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Systematic Review

Clinical effects of pre-adjusted edgewise orthodontic brackets: a systematic review and meta-analysis

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SUMMARY

BACKGROUND: Fixed-appliance treatment is a major part of orthodontic treatment, but clinical evidence remains scarce.

OBJECTIVES: Objective of this systematic review was to investigate how the therapeutic effects and side-effects of brackets used during the fixed-appliance orthodontic treatment are affected by their characteristics.

SEARCH METHODS AND SELECTION CRITERIA: We searched MEDLINE and 18 other databases through April 2012 without restrictions for randomized controlled trials and quasi-randomized controlled trials investigating any bracket characteristic.

DATA COLLECTION AND ANALYSIS: After duplicate selection and extraction procedures, risk of bias was assessed also in duplicate according to Cochrane guidelines and quality of evidence according to the Grades of Recommendation. Assessment, Development and Evaluation approach. Random-effects meta-analyses, subgroup analyses, and sensitivity analyses were performed with the corresponding 95 per cent confidence intervals (CI) and 95 per cent prediction intervals (PI).

RESULTS: We included 25 trials on 1321 patients, with most comparing self-ligated (SL) and conventional brackets. Based on the meta-analyses, the duration of orthodontic treatment was on average 2.01 months longer among patients with SL brackets (95 per cent CI: 0.45 to 3.57). The 95 per cent PIs for a future trial indicated that the difference could be considerable (−1.46 to 5.47 months). Treatment characteristics, outcomes, and side-effects were clinically similar between SL and conventional brackets. For most bracket characteristics, evidence is insufficient. Some meta-analyses included trials with high risk of bias, but sensitivity analyses indicated robustness.

CONCLUSIONS: Based on existing evidence, no clinical recommendation can be made regarding the bracket material or different ligation modules. For SL brackets, no conclusive benefits could be proven, while their use was associated with longer treatment durations.

Introduction

Fixed-appliance treatment has become an integral part in modern orthodontics and has been a major focus point of orthodontic research. Research has mainly focused on aesthetic conventionally ligated (CL) brackets and the re-emergence of self-ligated (SL) brackets with their subsequent commercial success.

Aesthetic brackets are mainly represented by plastic and ceramic brackets (with or without metallic inserts). Ceramic brackets have a number of advantages, including superior mechanical and optical properties, while being biologically inert (Eliades, 2007). Their disadvantages include higher friction, higher tie-wing fracture susceptibility, and enamel damage during debonding (Schumacher *et al.*, 1990; Ghafari, 1992). Concerns regarding current plastic brackets include adequacy of their mechanical properties, impaired torque capacity, their cyclic softening effect, and possible toxic effects by released substances (Feldner *et al.*, 1994; Kusy and Whitley, 2005; Zinelis *et al.*, 2005).

SL brackets have attracted much attention in recent years and their use has increased considerably. Constant archwire engagement, reduced friction, reduction of needed appointments, reduction of generated forces and moments, greater arch expansion with/without buccal bone apposition, and reduced incisor proclination are some of the benefits attributed to SL brackets (Harradine, 2001; Ehsani *et al.*, 2009; Marshall *et al.*, 2010; Sifakakis *et al.*, 2010). Reported disadvantages include higher cost, failure of the closing mechanism, higher profile, and reduced torque expression (Morina *et al.*, 2008).

Although commercial and scientific interest has followed bracket developments, a lack of clinical evidence exists.

Bracket material choice is still mainly chosen according to aesthetic needs of the patients and *in vitro* data (Eliades *et al.*, 2004; Rosvall *et al.*, 2009). SL brackets' knowledge is still based on *in vitro* data, observational clinical data, or marketing claims (Pandis *et al.*, 2006a; Hamilton *et al.*, 2008; Pandis et al 2008a; Pandis *et al.*, 2008b; Miles, 2009; O'Brien and Sandler, 2010; Pandis *et al.*, 2010a). However, advantages from *in vitro* or *in silico* studies cannot be directly extrapolated to clinical practice (Burrow, 2009; Turpin, 2009), due to intraoral aging of the various bracket-wire components (Eliades *et al.*, 2000; Eliades and Bourauel, 2005; Pandis *et al.*, 2007a; Ali *et al.*, 2012). Additionally, clear benefits of SL brackets, such as savings in chair time and longer between-appointment intervals, should be viewed in conjunction with treatment duration and efficiency.

Although systematic assessments for most bracket characteristics are scarce, existing evidence on SL brackets has been previously quantitatively assessed (Chen *et al.*, 2010; Fleming and Johal, 2010; Čelar *et al.*, 2013). However, conclusions may be distorted by inclusion of non-randomized studies, limited identification of eligible trials, or issues during qualitative/quantitative data synthesis (Papageorgiou *et al.*, 2011; Papageorgiou *et al.*, 2013). In particular, evaluation of the validity of the undertaken meta-analyses (Guyatt *et al.*, 2011) and their translation in future clinical settings (Higgins *et al.*, 2009) could aid in drawing robust conclusions. Finally, most published research has focused on a single characteristic of the bracket, without considering the bracket-archwire interaction (Miles, 2008). This systematic review appraises existing randomized and quasi-randomized trials regarding the role of the various characteristics of orthodontic brackets (material, slot size, ligation type, etc) and their combination with specific wires on their clinical effectiveness and associated side-effects during fixed-appliance orthodontic treatment. This review follows a previous review on the effectiveness of orthodontic archwires (Papageorgiou *et al.*, manuscript in preparation).

Materials and methods

This review's pre-defined protocol was based on the Cochrane guidelines (Higgins and Green, 2011) and is reported according to the PRISMA statement (Liberati *et al.*, 2009) and its extension for abstracts (Beller *et al.*, 2013). The inclusion criteria were 1. randomized controlled trials (RCTs) and quasi-RCTs, 2. human patients of any age or gender that received fixed-appliance orthodontic treatment, and 3. comparable patients for age, gender, and malocclusion receiving therapy with any type of bracket different from the first group (no untreated control groups). Trials were excluded, if the compared groups did not differ in at least one from the following characteristics: 1. bracket material, 2. bracket ligation type (CL versus SL brackets), 3. ligation module for CL brackets (e.g. elastomeric versus stainless steel ligatures), or 4. bracket slot size. After extensive unrestricted electronic and manual literature searches (Supplementary Table 1), duplicate procedures of study selection, data extraction, and Cochrane risk of bias assessment were conducted by two unblinded authors (SNP and KP). The quality of evidence and strength of recommendations for each meta-analysis outcome were ultimately assessed based on the Grades of Recommendation. Assessment, Development and Evaluation (GRADE) approach (Guyatt *et al.*, 2011). Disagreements were resolved by a third author (IK) and agreement was measured with an unweighted kappa.

A random-effects model (DerSimonian and Laird, 1986) was chosen to pool data, since the observed effects were expected to differ across studies due to differences in the sample (i.e. patient's dental/skeletal age) and implementation (i.e. treatment with/without extractions or different mechanics used). In case of meta-analyses with three or more trials, 95 per cent prediction intervals (PI) (Higgins *et al.*, 2009; Graham and Moran, 2012) were calculated to predict treatment effects in a new trial (reported here only for significant meta-analyses). The extent and impact of between-study heterogeneity was assessed by inspecting the forest plots and by calculating the tau-squared and the I^2 statistic, respectively. When heterogeneity was present (I^2 between 25 and 75 per cent), possible sources of heterogeneity were sought with stratification by bracket/archwire or treatment characteristics. When heterogeneity was greater than 75 per cent, data were not pooled. If a sufficient number of trials were identified ($n > 7$), analyses were planned for "small-study effects" and publication bias [a contour-enhanced funnel plot (Peters *et al.*, 2008) and Egger's weighted test (Egger *et al.*, 1997)].

Mean differences (MD) or standardized mean differences (SMD) for continuous outcomes and risk ratios for dichotomous outcomes and their corresponding 95 per cent confidence intervals (CI) were calculated. When possible, exploratory stratified analyses according the bracket/archwire characteristics used to define the groups were performed with pre-specified mixed-effects subgroup (SG) analyses: (e.g. SL versus CL brackets; metallic versus ceramic brackets). Robustness of the results was *a priori* to be checked according to 1. severity of the initial malocclusion and 2. the inclusion of extractions in the treatment plan. *A priori* sensitivity analyses for each outcome were planned based on the improvement of the GRADE classification. All analyses were done in Stata version 10 (StataCorp LP, College Station, Texas, USA) with the 'metan' (random-effects meta-analysis), 'rfdist' (prediction intervals) and 'metareg' macros (mixed-effects SG analysis with the Knapp-Hartung modification(Knapp and Hartung, 2003)). Significance (α) was set at 0.05, except for a 0.10 used for the heterogeneity tests (Ioannidis, 2008).

Results

A total 1528 citations were identified electronically and 9 more manually (Supplementary Figure 1). After duplicate exclusion, 762 articles were screened and another 632 articles were excluded on the basis of title and abstract. From the 130 articles that remained, 105 articles were excluded on the basis of their full-text or other reasons. A total of 15 trial authors were finally contacted for full-text provision, clarifications or additional unpublished data, while two authors' e-mails could not be found (Bhavra G S, Garg D). From the 15 trial authors, 9 trialists responded (Cattaneo P, Cobourne M T, Conti A C, Fleming P S, Johansson K, Kohli S, Miles P G, Pandis N, Pringle A) and 4 trialists did not (de Almeida M R, Jiang L Q, Wahab R, Walker B). Another 15 articles were excluded from the present review, as they assessed archwire characteristics. Finally a number of possibly eligible trials ($n = 8$) were excluded: no response and trial was deemed ineligible (Garg D, Gaspar Ribeiro D A), abstract/posters with no available text (Bhavra GS, Hada D), and ongoing trials (Clinicaltrials.gov identifier: NCT01320657, ISRCTN identifiers: ISRCTN68289972, Fleming P.S. thesis, Kaklamanos E.G. thesis) (Details available upon request).

A total of 25 full-text reports were finally included, describing 1321 patients included in 23 trials published between 1998 and 2012 (Supplementary Table 2). Three publications (Scott *et al.*, 2008a; Scott *et al.*, 2008b; DiBiase *et al.*, 2011) reported data from the same trial. Miles and Weyant (2010) reported also time taken to tie and untie the SL brackets, but this outcome was not included in our protocol and is not reported here. The bracket and archwire products used in the included trials are provided separately in Supplementary Table 3. The kappa score for the selection of studies, the data extraction and the risk of bias assessment were 0.870, 0.916, and 0.921, respectively, indicating an almost perfect level of inter-reviewer agreement.

The characteristics and risk of bias for the 25 trials included are shown in Table 1 and Supplementary Table 4–5, respectively. A total of three split-mouth trials were included and all used appropriate statistical methods (paired *t*-tests and Wilcoxon signed-rank test). No trial from the 19 that had dropouts carried out an intention-to-treat analysis. Only 10 trials (40 per cent) reported *a priori* calculating sample size although that was not always adequately assessed. The included trials primarily assessed either characteristics of CL brackets (slot size, type of ligature used, etc), characteristics of SL brackets or compared CL brackets with SL brackets. Summary of finding tables for the meta-analyses according to the GRADE approach are provided in Table 2 and Supplementary Table 6. Where no meta-analysis was feasible, only quick references are made, while the details are included as supplementaries.

Assessment of either CL or SL brackets

No trial primarily investigated the effect of bracket material and no indirect comparison was possible, as all ceramic brackets used were SL, had a metal insert, and were compared with CL metal brackets. The bracket slot size was assessed in two included trials, which found no consistent difference between 0.022" and 0.018" brackets (Supplementary 1).

Regarding the module used for the ligation of the CL brackets, inadequate data existed for the comparison of SS, conventional elastomeric or low friction elastomeric modules (Supplementary 2).

The comparison of active versus passive SL brackets was made separately from three trials, which, however, found no significant difference between them (Supplementary 3).

Comparison of CL and SL Brackets

Comparison of SL and CL brackets during tooth alignment

SL orthodontic brackets were assessed by a total of 24 included trials, with most studies comparing SL and CL brackets.

Duration of orthodontic treatment

Duration of orthodontic treatment was assessed in terms of time needed to finish the 1. early alignment phase (up to 3 months), 2. complete alignment phase, and 3. complete orthodontic treatment (removal of appliances). As extreme between-study heterogeneity was identified ($I^2 > 75$ per cent), no meta-analysis was made for the early alignment phase. Time to complete the alignment phase of orthodontic treatment was found not to be significantly higher in the SL group (Supplementary Figure 2). Meta-analysis for the overall duration of the orthodontic treatment from four trials was found to be significantly longer in the SL group by 2.01 months (Figure 1). Based on 95 per cent PIs, orthodontic treatment in a future setting could take 1.46 months less to 5.47 months more for patients treated with SL brackets. Results were not affected by inclusion of extractions in the treatment [in two (Fleming *et al.*, 2010; DiBiase *et al.*, 2011) out of four trials; $P_{SG} = 0.844$] or use of M_{act} NiTi archwires [three (Cattaneo *et al.*, 2011; DiBiase *et al.*, 2011; Johansson and Lundström, 2012) out of four trials] instead of M_{stab} NiTi ($P_{SG} = 0.574$).

The number of appointments between SL and CL groups was compared in three included trials. Meta-analysis indicated the number of needed appointments was not significantly greater for patients treated with SL brackets compared to CL brackets (Supplementary Figure 3).

Treatment outcomes

Treatment outcomes between patients treated with SL and CL brackets were assessed by changes in tooth alignment, changes of malocclusion severity indices, and changes of the dental arch in the three planes. Changes in tooth alignment were measured by Little's irregularity index (LII) or its 3D analogue, and as consistency between them was

Table 1 Main characteristics of included trials regarding different brackets included in the systematic review (RCT, randomized controlled trial; SS, stainless steel; SL, self-ligated; M_{act}, martensitic-active; CuNiTi, Copper-Nickel-Titanium; β-Ti, beta Titanium; A_{act}, austenitic-active; NiTi, Nickel-Titanium; NR, not reported; CL, conventionally ligated; M_{stab}, martensitic-stabilized; max, maxilla; Rh, Rhodium.).

Trial	Design	Setting (country; clinic; recruitment dates; mean follow-up; %dropouts)	Bracket/ligature	Archwire(s)
Cattaneo *et al.* (2011)*	Single-centre single-blind two-arm parallel RCT	Denmark; university; from December 2004 to November 2009; 21.8 months; 36% dropouts	**Gp1**: SS passive SL 0.022" brackets/None	A1: 0.014" M_{act} CuNiTi 35°C A2: 0.014 × 0.025" M_{act} CuNiTi 35°C A3: 0.018 × 0.025" M_{act} CuNiTi 35°C A4: 0.019 × 0.025" SS A5: 0.019 × 0.025" β-Ti or SS
			Gp2: SS active SL 0.022" brackets/None	A1: 0.014" A_{act} NiTi A2: 0.018 × 0.018" A_{act} NiTi A3: 0.019 × 0.025" A_{act} NiTi A4: 0.019 × 0.025" SS A5: 0.019 × 0.025" β-Ti or SS
Cobb *et al.* (1998)	Single-centre three-arm parallel RCT	USA; university; recruitment dates NR; 12 months; 2% dropouts	**GpA**: SS CL 0.018" brackets/Elastomeric **GpB**: SS CL 0.022" brackets/Elastomeric	**Gp1:** 0.016" A_{act} NiTi **Gp2:** 0.016" N^+ implanted A_{act} NiTi **Gp3:** 0.0175" multistranded SS
DiBiase *et al.* (2011)*	Multicentre two-arm parallel RCT	England; university/hospital; recruitment dates NR; 23.8 months; 22.6% dropouts	**Gp1**: Polycarbonate with SS slot passive SL 0.022" brackets/None **Gp2**: SS CL 0.022" brackets/Elastomeric	A1: 0.014" M_{act} CuNiTi 35°C A2: 0.014 × 0.025" M_{act} CuNiTi 35°C A3: 0.018 × 0.025" M_{act} CuNiTi 35°C A4: 0.019 × 0.025" SS
Fleming *et al.* (2009a)*	Multicentre two-arm parallel RCT	England; university/hospital; from April 2006 to October 2006; 8.3 months; 9.1% dropouts	**Gp1**: SS passive SL 0.022" brackets/None **Gp2**: SS CL 0.022" brackets/Elastomeric or SS	A1: 0.016" M_{stab} NiTi A2: 0.017 × 0.025" M_{stab} NiTi A3: 0.019 × 0.025" M_{stab} NiTi A4: 0.019 × 0.025" SS
Fleming *et al.* (2009b)*	Multicentre two-arm parallel RCT	England; university/hospital; from April 2006 to October 2006; 1.9 months; 1.5% dropouts	**Gp1**: SS passive SL 0.022" brackets/None **Gp2**: SS CL 0.022" brackets/Elastomeric (elastomeric in figure-eight form or SS ligatures in areas with marked irregularity)	A1: 0.016" M_{act} NiTi
Fleming *et al.* (2009c)*	Multicentre two-arm parallel RCT	England; university/hospital; from April 2006 to October 2006; 7 days; 27.3% dropouts	**Gp1**: SS passive SL 0.022" brackets/None **Gp2**: SS CL 0.022" brackets/Elastomeric (SS ligatures in areas with marked irregularity)	A1: 0.016" M_{act} NiTi
Fleming *et al.* (2010)*	Multicentre two-arm parallel RCT	England; university/hospital; from May 2006 to September 2006; 9.9 months; 18.2% dropouts	**Gp1**: SS passive SL 0.022" brackets/None **Gp2**: SS CL 0.022" brackets/Elastomeric or SS	A1: 0.016" M_{stab} NiTi A2: 0.017 × 0.025" M_{stab} NiTi A3: 0.019 × 0.025" M_{stab} NiTi A4: 0.019 × 0.025" SS
Jiang *et al.* (2009)	Single-centre two-arm parallel RCT	China; university; from December 2008 to NR; 7 days; 15% dropouts	**Gp1:** SS passive SL slot size NR brackets/None **Gp2:** CL slot size brackets/NR	A1: 0.014" M_{act} NiTi
Johansson and Lundström (2012)	Single-centre single-blind two-arm parallel RCT	Sweden; hospital; from January 2007 to August 2007; 19.3 months; 10% dropouts	**Gp1**: SS active SL 0.022" brackets/None **Gp2**: SS CL 0.022" brackets/NR	A1: 0.014" M_{stab} NiTi A2: 0.020 × 0.020" M_{act} NiTi A3: 0.019 × 0.025" SS
Kohli and Kohli (2012)	Single-centre single-blind two-arm parallel RCT	India; private practice; recruitment dates NR; 7 days; 14% dropouts	**Gp1:** SS active SL 0.022" brackets/None **Gp1:** SS passive SL 0.022" brackets/None	**A1:** 0.016" M_{act} NiTi
Leite *et al.* (2012)*	Single-centre single-blind two-arm parallel RCT	Brazil; university; recruitment dates from March 2009 to Decemeber 2010; 6 months; 0% dropouts	**Gp1**: SS passive SL 0.022" brackets/None **Gp2**: SS CL 0.022" brackets/SS	A1: 0.013" M_{stab} NiTi A2: 0.014" M_{stab} NiTi A3: 0.016" M_{stab} NiTi

Table 1 (Continued).

Trial	Design	Setting (country; clinic; recruitment dates; mean follow-up; %dropouts)	Bracket/ligature	Archwire(s)
Mezomo *et al.* (2011)	Single-centre two-arm split-mouth RCT	Brazil; university; recruitment dates NR; 12 weeks; dropouts NR	**Gp1:** SS passive SL 0.022" brackets/None **Gp2:** SS CL 0.022" brackets/Elastomeric	A1: 0.0155 × 0.0175" SS coaxial A2: 0.016" SS A3: 0.018" extra-hard SS
Miles (2005)	Single-centre single-blind two-arm parallel quasi-RCT	Australia; private practice; recruitment dates NR; 20 weeks; 3.3% dropouts (including 1.7% exclusions for balance)	**Gp1**: SS passive SL 0.022" brackets/None **Gp2**: SS CL 0.022" brackets/Elastomeric (figure-eight form or SS ligatures in areas of with excessive irregularity)	A1: 0.014" M_{act} CuNiTi 35°C A2: 0.016 × 0.025" M_{act} CuNiTi 35°C
Miles *et al.* (2006)	Single-centre single-blind two-arm split-mouth quasi-RCT	Australia; private practice; recruitment dates NR; 20 weeks; 3.3% dropouts (including 1.7% exclusions for balance)	**Gp1**: SS passive SL 0.022" brackets/None **Gp2**: SS CL 0.022" brackets/Elastomeric (figure-eight form or SS ligatures in areas of with excessive irregularity)	A1: 0.014" M_{act} CuNiTi 35°C A2: 0.016 × 0.025" M_{act} CuNiTi 35°C
Miles (2007)	Single-centre two-arm split-mouth quasi-RCT	Australia; private practice; recruitment dates NR; 4.1 months; 31.6% dropouts	**Common:** *Max anterior*—ceramic CL 0.018" brackets *Man anterior*—SS CL 0.018" brackets **Gp1:** *Max posterior*—SS passive SL 0.018" brackets/None **Gp2:** *Max posterior*—SS CL 0.018" brackets/Elastomeric	(After initial alignment) A1: 0.016 × 0.022" SS
Miles and Weyant (2010)	Single-centre single-blind two-arm parallel RCT	Australia; private practice; recruitment dates NR; 10 weeks; 11.8% dropouts (including 2.9% exclusions for balance)	**Gp1**: *Anterior*—ceramic with Rh-coated clip active SL 0.018" brackets/None *Posterior*—SS active SL 0.018" brackets/None **Gp2**: *Anterior*—ceramic CL 0.018" brackets/Elastomeric coated *Posterior*—SS CL 0.018" brackets/Elastomeric	A1: 0.014" M_{act} NiTi 37°C
Pandis *et al.* (2007b)*	Single-centre single-blind two-arm parallel quasi-RCT	Greece; private practice; dates from September 2004 to July 2005; 3.4 months; 0% dropouts	**Gp1**: SS passive SL 0.022" brackets/None **Gp2**: SS CL 0.022" brackets/(Mainly) elastomeric, often in a figure-eight form.	A1: 0.016" M_{act} CuNiTi 35°C A2: 0.020" A_{act} NiTi A1: 0.014" M_{act} CuNiTi 35°C A2: 0.014 × 0.025" M_{act} CuNiTi 35°C
Pandis *et al.* (2010b)*	Single-centre two-arm parallel quasi-RCT	Greece; private practice; from October 2007 to March 2008; 2.9 months; 0% dropouts	**Gp1**: SS active SL 0.022" brackets/None **Gp2**: SS CL 0.022" brackets/Elastomeric	A1: 0.014" or 0.016" M_{stab} NiTi
Pandis et al. (2010c)*	Single-centre two-arm parallel RCT	Greece; private practice; from March 2007 to November 2008; 95.5 days; 5.7% dropouts	**Gp1**: SS passive SL 0.022" brackets/None **Gp2**: SS active SL 0.022" brackets/None	A1: 0.014" M_{act} CuNiTi 35°C A2: 0.016 × 0.025" M_{act} CuNiTi 35°C
Pandis *et al.* (2011)*	Single-centre single-blind two-arm parallel RCT	Greece; private practice; from June 2009 to March 2010; duration 5.9 months; 0% dropouts	**Gp1**: SS passive SL 0.022" brackets/None **Gp2**: SS CL 0.022" brackets/Elastomeric	A1: 0.014" M_{act} CuNiTi 35°C A2: 0.014 × 0.025" M_{act} CuNiTi 35°C A3: 0.016 × 0.025" SS
Pringle *et al.* (2009)	Multicentre two-arm parallel RCT	England; hospital/private practice; from July 2005 to April 2006; 8 days; 21.2% dropouts	**Gp1**: Polycarbonate with SS slot passive SL 0.022" brackets/None **Gp2**: SS CL 0.022" brackets/Elastomeric	A1: 0.014" M_{act} CuNiTi 35°C
Scott *et al.* (2008a)*	Multicentre two-arm parallel RCT	England; university/hospital; recruitment dates NR; 8.3 months; 3.2% dropouts	**Gp1**: Polycarbonate with SS slot passive SL 0.022" brackets/None **Gp2**: SS CL 0.022" brackets/Elastomeric	A1: 0.014" M_{act} CuNiTi 35°C A2: 0.014 × 0.025" M_{act} CuNiTi 35°C A3: 0.018 × 0.025" M_{act} CuNiTi 35°C A4: 0.019 × 0.025" SS

Table 1 (Continued).

Trial	Design	Setting (country; clinic; recruitment dates; mean follow-up; %dropouts)	Bracket/ligature	Archwire(s)
Scott *et al.* (2008b)*	Multicentre two-arm parallel RCT	England; university/hospital; recruitment dates NR; 7 days; 3.2% dropouts	**Gp1**: Polycarbonate with SS slot passive SL 0.022" brackets/None **Gp2**: SS CL 0.022" brackets/Elastomeric	A1: 0.014" M_{act} CuNiTi 35°C
Uzdil (2008)	Single-centre four-arm parallel RCT	Turkey; university; recruitment dates NR; duration NR; dropouts NR	**Gp1**: SS passive SL 0.022" brackets/None **Gp2**: SS passive SL 0.018" brackets/None **Gp3**: SS CL 0.018" brackets/Elastomeric **Gp4**: SS CL 0.018" brackets/ Low friction elastomeric	A1: 0.014" M_{act} CuNiTi 35°C
Wahab *et al.* (2012)	Multicentre two-arm parallel RCT	Malaysia; university/private; recruitment dates NR; 16 months; 3.3% dropouts	**Gp1**: Polycarbonate with SS slot passive SL 0.025" brackets/None (laceback) **Gp2**: SS CL 0.025" brackets/Elastomeric (laceback)	A1: 0.014" M_{stab} NiTi

*Including data from communication with trialists.

Table 2 Grades of Recommendation. Assessment, Development and Evaluation (GRADE) summary of findings table for meta-analyses on bracket data (continuous outcomes). SL, self-ligated; CL, conventionally ligated; CI, confidence interval; Tx, treatment; SG, subgroup; M_{act}, martensitic-active; NiTi, Nickel-Titanium; M_{stab}, martensitic-stabilized; PI, prediction interval; LII, Little's irregularity index; 3D, three dimensional; PAR, peer assessment rating; ICON, index of complexity, outcome and need; SMD, standardized mean difference; VAS, visual analogue score; LS, Likert scale; EARR, external apical root resorption.

Patients: receiving fixed appliances for tooth alignment; **Settings:** university, hospital and private practice; **Intervention:** SL brackets; **Comparison:** CL brackets

Outcome (follow-up); archwires used	**Illustrative comparative risks (95% CI)**		**No. of partici-pants (trials)**	**Quality of evidence (GRADE)**	**Comments**
	Assumed risk	Corresponding risk			
	CL brackets	**SL brackets**			
Tx duration; alignment (follow-up in months until the final alignment phase) Including M_{act} NiTi (2)/ only M_{stab} NiTi(1)	The mean duration ranged across CL groups from **5.5 to 8.2 months**	The mean duration in the SL groups was **0.30 months longer** (from 0.23 lower to 0.83 higher)	170 (3)	⊕⊕⊕○ **moderate***	$P = 0.260$; $I^2 = 0\%$; non-significant archwire SG ($P_{SG} = 0.679$).
Tx duration; complete treatment (follow-up in months from appliance placement to removal) Including M_{act} NiTi (2)/ only M_{stab} NiTi(1)	The mean duration ranged across CL groups from **18.2 to 23.0 months**	The mean duration in the SL groups was **2.01 months longer** (from 0.45 to 3.57 higher)	233 (4)	⊕⊕⊕○ **moderate***	$P = \mathbf{0.001}$; $I^2 = 0\%$; 95% PI: −1.46 to 5.47 months; non-significant archwire SG ($P_{SG} = 0.574$).

Table 2 (Continued).

Patients: receiving fixed appliances for tooth alignment; **Settings:** university, hospital and private practice; **Intervention:** SL brackets; **Comparison:** CL brackets

Outcome (follow-up); archwires used	**Illustrative comparative risks (95% CI)**		**No. of participants (trials)**	**Quality of evidence (GRADE)**	**Comments**
	Assumed risk	Corresponding risk			
	CL brackets	**SL brackets**			
Number of appointments (follow-up: 19.3 to 23.8 months) Including M_{act} NiTi (2)/ only M_{stab} NiTi(1)	The mean number of appointments ranged across CL groups from **14.1 to 15.7** appointments	The mean number of appointments in the SL groups was **0.79 appointment greater** (from 0.51 lower to 2.09 higher)	192 (3)	⊕⊕⊕⊕ **high**	$P = 0.230$; $I^2 = 6\%$; non-significant archwire SG ($P_{SG} = 0.539$).
Tooth alignment (reduction of LII scores & 3D analogue of it)*** mm of LII (follow-up: 1.6 to 4.7 months) M_{act} NiTi(5)/ M_{stab} NiTi (1)	The mean LII reduction ranged across CL groups from **1.5 to 12.6 mm**	The mean LII reduction in the SL groups was **0.05 mm lower** (from 0.46 lower to 0.36 higher)	330 (6)	⊕⊕○○ **low****	$P = 0.630$; $I^2 = 19\%$; effects by five parallel and one split-mouth trial did not differ and were pooled****; significant archwire SG (P_{SG} **= 0.076**) with M_{act} NiTi: −0.03 (−0.38 to 0.31) & M_{stab} NiTi: −4.00 (−7.28 to −0.72).
Outcome of orthodontic Tx (reduction of PAR & ICON scores)*** Points on PAR: 0 to 50 (usually) (follow-up: 19.3 to 23.8 months) M_{act} NiTi (2)/ M_{stab} NiTi(1)	The mean PAR reduction in the CL groups was **22.3 points**	The mean PAR reduction in the SL groups was **0.9 points lower** (from2.7 lower to 0.8 higher)	192 (3)	⊕⊕⊕⊕ **high**	Scores estimated using an SMD of −0.15 (−0.44 to 0.13) for PAR and ICON scores; $P = 0.300$; $I^2 = 0\%$; non-significant archwire SG ($P_{SG} = 0.846$).
Intercanine width change (follow-up: 3.4–8.3 months) M_{act} NiTi (4)/ M_{stab} NiTi (1)	The mean intercanine width change ranged across CL groups from **1.2 to 7.4 mm**	The mean intercanine width change in the SL groups was **0.54 mm lower** (from 0.89 to 0.18 lower)	284 (5)	⊕⊕⊕○ **moderate***	P = **0.003**; $I^2 = 0\%$; 95% PI: −1.11 to 0.04 mm; non-significant archwire SG ($P_{SG} = 0.615$).
Intermolar width change (follow-up: 3.4–8.3 months) M_{act} NiTi (4)/ M_{stab} NiTi (1)	The mean intermolar width change ranged across CL groups from **−0.6 to 1.5 mm**	The mean intermolar width change in the SL groups was **0.53 mm greater** (from 0.09 to 0.98 higher)	284 (5)	⊕⊕⊕○ **moderate***	P = **0.020**; $I^2 = 23\%$; 95% PI: −0.53 to 1.60 mm; non-significant archwire SG ($P_{SG} = 0.397$).
Incisor inclination change Based on the angle mandibular incisor-mandibular plane (follow-up: 3.4–8.3 months) M_{act} NiTi (2)/ M_{stab} NiTi(1)	The mean incisor inclination change ranged across CL groups from **1.4 to 6.2 °**	The mean incisor inclination change in the SL groups was **0.06° higher** (from 0.50 lower to 0.61 higher)	174 (3)	⊕⊕⊕○ **moderate***	$P = 0.840$; $I^2 = 0\%$; non-significant archwire SG ($P_{SG} = 0.717$).
Pain intensity on the first day Points on VAS scale: 0–100 mm M_{act} NiTi (5)	The mean pain intensity in the CL groups was **67.7 mm**	The mean pain intensity in the SL groups was **3.57 mm lower** (from 8.02 lower to 0.71 higher)	266 (5)	⊕⊕⊕○ **moderate***	Scores estimated using an SMD of −0.21 (−0.45 to 0.03) for VAS and LS scores***; $P = 0.100$; $I^2 = 0\%$
Pain intensity on the third day Points on VAS scale: 0–100 mm M_{act} NiTi (5)	The mean pain intensity in the CL groups was **17.3 mm**	The mean pain intensity in the SL groups was **2.53 mm lower** (from 8.97 lower to 4.14 higher)	266 (5)	⊕⊕⊕○ **moderate***	Scores estimated using an SMD of −0.11 (−0.40 to 0.18) for VAS and LS scores***; $P = 0.460$; $I^2 = 27\%$
Pain intensity on seventh day Points on VAS scale: 0–100 mm M_{act} NiTi (5)	The mean pain intensity in the CL groups was **5.93 mm**	The mean pain intensity in the SL groups was **0.64 mm lower** (from 4.12 lower to 2.96 higher)	266 (5)	⊕⊕⊕○ **moderate***	Scores estimated using an SMD of −0.05 (−0.33 to 0.23) for VAS and LS scores***; $P = 0.740$; $I^2 = 23\%$
EARR at mandibular central incisor (follow-up: 6.0–8.3 months) M_{act} NiTi (1)/M_{stab} NiTi(1)	The mean EARR ranged across CL groups from **0.3 to 1.2 mm**	The mean EARR in the SL groups was **0.25 mm greater** (from 0.47 lower to 0.96 higher)	79 (2)	⊕⊕⊕⊕ **high**	$P = 0.500$; $I^2 = 33\%$

*Downgraded by 1 for risk of bias: overall risk of bias judged as moderate.
**Downgraded by 2 for risk of bias: overall risk of bias judged as high.
***No significant difference between data from the two outcome measures (between-subgroups analysis).
****Mean Differences (95% CIs) for parallel trials: −0.05 (−0.54–0.45) and for split-mouth trial: −0.10 (−1.44–1.24) with no difference ($P_{SG} = 0.947$).
Bold *P*-values indicate statistical significance.

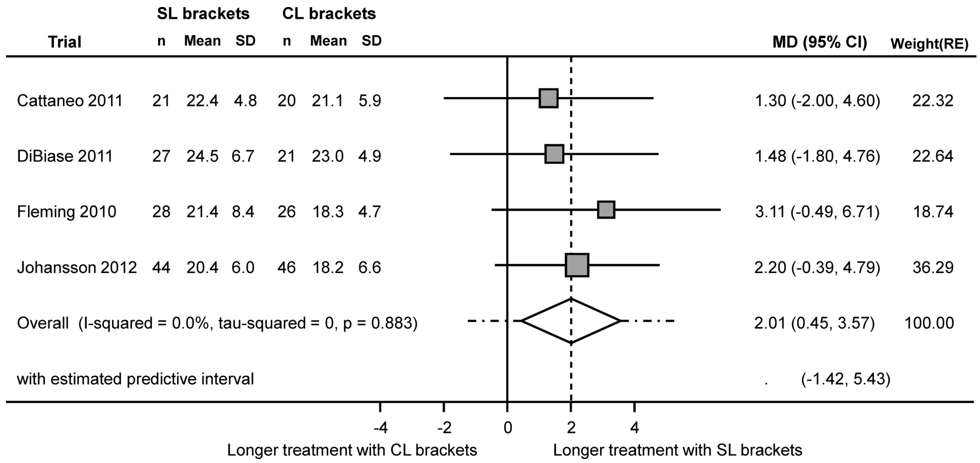

Figure 1 Forest plot for meta-analysis of overall orthodontic treatment duration from four trials (Fleming *et al.*, 2010; Cattaneo *et al.*, 2011; DiBiase *et al.*, 2011; Johansson and Lundström, 2012); prediction interval for the treatment effect of a new trial given as a horizontal dotted line; estimates to the right indicate longer duration for self-ligated (SL) groups. SL, self-ligated; CL, conventionally-ligated; SD, standard deviation; MD, mean difference; RE, random-effects model.

found, they were pooled together. Between patients treated with SL and CL brackets, no significant difference in tooth alignment was found, whether statistically (P = 0.630) or clinically (0.05 mm) significant (Figure 2). However, the effectiveness of SL and CL brackets was similar only when M_{act} NiTi archwires were used. In the one trial with M_{stab} NiTi archwires, patients treated with SL brackets had a significantly lower LII reduction (MD = −4.00 mm; 95 per cent CI: −7.28 to −0.72 mm) than those treated with CL brackets; (MD = −0.001 mm; 95 per cent CI: −0.33 to 0.33 mm; P_{SG} = 0.076).

Changes in malocclusion severity during treatment were measured with the Peer Assessment Rating (PAR) and the Index of Outcome, Complexity and Need (ICON) index. Synthesis through the SMD indicated that no significant difference existed between the SL and CL groups (Supplementary Figure 4). Re-expressing the SMD into the PAR index, patients treated with SL brackets had a PAR reduction lower than the CL group by 0.9 points.

Changes of the dental arch in the transverse plane during orthodontic treatment were assessed with the interpremolar width (at the first or second premolar) by one trial and with the intercanine width and the intermolar width by five trials. Meta-analysis of the intercanine width showed that the use of SL brackets was associated with an intercanine width significantly lower by 0.54 mm from the CL group (P = 0.003) (Figure 3a). Based on the 95 per cent PIs, patients treated with SL brackets in a future trial could have from 1.11 mm lower to 0.04 mm higher intercanine width than those treated with CL brackets. On the other hand, meta-analysis of the intermolar width showed that the use of SL brackets was associated with an intermolar width significantly higher by 0.53 mm more expansion (P = 0.020) (Figure 3b). Based on the 95 per cent PIs, patients treated with SL brackets in a future trial could have from 0.53 mm lower to 1.60 mm higher intermolar width than those treated with CL brackets.

Other changes of the dental arch assessed included the arch length, the sum of the right and left first molar-incisal papilla distances and the buccolingual inclination of the mandibular incisor. The first two outcomes were reported from a single trial each. No difference was reported between SL and CL groups for the arch length (Scott *et al.*, 2008a) or the first molar-incisal papilla distance (Uzdil, 2008). Meta-analysis of the buccolingual inclination of the mandibular incisor from three trials indicated no significant difference between SL and CL groups (MD = 0.06 degree, P = 0.840; Supplementary Figure 5).

Treatment side-effects

Pain intensity after initial archwire placement and at various timepoints during the next 7 days was assessed by a number of trials using the Visual Analogue Scale and the Likert Scale. Meta-analysis with the SMD could be made for the reported pain intensity at 4 hours and on the first, third, and seventh day after archwire placement. However, readers are prompted to the review by Čelar *et al.* (2013), where pain intensity after archwire insertion is discussed comprehensively. For pain intensity 4 hours after archwire placement, no additional data existed. For the next three timepoints, another trial was added to the four previous trials identified in the previous review, without however significantly altering the estimate summary. The results of the meta-analyses are provided in Table 2 and Supplementary Figures 6–8. Detailed use of analgesics was reported by two trials, while individual patient data were provided for a third trial (Pringle *et al.*, 2009). Meta-analysis of three trials indicated no significant difference in analgesic use between patients treated with SL brackets or CL brackets (Supplementary Figure 9).

Investigated side-effects included treatment-induced External Apical Root Resorption (EARR) and bracket

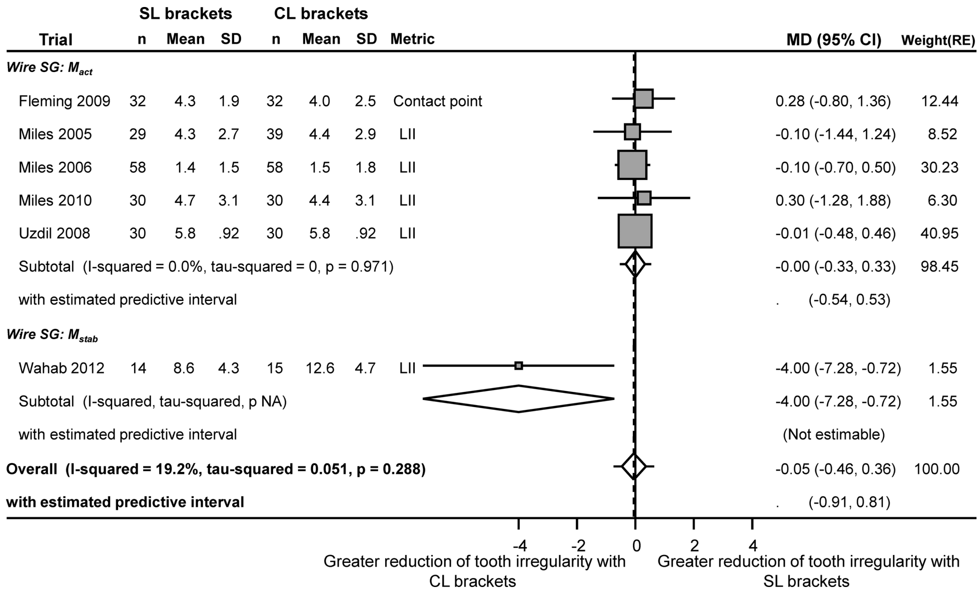

Figure 2 Forest plot for meta-analysis of change in tooth irregularity from six trials (Miles, 2005; Miles *et al.*, 2006; Uzdil, 2008; Fleming *et al.*, 2009b; Miles and Weyant, 2010; Wahab *et al.*, 2012); prediction interval for the treatment effect of a new trial given as a horizontal dotted line; estimates to the right indicate greater reduction of tooth irregularity for self-ligated (SL) groups. SL, self-ligated; CL, conventionally-ligated; SD, standard deviation; MD, mean difference; RE, random-effects model; SG, subgroup; Mact, martensitic-active Nickel-Titanium; LII, Little's irregularity index; Mstab, martensitic-stabilized Nickel-Titanium.

debonding or breakage. Meta-analysis of EARR at the mandibular central incisor showed that patients in the SL groups had 0.25 mm greater EARR than the CL groups, which was neither statistically nor clinically significant (Supplementary Figure 10). SL brackets were reported separately by two trials to be more significant to either debonding or breakage (Supplementary 4).

Sensitivity analyses for all meta-analysis outcomes are given in Supplementary Table 7 and showed that the meta-analyses' results were robust.

Comparison of SL and CL brackets during space closure

Closure of extraction spaces was investigated by two identified trials, which found no significant difference between bracket groups (Supplementary 5).

Discussion

This systematic review included a total of 25 trials with 1321 patients. A striking lack of evidence exists regarding bracket material, bracket slot size and ligation module for CL brackets. The majority of identified trials compared SL brackets with CL brackets. All conclusions are made in conjunction with the risk of bias, the GRADE classification, and methodological issues like sample size adequacy and appropriateness of statistics used. Also, certain trials were excluded on the basis of their design, like an identified split-mouth trial of fluoride-releasing elastomeric ligatures, which was excluded due to possible contamination (Mattick *et al.*, 2001).

No trial was identified primarily investigating the effect of bracket material on orthodontic therapy. All ceramic brackets used were SL brackets with a metal insert and no comparison solely on the basis of material could be made (even indirectly). Bracket slot size was assessed only as a secondary outcome in two trials, with no meta-analysis possible. Obviously, this factor must be viewed in conjunction with the slot-wire play (Gioka and Eliades, 2004; Burrow, 2009; Tominaga *et al.*, 2012).

No formal assessment could be made for the effectiveness of the different modules used to engage the archwire into CL brackets. Polyurethane-based elastomers lose approximately 50 per cent of the force applied within the first 24 hours (Taloumis *et al.*, 1997). More force dissipation could take place intraorally due to pH fluctuations, temperature variations, enzyme action, and mechanical loading. For this reason, SS ligatures have been suggested as more efficient, especially for tooth rotations (Rock and Wilson, 1989). On the other hand, SS ligatures exert higher moments, which may exceed the biological range (Bednar and Gruendeman, 1993). Many types of non-conventional ligatures including fluoride-releasing or reduced-friction ligatures, have been tested in the dry or the wet state (Khambay *et al.*, 2004; Franchi *et al.*, 2009; Mantel, 2011), but no clinical evidence exists.

Self-ligation was by far the subject assessed by the majority of included trials. Although duration of the alignment phase was identical, duration of the complete orthodontic treatment was significantly higher by 2 months on average in patients treated with SL brackets. Based on the 95 per cent PIs, a future treatment with SL brackets could

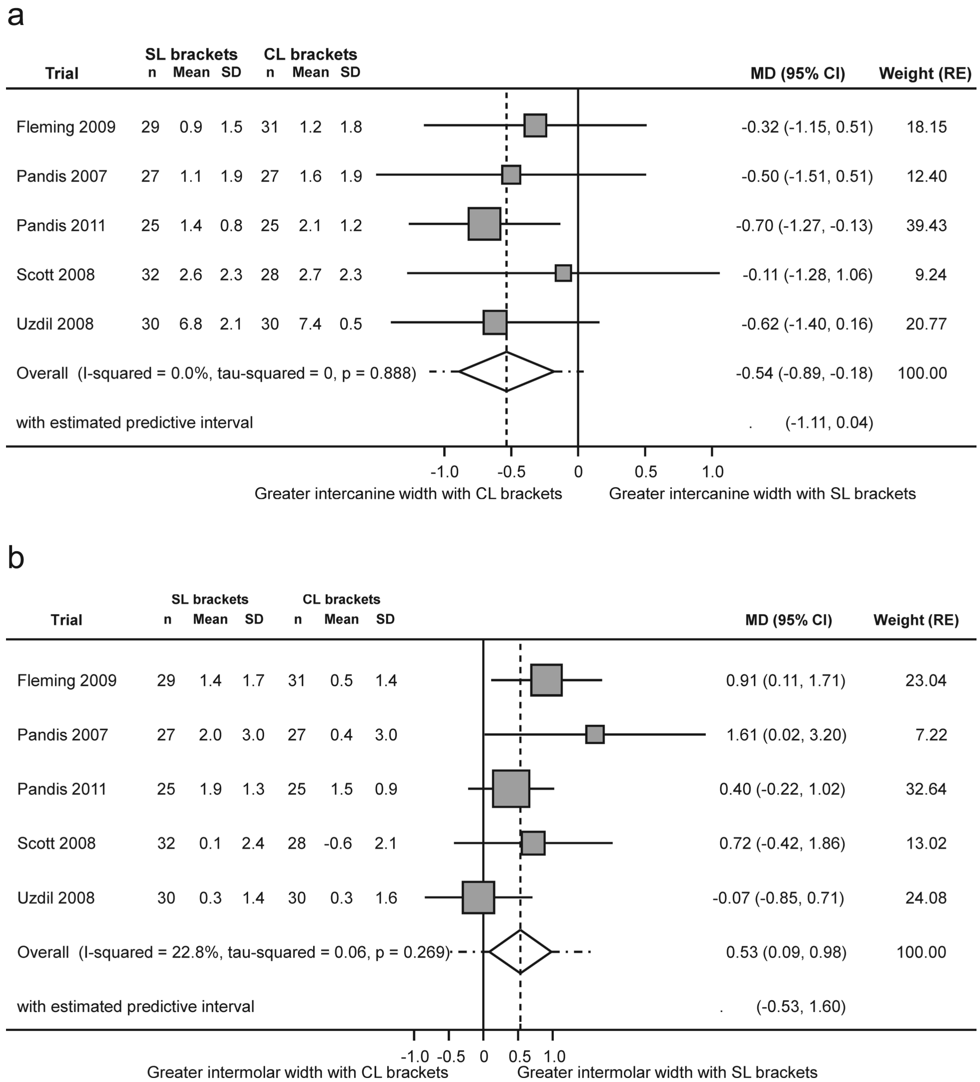

Figure 3 Forest plot for meta-analysis of (a) intercanine width from five trials (Pandis *et al.*, 2007b; Scott *et al.*, 2008a; Uzdil, 2008; Fleming *et al.*, 2009a; Pandis *et al.*, 2011); prediction interval for the treatment effect of a new trial given as a horizontal dotted line; estimates to the right indicate greater intercanine width for self-ligated (SL) groups and (b) intermolar width from five trials (Pandis *et al.*, 2007b; Scott *et al.*, 2008a; Uzdil, 2008; Fleming *et al.*, 2009a; Pandis *et al.*, 2011); prediction interval for the treatment effect of a new trial given as a horizontal dotted line; estimates to the right indicate greater intermolar width for SL groups. SL, self-ligated; CL, conventionally-ligated; SD, standard deviation; MD, mean difference; RE, random-effects model.

take from 1.5 months shorter to 5.5 months longer than with CL brackets. Although teeth extractions, archwire type, or study quality had no effect on this estimate, there are many other factors that could influence treatment duration (Mavreas and Athanasiou, 2008). An explanation, for this considerable difference could be difficulties reported during finishing with SL brackets (Harradine and Birnie, 1996), which lead some orthodontists to change to CL brackets for the finishing and detailing phases (Prettyman *et al.*, 2012). Torque expression is believed to be influenced by characteristics of both the archwire and the bracket (Pandis *et al.*, 2008c; Huang *et al.*, 2009; Sifakakis *et al.*, 2012). In any case, a reduction in duration of the alignment phase or the orthodontic treatment (due to lower friction) cannot be supported.

The number of needed appointments was slightly greater for the SL groups but to no statistically significant extent. However, time between appointments was not assessed in any of the trials. Observational data indicate longer appointment intervals for patients treated with SL brackets compared with CL brackets (Kai, 2010). The increased fracture risk of retrieved NiTi archwires (Bourauel *et al.*, 2008) must also be taken into account when planning longer appointment intervals (Harradine, 2003), especially as the actual fracture cause remains unclear (Zinelis *et al.*, 2007).

Treatment effectiveness in terms of tooth alignment did not differ between patients treated with SL and CL brackets. This seems to support the claims that the archwire binding-releasing phenomenon plays a much greater role than the bracket-archwire friction (Southard *et al.*, 2007; Fansa *et al.*, 2009). Interestingly, stratification by archwire type indicated that the efficiency of the two systems was comparable only with use of M_{act} NiTi archwires. When using M_{stab} NiTi archwires, SL brackets were less effective than CL brackets in tooth alignment (i.e. associated with 4 mm less irregularity alleviation). Although the SGs in the analysis were not adequate and the results have to be confirmed by future trials, this could justify the use of 'high-technology archwires' that is suggested by SL brackets' manufacturers. The proposed theoretical basis for this is the complete archwire engagement (even for considerably displaced teeth), while exerting minimal forces, which do not endanger the periodontal vascular supply, and allow more freedom for the teeth to move individually. However, no justification yet exists.

The importance of dental effects of SL brackets is questionable. Dental arches of patients treated with SL brackets were narrower at the canines and wider at the molars than those treated with CL brackets. Theoretically, reduced friction is coupled with lower, physiologically harmonious forces that promote alveolar bone generation and allow for greater lateral expansion (Damon, 2005). However, in both cases an average difference of about 0.5 mm is probably of little clinical significance, as changes in intermolar width of 1–2 mm translate in 0.3–0.6 mm of arch perimeter (Germane *et al.*, 1991). The minimal difference of active or passive SL brackets compared with CL brackets regarding arch dimensions, molar inclination, or incisor inclination was confirmed by a recently published RCT (Fleming *et al.*, 2013). This was published after review procedures had ended and will be included in the first review's update. Nevertheless, the factor of wire arch shape was not taken into account in this review and could have influenced the results. Finally, a previously reported lower mandibular incisor inclination reported for SL brackets, possibly indicating expansion & distalisation without incisor flaring (Paquette, 2011), was not confirmed by this review.

Pain intensity after archwire insertion was not different among patients treated with SL and CL brackets, which has been already reported (Čelar *et al.*, 2013). No difference in EARR was found from two included trials and evidence was graded high. However, EARR is not solely dependent on orthodontic treatment, and in order to explore EARR in association with bracket use, additional well-designed and explicitly reported trials are needed. Finally, no trial was found assessing the periodontal/microbiological outcomes or outcomes regarding the post-treatment stability and relapse in association with bracket type.

No significant difference between passive and active SL brackets on treatment duration, transverse dental effects, incisor inclination, or pain intensity was found. Passive SL brackets have been reported to present less frictional resistance (Thorstenson and Kusy, 2002; Budd *et al.*, 2008) and also to exert higher moments during derotation (Pandis *et al.*, 2008c). Active SL brackets have been reported to exert lower force values in the lingual direction during simulated first-order corrections (Pandis *et al.*, 2008d) although these forces are not always lower than CL brackets (Brezniak *et al.*, 2010). It seems that the archwire may play a greater role than the sliding mechanism during first- and second-order correction although the exertion of force or moments may be more complicated. The fact that active SL brackets were not superior in torque deliverance (Badawi *et al.*, 2008), as reported *in vitro*, could be attributed to differences in archwire play (Huang *et al.*, 2012). Clinical evidence does not seem to support such a difference between SL and CL brackets (Pandis *et al.*, 2006b; Major *et al.*, 2011; Brauchli *et al.*, 2012) or use a third 'interactive' SL bracket category.

This review was based on standard guidelines and apart from published trials, unpublished/ongoing ones were inquired upon, while additional data were provided from communication with trialists. Blinding is not always possible, and when not, it is inappropriate to describe all such studies as of 'low quality'. So, unlike previous reports, blinding of the orthodontist or the patients was considered as adequate when it was partly done or attempted. Unclear classifications were not resolved by exclusion of the trial, but included, and communication attempts were made in order to clarify them (although not all of them were ultimately clarified). Sensitivity analyses took account of sources of bias and showed that results were robust. Methodological adequacy of trials was assessed in terms of risk of bias, sample size calculations, method error assessment, and appropriateness of statistics used [as for example in split-mouth trials (Lesaffre *et al.*, 2009)]. Between-study heterogeneity was incorporated in a clinically justified random-effects model, while the 95 per cent PIs were calculated, as robust conclusions from random-effects meta-analyses mandate their use. Finally, the GRADE approach was used to evaluate the strength of recommendations. The review is to be updated in 4–5 years or earlier if many new trials are identified.

The major limitation of this review is the lack of substantial high-level evidence for many of the interventions and outcomes included. This is especially of interest for outcomes, like root resorption and stability, as biology, and not mechanics, seems to be the major limiting factor in orthodontics (Burrow, 2009). Secondly, the lack of consistent reporting across studies, missing data due to non-response of trialists and inability to examine publication bias or other reporting biases could further the risk of bias.

Conclusions

There is insufficient evidence at present to make recommendation for the effect of bracket material, ligature type for CL brackets, and clip mode of the SL brackets regarding treatment efficiency/efficacy or potential side-effects. We cannot make a qualified recommendation for the use of SL brackets on fixed-appliance orthodontic patients on the basis of efficiency, effectiveness, or side-effects. Use of SL brackets seems to be significantly associated with a longer treatment by 2 months on average, a minimal increase in intercanine width, and a minimal decrease in intermolar width.

The present systematic review highlighted the need for additional parallel RCTs according to the Consolidated Standards of Reporting Trials statement in order to safely make clinical recommendations about the materials, size, and ligation of orthodontic brackets. Such RCTs should have adequate sample size, minimize any bias, explicitly report the trial's procedures and results and preferably take into consideration possible influencing factors like tooth extractions and type of archwire used. Other characteristics to be assessed in the future are bracket prescription, different adhesive/brackets combinations, or lingual bracket placement.

Supplementary material

Supplementary materials are available at *European Journal of Orthodontics* online.

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