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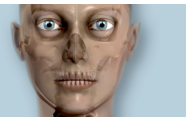

REVIEW ARTICLE

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A systematic review and meta-analysis of experimental clinical evidence on initial aligning archwires and archwire sequences

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Abstract

The aim of the study was to assess treatment effects and potential side effects of different archwires used on patients receiving orthodontic therapy. Electronic and manual unrestricted searches were conducted in 19 databases including MEDLINE, Cochrane Library, and Google Scholar until April 2012 to identify randomized controlled trials (RCTs) and quasi-RCTs. After duplicate study selection, data extraction, risk of bias assessment with the Cochrane risk of bias tool, and narrative analysis, mean differences (MDs) with confidence intervals (CIs) of similar studies were pooled using a random-effects model and evaluated with GRADE. A total of 16 RCTs were included assessing different archwire characteristics on 1108 patients. Regarding initial archwires, meta-analysis of two trials found slightly greater irregularity correction with an austenitic-active nickel-titanium (NiTi) compared with an martensitic-stabilized NiTi archwire (corresponding to MD: 1.11 mm, 95% CI: −0.38 to 2.61). Regarding archwire sequences, meta-analysis of two trials found it took patient treated with a sequence of martensitic-active copper-nickel-titanium (CuNiTi) slightly longer to reach the working archwire (MD: 0.54 months, 95% CI: −0.87 to 1.95) compared with a martensitic-stabilized NiTi sequence. However, patients treated with a sequence of martensitic-active CuNiTi archwires reported general greater pain intensity on the Likert scale 4 h and 1 day after placement of each archwire, compared with a martensitic-stabilized NiTi sequence. Although confidence in effect estimates ranged from moderate to high, meta-analyses could be performed only for limited comparisons, while inconsistency might pose a threat to some of them. At this point, there is insufficient data to make recommendations about the majority of initial archwires or for a specific archwire sequence.

Key words: aligning archwire; alignment; archwire sequence; bracket; fixed orthodontic treatment; initial archwire; orthodontic archwire

Introduction

Rationale

Developments in the last decades regarding orthodontic archwires used during fixed appliance treatment include the introduction of various archwires from NiTi alloys, multistranded archwires and esthetic coated or uncoated archwires.

Developments of orthodontic archwires based on NiTi alloys using a recent classification (1) and in chronological order include 1) the martensitic-stabilized (M_{stab}) – conventional – NiTi, 2) the austenitic-active (A_{act}) – *known as superelastic* – NiTi, 3) the martensitic-active (M_{act}) – *heat-activated* – NiTi or copper-nickel-titanium (CuNiTi), and 4) the graded M_{act} NiTi archwires. The *in vitro* beneficial properties of the last three categories of NiTi archwires have been previously documented (1–4), but have not been confirmed clinically (5–7). Retrieval analyses indicated that intra-oral aging (8) may alter the physical properties of the NiTi archwires (9, 10), the bracket (11) or ligation modules (12).

Multistranded stainless steel (SS) archwires have been developed to fulfill the requirements of an ideal archwire (1) and have been proposed as an economical alternative to NiTi archwires (13, 14), as they are equally efficient (15) and produce low force and moment levels (16). Various attempts at the development of an esthetic archwire have been made (17–19). Recently, shape memory polymeric archwires were developed (20, 21), in which moieties in the material act as molecular switches upon irradiation with UV light of $\lambda < 260$ nm (22).

Archwire sequences used in clinical practice vary greatly, with first coming the use of a NiTi archwire followed by beta titanium or SS archwires and a mean number of four to five archwires per sequence being a popular choice among orthodontists (23, 24). In general, the orthodontist strives to use archwires with greater stiffness and smaller range moving from the aligning phase to the working and finally the finishing phase. Investigating a specific archwire sequence is based on the need to establish a standard way of reaching the working archwire, which will be clinically effective and biologically sound (25, 26).

Previous systematic reviews have attempted to summarize evidence regarding initial aligning archwires (27) or specific sequences of archwires (28). However, inclusion of observational studies, limited literature search, and exclusion of gray literature may limit the value and validity of a systematic review/meta-analysis (29, 30). Also, most knowledge syntheses focus on a single archwire characteristic, although it is not agreed whether it is the bracket, the archwire, or their interaction that mainly influences the mechanical behavior of the bracket–archwire complex (31, 32). Therefore, investigation of the bracket–archwire complex may be more appropriate. As earlier reviews included trials up to 2008 or 2009, an update was decided.

Objectives

This systematic review aims to critically appraise existing evidence from randomized controlled trials (RCTs) and quasi-RCTs regarding the effectiveness, efficiency, and potential side effects of the various archwires used during fixed appliance orthodontic treatment.

Methods

Protocol

This review's protocol was made *a priori* based on the guidelines of the PRISMA statement (33), its extension for abstracts (34), and the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0 (35).

Eligibility criteria

Type of studies

Randomized controlled trials (RCTs) and quasi-RCTs (36) of parallel or split-mouth design. Split-mouth trials were eligible, if no carryover effect was possible and clustering (or pairing) of teeth was taken statistically into account (37–39). When trial reports used the word 'random' once, but no further information was given, the

authors were contacted to clarify whether true randomization had taken place.

Type of participants

Humans of any age or sex.

Intervention

Placement of initial archwire and/or of the following archwire sequence in the frame of orthodontic therapy with fixed orthodontic appliances to correct existing malocclusion. In order for a study to be included, all of the patient's teeth of one or both jaws (excluding third and possibly second molars) were required to have received treatment with fixed orthodontic appliances and archwire(s).

Comparison

Comparable patients for age, sex, and malocclusion receiving therapy with another combination of archwire and bracket (no untreated control groups). Trials were excluded, if the comparison group did not differ from the experimental group in at least one from the following characteristics: 1) archwire material, 2) archwire cross-section shape, or 3) archwire cross-section size.

Primary outcome

Tooth alignment as measured by 2-D or 3-D (intertooth) contact point differences or reduction in Little's Irregularity Index (LII) (40). Alternatively, the outcome of orthodontic treatment was included and measured in Peer Assessment Rating (PAR) scores (41), the Index of Outcome, Complexity and Need (ICON) (42), or any other valid measuring method of malocclusion severity. Both overall correction of the dental arch and correction of the labial/buccal segments were included.

Secondary outcomes

1) Time to misalignment correction (where not defined, a final cutoff value of 2 mm irregularity was deemed adequate), 2) time to proceed to the next archwire in the sequence, 3) time to reach the working archwire, 4) treatment duration, 5) number of appointments, 6) space closure of extraction sites, 7) dental/skeletal changes, 8) patient-reported pain intensity measurement by visual analog scale (VAS) (43), Likert scale (LS) (44), or other valid scale, 9) clinician-prescribed or self-prescribed analgesics use, 10) bracket failure (only for identical groups regarding bonding systems used), 11) archwire fracture, 12) External Apical Root Resorption (EARR), and 13) post-treatment stability and relapse.

Studies were excluded if: 1) different arch forms or bendings of identical archwires were compared (i.e., preformed vs. computer-aided bended archwires, etc.) or 2) patients had previous active treatment or relevant medical history.

Information sources, search, study selection, and data collection process

Systematic searches for RCTs and quasi-RCTs (completed or ongoing) were conducted. A total of 19 general, open-access, regional, or gray literature databases were searched from their inception up to April 2012, including MEDLINE, Cochrane Library, Google Scholar, and Clinical Trials (Table S1). There was no language, publication year, or publication status (i.e., unpublished articles) restriction. Translations of papers were arranged where necessary.

The reference and citation lists of all included trials and relevant reviews were scanned for additional entries. Manual updates of journals and databases were made weekly up to July 2012. Corresponding authors of registered trials, conference abstracts, and posters were inquired on their current status.

One author (SNP) screened all titles and abstracts obtained from the database searches. Two authors (SNP and KP) reviewed unblinded (45) the full text of potentially relevant studies and completed pre-defined data extraction forms. Corresponding authors were contacted for clarifications [with open-ended questions to avoid overly positive answers (35)], missed trials, and further data.

Risk of bias in individual or across studies

Two authors (SNP and KP) independently assessed the risk of bias of the included studies

using the Cochrane Collaboration's tool for assessing risk of bias (46), guided by the Cochrane Handbook for Systematic Reviews of Interventions (35). Each RCT was assigned an overall risk of bias in terms of high risk ('high' for ≥2 key domains), unclear risk ('unclear' for ≥2 key domains), and low risk for the remaining. The exact definitions used for each of the domains were pre-specified in the protocol (available on request).

The quality of evidence and strength of recommendations for each meta-analysis outcome were ultimately assessed according to the GRADE approach (Grades of Recommendation, Assessment, Development, and Evaluation) (47).

Disagreements concerning study selection, data extraction, or risk of bias were settled by a third author (IK), and agreement was assessed using the unweighted κ coefficient (48). The two authors were calibrated before the actual procedures by pilot running the search results of a previous systematic review (49) regarding all duplicate procedures, until almost perfect agreement ($\kappa > 0.8$) was reached both between authors and with the results of that review.

Summary measures, synthesis of results, and additional analyses

Data were considered suitable for pooling if similar interventions were used in the same way and similar outcomes were reported. A random-effects model as proposed by DerSimonian and Laird (50) was chosen, because the observed effect was 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% prediction intervals (PIs) (51, 52) were calculated to predict treatment effects in a new trial. Although all 95% PIs were calculated, only PIs for significant meta-analyses are provided here (the remainder being available on request).

The extent and impact of between-study heterogeneity were 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%), possible sources of heterogeneity were sought with stratification by bracket/archwire or treatment characteristics. When heterogeneity was >75%, data were not pooled. If a sufficient number of trials were identified ($n > 7$), analyses were planned for 'small-study effects' and publication bias.

All analyses were carried on the basis of intention-to-treat (worst-case analysis) when possible. Experimental groups were defined by characteristics of the bracket–archwire complex, as listed in the inclusion criteria section. For example, a possible comparison could be a trial arm of conventionally ligated (CL) metallic 0.022″ brackets with a 0.016″ M_{act} CuNiTi initial archwire versus a trial arm of self-ligating (SL) ceramic 0.022″ brackets with a 0.014″ M_{stab} NiTi archwire. When two or more arms were classified, the same (for example two different brands of brackets identical to all characteristics), fixed-effect meta-analysis was used to merge them, prior to comparison with the group that differed. For trials providing before-and-after data for two groups but no increments, a modest pre-/post-correlation of 0.25 was used (after sensitivity analyses with 0.25, 0.50, and 0.75). Split-mouth trials were meta-analyzed separately from parallel trials, identifying differences in effect size due to design and pooled only if similar (39), as data for the 'inverse variance method' were often unavailable.

Mean differences (MD) or standardized mean differences (SMD) for continuous outcomes and their corresponding 95% confidence intervals (CIs) were calculated. When possible, exploratory stratified analyses according to the bracket/archwire characteristics used to define the groups were performed with pre-specified subgroup analyses (SG): (i.e., SL vs. CL brackets; metallic vs. 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. RevMan version 5.1 (Nordic Cochrane Centre, Cochrane

Collaboration, Copenhagen, Denmark) was used to carry out the meta-analyses for comparable trials and outcomes, and Stata version 10 (StataCorp LP, College Station, TX, USA) was used for calculating Cohen's κ and 95% PIs. Significance (α) was set at 0.05, except for a 0.10 used for the heterogeneity tests (53).

Results

Study selection

A total of 1528 citations were identified electronically and nine more manually (Fig. 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, 106 articles were excluded on the basis of their full text. Eleven articles more were finally not included, as no full text was obtained. A total of 18 trial authors were contacted for full-text provision, clarifications, or additional unpublished data. Two author e-mails could not be found, while six trialists responded. Another 24 articles were excluded from the present review, as they assessed bracket characteristics. Finally, a number of possibly eligible trials (n = 8) were excluded: No response and trial were deemed ineligible (54), abstract/posters with no available text (55–58), and ongoing trials (ISRCTN identifiers: ISRCTN38412478, ISRCTN75477546).

Study characteristics and risk of bias

A total of 16 full-text reports were finally included, describing 1108 patients included in

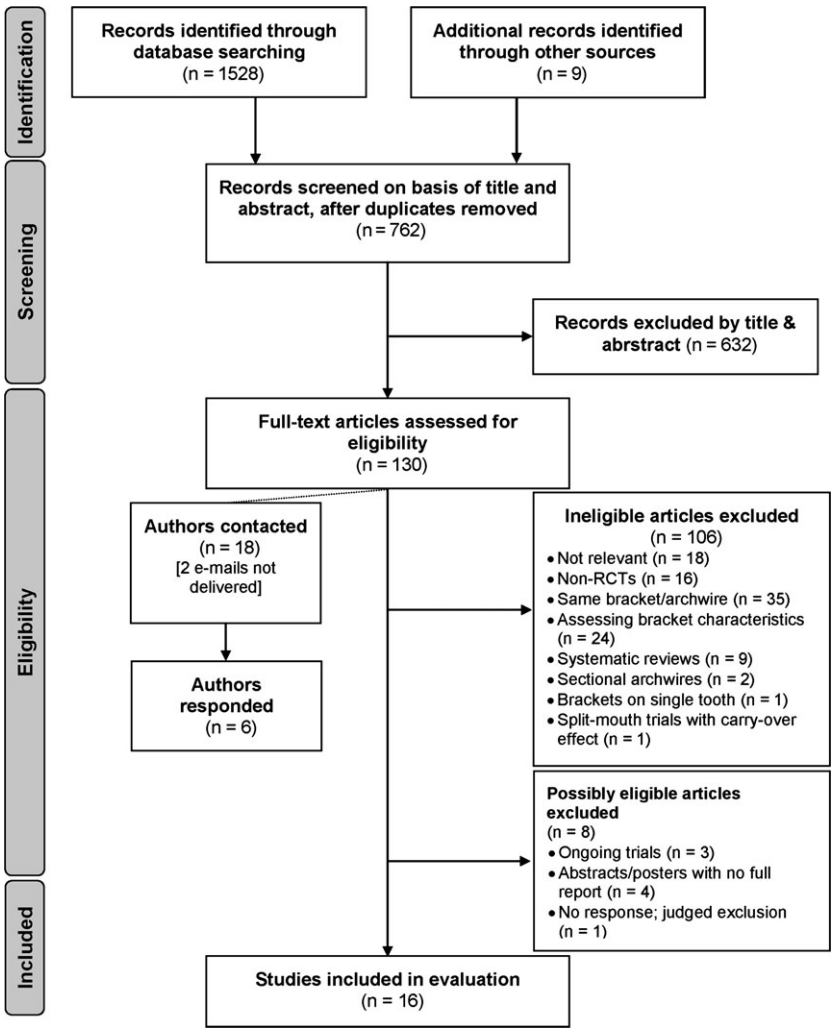

Fig. 1. PRISMA flow diagram of the study selection procedure.

16 RCTs published between 1990 and 2012. All trial reports were in English, except for one in Chinese (59). The bracket and archwire products used in the included trials are provided separately in Table S2. 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 (48).

Trial characteristics and risk of bias assessment for each of the 16 trials, based on published data and author communication, are given in Table 1, Table S3, Table 2, Table S4, and Table 3, respectively. One split-mouth trial (60) was included, which used appropriate statistical methods (Wilcoxon signed-rank test). Only three trials (61–63) provided a CONSORT flowchart with complete patient data.

Trials on initial archwires

A total of 13 trials with 863 patients were included, assessing various factors: cross-section of archwires (64), N^+ implantation of archwires (60, 65), and archwire materials (61–63, 66–71). The association of archwire cross-section size with reported pain intensity during the first 7 days after initial archwire placement was investigated by Erdinç and Dinçer (64), who reported significantly less pain and lower analgesic use in the 0.016″ group compared with the 0.014″ group. The method of N^+ ion implantation of β-Ti or NiTi archwires, to alter surface roughness and presumably facilitate easier sliding, was investigated in two trials (60, 65) that did not find a significant improvement.

M_{act} NiTi archwires

The use of an initial M_{act} NiTi compared with a M_{stab} NiTi archwire was assessed in two trials that reported no significant difference on alleviation of tooth irregularity (69) or time to align the anterior teeth (62).

The use of an initial M_{act} NiTi compared with an A_{act} NiTi archwire was assessed in three trials, two of which found no difference in tooth alignment (69, 70). In the third trial (72), patients treated with a M_{act} NiTi initial archwire were reported to have lower pain intensity (VAS) at the second, third, and fourth day after archwire insertion. Treatment efficacy between patients treated with M_{act} NiTi compared with a multistranded SS initial archwires was assessed on the basis of 3-D contact point movement by two trials (66, 70) that found no significant difference, while issues of sample adequacy and existing bias may reduce validity of the results.

A_{act} NiTi archwires

As stated above, significant differences in pain intensity or analgesic use were found after an initial A_{act} NiTi or a M_{act} NiTi archwire (72).

The use of an initial A_{act} NiTi archwire was compared with a M_{stab} NiTi archwire in terms of 3-D contact point movement (61, 70), LII reduction (69), and pain intensity (67). The SMD was used to pool contact point movement, and LII reductions from two trials were pooled, while data from the third one were unavailable. Meta-analysis showed that use of A_{act} NiTi initial archwires was associated with a small and statistically nonsignificant benefit in irregularity alleviation compared with M_{stab} NiTi initial archwires (Table 4; Fig. 2), with evidence being classified according to GRADE as ‘moderate’. Finally, pain intensity and analgesic use differed significantly between groups only at the fourth day, with the A_{act} NiTi group reporting less pain.

Pain after engagement of an initial A_{act} NiTi archwire was compared in a trial to a multistranded SS archwire (68), without finding significant differences. Regarding the comparison of alignment efficiency, the results were contradictory, with one trial finding no difference in LII reduction (69) and one trial finding significantly higher 3-D contact point movement of the anterior segment for the A_{act} NiTi compared with the multistranded SS archwires (71).

Multistranded archwires

As stated above for each type of NiTi archwire, no differences were found between multistranded SS archwires compared with A_{act} NiTi archwires in terms of intertooth contact point movement (70, 71) or patient pain intensity (68). Moreover, no difference was found between

Table 1. **Main characteristics of included trials regarding initial archwires**

Trial First author	Design	Setting (country; clinic; recruitment dates; mean follow-up; % dropouts)	Bracket/ligature	Initial archwire (A1)
Cioffi (72)	Single-center double-blind two-arm parallel RCT	Italy; university; January 2009-NR; 7 days; 0% dropouts	SS CL 0.022″ brackets/ elastomeric	Gp1: 0.016″ A_{act} NiTi Gp2: 0.016″ M_{act} NiTi
Cobb III (65)	Single-center three-arm parallel RCT	USA; university; recruitment dates NR; 12 months; 2% dropouts	GpA: SS CL 0.018″ brackets/ elastomeric	Gp1: 0.016″ A_{act} NiTi Gp2: 0.016″ N^+ implanted A_{act} NiTi
			GpB: SS CL 0.022″ brackets/ elastomeric	Gp3: 0.0175″ multistranded SS
Erdinç (64)	Single-center two-arm parallel RCT	Turkey; university; recruitment dates NR; 7 days; 0% dropouts	SS CL 0.018″ brackets/NR	Gp1: 0.014″ M_{stab} NiTi Gp2: 0.016″ M_{stab} NiTi
Evans (66)	Multicenter three-arm parallel RCT	Country NR; setting NR; recruitment dates NR; 8 weeks; 9% dropouts	SS slot size NR CL brackets/ elastomeric (usually)	Gp1: 0.016 × 0.022″ medium force M_{act} NiTi 28°C Gp2: 0.016 × 0.022″ graded M_{act} NiTi 32.5°C Gp3: 0.0155″ multistranded SS
Fernandes (67)	Multicenter two-arm parallel RCT	Norway; university/private; recruitment dates NR; 7 days; 7.4% dropouts (regarding the pain recordings)	(brackets were standardized) SS CL slot size NR brackets/NR	Gp1: 0.014″ light force A_{act} NiTi Gp2: 0.014″ M_{stab} NiTi
Jones (68)	Single-center two-arm parallel RCT	Wales; university; recruitment dates NR; 15 days; 6.7% dropouts	SS CL 0.018″ brackets/NR	Gp1: 0.014″ heavy A_{act} NiTi Gp2: 0.015″ multistranded SS
Kula (60)	Single-center triple-blind two-arm split-mouth RCT	USA; setting NR; recruitment dates NR; 6 months (maximum); 23.1% dropouts	SS CL 0.022″ brackets/ elastomeric	Gp1: 0.019 × 0.025″ β-Ti Gp2: 0.019 × 0.025″ N^+ implanted β-Ti
O'Brien (61)[#]	Single-center two-arm parallel RCT	England; university; recruitment dates NR; 5 weeks; dropouts NR	SS CL 0.018″ brackets/ elastomeric or SS	Gp1: 0.016″ A_{act} NiTi Gp2: 0.016″ M_{stab} NiTi
Ong (69)	Single-center double-blind three-arm parallel RCT	Australia; private; recruitment dates NR; 4.1 months; 3.8% dropouts	SS CL 0.018″ brackets/ elastomeric	Gp1: 0.014″ M_{stab} NiTi Gp2: 0.014″ A_{act} NiTi Gp3: 0.014″ M_{act} CuNiTi 35°C
Pandis (62)[#]	Single-center double-blind two-arm parallel RCT	Greece; private; December 2006 –December 2007; 6 months; 0% dropouts	SS active SL 0.022″ brackets/None	Gp1: 0.016″ M_{act} CuNiTi 35°C Gp2: 0.016″ M_{stab} NiTi

Table 1. **(continued)**

Trial First author	Design	Setting (country; clinic; recruitment dates; mean follow-up; % dropouts)	Bracket/ligature	Initial archwire (A1)
Quintao (70)	Single-center four-arm parallel RCT	Brazil; university; recruitment dates NR; 8 weeks; dropouts NR	SS CL 0.022″ brackets/NR	Gp1: 0.016″ light force A_{act} NiTi Gp2: 0.016″ M_{act} NiTi Gp3: 0.0155″ multistranded SS Gp4: 0.014″ SS
Sebastian (63)	Single-center double-blind two-arm parallel RCT	India; university; recruitment dates NR; 12 weeks; 0% dropouts	SS CL 0.022″ brackets/ elastomeric (usually) and SS	Gp1: 0.016″ multistranded A_{act} NiTi Gp2: 0.016″ A_{act} NiTi
West (71)	Single-center two-arm parallel RCT	Ireland; setting NR; recruitment dates NR; 6 weeks; dropouts NR	SS CL slot NR brackets/NR	Gp1: 0.014″ A_{act} NiTi Gp2: 0.0155″ multistranded SS

A1, first archwire; RCT, randomized controlled trial; NR, not reported; SS, stainless steel; CL, conventionally ligated; Gp, group; A_{act}, austenitic-active; NiTi, nickel-titanium; M_{act}, martensitic-active; M_{stab}, martensitic-stabilized; β-Ti, beta titanium; SL, self-ligating; [#]including data from author communication.

multistranded SS archwires compared with M_{act} NiTi archwires in terms of intertooth contact point movement (66, 70). In contrast, multistranded A_{act} NiTi archwires were reported to be significantly more efficient in terms of 3-D contact point movement than its single-stranded analogs.

Trials on archwire sequences

Four trials (59, 69, 73, 74) investigated archwire sequences used on 364 patients with SS CL brackets. AlQabandi et al. (73) compared a sequence of round SS archwires with progressively greater cross-section with a sequence of a rectangular M_{act} CuNiTi archwire, followed by a rectangular SS archwire and found no significant difference in treatment effects.

Ji et al. (59) similarly compared a sequence of four progressively larger round M_{stab} NiTi archwires, followed by two rectangular SS archwires and a sequence of 0.016″ M_{act} round NiTi, followed by a rectangular M_{act} NiTi and a rectangular SS archwire. No significant difference was found in treatment duration or bracket failure between the groups, while significantly more archwire fractures were observed in the first (M_{stab} NiTi) group. Nevertheless, caution is advised due to the lack of sample size calculation, the unclear risk of bias, and the lack of complete reporting that precluded direct assessment.

Mandall et al. (74) randomized patients in three sequences including various NiTi, CuNiTi, and SS archwires, which are all manufactured by the same company (Table S2). Assessed outcomes included time/appointments to reach the working archwire, pain intensity (LS) after archwire insertion, and EARR of the maxillary central incisor. No significant difference was found among groups for any outcome in the maxillary arch. In the mandibular arch, however, significantly less time to reach the working archwire and significantly lower pain intensity (LS) at 4 h, the first and the seventh day after insertion were reported for the archwire sequence 'round and then rectangular M_{stab} NiTi' (Gp1) compared with the sequence 'round M_{stab} NiTi and then round SS' (Gp2). Also, significantly lower pain intensity (LS) at the first, third, and seventh day after insertion was reported for the 'round then rectangular M_{stab} NiTi' sequence compared with the sequence 'rectangular M_{act} CuNiTi.'

Table 2. **Main characteristics of included trials regarding sequences of archwires**

Trial First author	Design	Setting (country; clinic; recruitment dates; mean follow-up; % dropouts)	Bracket/ligature	Archwire sequence
AlQabandi (73)	Single-center two-arm parallel RCT	USA; university; recruitment dates NR; 6.2 months; dropouts NR	SS CL 0.018″ brackets/NR	Gp1: A1-??: SS (progressively larger cross-section archwires) A(last): 0.016″ SS Gp2: A1: (15 patients) 0.016 × 0.022″ M_{act} CuNiTi 35–37°C A2: 0.016 × 0.022″ SS
Ji (59)	Single-center two-arm parallel RCT	China; university; July 2006–November 2008; 5.0 months; 0% dropouts	SS CL 0.022″ brackets/NR	Gp1: A1: 0.012″ M_{stab} NiTi A2: 0.014″ M_{stab} NiTi A3: 0.016″ M_{stab} NiTi A4: 0.018″ M_{stab} NiTi A5: 0.018 × 0.025″ SS A6: 0.019 × 0.025″ SS Gp2: A1: 0.016″ M_{act} NiTi (0.012″ in severe crowding) A2: 0.019 × 0.025″ M_{act} NiTi A3: 0.019 × 0.025″ SS
Mandall (74)[#]	Multicenter single-blind three-arm parallel RCT	England; university/hospital/private; recruitment dates NR; 9.3 months (until placement of the last working archwire); 9.7% dropouts	SS CL 0.022″ brackets/ligation methods left to clinical judgment; ultimately found to be equally divided among groups	Gp1: A1: 0.016″ M_{stab} NiTi A2: 0.018 × 0.025″ M_{stab} NiTi A3: 0.019 × 0.025″ SS Gp2: A1: 0.016″ M_{stab} NiTi A2: 0.016″ SS A3: 0.020″ SS Gp3: A1: 0.016 × 0.022″ M_{act} CuNiTi 35°C A2: 0.019 × 0.025″ M_{act} CuNiTi 35°C A3: 0.019 × 0.025″ SS

Table 2. **(continued)**

Trial First author	Design	Setting (country; clinic; recruitment dates; mean follow-up; % dropouts)	Bracket/ligature	Archwire sequence
Ong (69)	Single-center double-blind three-arm parallel RCT	Australia; private; recruitment dates NR; 4.1 months; 3.8% dropouts	SS CL 0.018″ brackets/ elastomeric	Gp1: A1: 0.014″ M_{stab} NiTi A2: 0.017 × 0.017″ M_{act} NiTi 27°C A3: 0.016 × 0.022″ SS Gp2: A1: 0.014″ A_{act} NiTi A2: 0.016 × 0.022″ graded M_{act} NiTi 32.5°C A3: 0.016 × 0.022″ SS Gp3: A1: 0.014″ M_{act} CuNiTi 35°C A2: 0.014 × 0.025″ M_{act} CuNiTi 35°C A3: 0.016 × 0.022″ SS

RCT, randomized controlled trial; NR, not reported; SS, stainless steel; CL, conventionally ligated; Gp, group; M_{act}, martensitic-active; CuNiTi, copper-nickel-titanium; M_{stab}, martensitic-stabilized; NiTi, nickel-titanium; A_{act}, austenitic-active; #including data from author communication.

Table 3. **Assessment of risk of bias* in randomized controlled trials included in the systematic review**

Trial First author	Sequence generation	Allocation concealment	Blinding (clinician/patients)	Blinding (assessor)	Incomplete outcome data	Selective outcome reporting	Other biases	Overall
AlQabandi (73)	??	??	??	–	??	+	+	??
Cobb (65)	+	??	??	??	??	??	??	??
Cioffi (72)	+	+	+	+	+	–	+	+
Erdinç (64)	??	??	??	??	–	+	??	??
Evans (66)	??	??	??	–	??	–	??	–
Fernandes (67)	??	??	??	??	–	+	??	??
Ji (59)	??	??	??	+	+	–	??	??
Jones (68)	??	??	??	+	??	+	??	??
Kula (60)	??	??	+	+	–	+	??	??
Mandall (74)†	+	+	+	+	+	+	+	+
O'Brien (61)†	+	??	??	+	–	+	+	??
Ong (69)	+	+	+	+	+	+	+	+
Pandis (62)†	+	+	+	+	+	+	+	+
Quintao (70)	??	??	??	–	??	+	??	??
Sebastian (63)	+	+	+	+	+	+	??	+
West (71)	+	??	??	–	??	+	??	??

+: adequately assessed (low risk of bias); –: inadequately assessed (high risk of bias); ??: unclear.
*Based on Cochrane risk-of-bias tool (35). The excerpts of the included studies that were used to make the judgement are available upon request from the review authors.
†Including data from author communication.

Table 4. **GRADE summary of findings table for meta-analyses on initial archwires' data**

Patients: receiving fixed appliances for tooth alignment
Settings: private practice (not reported for one trial)
Intervention: A_{act} NiTi initial archwire
Comparison: M_{stab} NiTi initial archwire

Outcome (follow-up) Brackets used	Illustrative comparative risks* (95% CI) Assumed risk M_{stab} NiTi Gp	Corresponding risk A_{act} NiTi Gp	No. of participants [trials]	Quality of evidence (GRADE)	Comments
Tooth alignment (reduction of LII scores and 3-D contact point movement)* mm of LII (follow-up: 5 weeks) CL brackets	Mean LII reduction in M_{stab} NiTi groups 3.7 mm	Mean LII reduction in A_{act} NiTi groups 1.11 mm higher (0.38 lower to 2.61 higher)	126 [2 (61, 69)]	⊕⊕⊕○ Moderate†	Scores estimated using a SMD of 0.26 (−0.09 to 0.61) for LII and contact point movement; $p = 0.140$; $I^2 = 0\%$

A_{act}, austenitic-active; NiTi, nickel-titanium; M_{stab}, martensitic-stabilized; CI, confidence interval; Gp, group; LII, Little's irregularity index; 3-D, three-dimensional; CL, conventionally ligated; SMD, standardized mean difference.
*No significant difference between data from the two outcome measures (between-subgroups analysis).
†Downgraded by 1 for risk of bias in one trial: risk of attrition bias and possibly incomplete blinding.

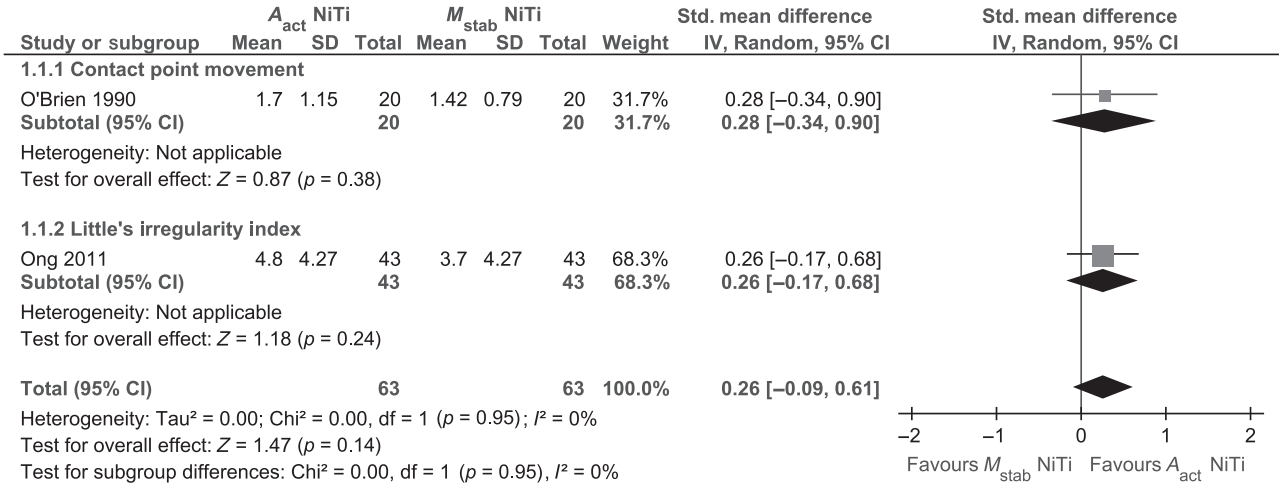

Fig. 2. Forest plot for meta-analysis of tooth alignment between an A_{act} nickel-titanium (NiTi) and a M_{stab} NiTi initial archwire.

Ong et al. (69) randomized patients in three sequences with NiTi and CuNiTi archwires from three different companies (Table S2). No significant difference was found in time to reach the working archwire and pain intensity (LS) at 4 h and on the first, third, or seventh day after insertion between any two archwire sequence groups. Significantly higher alleviation of the mandibular anterior irregularity (LII) was reported for the second trial arm (GAC sequence) compared with the third trial arm (Ormco sequence), when the third archwire was reached (difference in LII reduction = 1.9 mm, 95% CI: 0.16–3.64 mm, $p = 0.030$).

The last two trials (69, 74) were pooled to compare the M_{act} CuNiTi sequence with the M_{stab} NiTi sequence of each trial. The forest plots are presented in Figs 3 and 4, while the

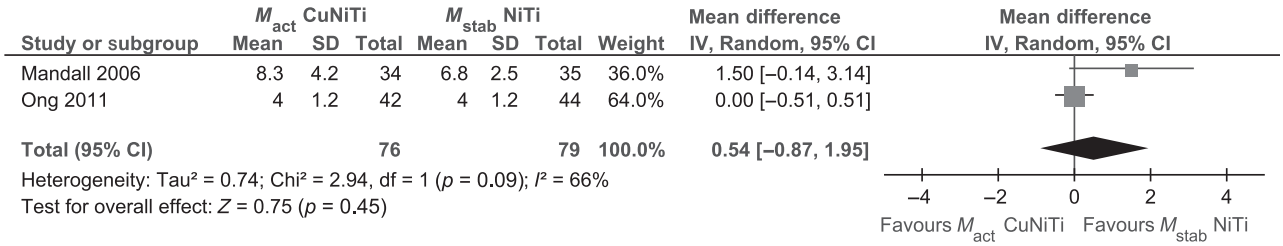

Fig. 3. Forest plot for the meta-analysis of time to reach the working archwire between a M_{act} CuNiTi and a M_{stab} nickel-titanium (NiTi) archwire sequence.

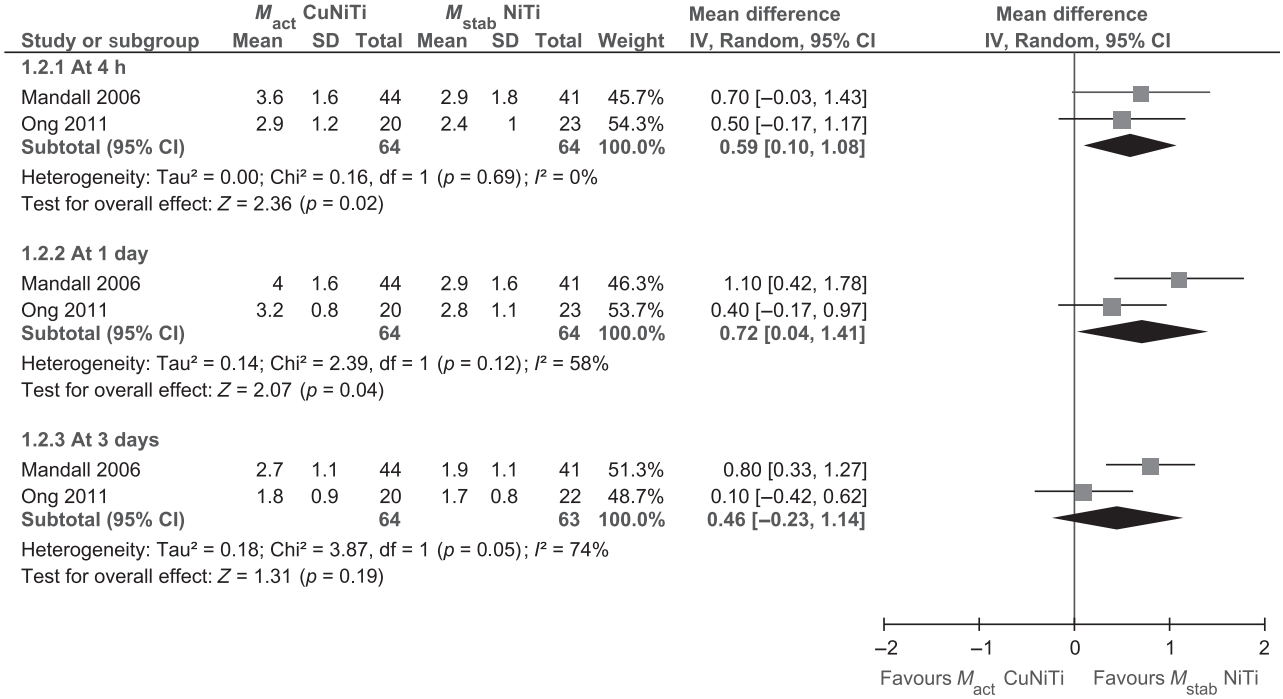

Fig. 4. Forest plot for meta-analysis of pain intensity (Likert Scale) after placement of archwire between a M_{act} CuNiTi and a M_{stab} nickel-titanium (NiTi) archwire sequence (reported means of values after first, second, and third archwire).

results of meta-analyses together with the quality of evidence according to GRADE are provided in Table 5. No significant difference between the two sequences was found regarding the time to reach the working archwire (Fig. 3). Patients treated with the M_{act} CuNiTi sequence reported generally greater pain intensity compared to those treated with the M_{stab} NiTi sequence (Fig. 4), which was significant at 4 h and on the first day after insertion. The small number of trials precluded any heterogeneity explanations, while meta-analysis for reported pain on the seventh day was not undertaken due to extreme heterogeneity ($I^2 > 75\%$). The quality of recommendations according to GRADE was moderate to high.

Due to the small number of studies included for each outcome, no formal assessment of 'small-study effects' (including publication bias), subgroup analysis according to bracket or treatment characteristics or sensitivity analysis could be undertaken.

Discussion

Summary of evidence

This systematic review included 16 trials with considerable variations in trial conduct and outcome reporting and a total of 1108 patients. A considerable lack of evidence exists regarding both the various initial archwires and complete

Table 5. **GRADE summary of findings table for meta-analyses on archwire sequences' data**

Patients: receiving fixed appliances for tooth alignment
Settings: university, hospital and private practice
Intervention: sequence of M_{act} CuNiTi archwires
Comparison: sequence of M_{stab} NiTi archwires

Outcome (follow-up) Brackets used	Illustrative comparative risks* (95% CI) Assumed risk NiTi sequence	Corresponding risk CuNiTi sequence	No of participants [trials]	Quality of evidence (GRADE)	Comments
Time to working archwire (CL brackets)	Mean time to reach working archwire ranged across NiTi groups from 4.0 to 6.8 months	Mean time to reach working archwire in the CuNiTi groups 0.54 month greater (0.87 lower to 1.95 higher)	155 [2 (69, 74)]	⊕⊕⊕○ Moderate*	$p = 0.450$; $I^2 = 66\%$
Pain intensity at 4 h on LS scale: 0–7 (CL brackets)	Mean pain intensity ranged across NiTi groups from 2.4 to 2.9 points	Mean pain intensity in CuNiTi groups 0.59 points greater (0.10–1.08 higher)	128 [2 (69, 74)]	⊕⊕⊕⊕ High	$p = 0.020$; $I^2 = 0\%$
Pain intensity on first day Points on LS scale: 0–7 (CL brackets)	Mean pain intensity ranged across NiTi groups from 2.8 to 2.9 points	Mean pain intensity in CuNiTi groups 0.72 points greater (0.04–1.41 higher)	128 [2 (69, 74)]	⊕⊕⊕○ Moderate†	$p = 0.040$; $I^2 = 58\%$
Pain intensity on third day Points on LS scale: 0–7 (CL brackets)	Mean pain intensity ranged across NiTi groups from 1.7 to 1.9 points	Mean pain intensity in CuNiTi groups 0.46 points greater (0.23 lower to 1.14 higher)	127 [2 (69, 74)]	⊕⊕⊕○ Moderate†	$p = 0.190$; $I^2 = 74\%$

M_{act}, martensitic-active; CuNiTi, copper-nickel-titanium; M_{stab}, martensitic-stabilized; NiTi, nickel-titanium; CI, confidence interval; CL, conventionally ligated; LS, Likert scale.
*Downgraded by 1 for inconsistency: moderate heterogeneity and confidence regarding decision could be possibly affected by heterogeneity.
†Did not downgrade for inconsistency: moderate to high heterogeneity, but decision regarding clinical decision unaffected.

archwire sequences that are commercially available.

Orthodontic mechanotherapy has been based on the incremental variation of archwire dimension or archwire material (and modulus of elasticity) (75). The effect of the size and shape of the archwire's cross-section could not be assessed in this review. Various authors have reported a correlation between frictional behavior and vertical wire dimension (76–78), with friction increasing as vertical wire dimension becomes greater. Conversely, an increased clearance between wire and bracket results in reduced friction, as well as in diminished control during tooth movement (79). Regarding the cross-section shape, even an artificially induced

beveling of rectangular archwires can reduce friction (80).

Ion implantation of β-Ti or NiTi archwires was assessed independently by two trials with no significant effect found. These investigations are based on *in vitro* data showing that altering of the surface roughness of the archwire may reduce corrosion, friction and possibly enable faster sliding of the archwire (81–83). However, this may hold true only when both opposing surfaces have been ion implanted (60). Also, NiTi archwires are subject to surface alterations by intra-oral conditions and/or bracket engagement (10), which could modify their performance. The idea that surface roughness and friction reduction is crucial to efficient mechanics also forms the basis of using metal or silica inserts or glazed slot bases in ceramic brackets (84). Although current evidence suggests that the clinical role of friction may have been overestimated (85), further research under non-simplified conditions and in collaboration with biomedical engineers is recommended (86).

A wide variety of NiTi-based archwires is available, which have been studied extensively *in vitro* (5, 7, 15, 83, 87–89). Factors of archwires that must be taken into account are their biocompatibility (90) and intra-oral aging (8, 91), followed by an increased risk of fracture (9), especially when planning longer appointment intervals, although the actual causes remain unclear (92).

Limited data preclude firm conclusions on the use of M_{act} NiTi archwires. Pandis et al. (62) reported no significant advantage in alleviation of mandibular anterior tooth irregularity compared with M_{stab} NiTi, while Cioffi et al. (72) reported lower pain intensity at the second, third, and fourth day after placement compared with A_{act} NiTi. Both studies provide evidence that would be rated as 'high quality' by the GRADE approach; nevertheless, additional studies are needed.

Meta-analysis of two trials found that A_{act} NiTi was slightly more effective in tooth alignment than M_{stab} NiTi, although not to a significant extent. However, this difference must be verified by subsequent large studies, as the small number of trials or differences in trial conduct and outcomes reported could have affected this estimate. Nevertheless, many of the included trials reported that considerable wire deflections are needed for the superelastic plateau of A_{act} archwires to be clinically useful (93). Also, recent observational evidence indicates that the bracket prescription may possibly affect the clinical performance of A_{act} NiTi archwires (94).

No clear conclusions can be made for the use of multistranded archwires due to the diverse comparisons between single- and multistranded archwires and serious methodological issues. In the trial of Sebastian et al. (63), a significant advantage of the multistranded A_{act} NiTi archwire was reported compared with its single-stranded analog with the provided evidence rated as 'high quality'.

Many different esthetic archwire coatings have been used to improve the frictional and esthetic characteristics of orthodontic archwires (95), with a number of issues identified. For example, epoxy resin-coated A_{act} NiTi archwires have been reported to produce lower loading and unloading force values than uncoated archwires of the same nominal dimensions for CL brackets and even more with SL brackets (96). Also, retrieved specimens presented increased surface roughness, deterioration of esthetics, and reduction of unloading force values, the latter being observed for CL and not SL brackets (18). On the other hand, certain coatings of archwires may prevent or minimize archwire corrosion of orthodontic archwires intra-orally (97).

The use of an archwire sequence of M_{act} CuNiTi was found to be associated with greater pain intensity compared with a sequence of M_{stab} NiTi at 4 h and 1 day after archwire insertion. This issue should not be taken lightly, as post-insertion pain is more intense and lasts longer than post-extraction pain (98). Orthodontic pain may be influenced by numerous factors (99), which may lead to poor patient compliance or treatment discontinuation (100, 101) and are believed to be associated with the amount of force applied to the tooth (102). Also, the two

identified and pooled trials of archwire sequences differed in some aspects. Mandall et al. (74) used sequences from a single company, while Ong et al. (69) from three different companies. Archwire change in Mandall et al. was made when the archwire was passive, while in Ong et al. when the archwire could be completely engaged. Finally, Ong et al. used brackets of smaller slot size than Mandall et al. (0.018″ vs. 0.022″), resulting in reduced slot-wire play and potentially more efficient treatment, although this has not yet been empirically proven (103).

Strengths and limitations

The conduct and reporting of this review was based on standard guidelines (33–35). Apart from published articles, unpublished/ongoing trials were inquired upon and additional data were provided after communication with trialists. Blinding is not always possible, and when not, it is inappropriate to describe all such studies as of 'low quality' (35). Unclear classifications were not resolved by exclusion of the trial, but included, reported, and will be improved in a following update (planned in 5–6 years). Sensitivity analyses took into account sources of unclear or high risk of bias. Methodological adequacy of included trials was assessed in terms of within-study risk of bias, sample size calculations, assessment of the method error, and appropriateness of statistics used [as for example in split-mouth trials (39)]. Between-study heterogeneity was both tested and included in the random-effects model, while the 95% PIs were calculated, because robust conclusions from random-effects meta-analyses mandate their use (52). Finally, the GRADE approach was used to evaluate the across studies evidence provided by the meta-analyses (47). However, the major limitation of this review is the lack of substantial high-level evidence for many of the interventions and outcomes assessed. Secondly, the lack of consistent reporting across studies, missing data due to non-response of trialists, and inability to examine publication bias and other reporting biases may have increased the risk of bias.

Conclusions

There is insufficient data at present to make recommendations for the use of any available archwire type regarding effectiveness, efficacy, treatment outcome, or potential side effects. The meta-analyses conducted are limited by the small number of trials and methodological issues and must therefore be subsequently confirmed.

Regarding initial archwires, meta-analysis of two trials indicates that in CL brackets, use of an austenitic-active NiTi initial archwire was not significantly more effective in tooth alignment than a martensitic-stabilized NiTi archwire (moderate evidence quality).

Regarding archwire sequences, meta-analysis of two trials indicates that in CL brackets, a sequence of martensitic-active CuNiTi archwires compared with a sequence of martensitic-stabilized NiTi archwires:

- Has no effect on time needed to reach the working archwire (moderate evidence), and
- Results in greater patient-reported pain intensity, which was statistically significant 4 h and 1 day after placement of each archwire (moderate to high evidence).

The clinical effects of orthodontic archwires should be evaluated in parallel RCTs, reported according to the CONSORT statement and with detailed intervention and outcome data to justify their use.

Clinical relevance

Regarding initial archwires, superelastic NiTi archwire was not more effective in tooth alignment compared with conventional NiTi. Regarding sequences of archwires, use of a heat-activated NiTi archwire sequence was associated with greater pain intensity 4 h and 1 day after insertion of each archwire, but did not differ in terms of effectiveness from a conventional NiTi archwire sequence. Further studies are needed to justify the clinical superiority of any type of archwire used during orthodontic treatment over another.

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Conflict of interest

The authors report no commercial, proprietary, or financial interest in the products or companies described in this article.

Literature search update

An update of the systematic literature search was undertaken after acceptance of the paper on April first, 2014 in four databases (Cochrane Library, MEDLINE, Scopus, and ISI Web of Knowledge) using the same search strategies as listed in Table S1. After study selection, two additional eligible studies were identified (Gravina MA, Brunharo IH, Fraga MR, Artese F, Campos MJ, Vitral RW et al. Clinical evaluation of dental alignment and leveling with three different types of orthodontic wires. *Dental Press J Orthod* 2013;18:31–7 & Sandhu SS, Sandhu J. A randomized clinical trial investigating pain associated with superelastic nickel-titanium and multistranded stainless steel archwires during the initial leveling and aligning phase of orthodontic treatment. *J Orthod* 2013;40:276–85) and it was judged that they would not overly influence the review's conclusions. They are planned to be incorporated in a future update of the systematic review.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Search strategies used for each database with the corresponding results.

Table S2. Product names of brackets and archwires used in the included trials.

Table S3. Supplementary trial characteristics from Table 1.

Table S4. Supplementary trial characteristics from Table 2.