

Self-Ligating Brackets in Orthodontics

A Systematic Review

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ABSTRACT

Objective: To evaluate the clinical differences in relation to the use of self-ligating brackets in orthodontics.

Materials and Methods: Electronic databases were searched; no restrictions relating to publication status or language of publication were applied. Randomized controlled trials (RCTs) and controlled clinical trials (CCTs) investigating the influence of bracket type on alignment efficiency, subjective pain experience, bond failure rate, arch dimensional changes, rate of orthodontic space closure, periodontal outcomes, and root resorption were selected. Both authors were involved in study selection, validity assessment, and data extraction. Disagreements were resolved by discussion.

Results: Six RCTs and 11 CCTs were identified. Meta-analysis of the influence of bracket type on subjective pain experience failed to demonstrate a significant advantage for either type of appliance. Statistical analysis of other outcomes was unfeasible because of inadequate methodological design and heterogenous designs.

Conclusions: At this stage there is insufficient high-quality evidence to support the use of self-ligating fixed orthodontic appliances over conventional appliance systems or vice versa. (*Angle Orthod.* 2010;80:575–584.)

KEY WORDS: Self-ligating; Orthodontic; Fixed appliance; Systematic; Meta-analysis

INTRODUCTION

Self-ligating brackets (SLBs) are not new conceptually, having been pioneered in the 1930s. They have undergone a revival over the past 30 years with a variety of new appliances being developed. A host of advantages over conventional appliance systems have been claimed typically relating to reduced frictional resistance.^{1–4}

The most compelling potential advantages attributed to SLBs are a reduction in overall treatment time^{5,6} and less associated subjective discomfort.⁷ Other purported improvements include more efficient chairside manipulation⁸ and promotion of periodontal health due to poorer

biohostability. Preliminary retrospective research has pointed to a definite advantage, with a reduction in overall treatment time of 4 to 7 months and a similar decrease in required appointments.^{5,6} Consequently, the use of SLBs has increased exponentially; over 42% of American practitioners surveyed reported using at least one system in 2008.⁹ This figure was just 8.7% in 2002.¹⁰

Retrospective research may be confounded by a variety of factors including operator enthusiasm, different appointment intervals and archwire sequences, and multiple operators. However, prospective research relating to SLBs has emerged in recent years.

The purpose of this systematic review is to evaluate the clinically significant effects of SLBs on orthodontic treatment with respect to the quality of scientific evidence and the methodology of those reports. An understanding of clinical evidence on the impact of SLBs on orthodontic treatment would inform the orthodontist's decisions in relation to their choice of fixed appliance system.

MATERIALS AND METHODS

To be included in the review, trials had to meet the following selection criteria:

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- Study design: Randomized and controlled clinical trials.
- Participants: Patients with full arch, fixed orthodontic appliance(s) treated with SLBs or conventional brackets (CBs).
- Interventions: Fixed appliance orthodontic treatment involving SLBs or CBs.
- Outcome measures: The outcome measures were alignment efficiency, pain experience, arch dimensional changes, rate of orthodontic space closure, bond failure rate, and periodontal effects related to both SLB and CB systems.

The efficiency of arch alignment, subjective pain experience, arch dimensional changes, rate of orthodontic space closure, and periodontal effects related to both appliances were recorded. Dichotomous data on the attachment failure rate related to each appliance were also noted.

Search Strategy for Identification of Studies

The following electronic databases were searched: MEDLINE via OVID (1950 to April 2009; see Appendix), EMBASE (1980 to April 2009), and Cochrane Central Register of Controlled Trials (The Cochrane Library, 2009). Language restrictions were not applied. Unpublished or “gray” literature was searched using ClinicalTrials.gov (www.clinicaltrials.gov) and the National Research Register (www.controlled-trials.com) using the term, “orthodontic and bracket.” In addition, Pro-Quest Dissertation Abstracts and Thesis database was searched (www.lib.umi.com/dissertations) using “orthodontic*” and “ligat*.” Conference proceedings and abstracts were also searched. Authors were contacted to identify unpublished or ongoing clinical trials and to clarify data as required. Reference lists of the included studies were screened for relevant research.

Assessment of Relevance, Validity, and Data Extraction

Assessment of research for inclusion in the review and assessment of validity and extraction of data were performed independently and in duplicate by two authors who were not blinded to the authors or the results of the research. Disagreements were resolved by discussion.

Six key methodological criteria were assessed: sample size calculation, random sequence generation, allocation concealment, reporting of withdrawals, blinding of measurement assessment, and the use of intention to treat analysis. An overall assessment of risk of bias (high, medium, low) was undertaken for each included trial using Cochrane Collaboration criteria. When five or more quality items were met, studies were considered to have a low risk of bias; three or more had medium risk; studies fulfilling less

than three criteria were deemed to have high risk of bias. Only those at low to medium risk of bias were to be considered for meta-analysis.

Data Synthesis

A data extraction form was used to tabulate data on the outcomes of interest. Pain intensity using a visual analog scale (VAS) was obtained at all available time intervals. Pain scores assessed by means other than a zero-to-100 VAS were to be equated with this scale by multiplying the original scale employed by an appropriate factor.

Heterogeneity of the clinical studies was gauged by referring to each study assessing treatment protocol, timing of data collection, and measurement technique. Statistical heterogeneity was to be assessed by inspecting a graphical display of the estimated treatment effects from the trials along with their 95% confidence intervals. Chi-squared and I-squared tests for homogeneity were undertaken prior to each meta-analysis. Meta-analyses would also be possible only on studies reporting the same outcome measures at similar time intervals. Mean differences, standard deviations, and 95% confidence intervals were to be calculated for individual trials and combined using a random-effects model. Where necessary, sensitivity analyses were to be done with regard to the individual quality criteria, risk of bias, and publication status.

RESULTS

Description of Studies

Forty-three trials were initially deemed potentially relevant to the review, 42 being derived from MEDLINE via OVID and 1 study from the National Research Register¹¹ (www.controlled-trials.com). Following detailed assessment, 13 satisfied the inclusion criteria. One of these was subsequently omitted following retrieval of the full-text article; the remaining 30 studies were also excluded. However, after we contacted the authors of published trials, a further five studies were included. Of the 17 papers selected, 6 were randomized controlled trials (Table 1^{11–27}).

Outcomes assessed include alleviation of irregularity using Little’s irregularity index, subjective pain experience recorded using VASs, rate of orthodontic space closure, dimensional changes during orthodontic alignment, plaque retention, extent of root resorption developing during treatment, and attachment debond rate related to either appliance system.

Methodological Quality of Included Studies

The methodological quality of the trials considered in the review is presented in Table 2.^{11–27} A priori sample-

size calculations were undertaken in just six of the studies.^{11,12,14,18,21,24} Generation of the random-number sequence was considered adequate in six trials using computer-generated random allocation.^{11,12,14,17,18,24} In many of the studies, allocation was performed using a quasi-random method, with consecutive subjects being alternated between appliances. Six trials had acceptable allocation concealment.^{11,12,14,17,18,24} Group allocation was not concealed in the split-mouth studies.^{13,19,20}

Outcome assessment was blind in five studies.^{12,14,20–22} There were no dropouts in six studies^{16,19,21–23,27}; in studies with dropout, those lost to follow-up were reported on. However, statistical analysis was invariably per protocol with dropouts excluded from analysis. Overall, six studies were deemed to be at low risk of bias.^{11,12,14,17,18,24}

Efficiency of Initial Orthodontic Alignment

Five trials considered the efficiency of initial orthodontic alignment.^{12–16} One study used a three-dimensional measuring technique, making comparison unfeasible.¹² The remaining studies used two-dimensional measurement^{13–16}; one of these trials incorporated a split-mouth design allowing consideration of just four mandibular contact points.¹³ Alignment efficiency was assessed in the mandibular arch in all cases, with four studies confined to the lower anterior region and one study considering the arch from first molar to first molar.¹²

Miles et al,¹³ Scott et al,¹⁴ and Miles¹⁵ followed similar treatment protocols with alignment efficiency assessed using Little's irregularity index in the mandibular arch recorded at similar intervals. Scott et al¹⁴ assessed changes in the irregularity index 8 weeks after appliance placement; Miles¹⁵ and Miles et al¹³ both assessed residual irregularity 10 weeks and 20 weeks after placement of appliances. However, two of the studies^{13,15} failed to include standard deviations and were at high risk of bias, precluding meta-analysis. Instead of measuring the amount of irregularity relieved in a given time frame, Pandis et al¹⁶ calculated the time taken for alignment of the lower anteriors to occur.

Subjective Pain Experience

Four trials investigated subjective pain experience after initial placement of the appliances.^{11,13,17,18} Of these, one split-mouth study considered pain reports after both the first and second visits, with patients indicating which system was associated with the greatest discomfort.¹³ Data in three of the trials are presented as continuous pain scores from 0 to 100 on a 100-mm VAS.^{11,17,18} One trial reported pain scores at 15 time intervals¹¹; two trials used four time points: 4 hours, 24 hours, 3 days, and 7 days after appliance

placement. The findings from these studies conflicted slightly with one study reporting a tendency to less pain experience with Damon 3 SLBs, although this finding did not reach statistical significance.¹¹ Reported pain peaked within 24 hours^{11,17,18} before subsiding to near baseline levels 7 days after appliance placement. Three studies^{11,17,18} were regarded as being at low risk of bias, and they reported similar outcomes permitting statistical comparison; pain scores at four analogous time intervals were extracted from each study to facilitate this.¹¹ Pain intensity over the first 7 days was reported in three studies involving 160 patients, with 83 in the SLB group and 77 in the CB group. Patients in the SLB group reported a mean difference in pain intensity of 0.99 to 5.66 points lower than in the CB group, the greatest difference being reported 3 days after appliance placement (Figures 1–4). However, differences were not of statistical significance.

Two studies^{13,18} reported greater pain experience during chairside manipulation of self-ligating appliances. However, as the mechanisms of archwire engagement and disengagement are very different using SmartClip¹⁸ and Damon 2,¹³ it was felt that direct statistical comparison of this research finding would be invalid.

Bond Failure Rate

Two studies have considered failure of bonded attachments over 20 weeks¹³ and 12 months.¹⁹ The date used for assessing failure or time taken for failure to occur was not reported, and only first-time failures for each tooth were recorded. No significant differences were noted in the more extensive study.¹⁹

Plaque Retention and Periodontal Health

Two trials have compared the impact of SLBs and elastomeric ligation on plaque retention.^{20,21} A split-mouth design was used in one study assaying plaque specimens harnessed 1 and 5 weeks after bonding.²⁰ Longer term effects of bracket system on periodontal health and accumulation of debris has also been assessed.²²

Pellegrini et al²⁰ investigated the influence of method of archwire ligation on plaque retention using ATP-driven bioluminescence to assess bacterial load. Mean streptococcal and total bacterial levels harvested from tooth surfaces were lower with the SLB ($P < .05$). A further prospective trial, however, failed to show an association between bracket type and bacterial load.²¹ This finding may reflect the different measurement technique employed involving estimation of salivary levels of *Streptococcus mutans*.²¹

Furthermore, Pandis et al²² failed to demonstrate a link between bracket type and periodontal health following removal of orthodontic appliances. It appears that, while bracket type might influence bacterial load

Table 1. Summary of Included Research

Study	Methods	Participants	Interventions	Outcomes	Notes
Pringle et al (2009) ¹¹	RCT. Observed for 8 d after appliance placement	52 of 66 patients analyzed. Mean age: TruStraight, 16.1 (7.4) y; Damon 3, 15.2 (6.8). 24 male, 28 female	Group 1: 28 patients with TruStraight Group 2: 24 patients with Damon 3	Subjective pain experience at 2 time intervals on 8 consecutive d after appliance placement	
Fleming et al (2009) ¹²	RCT. Observed at 8 wk	65 patients. Mean age, 16.28 (2.68) y. 22 male, 43 female	Group 1: 32 patients with SmartClip Group 2: 33 patients with Victory	Rate of initial alignment lower 6–6	Measurements were recorded in 3 dimensions
Miles et al (2006) ¹³	CCT. Split-mouth design. Observed at 10 and 20 wk	58 consecutive patients. Mean age, 16.3 y. 18 male, 40 female	Lower appliance with Damon 2 or Victory brackets in alternate quadrants	Rate of initial alignment lower 3–3 Pain experienced at chairside and after appliance manipulation Bracket failure rate recorded	Contact point between central incisors omitted
Scott et al (2008) ¹⁴	RCT. Observed at 8 wk and after mandibular alignment	62 patients recruited. Mean age, 16.27 (4.47) y. 32 male, 30 female	Group 1: 33 patients with Damon 3 Group 2: 29 patients with Synthesis	Rate of initial alignment lower 3–3 Time taken (days) to align lower arch in $0.019 \times 0.025''$ SSW ^a Root shortening of mandibular incisors	
Miles (2005) ¹⁵	CCT. Observed at 10 and 20 wk	48 patients. Mean age, 17.1 y. 26 male, 32 female	Group 1: 24 patients with SmartClip Group 2: 24 patients with Victory	Rate of initial alignment lower 3–3	
Pandis et al (2007) ¹⁶	CCT. Observed until alignment achieved	54 patients. Mean age, 13.7 (1.38) y. 11 male, 43 female	Group 1: 27 patients with Damon 2 Group 2: 27 patients with GAC Microarch	Time taken (days) to align lower 3–3	
Scott et al (2008) ¹⁷	RCT. Observed for 1 wk after appliance placement	62 patients recruited. Mean age, 16.27 (4.47) y. 32 male, 30 female	Group 1: 33 patients with Damon 3 Group 2: 29 patients with Synthesis	Subjective pain experience at 4 h, 24 h, 3 d, and 7 d after appliance placement Analgesic consumption	
Fleming et al (2009) ¹⁸	RCT. Observed for 1 wk after appliance placement and at chairside	48 of 66 patients analyzed. Mean age, 15.96 (2.56) y. 16 male, 32 female	Group 1: 26 patients with SmartClip Group 2: 22 patients with Victory	Subjective pain experience at 4 h, 24 h, 3 d, and 7 d after appliance placement Analgesic consumption Pain experience at chairside	
Pandis et al (2006) ¹⁹	CCT. Split-mouth	62 patients. Mean age 14 y. 23 male, 39 female	Group 1: 43 patients with Damon 2 Group 2: 19 patients with GAC Microarch Appliances were bonded with Transbond Plus and Transbond XT (3M Unitek) or OrthoSolo and Enlight (ORMCO)	Bracket failure rate over a 12-mo period	First time failures only were recorded
Pellegrini et al (2009) ²⁰	CCT. Split-mouth. Observed 1 and 5 wk after appliance placement	18 patients. Mean age, 13.9 y. 5 male, 13 female	In-Ovation R or MiniOvation brackets on alternate lateral incisors	Mean bacterial counts and ATP-driven bioluminescence determinations	

Table 1. Continued

Study	Methods	Participants	Interventions	Outcomes	Notes
Pandis et al (2008) ²¹	CCT. Observed 87 d after appliance placement	32 patients. Mean age, 13.6 (1.5) y. 16 male, 16 female	Group 1: 16 patients with Damon 2 Group 2: 16 patients with GAC Microarch	<i>S mutans</i> counts	
Pandis et al (2008) ²²	CCT. Periodontal examination before and after orthodontic treatment	100 patients. Age range, 12–17 y. 36 male, 64 female	Group 1: 50 patients with In-Ovation R Group 2: 50 patients with GAC Microarch	Plaque, gingival, and calculus indices, and probing depth for mesial, buccal, and distal aspects of mandibular 3–3	
Pandis et al (2006) ²³	CCT. Observed after orthodontic alignment	105 patients. Mean age, 16.14 (2.9) y. 36 male, 69 female	Group 1: 52 patients with Damon 2 Group 2: 53 patients with GAC Microarch	Change in inclination of U1 to SN and NA lines during treatment	
Fleming et al (2009) ²⁴	RCT. Observed at 30 wk after appliance placement	60 patients. Mean age, 16.35 (2.73) y. 21 male, 39 female	Group 1: 29 patients with SmartClip Group 2: 31 patients with Victory	Transverse dimensional change and incisor inclination change	
Pandis et al (2009) ²⁵	CCT. Observed after orthodontic treatment	54 patients. Mean age, 13.8 (1.5) y. 11 male, 43 female	Group 1: 27 patients with Damon 2 Group 2: 27 patients with GAC Microarch	Transverse dimensional change and incisor inclination change	
Miles (2007) ²⁶	CCT. Split-mouth. Observed at 5 weekly intervals during space closure	13 patients analyzed. Median age, 13.1 y. 5 male, 8 female	Clarity appliance placed upper 3-3 with SmartClip or Victory brackets on 2nd premolars	Rate of orthodontic space closure	
Pandis et al (2008) ²⁷	CCT. Observed after orthodontic treatment	96 patients. Mean age, 13.21 (1.64) y. 29 male, 67 female	Group 1: 48 patients with Damon 2 Group 2: 48 patients with GAC Microarch	Root length before and after treatment on panoramic radiographs	

^a SSW indicates stainless steel wire.

Table 2. Methodological Assessment of Included Trials

Study	Design	Sample Size Calculation	Random Sequence Generation	Allocation Concealment	Reporting of Withdrawals	ITT	Blinding of Measurement	Risk of Bias
Pringle et al (2009) ¹¹	RCT ^b	Yes	Yes	Yes	Yes	No	No	Low
Fleming et al (2009) ¹²	RCT	Yes	Yes	Yes	Yes	No	Yes	Low
Miles et al (2006) ¹³	CCT ^c	No	Alternate	No	Yes	No	No	High
Scott et al (2008) ¹⁴	RCT ^d	Yes	Yes	Yes	Yes	No	Yes	Low
Miles (2005) ¹⁵	CCT	No	Alternate	No	Yes	No	No	High
Pandis et al (2007) ¹⁶	CCT	No	Alternate	No	None	–	No	Medium
Scott et al (2008) ¹⁷	RCT	n/a ^a	Yes	Yes	Yes	No	No	Low
Fleming et al (2009) ¹⁸	RCT	Yes	Yes	Yes	Yes	No	No	Low
Pandis et al (2006) ¹⁹	CCT	No	Alternate	No	None	–	No	Medium
Pellegrini et al (2009) ^{20*}	CCT	No	Unclear	Unclear	Yes	No	Yes	Medium
Pandis et al (2008) ²¹	CCT	Yes	Alternate	No	None	–	Yes	Medium
Pandis et al (2008) ²²	CCT	No	Alternate	No	None	–	Yes	Medium
Pandis et al (2006) ²³	CCT	No	Alternate	No	None	–	No	Medium
Fleming et al (2009) ²⁴	RCT	Yes	Yes	Yes	Yes	No	No	Low
Pandis et al (2009) ²⁵	CCT	No	Alternate	No	Yes	No	No	High
Miles (2007) ²⁶	CCT	No	Alternate	No	Yes	No	No	High
Pandis et al (2008) ²⁷	CCT	No	Alternate	No	None	–	No	Medium

^a Intention to treat analysis.

^b RCT signifies randomized controlled trial.

^c CCT signifies controlled clinical trial.

^d Sample size was dictated by allied research on this population.¹⁴

* Author contacted to clarify randomization. No reply was received.

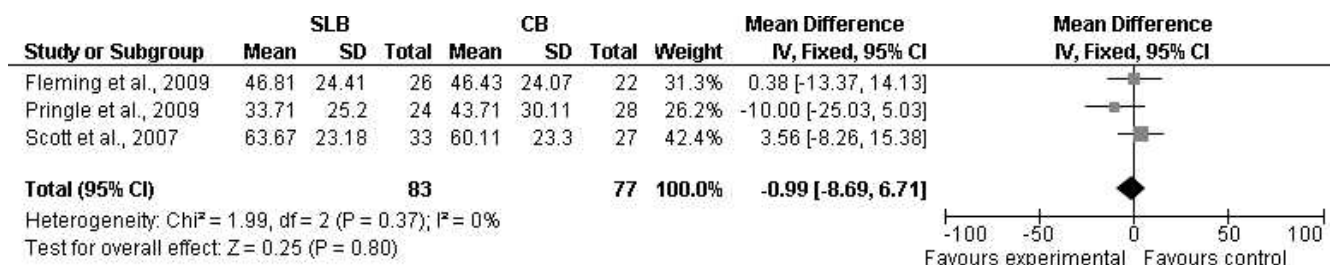


Figure 1. Meta-analysis and forest plot of pain scores (VAS) 4 hours after appliance placement in experimental (SLB) and control (CB) groups. VAS indicates visual analog scale; SLB indicates self-ligating bracket; CB indicates conventional bracket.

with appliances in situ, this effect may not be sustained after treatment.

Torque Expression and Arch Dimensional Change

In relation to the mandibular arch, Pandis et al,¹⁶ Fleming et al,²⁴ and Pandis et al²⁵ reported identical incisor proclination and intercanine expansion with both appliance systems during arch alignment. Statistically greater intermolar expansion with self-ligating appliances has been shown in the latter studies.^{24,25} Similar findings were not observed by Scott et al,¹⁴ although this study involved assessment after mandibular premolar extraction, precluding direct comparison. There were insufficient trials of low- or medium-bias risk in homogenous groups to allow meta-analysis of this outcome.

Orthodontic Space Closure

Only one study considered the rate of orthodontic space closure²⁶ at intervals of 5 weeks until complete space closure was achieved. This study had an inadequate sample size, with 4 of 18 subjects (22%) failing to complete the study. Posted archwires were used on both sides; therefore, tooth movement on one side may not have been independent of the other.

Apical Root Resorption

Pandis et al,²⁷ using panoramic radiographs, reported no mean difference in the amount of apical root resorption of the maxillary incisors with Microarch and Damon 2 systems. Similar results were obtained by Scott et al,¹⁴ who assessed changes in root lengths of

mandibular incisors on periapical radiographs following arch alignment. The mean amount of resorption was slightly greater with the Damon 3 appliance (2.26 vs 1.21 mm), although the difference failed to reach statistical significance.

DISCUSSION

Most of the studies included were considered to be at low to medium risk of bias. However, a priori sample size calculations were reported in only six studies, increasing the risk of false negative outcomes. The method of randomization and allocation concealment was often inadequate or incompletely reported. Many studies used alternate allocation, which precluded concealment of the participant to group allocation. Seven studies reported no dropouts; in the remaining studies, dropouts were clearly outlined. A CONSORT flow diagram was included in just four studies.^{11,14,17,25}

Per-protocol analysis was used in all studies, with dropouts being excluded from statistical analysis. Intention-to-treat analysis would be a more appropriate technique ensuring consideration of all subjects initially randomized, maintaining the benefits of randomization throughout the trial. Further prospective research in this area should be reported in accordance with the CONSORT guidelines²⁸; this will improve the quality of research studies, permitting further meta-analyses, and will make components of research including method of randomization and allocation concealment more transparent.

Meta-analysis of the influence of bracket type on pain experience confirmed that SLBs do not have a clinically significant bearing on subjective pain experience. The

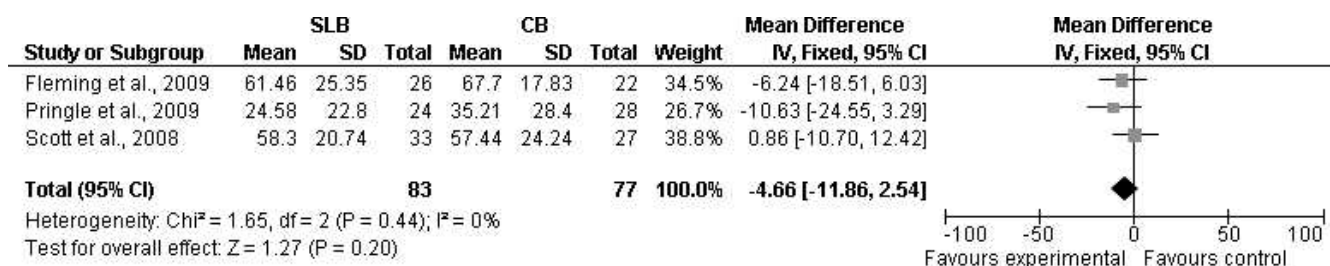


Figure 2. Meta-analysis and forest plot of pain scores (VAS) 24 hours after appliance placement in experimental (SLB) and control (CB) groups.

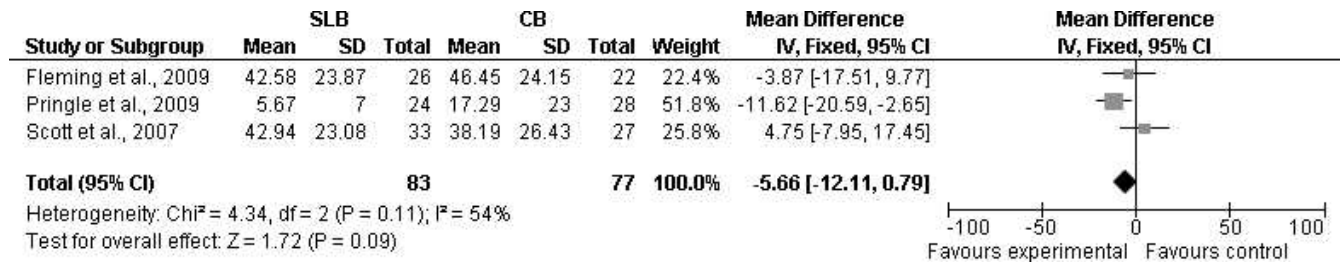


Figure 3. Meta-analysis and forest plot of pain scores (VAS) 72 hours after appliance placement in experimental (SLB) and control (CB) groups.

three studies included in the meta-analysis had discordant findings; one favored SLBs¹¹ and the other two studies demonstrated little difference between appliance systems. We can only speculate as to why this discrepancy arose; all studies were of high methodological quality and were carried out in similar settings, with analogous age and gender distribution.^{11,17,18} The failure to highlight a significant bracket-related effect is compatible with previous research, which has failed to demonstrate a link between archwire material²⁹ or dimension³⁰ and pain experience. Clearly, pain is influenced by a variety of factors, with individual susceptibility being critical. Consequently, to definitively address this question, a well-designed, prospective study of a large sample is required.

Prospective research considering surrogate measures of treatment efficiency, including the efficiency of orthodontic alignment and rate of space closure, has shown little difference between fixed appliance types, with remarkable consistency. These findings are incompatible with retrospective research findings^{5,6} and with manufacturers' claims of superior clinical performance. However, statistical comparison of these studies was not performed in view of differences in measuring alignment, methodological inadequacies related to some of the research, and incomplete reporting of results.

Arch dimensional changes arising with SLBs and conventional systems appear to be similar: identical levels of incisor proclination and intercanine expansion developed in both systems.^{16,23-25} This outcome is at odds with claims that low-friction systems respond differently under soft tissue pressures. Nevertheless, two studies have suggested that greater mandibular intermolar expansion develops during alignment with SLBs.^{24,25}

The finding of lower bacterial and streptococcal loads surrounding SLBs compared with conventional brackets during the initial stages of orthodontic treatment is of interest.²⁰ Longer term follow-up has highlighted the capacity of periodontal tissues to recover from this initial insult following appliance removal.²² Nevertheless, it is unclear whether increased plaque accumulation has other detrimental effects, particularly decalcification. Further research is required to investigate this relationship further.

While evidence regarding the clinical application of SLBs is beginning to accumulate, the influence of bracket type on oral health-related quality of life is uninvestigated. There has also been no direct prospective comparison of overall treatment duration with conventional brackets and SLBs. Further research should be reported in accordance with the CONSORT guidelines²⁸ and should have adequate sample size to avoid Type II error.

CONCLUSIONS

- There is insufficient evidence to support the use of self-ligating fixed orthodontic appliances over conventional appliance systems or vice versa.
- SLBs do not confer particular advantage with regard to subjective pain experience.
- There is insufficient evidence suggesting that orthodontic treatment is more or less efficient with SLBs.

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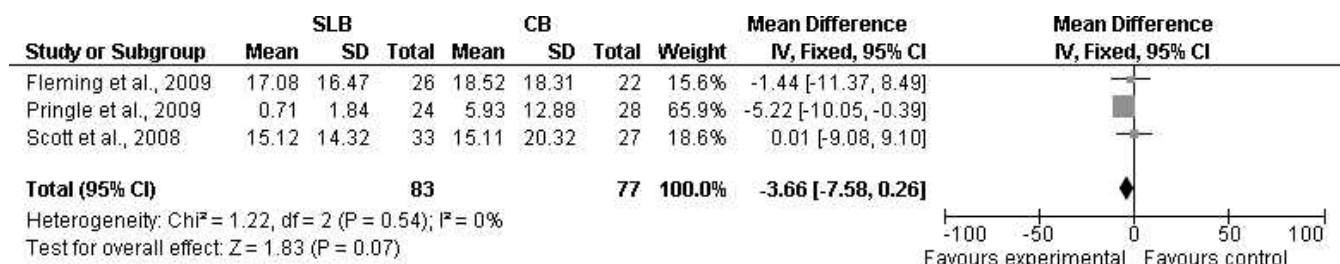


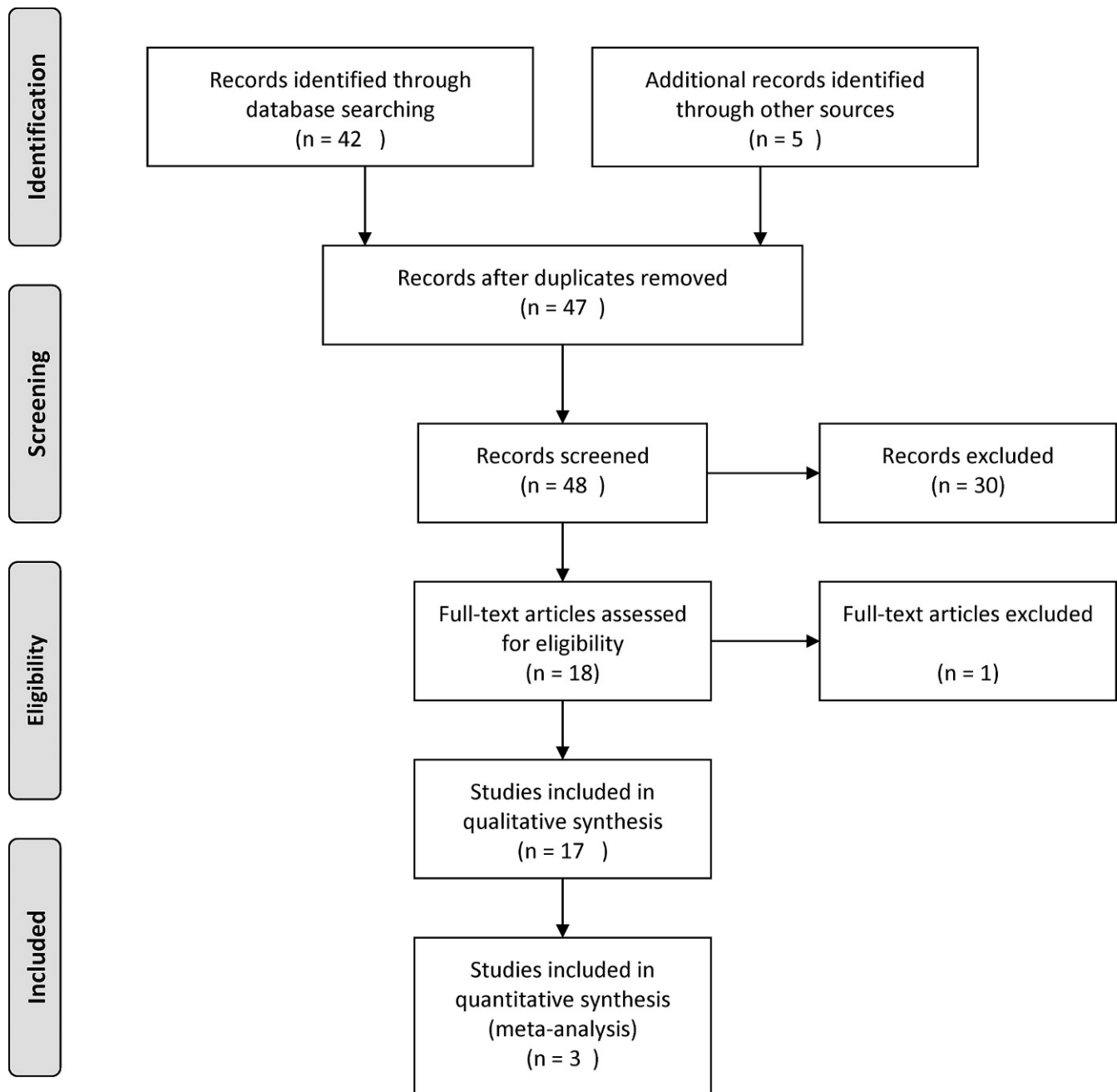
Figure 4. Meta-analysis and forest plot of pain scores (VAS) 7 days after appliance placement in experimental (SLB) and control (CB) groups.

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APPENDIX 1

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APPENDIX 2

- 1 RANDOMIZED CONTROLLED TRIAL.pt. (272711)
 2 CONTROLLED CLINICAL TRIAL.pt. (79394)
 3 RANDOMIZED CONTROLLED TRIALS.sh. (0)
 4 RANDOM ALLOCATION.sh. (64632)
 5 DOUBLE BLIND METHOD.sh. (101818)
 6 SINGLE BLIND METHOD.sh. (12964)
 7 or/1-6 (408191)
 8 (ANIMALS not HUMANS).sh. (3290537)
 9 7 not 8 (377322)
 10 CLINICAL TRIAL.pt. (453141)
 11 exp Clinical Trial/ (576329)
 12 (clin\$ adj25 trial\$.ti,ab. (160255)
 13 ((sing\$ or doubl\$ or trebl\$ or tripl\$) adj25 (blind\$ or mask\$)).ti,ab. (101760)
 14 PLACEBOS.sh. (27991)
 15 placebo\$.ti,ab. (116671)
 16 random\$.ti,ab. (445674)
 17 RESEARCH DESIGN.sh. (56256)
 18 or/10-17 (970709)
 19 18 not 8 (898433)
 20 19 not 9 (534857)
 21 9 or 20 (912179)
 22 exp ORTHODONTICS/ (34694)
 23 orthod\$.mp. (39934)
 24 22 or 23 (43726)
 25 (bracket\$ or brace\$ or appliance\$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (26892)
 26 (self ligat\$ or ligat\$ or low friction\$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (60515)
 27 25 and 24 and 26 (317)
 28 27 and 21 (42)