Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)

El-Angbawi A, McIntyre GT, Fleming PS, Bearn DR

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TABLE OF CONTENTS

Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)

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i

[Intervention Review]

Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment

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ABSTRACT

Background

Accelerating the rate of tooth movement may help to reduce the duration of orthodontic treatment and associated unwanted effects including root resorption and enamel demineralisation. Several methods, including surgical and non-surgical adjuncts, have been advocated to accelerate the rate of tooth movement. Non-surgical techniques include low-intensity laser irradiation, resonance vibration, pulsed electromagnetic fields, electrical currents and pharmacological approaches.

Objectives

To assess the effect of non-surgical adjunctive interventions on the rate of orthodontic tooth movement and the overall duration of treatment.

Search methods

We searched the following databases on 25 November 2014: the Cochrane Oral Health Group's Trials Register (November 2014), the Cochrane Central Register of Controlled Trials (CENTRAL; The Cochrane Library 2014, Issue 10), MEDLINE via OVID (1946 to November 2014), EMBASE via OVID (1980 to November 2014), LILACS via BIREME (1980 to November 2014), metaRegister of Controlled Trials (November 2014), the US National Institutes of Health Trials Register (ClinicalTrials.gov; November 2014) and the WHO International Clinical Trials Registry Platform (November 2014). We checked the reference lists of all trials identified for further studies. There were no restrictions regarding language or date of publication in the searches of the electronic databases.

Selection criteria

We included randomised controlled trials (RCTs) of people receiving orthodontic treatment using fixed appliances along with non-surgical adjunctive interventions to accelerate tooth movement. We excluded non-parallel design studies (for example, split-mouth) as we regarded them as inappropriate for assessment of the effects of this type of intervention.

Data collection and analysis

Two review authors were responsible for study selection, risk of bias assessment and data extraction; they carried out these tasks independently. Any disagreements were resolved by discussion amongst the review team to reach consensus. The review authors contacted the corresponding authors of trials to obtain missing information and data to allow calculation of mean differences (MD), 95% confidence intervals (CI) or risk ratios (RR) when these were not reported.

Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)

1

Main results

We included two studies in this review, which were both assessed as being at high risk of bias. The two studies, involving a total of 111 participants, compared the use of Tooth Masseuse and OrthoAccel with conventional treatment mechanics during orthodontic alignment and canine retraction phases, respectively. Both studies included objective assessment of the amount or rate of tooth movement, but we were not able to meta-analyse this data as they used different outcome measurements at different stages of the orthodontic treatment process. One study measured subjective evaluation of pain and discomfort and the other evaluated adverse effects. The studies did not directly report either the duration of orthodontic treatment or the number of visits during active treatment.

Using the Tooth Masseuse with 111 Hz at 0.06 Newtons (N) for 20 minutes daily resulted in greater reduction in irregularity in the lower incisor region over 10 weeks, assessed using Little's Irregularity Index (LII) with a mean difference (MD) of 0.6 mm (95% confidence interval (CI) -0.94 to 2.34) when compared to the control group. Pain and discomfort increased at six to eight hours after arch wire placement and after seven days, with minimal difference between the intervention and control groups. No statistical tests were provided for either variable and the differences between the two groups were not clinically important.

Using OrthoAccel with 30 Hz at 0.25 N for 20 minutes daily produced a higher rate of maxillary canine distalisation in comparison to the control group (MD 0.37 mm/month; 95% CI -0.07 to 0.81; P = 0.05). Whilst this difference suggested 50% faster tooth movement using the vibrational appliance, the absolute differences were marginal and deemed clinically unimportant. Similar levels of non-serious adverse effects were reported in the intervention and control groups with a risk ratio of 0.96 (95% CI 0.32 to 2.85).

Overall, the quality of the evidence was very low and therefore we cannot rely on the findings.

Authors' conclusions

There is very little clinical research concerning the effectiveness of non-surgical interventions to accelerate orthodontic treatment. The available evidence is of very low quality and so it is not possible to determine if there is a positive effect of non-surgical adjunctive interventions to accelerate tooth movement. Although there have been claims that there may be a positive effect of light vibrational forces, results of the current studies do not reach either statistical or clinical significance. Further well-designed and rigorous RCTs with longer follow-up periods are required to determine whether non-surgical interventions may result in a clinically important reduction in the duration of orthodontic treatment, without any adverse effects.

PLAIN LANGUAGE SUMMARY

Additional, non-surgical treatments for accelerating tooth movement in dental patients being treated with fixed braces

Review question
What effect do non-surgical adjuncts have on the length of time it takes for teeth to move when treated with fixed braces, and the overall time required for orthodontic treatment?

Background
Throughout the world, orthodontic treatment is used to correct the position of teeth in adolescents and adults when they experience problems. Braces are orthodontic appliances made up of brackets glued to the teeth and then connected by wires in order to exert pressure on the teeth to move them and improve their positioning. Depending on the problem, the length of time for treatment may range from several months to several years. However, most treatments take on average, around 24 months. Accelerating the rate of tooth movement may help to reduce the length of time needed for a course of treatment and may reduce the unwanted effects of orthodontic treatment that can sometimes occur, such as tooth decay and the shortening of the tooth root. Several methods, including surgical and non-surgical treatments, have been suggested to accelerate orthodontic tooth movement. The evidence relating to non-surgical procedures to accelerate orthodontic tooth movement is assessed in this review.

Study characteristics

Authors for the Cochrane Oral Health Group carried out this review of existing studies. The evidence on which it is based is current up to 26 November 2014.

We included two studies involving a total of 111 participants in this review. A single orthodontic specialist in a private practice in Australia carried out one study, while the other study was conducted on patients treated by orthodontic residents in a university hospital seating in the United States of America. In one study, the age of participants ranged from 11 to 15 years old, and in the second, the average age of participants was 21 years. The studies evaluated the additional use of two devices that use light vibrational forces - Tooth Masseuse in people receiving conventional fixed appliance treatment during the tooth alignment stage and OrthoAccel for those receiving conventional fixed appliance treatment for the space closure stage in orthodontic treatment. Participants receiving additional treatment with the devices were compared to those receiving only the conventional treatment. The trials evaluated different aspects of orthodontic tooth movement and side effects.

Key results

Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)

2

The studies evaluated three outcomes: rate of tooth movement; patient perception of pain and discomfort, and unwanted side effects. There were substantial differences between the studies, which meant that we were unable to combine the results.

From the limited evidence available, it is not possible to establish if the use of vibrational forces during treatment with fixed orthodontic appliances has a significant beneficial or harmful effect on either the rate of orthodontic tooth movement or the duration of treatment.

Quality of the evidence

The quality of evidence was very low.

Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)

3

SUMMARY OF FINDINGS

Summary of findings for the main comparison.

Non-surgical adjunctive interventions compared with conventional orthodontic treatment for accelerating the rate of orthodontic tooth movement

Patient or population: Orthodontic patients with malocclusion

Settings: Private orthodontic practice

Intervention: Non-surgical adjunctive interventions

Comparison: Conventional orthodontic treatment

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Partici-pants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Convention-al orthodontic treatment	Non-surgical adjunctive in-tervention				
Duration of active ortho-dontic treatment						Not investigated by included studies
Rate of tooth move-ment: reduction in the Little's irregularity in-dex (LII) during align-ment stage due to tooth movement during the first 10 weeks of the alignment stage in mm	The mean re-duction in the LII score in the control group was 3.4 mm	The mean re-duction in the LII score in intervention group was 0.6 mm higher (95% CI -0.94 to 2.34)		64 participants (1 study)	⊕⊝⊝⊝ **very low** [1]	• One study Miles 2012 • No statistical tests provided, however, confi-dence intervals indicate no statistical signifi-cant difference. • Outcome was also measured at 5 and 8 weeks with intervention group LII reduction 0.9 mm higher (95% CI -1.72 to 2.62) and at 0.3 mm higher (95% CI -0.95 to 1.55), respectively
Rate of tooth move-ment: rate of orthodon-tic tooth movement in the maxillary arch dur-ing space closure in mm/ month	The mean rate of tooth move-ment in the control group was 0.79 mm/ month	The mean rate of orthodontic tooth movement in the intervention groups was 0.37 mm/ month		45 participants (1 study)	⊕⊝⊝⊝ **very low** [2]	• One study Pavlin 2015 • Stratification was done for age (subgroups 12 to 19 years and 20 to 40). The authors did not report the outcome of each subgroup sepa-rately. • In this study the space closure was done by using either en masse retraction or canine retraction and that was according to sam-ple stratification during the randomisation

		higher (95% CI -0.07 to 0.81)				process. The author did not report the outcome of each group separately.
Improvement in occlusion						Not investigated by the included studies.
Patient-centred outcomes: Pain and discomfort using visual analogue scale (VAS; 0 to 100 mm)	The mean pain and discomfort VAS score was 47.6 in the control group after one day from ligating the arch wire	The mean pain and discomfort VAS score in the intervention groups was 6.1 points lower (95% CI -6.60 to 18.80)		64 participants (1 study)	⊕⊖⊖⊖ **very low**[1]	• One study Miles 2012 • No statistical tests provided, however, confidence intervals indicate no statistical significant difference. • Outcome was also measured at the time of ligation, 6 to 8 hours, 3 days and 7 days after initial arch wire, with intervention group VAS score 4.3 higher (95% CI -2.19 to 10.79), 0.8 higher (95% CI -11.37 to 12.25), 1.1 lower (95% CI -7.27 to 9.47) and 1.5 lower (95% CI -1.96 to 4.97) respectively. • Studies did not measure patient-centred outcomes of impact of fixed appliances on daily life and quality of life
Harms: Serious adverse effects	0	0	RR 1	45 participants (1 study)	⊕⊖⊖⊖ **very low**[2]	• One study Pavlin 2015 • No serious effects were reported for any of the study groups during treatment.
Harms: Non-serious adverse effects during treatment, including: gastrointestinal disorders, general disorders , injury, poisoning and procedural complications, musculoskeletal and connective tissue disorders, nervous system disorders and respiratory, thoracic and mediastinal disorders.	230 per 1000	220 per 1000 (74 to 656)	RR 0.96 (95% CI 0.32 to 2.85)	45 participants (1 study)	⊕⊖⊖⊖ **very low**[2]	• One study Pavlin 2015

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk Ratio.

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

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[1] Downgraded one level for limitation in design and implementation due to unclear risk of allocation bias, performance bias and other sources of bias. Downgraded one level for imprecision (single study Miles 2012). Also downgraded one level for indirectness of evidence (surrogate results).
[2] Downgraded one level for limitation in design and implementation due to unclear risk of selection bias, detection bias, attrition bias, reporting bias and other sources of bias. Downgraded one level for imprecision (single study Pavlin 2015). Also downgraded one level for indirectness of evidence (surrogate results).

Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)

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6

Cochrane Database of Systematic Reviews

BACKGROUND

Description of the condition

Deviation from a normal bite can be defined as malocclusion (Andrews 1972). It is a common dental problem with a range of prevalence among different ethnic populations, with more than a quarter of adolescents classified as being in need of orthodontic treatment (Migale 2009; Mtaya 2009; Tausche 2004). Malocclusion can cause aesthetic and functional problems, which can lead to a negative impact on quality of life (Dimberg 2015). Malocclusion is normally corrected using orthodontic treatment, which includes fixed or removable orthodontic appliances, or both.

There are clear benefits of effective and efficient fixed orthodontic treatment to patients, clinicians, and health service providers. Effective orthodontic treatment is accomplished by delivering planned treatment goals over the shortest time possible, with minimal biological side effects and high levels of patient satisfaction. The duration of orthodontic treatment may range from several months to several years, with the majority of comprehensive treatment taking approximately 24 months to complete (Mavreas 2008). This can be extended for patients with a severe malocclusion. Reducing treatment duration can limit the risk of undesirable effects and associated cost, and can increase patient satisfaction (Riedmann 1999; Segal 2004).

Several factors can influence the duration of treatment, including both patient-related and treatment-related aspects (Fisher 2010; Mavreas 2008). An increased duration of treatment is undesirable, due to the increased risk of exposing patients to additional biological side effects (e.g. root shortening or decalcification). Several conventional treatment modalities have been suggested to reduce the duration of orthodontic treatment (Germec 2008; Sebastian 2012). Similarly, in the last few decades, non-conventional adjunctive techniques have been developed to reduce treatment duration by accelerating the rate of tooth movement. These include surgical interventions (e.g. surgical corticotomy) and non-surgical interventions (e.g. low laser therapy and mechanical vibration).

Description of the intervention

The proposed non-surgical adjunctive interventions to accelerate orthodontic tooth movement include:

- Low energy laser radiation directed to the mucosa of the targeted teeth;
- Intermittent resonance vibration using an electrical appliance fitted into the orthodontic appliance or the teeth;
- Pulsed electromagnetic waves using integrated circuits placed in an oral appliance;
- Chewing gum or muscle exercise;
- Pharmacological methods; and
- Novel methods as they are described by authors.

These interventions are used during conventional fixed appliance orthodontic treatment therapy, and are undertaken by the clinician in a clinical setting during additional scheduled visits (e.g. low energy laser radiation), or can be fitted in an oral appliance and used by the patient on a daily or weekly basis following the clinician's prescription (e.g. pulsed electromagnetic waves and intermittent electrical vibration).

How the intervention might work

Orthodontic tooth movement occurs due to a sterile inflammatory process that results in bone resorption and deposition, which is known as bone remodelling (Zainal 2011). Bone cells (osteoclasts and osteoblasts) responsible for remodelling are the main target of non-surgical interventions for accelerating tooth movement. This is because it has been proposed that such interventions can act as a bio-stimulus to increase the activity of bone cells (Tortamano 2009). The increased bone remodelling rate can increase the rate of tooth movement, which may lead to a reduction in the duration of orthodontic treatment.

Why it is important to do this review

The Cochrane Oral Health Group undertook an extensive prioritisation exercise in 2014 to identify a core portfolio of titles that were the most clinically important ones to maintain on the Cochrane Library (Worthington 2015). Consequently, this review was identified as a priority title by the orthodontic expert panel (Cochrane OHG priority review portfolio).

The duration of treatment is an important aspect of successful and effective orthodontic therapy. Comprehensive fixed appliance orthodontic treatment usually takes about two years to complete and can be influenced by different factors, including patient-related and treatment-related aspects. Reduction in the duration of orthodontic treatment can reduce the exposure of patients to risks associated with treatment and related cost, and can increase patient satisfaction. This systematic review assessed the available evidence for the effect of non-surgical adjunctive interventions on the reduction of orthodontic treatment duration by accelerating orthodontic tooth movement. In addition, the effect on treatment outcome, biological side effects and patient perception were evaluated. This provides the orthodontic clinician with evidence about the effectiveness and safety of non-surgical adjunctive interventions for accelerating orthodontic tooth movement.

OBJECTIVES

To assess the effect of non-surgical adjunctive interventions for accelerating the rate of orthodontic tooth movement and reducing the duration of orthodontic treatment.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs), irrespective of publication status or language of publication. Non-parallel design studies (e.g. split-mouth) were determined to be inappropriate for this type of investigation. This is mainly because this type of study design may introduce 'carry-across effects' which potentially allow interventions to have effects on experimental units other than those to which they were assigned. There was no restriction in the length of follow-up.

Types of participants

We included studies of individuals, of any age, receiving orthodontic treatment with fixed appliances that incorporated the adjunctive use of non-surgical interventions to accelerate tooth movement. We excluded studies that included patients who were

treated with orthognathic surgery, participants with cleft lip or palate, or with other craniofacial syndromes or deformities, as these patients would routinely have a combination of orthodontic and surgical treatment, which can influence the outcome, duration and side effects of the treatment.

Types of interventions

- Active interventions: any form of fixed appliance orthodontic treatment incorporating the use of non-surgical adjunctive interventions for accelerating orthodontic tooth movement
- Control: any form of fixed appliance orthodontic treatment without the use of non-surgical adjunctive interventions for accelerating orthodontic tooth movement

Types of outcome measures

Primary outcomes

- Rate of tooth movement determined by millimetres of tooth movement per week or month
- Duration of active orthodontic treatment, number of visits during active treatment (scheduled and unscheduled), and duration of appointments

Secondary outcomes

- Improvement in occlusion, as judged using Peer Assessment Rating (PAR) or other validated scale, recorded at the completion of active orthodontic treatment
- Patient-centred outcomes: impact of fixed appliances on daily life, quality of life and pain experience
- Harms arising during the course of orthodontic treatment including gingival and periodontal problems, anchorage loss, and iatrogenic damage to teeth (e.g. caries or decalcification, root resorption)
- Prolonged stability of treatment outcome using validated methods, e.g. Little's irregularity index (LII)
- Cost of treatment
- Safety of the adjunctive intervention

Search methods for identification of studies

For the identification of studies included or considered for this review, we developed detailed search strategies for each database that was searched. These were based on the search strategy developed for MEDLINE, and revised appropriately for each database.

Electronic searches

We searched the following databases:

- The Cochrane Oral Health Group's Trials Register (November 2014; see Appendix 1);
- The Cochrane Central Register of Controlled Trials (CENTRAL; *The Cochrane Library 2014*, Issue 10; see Appendix 2);
- MEDLINE via OVID (1946 to November 2014; see Appendix 3);
- EMBASE via OVID (1980 to November 2014; see Appendix 4);
- LILACS via BIREME (1980 to November 2014; see Appendix 5).

The MEDLINE subject search was linked to the Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomised trials in MEDLINE: sensitivity maximising version (2008 revision)

as referenced in Chapter 6.4.11.1 and detailed in box 6.4.c of the *Cochrane Handbook for Systematic Reviews of Interventions* (Lefebvre 2011).

Searching other resources

We examined the reference lists of relevant articles and contacted the investigators of included studies by electronic mail to ask for details of additional published and unpublished trials.

Ongoing trials

We conducted searches using the following databases to identify ongoing trials (see Appendix 6 for details of the search strategy):

- *meta*Register of Controlled Trials (*m*RCT) (November 2014);
- US National Institutes of Health Register (November 2014);
- World Health Organization International Clinical Trials Registry Platform Search Portal (ICTRP; November 2014).

We also contacted manufacturers of non-surgical adjuncts designed to accelerate orthodontic treatment for details of unpublished or ongoing trials.

Language

There were no language restrictions applied in the searches of the electronic databases.

Data collection and analysis

Selection of studies

Two review authors (AE and DB) independently assessed the titles and abstracts of studies identified by the searches. Full copies were obtained of all relevant and potentially relevant studies, and for studies that appeared to meet the inclusion criteria but for which there were insufficient data in the title and abstract to make a clear decision. The full-text papers were independently assessed by two review authors (AE and GM). Any disagreement on the eligibility of an included study was resolved through discussion and consensus. From this group of full-text papers, we recorded the studies not meeting the inclusion criteria, with reasons for exclusion, in the Characteristics of excluded studies section of the review.

Data extraction and management

Two review authors (AE and GM) independently extracted data. We used data extraction forms recording the year of publication, country of origin and details of the participants including demographic characteristics and the criteria for inclusion. We entered the study details into the Characteristics of included studies tables in Review Manager (RevMan) 5.3 (RevMan 2014). Any disagreements were resolved by consulting with a third review author.

The following details were also extracted if reported.

1. Trial methods: (a) allocation method; (b) sample size calculation; (c) masking of participants, trialists and outcome assessors; (d) exclusion of participants after randomisation and the proportion and reasons for sample attrition at follow-up.
2. Participants: (a) country of origin and study setting; (b) sample size; (c) age; (d) gender; (e) inclusion and exclusion criteria.
3. Intervention: (a) type; (b) materials and techniques used; (c) time of follow-up.

4. Control: (a) type; (b) materials and techniques used; (c) time of follow-up.
5. Outcomes: (a) primary and secondary outcomes mentioned in the Types of outcome measures section of this review.

Where stated, we recorded sources of funding. The review authors used this information to aid their assessment of investigator reporting bias and the validity of included trials.

Assessment of risk of bias in included studies

Two review authors (AE and GM) independently assessed the risk of bias for the selected trials using Cochrane's tool for assessing risk of bias, as described in section 8.5 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011a). We produced a 'Risk of bias' table for each included study in two parts. For each domain, we provided a description of what was reported to have happened in part one, whilst for the second part, we used this information to judge whether the risk of bias was low, high or unclear. The two review authors compared their assessments; any inconsistencies between them were discussed and resolved.

We assessed the following domains as being at low, high or unclear risk of bias:

- random sequence generation (selection bias);
- allocation concealment (selection bias);
- blinding of participants and personnel (performance bias);
- blinding of outcome assessors (detection bias);
- incomplete outcome data addressed (attrition bias);
- selective outcome reporting (reporting bias);
- other bias.

We categorised and reported the overall risk of bias of each included study according to the following:

- low risk of bias (plausible bias unlikely to seriously alter the results) if all domains were assessed at low risk of bias;
- unclear risk of bias (plausible bias that raises some doubt about the results) if one or more domains were assessed at unclear risk of bias; or
- high risk of bias (plausible bias that seriously weakens confidence in the results), if one or more domains were assessed at high risk of bias.

Measures of treatment effect

We calculated mean differences (MD) with 95% confidence intervals (CI) for continuous data, and risk ratios (RR) with 95% CI for dichotomous data. We contacted the corresponding authors of trials for original data where necessary.

Unit of analysis issues

We had anticipated that some of the included studies may have presented participant data from repeated or multiple site observations, or both, which may have lead to unit of analysis errors. Had this been the case, we would have followed the advice provided in section 9.3.4 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2011).

Dealing with missing data

In studies where data were unclear or missing, we contacted the principal investigators. If missing data were unavailable, we followed the advice given in section 16.1.2 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011b).

Assessment of heterogeneity

We assessed clinical heterogeneity by examining the characteristics of the studies, the similarity between the types of participants, the interventions and the outcomes, as specified in the criteria for included studies. We had intended to assess statistical heterogeneity using a Chi² test and the I² statistic, but this was not possible. We would have considered heterogeneity to be significant for the Chi² test when the P value was less than 0.10, with I² values of 30% to 60% indicating moderate heterogeneity, and over 60%, substantial heterogeneity (Higgins 2003).

Assessment of reporting biases

We had intended to assess publication bias according to the recommendations on testing for funnel plot asymmetry if a sufficient number of studies assessing similar interventions were identified for inclusion in this review, as described in section 10.4.3.1 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Sterne 2011). If asymmetry had been identified, we had planned to assess other possible causes and explore these in the discussion.

Data synthesis

We had planned to carry out meta-analyses where there were studies of similar comparisons reporting the same outcomes. We had planned to synthesise mean differences for continuous data, and risk ratios for dichotomous data. We had planned to use the fixed-effect model for meta-analyses. However, meta-analysis was not possible. We used additional tables to present the results from the included studies.

Subgroup analysis and investigation of heterogeneity

If a sufficient number of studies had been included with moderate, substantial or considerable heterogeneity (see Assessment of heterogeneity), we had planned to carry out subgroup analyses according to:

- type of non-surgical method used;
- age category (adolescents versus adults).

Sensitivity analysis

Had meta-analysis been possible, we would have performed sensitivity analyses, excluding studies with a high or unclear risk of bias.

Presentation of main results

Using GRADEPro software (GRADEpro 2014), we produced Summary of findings for the main comparison for the following outcomes, listed by priority.

1. Rate of tooth movement
2. Duration of orthodontic treatment, number of visits during active treatment (scheduled and unscheduled), and duration of appointments

3. Improvement in occlusion
4. Patient-centred outcomes: impact of fixed appliances on daily life, quality of life and pain experience
5. Harm arising during the course of orthodontic treatment: including gingival and periodontal problems, anchorage loss and iatrogenic damage to teeth (e.g. caries or demineralisation, root resorption)

We assessed the quality of the evidence as high, moderate, low or very low, with reference to the overall risk of bias for the included studies, the directness of the evidence, the inconsistency of the results, the precision of the estimates and the risk of publication bias.

RESULTS

Description of studies

See Characteristics of excluded studies and Characteristics of included studies.

Results of the search

The electronic searches identified 323 references with a further single reference identified through other sources. We examined the titles and abstracts of these studies for eligibility and eliminated all of those not matching the inclusion criteria. Seven potentially relevant studies were identified. We obtained full-text articles of two studies (Miles 2012; Pavlin 2015), and registry entries for six ongoing studies, one of which was the study registration for Pavlin 2015, and subjected them to further evaluation. After further assessment, we eliminated three of the registered ongoing studies as they had a split-mouth design (NCT02181439; IRCT138804022066N1; CTRI/2012/03/002488). Two potentially eligible ongoing studies are awaiting assessment as the trial authors were still recruiting participants (NCT02119455; JPRN-UMIN000013722). Although several attempts were made by the review authors to contact the authors of Pavlin 2015 using the correspondence address in the study registration, there was no response until the results were published, so the initial assessments were completed on the study registration information. Figure 1 shows the study selection process.

Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)

10

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Figure 1. Study flow diagram


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┌─────────────────────┐   ┌─────────────────────┐
│ 553 records         │   │ 1 additional        │
│ identified through  │   │ record identified   │
│ database            │   │ through other       │
│ searching           │   │ sources             │
└─────────────────────┘   └─────────────────────┘
              │                      │
              └──────────┬───────────┘
                         ▼
          ┌─────────────────────────┐
          │ 324 records left after  │
          │ duplicates removed      │
          └─────────────────────────┘
                         │
                         ▼
          ┌─────────────────────┐       ┌─────────────────────┐
          │ 324 records         │──────▶│ 316 records         │
          │ screened            │       │ rejected            │
          └─────────────────────┘       └─────────────────────┘
                         │
                         ▼
          ┌─────────────────────┐       ┌─────────────────────┐
          │ 7 studies (8        │       │ 3 studies           │
          │ reports)            │       │ excluded for        │
          │                     │       │ following reasons:  │
          │  • 2 full-text      │──────▶│                     │
          │    article          │       │  • split-mouth      │
          │  • 6 registered     │       │    design           │
          │    ongoing          │       │                     │
          │    study            │       └─────────────────────┘
          │    protocols        │
          └─────────────────────┘
                         │
                         ▼
          ┌─────────────────────┐
          │ 2 studies (3        │
          │ reports) included   │
          │                     │
          │ 2 were ongoing      │
          │ studies             │
          └─────────────────────┘
                         │
                         ▼
          ┌─────────────────────┐
          │ No studies          │
          │ included in         │
          │ quantitative        │
          │ synthesis           │
          │ (meta-analysis)     │
          └─────────────────────┘
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Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)   **11**

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Included studies

We included two studies in this review, reported in three publications (Miles 2012; Pavlin 2015). The two studies were designed to assess the influence of vibrational appliances as an adjunctive intervention on the rate of tooth movement. Both studies obtained ethical approval prior to commencement of the studies and recruitment of participants.

Characteristics of the trial settings and investigators

We included two studies in the current review. In Miles 2012, the treatment was carried out by a single specialist orthodontist in private orthodontic practice in Australia. In the Pavlin 2015 study, the patients received treatment at The University of Texas Science Centre Division of Orthodontics in the United States of America. The patients were treated by orthodontic residents under supervision of faculty members.

Miles 2012 investigated the reduction in irregularity for the mandibular anterior teeth during the first 10 weeks of fixed appliance orthodontic treatment at several time points (5, 8, and 10 weeks from the start of treatment). Pavlin 2015 assessed the rate of orthodontic movement of a maxillary canine tooth being distalised to close an extraction space for an average of 22 weeks.

Characteristics of the participants

A total of 111 participants (43 male and 68 female) were involved in the two studies (Miles 2012; Pavlin 2015). In Miles 2012, the age range of the participants (N = 66) was 11.1 to 15.7 years, with a similar mean age in the control and experiential groups of 13.1 (SE ± 0.18) years and 13.0 (SE ± 0.18) years, respectively; with more females (N = 40) recruited in the study than males (N = 26). The participants had a non-extraction orthodontic treatment plan with no impacted teeth requiring alignment. However, limited information was provided regarding the pre-treatment malocclusion. Little's Irregularity Index scores pre-treatment were 4.9 mm (SD ± 2.5) and 6.2 mm (SD ± 3.7) for the control and the experimental groups, respectively.

In Pavlin 2015, the average age of the participants (N = 45) was 21.6 (SD ± 8.2) years, with a similar mean age in the control and experiential groups of 21.4 (SD ± 7.8) and 21.8 (SD ± 8.7) years, respectively; more females (N = 28) were recruited in the study than males (N = 17). Participants had a minimum of 3 mm of extraction space that was to be closed by moving the maxillary canine distally. All participants received standard orthodontic treatment and temporary anchorage devices for tooth movement and space closure.

Characteristics of the interventions

A vibrational appliance was applied to the teeth for 20 minutes daily in the two studies to accelerate tooth movement, either to facilitate orthodontic space closure (Pavlin 2015), or to accelerate the alignment of the mandibular anterior teeth (Miles 2012). The device had a mouthpiece for the patient to lightly bite into with a linked extra-oral enclosure. The device provided a light vibrational force.

In the Miles 2012 study, the vibration appliance (Tooth Masseuse), which provided a vibrational frequency of 11 Hz and 0.06 Newtons (N; ~6.1 g), was applied immediately after the initial arch wire (0.014 inch NiTi) was placed, to accelerate the alignment of the mandibular anterior teeth. The same arch wire remained in place through the whole experimental period (10 weeks), and the participants were instructed to use the vibrational appliance daily for 20 minutes each session.

In the Pavlin 2015 study, the vibration appliance (OrthoAccel Device), which provided vibrational frequency of 30 Hz and 0.02 N, was applied to accelerate closing the extraction space, achieved by moving the maxillary anterior and canine teeth en masse, or the canine tooth distally, with the aid of a temporary anchorage device.

Characteristics of the outcomes

Outcomes assessed included primarily objective assessments of the amount and rate of tooth movement, in addition to subjective pain and discomfort experiences.

Specific clinical outcomes included:

1. Tooth movement: Miles 2012 assessed the amount of tooth alignment by measuring the reduction in the irregularity using Little's Irregularity Index (LII) at 0, 5 , 8 and 10 weeks after starting treatment. Pavlin 2015 assessed the rate of tooth movement per month by measuring the rate of maxillary canine distalisation to close an extraction space using a temporary anchorage device for an average of 22 weeks.

2. Pain experience: Miles 2012 investigated the levels of pain and discomfort during tooth alignment at five different time points (immediately after initial placement of fixed appliances, six to eight hours after, one day after, three days after, and at seven days) by asking participants to record pain and discomfort levels using a visual analogue scale.

The studies presented the outcome results as continuous data describing the mean and standard deviation, and dichotomous data describing participant numbers affected per study group. No statistical test results to compare the intervention outcomes were clearly mentioned in either of the studies. We considered a clinically significant difference would be a difference that could potentially have an impact on the overall duration of treatment.

Excluded studies

We excluded three ongoing studies due to a split-mouth study design (see Characteristics of excluded studies).
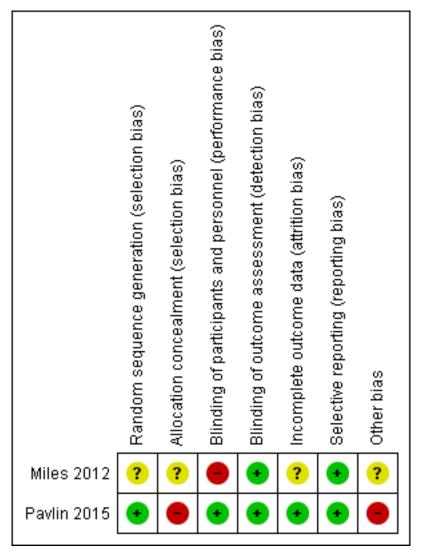
Risk of bias in included studies

Neither of the included studies had a low risk of bias in all of the domains. We assessed both as being at high risk of bias.

Further details of these assessments are given in the 'Risk of bias' table corresponding to each study in the Characteristics of included studies section. Overall ratings are also presented in the 'Risk of bias' summary in Figure 2.

Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)

12

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Figure 2.   Risk of bias summary: review authors' judgements about each risk of bias item for each included study

Allocation

Selection bias can be minimised when participants and study personnel cannot foresee the upcoming assignment. Pavlin 2015 clearly mentioned the randomisation procedure: "A third-party vendor provided computer generated randomisation scheduled with a block size of 4 and stratified"; however, the allocation concealment was not described. Miles 2012 reported "participants were randomly assigned in blocks of six"; however, the authors did not describe the randomisation method or the allocation concealment, so the risk of selection bias was unclear.

Blinding

Performance bias can be reduced by blinding both participants and study personnel to the type of intervention allocated. However, this can sometimes be unavoidable due to the nature of the intervention. In Miles 2012, although the clinician was blinded, the participants were not blinded to the type of intervention to which they were allocated; the study was rated as high risk of performance bias. Pavlin 2015 had a low risk of performance bias as the participants were blinded to the type of intervention allocated, and the control group participants were given a sham device,

which is an inactive device that was held in the mouth and looked identical to the active devices, but did not deliver any vibration.

Detection bias was rated as low risk in both Miles 2012 and Pavlin 2015 as the outcome investigator was blinded during data collection.

Incomplete outcome data

Miles 2012 reported incomplete outcome data with no clear description of how the missing data was dealt with. For the rate of orthodontic tooth movement outcome, two (3%) participants out of 66 were lost to follow-up; all the dropouts were from the experimental group. For the discomfort and pain outcome, there were eight (12.1%) dropouts (participants who did not complete VAS at the five time points) out of 66 study participants, five from the control group and three from the experimental group. Miles 2012 was assessed as unclear risk of bias, as it was not clear if the authors accounted for the missing data.

In Pavlin 2015, nine participants out of 45 (20%) were lost to follow-up, with five dropouts from the experimental group and four from the control group. However, the study was assessed as low risk

of bias as the authors accounted for the missing data by applying Intention-to-treat analysis.

Selective reporting

In Miles 2012, although the study protocol was not available, the outcomes listed in the 'Methods' section were comparable to the reported results. However, it was noticed that the results of the statistical tests (P value) comparing the two study groups were not reported. In general, we assessed the study as low risk of reporting bias.

The Pavlin 2015 study was registered in Clinicaltrials.gov, with all the proposed outcomes reported in an article in a peer-reviewed journal. The study was assessed as low risk of bias.

Other potential sources of bias

In Miles 2012, the pain and discomfort participant rating using VAS for the lower anterior teeth may have been confounded by the presence of upper fixed appliances, with the potential of influencing pain and perceived discomfort in the investigated lower arch. It was unclear whether the authors had planned to assess pain and discomfort for both arches or the lower arch only.

Pavlin 2015 was sponsored by OrthoAccel Technologies Inc, which is the manufacturer of the intervention appliance. It was mentioned on the clinicaltrial.gov website that there was a time-limited agreement between the principal investigators and the sponsor to review results before release to the public: "There is an agreement between Principal Investigators and the Sponsor that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is less than or equal to 60 days. The sponsor cannot require changes to the communication and cannot extend the embargo." We assessed the study at high risk of bias for other potential sources of bias.

In Pavlin 2015, it was not clear if the primary outcome measure for the rate of orthodontic tooth movement was for the canines only or en masse retraction of the six anterior teeth. Although stratification was done according to age and the technique of space closure (canine versus en masse retraction), the authors did not present the distribution and outcome for the technique of space closure subgroups. This may have influenced the rate of space closure in each group.

Effects of interventions

See: **Summary of findings for the main comparison**

Vibrational appliances as an adjunct to fixed braces versus conventional fixed braces treatment (control)

Primary outcomes

Rate of tooth movement

Both studies measured the rate of orthodontic tooth movement; however, different teeth and types of tooth movements were investigated in each study. Miles 2012 investigated the reduction in Little's Irregularity Index (LII) scores for the anterior mandibular teeth during the alignment stage for 10 weeks; while Pavlin 2015 investigated the rate of canine distalisation during the space closure stage in millimetres per month for an average of 22 weeks.

Due to the aforementioned clinically significant methodological differences between the two studies, we were unable to combine the outcomes in a meta-analysis. Therefore, the results for each study are discussed individually below.

Influence of a vibrational appliance versus conventional treatment (control) on the rate of anterior mandibular tooth movement during the alignment stage

Miles 2012 involved analysis of 64 children comparing vibrational appliance versus conventional treatment (control) by measuring the reduction in the LII score over 5, 8 and 10 weeks. This trial was judged to be at high risk of bias. The reduction in the LII score was higher in the intervention group with MD of 0.9 mm (95% CI -1.72 to 2.62) at 5 weeks; 0.3 mm (95% CI -0.95 to 1.55) at 8 weeks; and 0.7 mm (95% CI -0.94 to 2.34) at 10 weeks. No statistical tests were provided for the comparison between the two groups; however, based on the confidence intervals calculated, we concluded that there was no statistical difference between the two groups (Table 1).

Influence of vibrational appliance versus conventional treatment with placebo (control) on the rate of canine distalisation during the space closure stage

Pavlin 2015 was assessed to be at high risk of bias and analysed 45 people aged 12 to 40 years. The investigators compared the use of a vibrational appliance as an adjunct to fixed braces versus conventional fixed braces treatment with a placebo (control) by measuring the rate of maxillary canine distalisation during space closure to close a minimum of 3 mm space with average follow-up of 22 weeks. The authors reported that the difference in the rate of tooth movement (MD 0.37 mm/month; 95% CI -0.07 to 0.81) was statistically significant P = 0.05 (Table 2). However, based on the confidence intervals calculated for the mean differences, we concluded that there was no statistical difference between the two groups. In addition, the reported mean difference was considered to be clinically insignificant.

Duration of active orthodontic treatment

Neither of the included studies evaluated the influence of the vibrational appliance on the overall duration of orthodontic treatment. We felt that It was difficult and inaccurate to estimate the impact of the intervention on the overall duration of treatment from the available data.

Secondary outcomes

Patient-centred outcome: Pain and discomfort

Miles 2012

The participants from the intervention and control groups were instructed to record the level of discomfort at five different time points using a 100 mm visual analogue scale (Table 3). It was noted that pain and discomfort increased after six to eight hours after arch wire placement and dropped again after seven days, with minimal difference between the intervention and the control group. No statistical tests were provided for the comparison between the two groups; however, based on the confidence intervals calculated for the mean differences, we concluded that there was no statistical difference between the two groups. In addition, the difference between the two groups was considered clinically insignificant (Table 3).

Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)

14

Harms arising during the course of orthodontic treatment

Pavlin 2015

No serious adverse effects were reported in either the intervention or the control group during the study. A similar number of minimal non-serious adverse effects were reported in the Intervention group 5/23 (21.74%) and control group 5/22 (22.73%), with a RR of 0.96 (95% CI 0.32 to 2.85). The non-serious adverse effects included gastrointestinal disorders, general disorders, injury, poisoning and procedural complications, musculoskeletal and connective tissue disorders, nervous system disorders, and respiratory, thoracic and mediastinal disorders.

Other outcomes

None of the secondary outcomes mentioned below was investigated in either of the two included studies.

- Patient-centred outcomes: impact on daily life, quality of life
- Improvement in occlusion, as judged using a validated scale recorded at the completion of active orthodontic treatment
- Prolonged stability of treatment outcome using validated methods
- Cost of treatment

D I S C U S S I O N

Summary of main results

See Summary of findings for the main comparison for a summary of the main results.

Rate of tooth movement

The finding of the difference in reduction of Little's Irregularity Index (LII) in Miles 2012 is difficult to interpret due to the pre-treatment difference between the two groups, with the intervention group having a higher initial LII and therefore greater possibility for a reduction to be achieved. Given that this is the only included study that investigated tooth movement during alignment, and it was assessed at a high risk of bias, it is not possible to draw any conclusions on the data presented on rate of tooth movement.

Although Pavlin 2015 reported a mean difference of 0.37 mm/month (95% confidence interval (CI) -0.07 to 0.81) in the rate of canine distalisation between the two groups, which was reported to be statistically significant (P = 0.05); this has to be considered with caution. First, the reported 95% confidence interval did not confirm that the difference was statistically significant as it included zero (95% CI -0.07 to 0.81). Second, the reported difference is considered to be clinically insignificant.

Both studies assessed the rate of tooth movement as a primary outcome. However, it was not possible to combine the data from the two studies. Miles 2012 reported no significant advantage in the use of vibrational appliances on the rate of alignment of anterior teeth, while Pavlin 2015 demonstrated that vibrational appliances could increase the rate of canine distalisation during extraction space closure (see Table 2). It is important to mention that neither of the studies presented a mean difference that we deemed to be of clinical significance for the duration investigated.

Pain and discomfort during treatment

Miles 2012 reported no advantage in the use of a vibrational appliance in reducing pain and discomfort during the first week of fixed orthodontic appliance treatment, whilst Pavlin 2015 did not investigate pain and discomfort during treatment.

Harms during treatment

Pavlin 2015 reported no increase in the adverse effects due to the use of a vibrational appliances during orthodontic treatment. Miles 2012 did not measure harms.

Overall completeness and applicability of evidence

Currently, the evidence for non-surgical adjunctive interventions to increase the rate of tooth movement is incomplete. There are no data available for some interventions and the data for light vibrational forces is at high risk of bias with methodological flaws, meaning no conclusions can be drawn.

The participants in both studies are representative of the patient groups that would be treated in the majority of orthodontic settings, although the heterogeneity in Pavlin 2015 due to the mixture of children and adults compromises this. The LII used by Miles 2012 is a composite measure of irregularity so can be misleading when converted into millimetres per month of tooth movement for comparison. The latter is easier to interpret when appropriate, and was used by Pavlin 2015 .

It is important to note that in addition to the high risk of bias reported in the two included studies, the full orthodontic treatment duration and the reported outcomes cannot be considered to be representative of the entire orthodontic treatment duration. In other words, applying these results to the full duration of treatment is not realistic. It is important to interpret these results with caution as the methodology used for data collection was not described clearly and the study was rated as being at high risk of bias.

Quality of the evidence

We could not adequately assess the risk of bias in Miles 2012 due to the lack of information provided, but there was the possibility of allocation, attrition and other risks of bias. For Pavlin 2015, although the majority of domains were considered low risk of bias, the overall risk was assessed as high risk of bias due to the high risk of selection bias and other bias. Imprecision could have been avoided in both studies with appropriate sample sizes.

We downgraded the evidence by one level in respect of limitations in the study design, one for imprecision due to the small number of participants, and one for indirectness due to the use of surrogate outcomes as only the initial aligning stage of orthodontic treatment was assessed and the effect on overall treatment duration cannot be extrapolated from this. The overall quality of the evidence is therefore considered to be very low.

Potential biases in the review process

We used a broad search strategy with no language restrictions, and assessments were made independently by multiple authors. We are not aware of any biases in the review process. We excluded several published and ongoing studies because they were split-mouth studies. At this time, we believe that the potential cross-over effects of this design introduces a great risk of bias if we include this

Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)   **15**

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study design. The authors will continue to review this decision as evidence emerges from these ongoing studies.

Agreements and disagreements with other studies or reviews

In the last two years, several systematic reviews have been conducted to assess the effects of several types of surgical and non-surgical interventions in accelerating tooth movement (Gkantidis 2014; Kalemaj 2015; Long 2013). It was noticed that there is a lack of agreement amongst the reviews with regards to the reported effectiveness of some of the non-surgical interventions and the quality of evidence assessed. Gkantidis 2014 reported that there is moderate to weak evidence that non-surgical interventions (low energy laser, photobiomodulation or pulsed electromagnetic fields) can accelerate tooth movement. In contrast, Long 2013 suggested that low-level laser therapy is safe but unable to accelerate orthodontic tooth movement. Kalemaj 2015 reported that there is some evidence that low-level laser therapy can accelerate orthodontic tooth movement to a limited clinically insignificant degree. The inconsistency can be explained by the difference in the studies included in each review and the quality of evidence: Long 2013 and Gkantidis 2014 included RCTs and controlled clinical trials, while Kalemaj 2015 included RCTs including split-mouth design.

We decided to only include RCTs in this review. In addition, we excluded split-mouth design RCTs due to the potential for cross-over effect, which can potentially influence the assessed outcomes.

This explains the difference between our conclusion and the previously mentioned reviews.

AUTHORS' CONCLUSIONS

Implications for practice

There is insufficient evidence to conclude whether or not there is a positive effect of non-surgical adjunctive methods to accelerate tooth movement. Although there have been claims that there may be a positive effect of light vibrational forces, the results of the current studies do not reach either statistical or clinical significance and are at high risk of bias.

Implications for research

There is a clear need for well-designed and reported randomised clinical studies of the proposed non-surgical adjunctive methods to accelerate tooth movement. Due to cross-over effects, we would recommend that split-mouth designs are avoided. Future studies need to have sufficient number of participants to detect any clinically and statistically significant differences.

ACKNOWLEDGEMENTS

Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)

16

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Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)

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17

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)

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18

Miles 2012

Methods	Allocation: Randomised controlled trial
	Setting: Private practice, Pennsylvania, United States of America
	Sample size calculation: Calculated as 90% at 0.05 level to detect 20% faster alignment and reduction in irregularity
	Dropouts: 2 out of 66 participants did not complete the trial. The authors did not mention the reasons
Participants	66 participants with fixed orthodontic appliance 0.018 inch bracket slot system
	• Age 11 to 15 years old
	• Non-extraction treatment plan in the lower arch
	• No impacted or unerupted teeth
	• Participants living close to the orthodontic practice
Interventions	One Intervention group and one control group. Initial alignment of the lower anterior teeth using 0.018 x 0.025-inch bracket slot system brackets and 0.014-inch nickel titanium arch wire for 10 weeks.
	Intervention: The vibration appliance (Tooth Masseuse), which provided a vibrational frequency of 11 Hz and 0.06N (~6.1 g), was applied immediately after the initial arch wire was placed, to accelerate the alignment of the mandibular teeth. The participants were instructed to use the vibrational appliance daily for 20 minutes each session.
	Control: treated with initial arch wire only.
Outcomes	Primary outcome
	• The amount of tooth alignment measured by the reduction in the irregularity using Little's Irregularity Index at 0, 5 , 8 and 10 weeks of starting treatment.
	Secondary outcome
	• Pain and discomfort levels using visual analogue system during teeth alignment at 5 different time points (immediately after initial braces placement, 6 to 8 hours after fitting the braces, 1 day after, 3 days after and 7 days after)
Notes	Several attempts to contact authors with no response (invalid email address)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomly allocated in blocks of 6 as mentioned in page 214 "randomly assigned in blocks of six"
		No mention of how the randomisation was created
Allocation concealment (selection bias)	Unclear risk	No mention of allocation method
Blinding of participants and personnel (performance bias) All outcomes	High risk	Clinician and investigator blinded but not the participants as mentioned on page 216: "The clinician was blinded to the study participants at all appointments. Identification numbers were assigned to the models prior to the measurements to ensure blinding". When the participant is not blinded, it can influence the visual analogue scale (VAS) scoring for discomfort, which is scored by the participant.

Miles 2012 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessors were blinded during assessment, as mentioned on page 216: "Identification numbers were assigned to the models prior to the measurements to ensure blinding"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No mention of how missing data from participants who dropped out were dealt with, e.g. intention-to-treat analysis
Selective reporting (reporting bias)	Low risk	All planned outcomes reported, although neither P value for statistical testing of data nor the confidence intervals were reported. No protocol published
Other bias	Unclear risk	Pain may have occurred in other teeth in the lower or upper arch, which could have resulted in bias. The study appeared to be free of other forms of bias

Pavlin 2015

Methods	Allocation: Randomised Setting: Unknown Sample size calculation: "two-sided alpha of 0.05, and 80% power, a sample size of 16 subjects per group (total of 32) was required to detect a statistically significant difference between the groups" Intervention model: Parallel assignment with stratification "generated randomization schedule with a block size of 4 and stratified to insure that the number of subjects aged 12–19 years and aged 20–40 years, as well as the number of subjects with "separate canine retraction" versus "en masse retraction" were equally distributed between the groups." Dropouts: 9 out of 45 participants did not complete the trial
Participants	Age: 12 to 40 years Gender eligible for study: Both Accepts healthy volunteers: No Number of participants: 45 Inclusion criteria - Permanent dentition between the ages of 12 and 40 - Participants had maxillary first premolars extracted as part of the orthodontic treatment - Minimum of 3 mm of extraction space to be closed by distal movement of all 6 anterior teeth from canine to canine or by distal movement of the canines - Good oral hygiene and compliance Exclusion criteria - Any compromised medical or dental condition - Participant currently involved in any other study, lives significantly outside San Antonio, or both - Use of bisphosphonates - Pregnant females
Interventions	One intervention group and one control group

Pavlin 2015 *(Continued)*

- Intervention: OrthoAccel device provides a light vibration at 0.25 Newtons and 30 Hz frequency for 20 minutes daily.
- Control: Inactive sham device that is held in the mouth for 20 minutes a day.

Outcomes	**Primary outcome**
	- The rate of orthodontic movement of a maxillary canine tooth being distalised to close an extraction space.
	Secondary outcome
	- Adverse effects during treatment.
Notes	Study start date February 2009. Completed November 2011.
	Several attempts to contact authors and the sponsoring company with no response.
	The study was published as a peer reviewed article in September 2015 (Pavlin 2015).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Described as randomised clinical trial but no details provided "A third-party vendor provided a computer-generated randomization schedule with a block size of 4 and stratified to insure that the number of subjects aged 12–19 years and aged 20–40 years, as well as the number of subjects with "separate canine retraction" versus "en masse retraction" were equally distributed between the groups"
Allocation concealment (selection bias)	High risk	No mention of allocation method
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participant blinding: intervention and sham device nearly identical Operator blinding: "both the investigators and the subjects remained blinded to treatment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessor blinding: "Masking: Single Blind (Outcomes Assessor)" "The device was programmed to the assigned treatment by independent site personnel and both the investigators and the subjects remained blinded to treatment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Intention-to-treat analysis was done. From the data, the authors state the number analysed as N = 45, with a mention of the number of dropouts in each group.
Selective reporting (reporting bias)	Low risk	All outcomes outlined in the study registration were reported in the full article.
Other bias	High risk	The study was sponsored by OrthoAccel Technologies Inc, which is the manufacturer of the intervention appliance. It was mentioned in the clinicaltrial.gov registration that there was a time limited agreement between the principle investigator and the sponsor to review results before release to public: "There is an agreement between Principal Investigators and the Sponsor that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is less than or

Pavlin 2015 *(Continued)*

equal to 60 days. The sponsor cannot require changes to the communication and cannot extend the embargo."

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
CTRI/2012/03/002488	Study protocol evaluated, split-mouth randomised clinical trial
IRCT138804022066N1	Study protocol evaluated, split-mouth randomised clinical trial
NCT02181439	Study protocol evaluated, split-mouth randomised clinical trial

Characteristics of ongoing studies *[ordered by study ID]*

JPRN-UMIN000013722

Trial name or title	The effect of vibration on acceleration of orthodontic tooth movement
Methods	Cross-over, randomised, double blind - all involved are blinded
Participants	60 participants with malocclusion having fixed appliance orthodontic treatment
Interventions	To reveal the effect of vibration on acceleration of orthodontic tooth movement
Outcomes	Tooth movement Velocity of tooth movement Root resorption Evaluation about pain
Starting date	18/04/2014
Contact information	t-yamamo@m.tohoku.ac.jp
Notes	Several attempts to contact authors with no response http://apps.who.int/trialsearch/Trial2.aspx?TrialID=JPRN-UMIN000013722

NCT02119455

Trial name or title	Biomarkers of Orthodontic Tooth Movement With Fixed Appliances and Vibration Appliance Therapy
Methods	Allocation: Randomised Intervention Model: Parallel Assignment Masking: Single Blind (Outcomes Assessor) Primary Purpose: Treatment
Participants	Estimated number: 40 participants Age: 15 to 35 years

Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)

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22

Both genders

Inclusion criteria:

- Healthy, non-smoker with no systemic medical conditions and no routine medications
- 15 to 35 years of age at the time of bonding
- Non-extraction treatment plan or no extractions required in the first 6 months of treatment
- At least 5 mm of crowding in the mandibular arch
- Full-complement dentition 1st molar to 1st molar
- Good oral hygiene.

Exclusion criteria:

- Patients that require extractions as part of the orthodontic plan.
- Smoking or excessive alcohol consumption.
- Patients with edentulous areas
- Evidence of periodontal disease (any pocket depths more than 4 mm)
- Use of anti-inflammatory drugs within 2 days of bonding
- Active oral lesions (ulcerations, sores, mucositis, etc.)
- Uncontrolled diabetes
- Dentofacial deformities (cleft palate, hemifacial microsomia, etc.)
- Subjects routinely taking any of the following medications: Corticosteroids (including for asthma), bisphosphonates anti-inflammatories, nicotine patch, oestrogen, Opioids, growth Hormone, relaxin or anti-coagulants.
- Disease that could affect bone metabolism: Parathyroid or thyroid dysfunction, Osteoporosis, osteomalacia Vitamin D deficiency, fibrous dysplasia, Paget's Disease, multiple myeloma, osteogenesis Imperfecta, history of bone metastasis.

Interventions	Device: Vibration Device Subjects receiving the OrthoAccel Aura device will be instructed to use the device for 20 minutes/day per the manufacturer's instructions during the study period. The purpose of this study is to identify novel biological factors that are expressed in patients undergoing orthodontic tooth movement in conjunction with vibration appliance therapy and assess the rate of orthodontic alignment of mandibular anterior teeth.
Outcomes	Primary Outcome Measures: Changes in the expression of salivary biomarkers of bone remodeling (Time Frame: Up to Week 17 of alignment). Secondary Outcome Measures: • Alignment of Mandibular Anterior Teeth (Time Frame: Up to Week 17). The alignment will be evaluated using Little's Irregularity Index where the rate of tooth movement can be calculated. • Tooth Mobility (Time Frame: Up to Week 17). The degree of tooth mobility will be used, using a Periotest device (Siemens AG, Bensheim, Germany). • Orthodontic Pain Assessment (Time Frame: Up to Week 17). Subjects will be given a pain diary. The degree of pain will be assessed using a Visual Analogue Scale (VAS) ranging from 1 (least pain) to 10 (highest pain). • Oral Health Quality of Life (Time Frame: Up to Week 17). To assess the impact of the vibration appliance on the overall oral health quality of life of the subject, subjects will be given an Oral Health Impact Profile (OHIP-14) questionnaire.
Starting date	April 2014
Contact information	Contact: Flavio A Uribe, DDS, MDentSc furibe@uchc.edu Contact: Taranpreet K Chandhoke, DMD, PhD chandhoke@uchc.edu

Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)

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23

Notes	Estimated Study Completion Date: September 2016
	http://clinicaltrials.gov/show/NCT02119455 April 2014

ADDITIONAL TABLES

Table 1. Miles 2012: The effect of vibrational appliance on rate of tooth movement (alignment)

Time point	Control group LII mandibular arch Mean and SD in mm	LII percentage reduction in control group**	Intervention LII mandibular arch Mean and SD in mm	LII percentage reduction in intervention group**	Differnce between intervention and control groups LII mean difference mm (95%CI)**	Statistical test t-test
Number of participants analysed	33		31		Total = 64	
Initial LII score	4.9 (2.5)		6.2 (3.7)		1.3	Not provided
Reduction in LII score at 5 weeks	2.2 (± 2.82)*	45%	3.1(± 0.79)	50%	0.9 (-1.72 to 2.62)	Not provided
Reduction in LII score at 8 weeks	3.1 (± 2.4)	63%	3.4 (± 2.7)	55%	0.3 (-0.95 to 1.55)	Not provided
Reduction in LII score 10 weeks	3.4 (± 2.4)	69%	4.0 (± 3.3)	65%	0.6 (-0.94 to 2.34)	Not provided

** Figures not published but calculated by the current review authors.

Table 2. Pavlin 2015 The effect of vibrational appliance on the rate of orthodontic movement of a maxillary canine tooth

	Control group sham (Inactive Device)	Intervention group OrthoAccel Device	Mean difference	Statistical test
Number of participants analysed	22	23	45	0.05
The rate of orthodontic movement of a maxillary canine. Tooth being distalised to close an extraction space mean and 95% CI (millimetre per month)	0.79; 95% CI (0.49–1.09)	1.16; 95% CI (0.86–1.46)	0.37; 95% CI (-0.07 to 0.81)	

Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)

24

Table 3. Miles 2012 Pain and discomfort

Time point	Control group VAS mean mm (SD)	Intervention group VAS mean mm (SD)	Mean difference and 95% CI	Statistical test
T0 after wire placement	8.1 (12.3)	12.4 (13.3)	4.3 (-2.19 to 10.79)	Not provided
T1 after 6 to 8 hours	39.6 (25.8)	40.4 (20.8)	0.8 (-11.37 to 12.25)	Not provided
T2 after 1 day	47.6 (24.5)	41.5 (27.2)	6.1 (-6.60 to 18.80)	Not provided
T3 after 3 days	19.9 (15.5)	18.8 (18.5)	1.1 (-7.27 to 9.47)	Not provided
T4 after 7 days	5.5 (7.8)	4.0 (6.3)	1.5 (-1.96 to 4.97)	Not provided

A P P E N D I C E S

Appendix 1. Cochrane Oral Health Group Trials Register search strategy

1 (orthodontic*:ti,ab) AND (INREGISTER)
2 (((tooth and move*) or (teeth and move*)):ti,ab) AND (INREGISTER)
3 (#1 or #2) AND (INREGISTER)
4 (laser* :ti,ab) AND (INREGISTER)
5 ((electromagnetic and (energ* or wave* or radiation or pulse* or field*)):ti,ab) AND (INREGISTER)
6 ((electric* and (energ* or pulse* or wave* or current*)) :ti,ab) AND (INREGISTER)
7 (vibrat*:ti,ab) AND (INREGISTER)
8 (#4 or #5 or #6 or #7) AND (INREGISTER)
9 (#3 and #8) AND (INREGISTER)

Appendix 2. Cochrane Central Register of Controlled Trials (CENTRAL) search strategy

#1 [mh "Orthodontic appliances"]
#2 [mh "orthodontics, corrective"]
#3 orthodontic*
#4 ((tooth near/5 move*) or (teeth near/5 move*))
#5 {or #1-#4}
#6 [mh Lasers]
#7 laser*
#8 [mh "Electromagnetic radiation"]
#9 [mh "Electromagnetic fields"]
#10 (electromagnetic near/3 (energ* or wave* or radiation or pulse* or field*))
#11 (electric* near/3 (energ* or pulse* or wave* or current*))
#12 [mh ^Vibration]
#13 vibrat*
#14 {or #6-#13}
#15 #5 and #14

Appendix 3. MEDLINE (OVID) search strategy

1. exp Orthodontic appliances/
2. exp Orthodontics, corrective/
3. orthodontic.ti,ab.
4. ((tooth or teeth) adj5 move$).ti,ab.
5. or/1-4
6. exp Lasers/
7. laser$.ti,ab.
8. Electromagnetic radiation/
9. Electromagnetic fields/
10. (electromagnetic adj3 (energ$ or wave$ or radiation or pulse$ or field$)).ti,ab.

Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)

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11. (electric$ adj3 (energ$ or pulse$ or wave$ or current$)).ti,ab.
12. Vibration/
13. vibrat$.ti,ab.
14. or/6-13
15. 5 and 14

The above subject search will be linked to the Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomised trials in MEDLINE: sensitivity maximising version (2008 revision) as referenced in Chapter 6.4.11.1 and detailed in box 6.4.c of the*Cochrane Handbook for Systematic Reviews of Interventions*, Version 5.1.0 [updated March 2011] (Higgins 2011).

1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. randomized.ab.
4. placebo.ab.
5. drug therapy.fs.
6. randomly.ab.
7. trial.ab.
8. groups.ab.
9. or/1-8
10. exp animals/ not humans.sh.
11. 9 not 10

Appendix 4. EMBASE (OVID) search strategy

1. exp Orthodontic device/
2. exp Orthodontics/
3. orthodontic$.ti,ab.
4. ((tooth or teeth) adj5 move$).ti,ab.
5. or/1-4
6. exp Laser/
7. laser$.ti,ab.
8. Electromagnetic radiation/
9. Electromagnetic field/
10. (electromagnetic adj3 (energ$ or wave$ or radiation or pulse$ or field$)).ti,ab.
11. (electric$ adj3 (energ$ or pulse$ or wave$ or current$)).ti,ab.
12. Vibration/
13. vibrat$.ti,ab.
14. or/6-13
15. 5 and 14

The above subject search was linked to the Cochrane Oral Health Group filter for identifying RCTs in EMBASE via OVID:

1. random$.ti,ab.
2. factorial$.ti,ab.
3. (crossover$ or cross over$ or cross-over$).ti,ab.
4. placebo$.ti,ab.
5. (doubl$ adj blind$).ti,ab.
6. (singl$ adj blind$).ti,ab.
7. assign$.ti,ab.
8. allocat$.ti,ab.
9. volunteer$.ti,ab.
10. CROSSOVER PROCEDURE.sh.
11. DOUBLE-BLIND PROCEDURE.sh.
12. RANDOMIZED CONTROLLED TRIAL.sh.
13. SINGLE BLIND PROCEDURE.sh.
14. or/1-13
15. (exp animal/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans).ti.)
16. 14 NOT 15

Appendix 5. LILACS (BIREME) search strategy

Mh orthodontics or orthodontic$ or ortodon$ [Words] and Mh laser or laser$ or Mh Electromagnetic radiation or Mh Electromagnetic field or electromagnet$ or Mh Vibration or vibra$ [Words] and

Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)   **26**

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The above subject search was linked to the Brazilian Cochrane Center search strategy for LILACs via BIREME:

((Pt randomized controlled trial OR Pt controlled clinical trial OR Mh randomized controlled trials OR Mh random allocation OR Mh double-blind method OR Mh single-blind method) AND NOT (Ct animal AND NOT (Ct human and Ct animal)) OR (Pt clinical trial OR Ex E05.318.760.535$ OR (Tw clin$ AND (Tw trial$ OR Tw ensa$ OR Tw estud$ OR Tw experim$ OR Tw investiga$)) OR ((Tw singl$ OR Tw simple $ OR Tw doubl$ OR Tw doble$ OR Tw duplo$ OR Tw trebl$ OR Tw trip$) AND (Tw blind$ OR Tw cego$ OR Tw ciego$ OR Tw mask$ OR Tw mascar$)) OR Mh placebos OR Tw placebo$ OR (Tw random$ OR Tw randon$ OR Tw casual$ OR Tw acaso$ OR Tw azar OR Tw aleator$) OR Mh research design) AND NOT (Ct animal AND NOT (Ct human and Ct animal)) OR (Ct comparative study OR Ex E05.337$ OR Mh follow-up studies OR Mh prospective studies OR Tw control$ OR Tw prospectiv$ OR Tw volunt$ OR Tw volunteer$) AND NOT (Ct animal AND NOT (Ct human and Ct animal))) [Words]

Appendix 6. US National Institutes of Health Trials Register (ClinicalTrials.gov), WHO International Clinical Trials Registry Platform and metaRegister of Controlled Trials search strategy

orthodontic and laser
orthodontic and electromagnetic
orthodontic and vibration

WHAT'S NEW

Date	Event	Description
5 April 2016	Amended	References to ongoing and excluded studies added

CONTRIBUTIONS OF AUTHORS

Running searches: Cochrane Oral Health Group
Identifying relevant titles and abstracts from searches: Ahmed El-Angbawi (AE), Grant T McIntyre (GM), David R Bearn (DB)
Obtaining copies of trials: AE, GM
Selection of trials: AE, GM, DB
Extracting data from trials: AE, GM
Entering data into RevMan: AE
Carrying out risk of bias assessment: AE, GM
Carrying out analysis: AE, DB
Interpreting the data: AE, GM, DB & Padhraig Fleming (PF)
Drafting the final review: all review authors

DECLARATIONS OF INTEREST

There are no financial conflicts of interest; the review authors declare that they do not have any association with any parties who may have vested interests in the results of this review.

Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)

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27

Mayo Clinic, USA; National Center for Dental Hygiene Research & Practice, USA; New York University College of Dentistry, USA; and Royal College of Surgeons of Edinburgh, UK.

I N D E X   T E R M S

Medical Subject Headings (MeSH)

Cuspid; Pain Measurement; Randomized Controlled Trials as Topic [instrumentation]; Time Factors; Tooth Movement Techniques [adverse effects] [*methods]; Vibration [*therapeutic use]

MeSH check words

Adolescent; Child; Female; Humans; Male; Young Adult

Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment (Review)

28

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