	–	Full upper and lower appliance patients	–	14×0.014-in, 4×0.012-inch, 2×0.014- in nickel titanium (Nitinol, Unitek)	Fuji Ortho LC	60	60	3	0	System 1+	60	60	5	0	12 months
Wright et al. [23]	SM	09	12–20 years	–	Stainless steel orthodontic brackets (Forestadent, Straightwire, Andrews prescription)	Geristore	358	358	32	0	Phase II	358	358	11	0	12 months	
Fricker and Dip [24]	SM	10	–	Full upper and lower appliance patients	Ormesh universal light wire brackets (346–4,604) (Ormco Corp., Glendora, California) were bonded to the canines with Ormesh light wire brackets (340–4,601) bonded to the incisors	15×0.014-in, 4×0.016-in premium plus round stainless steel (A J Wilcock, Australia), one 0.014-in nickel titanium (Nitinol, Unitek, Monrovia, California)	Fuji II LC	60	60	2	0	System 1+	60	60	1	0	12 months

Table 2 (continued)

Article	Study design	DS	Age	Patients	Type of bracket bonded	Type of wire	RM-GIC treatment group					Composite resin treatment group					Follow-up period
							Type of material	BSL	*N*	*n*	LTF	Type of material	BSL	*N*	*n*	LTF	
Hegarty and Macfarlane [27]	SM	11	–	–	Stainless steel brackets (0.022–0.028-in. slot with mesh base, Orthos, Ormco, Glendora, California)	–	Fuji II LC	61*	61*	23**	0	Rely-a-bond	61*	61*	41**	0	12 months
Ireland and Sherriff [28]	SM	12	–	–	0.022-in Minitwin brackets	Archwire sequence: 0.012-in nickel titanium followed by 0.016-in nickel titanium	Fuji II LC	160	160	43	0	Right-on	157	157	20	0	18 months
Cacciafesta et al. [29]	SM	13	>18 years	Full upper and lower appliance patients	Stainless steel brackets with a 0.022-in slot (Orthos. Ormco), after teeth soaked with water	–	Fuji Ortho	404	404	32	0	System 1+	460	460	84	0	10 months
Cacciafesta et al. [30]	SM	14	–	Full upper and lower appliance patients	Stainless steel brackets with a 0.022-in slot (Orthos. Ormco), bonded on dry teeth	–	Fuji Ortho	110	110	38	0	System 1+	110	110	10	0	12 months
		15			Stainless steel brackets with a 0.022-in slot (Orthos. Ormco), after teeth soaked with saliva												

DS Dataset number; *SM* Split-mouth design; *PG* Parallel-group design; *BSL* Number of bonded teeth at baseline; *N* Number of teeth evaluated; *n* Number of bonding failures, *LTF* Loss-to-follow-up; *RM-GIC* Resin-modified glass-ionomer cement

*Number of patients, ** Number of patients with bond failure

Table 3 Results of individual datasets

Article	DS	RR	95% CI	*p* value
Summers et al. 2004 [18]	01	1.30	0.58–2.90	0.52
Choo et al. 2001 [19]	02	0.58	0.14–2.34	0.44
	03	0.61	0.15–2.46	0.48
	04	4.70	0.23–96.28	0.31
	05	0.99	0.14–6.84	0.99
Gaworski et al. 1999 [20]	06	3.36	1.78–6.34	0.0002[a]
Fowler 1998 [21]	07	1.14	0.87–1.50	0.35
Fricker and Dip, 1998 [22]	08	0.60	0.15–2.40	0.47
Wright et al. 1996 [23]	09	2.91	1.49–5.68	0.002[a]
Fricker and Dip, 1994 [24]	10	2.00	0.19–21.47	0.57
Hegarty and Macfarlane 2002 [27]	11	1.90	1.26–2.86	0.002[a]
Ireland and Sherriff 2002 [28]	12	2.11	1.30–3.42	0.002[a]
Cacciafesta et al. 1998 [29]	13	0.43	0.30–0.64	<0.0001[b]
Cacciafesta et al. 1999 [30]	14	3.80	1.99–7.24	<0.0001[a]
	15	0.93	0.46–1.90	0.85

DS Dataset number, *RR* relative risk, *CI* confidence interval

[a]Statistically significant difference, in favour of Composite resin

[b]Statistically significant difference, in favour of RM-GIC

bonding was done on dry teeth (DS 14). This may be due to the general hydrophobic nature of composite resin, which requires a dry surface for successful micro-retention. Such interpretation may seem to be confirmed by the results of the trial by Cacciafesta et al. [29], in which a better performance of RM-GIC was observed 10 months after bonding either of the two materials onto teeth soaked with water (DS 13). Such a factor is related to operator skills and clinical protocol. Together with the factor of time, i.e. a treatment period >14 months, this operator factor may explain the better clinical efficacy of composite resin as observed in some of the reviewed trials [23, 27–30]. However, the time factor alone may not be sufficient to justify a hypothesis that, for orthodontic bracket bonding, RM-GIC is inferior to composite resin, as indicated by the equivocal clinical results from one dataset (DS 01) after 1.32 years [18]. In addition, arguments favouring one material above the other while relying on the operator factor would need to take the different material (hydrophilic/hydrophobic) characteristics of RM-GIC and composite resin into account.

From the 15 individual datasets, nine were selected for pooling in two meta-analyses (Figs. 3 and 4). The selection was based on aspects of clinical and statistical heterogeneity. Only two clinical characteristics were considered for assessment for clinical heterogeneity: unit of investigation and study

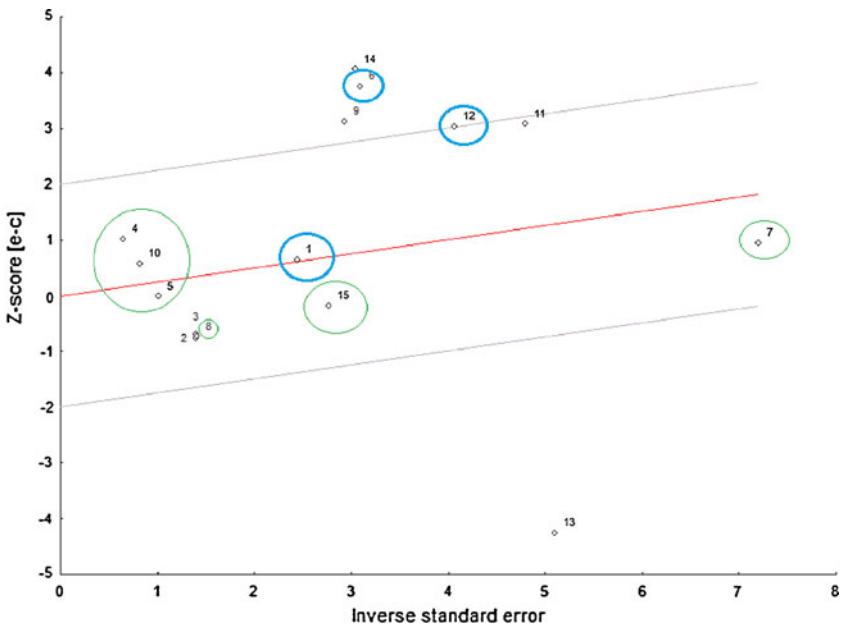
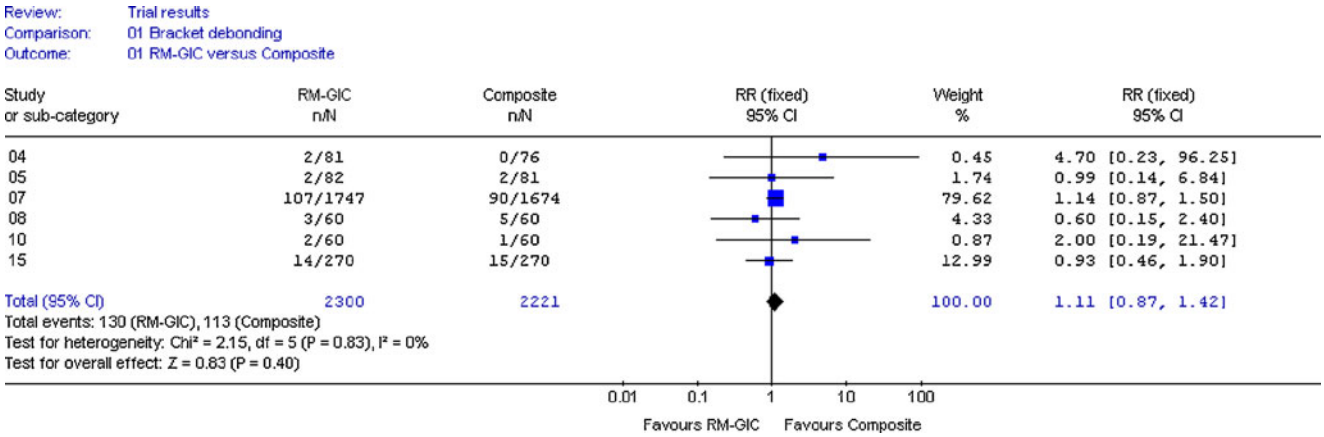


Fig. 2 Galbraith plot—investigation of heterogeneity between datasets (DS). *Green circles* DS 4, 5, 7, 8, 10 and 15 selected for meta-analysis 1 (see Fig. 3). *Blue circles* DS 1, 6 and 12 selected for meta-analysis 2 (see Fig. 4)

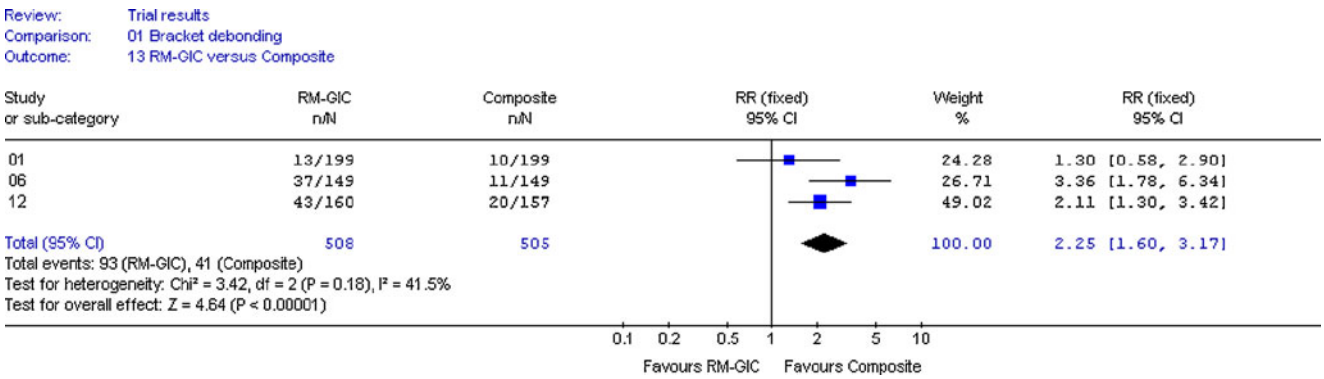


RM-GIC = Resin-modified glass-ionomer cement; n = number of teeth with failed bracket bonding; N = number of evaluated bonded teeth; CI = Confidence interval; RR = Relative risk; Study = Dataset number.

Fig. 3 Meta-analysis results after 12 months. *RM-GIC* Resin-modified glass-ionomer cement, *n* number of teeth with failed bracket bonding, *N* number of evaluated bonded teeth, *CI* confidence interval, *RR* relative risk, *study* dataset number

length. Choosing the unit of investigation as a criterion was justified, as a pooling of results derived from a number of patients (DS 11) together with results from a number of brackets (DS 01–10, 12–15) would have rendered the pooled result meaningless. The second aspect, study length, was based on the consideration that bonding strength weakens over time. These considerations were justified through the results provided by a Galbraith plot (Fig. 2). A further clinical aspect concerning heterogeneity, that of bonding on dry tooth surfaces (DS 14), was also identified through that method. The Galbraith plot has been developed as a tool for the investigation of heterogeneity between different sets of data [32]. The plot consists of a *y*-axis that shows the effect size divided by its standard error (*z* score) and an *x*-axis that shows the inverse of the standard error (SE). Each dataset is shown as a dot on the plot. At the centre of the Galbraith plot runs the regression line with two lines parallel to it at a two-standard deviation (SD) distance. A lack of heterogeneity is indicated when all dots are located in between the two SD lines. Empirical evidence has confirmed a significant association between the information displayed on the plot and the true presence of heterogeneity [32]. However, the results of a Galbraith plot are data driven, and investigation of heterogeneity should also take into account qualitative assessment of clinical and methodological characteristics of trials. In addition to the qualitative and graphical investigation of heterogeneity, use of the I^2 test to quantify the statistical heterogeneity in meta-analyses is recommended, owing to its high reproducibility [17, 32].

In this systematic review, all three approaches were utilised for assessment of heterogeneity. Qualitative assessment of clinical trial aspects was confirmed graphically. In addition, graphical investigation confirmed bonding on dry tooth surfaces as a further source of clinical heterogeneity. Dataset selection for the first meta-analysis (Fig. 3) was confirmed graphically, while the selection of datasets for



RM-GIC = Resin-modified glass-ionomer cement; n = number of teeth with failed bracket bonding; N = number of evaluated bonded teeth; CI = Confidence interval; RR = Relative risk; Study = Dataset number.

Fig. 4 Meta-analysis results after >14 months. *RM-GIC* Resin-modified glass-ionomer cement, *n* number of teeth with failed bracket bonding, *N* number of evaluated bonded teeth, *CI* confidence interval, *RR* relative risk, study dataset number

Table 4 Sensitivity analysis of pooled results

Meta-analysis	Effects model	Result
Group 1	Fixed effects model	RR 1.11 (95% CI, 0.87–1.42), p=0.40
		OR 1.12 (95% CI, 0.86–1.45), p=0.40
	Random effects model	RR 1.10 (95% CI, 0.86–1.41), p=0.43
		OR 1.11 (95% CI, 0.86–1.44), p=0.42
Group 2	Fixed effects model	RR 2.25 (95% CI, 1.60–3.17), p<0.0001
		OR 2.59 (95% CI, 1.74–3.84), p<0.00001
	Random effects model	RR 2.19 (95% CI, 1.37–3.50), p=0.01
		OR 2.48 (95% CI, 1.38–4.46), p=0.002

RR Relative risk, *OR* odds ratio, *CI* confidence interval

the second meta-analysis (Fig. 4) could not be confirmed graphically (Fig. 2). Nevertheless, statistical homogeneity for both dataset groups was confirmed by the I^2 test (p>0.10). On the basis of these results, the use of a fixed effects model was justified as having been appropriate for the pooling of both groups of datasets, as it showed that variations between the datasets are not excessive.

The results of the first meta-analysis (Fig. 3) indicate no difference between the two types of materials after 12 months, while the results of the second meta-analysis (Fig. 4) suggest a lower failure (debonding) rate for composite resin adhesives after periods longer than 14 months. The calculated relative risk of 2.25 (95% CI, 1.60–3.17) indicates that eight brackets out of 100 bonded with composite resin had failed over 14 months, compared to 18 out of 100 for the RM-GIC treatment group. The results of both meta-analyses were confirmed/not contradicted by the results of subsequent sensitivity analysis (Table 4). It has to be noted that both meta-analysis results are limited in strength because of the low number of available datasets (only six and three datasets, respectively), and that the latter appears even weaker and thus less robust in view of possible revision through trial evidence in future.

Validity of trial results and bias

Although the use of meta-analysis provides higher precision regarding trial results, the quality of the data is dependent upon the quality of the trials. Trial quality is derived from internal validity, i.e. the risk of under- and overestimation of the observed trials results through systematic error or bias. Overestimation has been observed to be the most common [33]. Egger et al. [34] reported a treatment effect overestimation of between 21% and 54% due to selection bias, solely caused by lack of allocation concealment during the randomisation process.

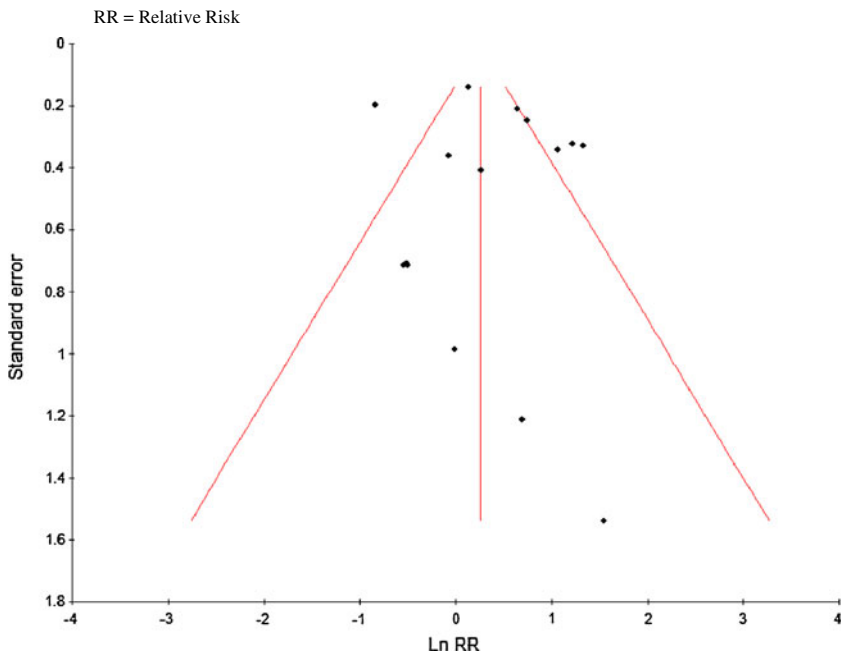


Fig. 5 Funnel plot of dataset results (test for publication bias)

Selection, detection/performance bias risk

Quality assessment showed that the findings of all of the accepted trials appeared to be limited by risk of selection and detection/performance bias.

It has been emphasised that selection bias can only be successfully prevented if the allocation sequence remains truly random and free from potential interference throughout the trial [13, 14]. Thus, it is important that trials should include an effective process for concealing the random allocation sequence and that, by the end of each trial, this process has indeed prevented direct observation and prediction of the random sequence allocation [13, 14]. Quality assessment in terms of the internal validity of trials should, therefore, be a measure of the result of random sequence allocation and allocation concealment and not only of it being recorded. All trials accepted in this systematic review failed to report not only on evidence of successful sequence allocation and allocation concealment results but also on necessary details about how sequence allocation and allocation concealment were attempted and whether these measures were successful.

Only one accepted trial followed a parallel group design [21]. All the others were based on a split-mouth study design. Split-mouth trials are common in dentistry. They have the advantage of using one patient for test and control. When more than one test and control tooth per patient is included, the resulting pairs should not be analysed as independent units, as such analysis would cause artificially narrower confidence intervals. However, these artificial changes may be considered to be only slight [35]. In this systematic review, all units of investigation (teeth with brackets; patients) were analysed as independent data, as the correction for the slight changes in confidence intervals would not have affected the general impact of selection bias on the relative risk (RR, 95% CI) per dataset (Table 3) due to lack of adequate randomisation in all trials.

Despite the advantage of using the same patient for test and control in split-mouth trials in testing the bonding efficacy of dental adhesives, a parallel-group study design might have been more appropriate. The chewing habits of study subjects utilising some parts of the dental arch more than others may have exerted more masticatoric stress on some brackets than on others. That may have favoured the clinical outcome of one type of adhesive above the other. The distribution of chewing habits among study subjects, if not directly investigated, remains an unknown factor. Random sequence generation, allocation and successful concealment of such allocation within the framework of a parallel-group study design would have, under condition of a sufficient number of study subjects, generated an even distribution of this unknown factor among test and control groups. Against this background, the use of a split-mouth study design has introduced the risk of selection bias. The single trial with a parallel-group study design [21] did not include any randomisation of study subjects. This also indicates a high risk of selection bias.

The use of a split-mouth study design in concert with the obvious differences in clinical appearance between RM-GIC and composite resin adhesives appears to have made successful blinding or masking impossible. For that reason, allocation to either treatment group was visible to patients, operators and evaluators. However, the difficulties of successful blinding still carry the danger of detection/performance bias, which may thus have affected the trials' results. Potential knowledge of superiority claims prior to the trial may have led patients to change their chewing habits, operators to place brackets more carefully or evaluators to apply evaluation criteria more subjectively. This in turn may have favoured the outcome of one type of treatment over the other, and an overestimation by over 50% in all trial results, as shown in Table 3 [34] may be assumed. The seriousness of such overestimation becomes clear when considering that, under condition of a 50% overestimation, the actual result for a test treatment would be a 20% higher relative risk (RR, 1.20) in comparison to the control, while the trial report would claim a 20% lower relative risk (RR, 0.80). Thus, in this example, the true result of the trial would constitute the complete opposite of the reported result. Such high percentages of over-estimation due to bias may, therefore, lead to situations where ineffective treatment procedures are presented as effective. Thus, all trial results identified in this systematic review need to be interpreted with caution.

Attrition and publication bias

The results of the quality assessment of all trials do not provide a basis for assumptions regarding any risk of attrition or publication bias.

Recommendations for further research

Systematic reviews are considered to provide the most comprehensive answers to clinical questions [36]. However, such evidence can only be as good as the quality of the trials reviewed. Although the trials accepted in this quantitative systematic review may be considered to be less affected by attrition and publication bias, their risk of selection and detection/performance bias is high. However, the precise effect of bias on the results remains unknown. Thus, the results need to be regarded with caution and require verification. Further high quality clinical trials are needed. Such trials should adopt a parallel group design that allows the use of randomisation and allocation concealment methods, which can effectively prevent direct

observation and prediction of the allocation sequence. A quantitative measurement regarding the success or failure of an adequate attempt to control against selection bias may be provided, for example, by inclusion of a test into trial methodology regarding the association of the trial endpoint with the probability $P\{E\}$ that a certain patient receives a certain treatment (test or control intervention) [13, 14]. In this regard, the use of the Berger–Exner test has been suggested to enable authors of trials to investigate whether selection bias has been introduced into their studies [13, 14]. Where bias risk has been found, it may be statistically adjusted [13]. Both outcomes should be included in the final trial report. In order to ensure that the lack of blinding may not have led to favouring one treatment over the other, trials should adopt and report procedures within their methodology and consequently be able to provide quantitative evidence that the established trial results were not affected by performance and detection bias. Future trials should, moreover, base their reporting on the CONSORT statement [37].

Conclusions

The current evidence suggests that there is no difference between RM-GIC and composite resin adhesives regarding the failure rate of orthodontic bracket bonding after 12 months but shows in favour of composite resin adhesives after a period of over 14 months. However, its risk of selection, detection and performance bias is high and may thus have diverted the observed trial results significantly away from the actual results. Consequently, further high quality randomised control trials are needed in order to answer more conclusively the question as to whether the clinical debonding (failure) rates of orthodontic brackets with RM-GIC or composite resin adhesives are the same.

Conflict of interest The authors declare that they have no conflict of interest.

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