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Surgical adjunctive procedures for accelerating orthodontic treatment (Review)

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[Intervention Review]

Surgical adjunctive procedures for accelerating orthodontic treatment

Padhraig S Fleming[1], Zbys Fedorowicz[2], Ama Johal[1], Ahmed El-Angbawi[3], Nikolaos Pandis[4]

[1]Barts and The London School of Medicine and Dentistry, Institute of Dentistry, Queen Mary University of London, London, UK. [2]Bahrain Branch, Cochrane, Awali, Bahrain. [3]School of Dentistry, University of Dundee, Dundee, UK. [4]Department of Orthodontics and Dentofacial Orthopedics, University of Bern, Bern, Switzerland

Contact address: Padhraig S Fleming, Barts and The London School of Medicine and Dentistry, Institute of Dentistry, Queen Mary University of London, New Road, London, E1 1BB, UK. padhraig.fleming@gmail.com.

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ABSTRACT

Background

A range of surgical and non-surgical techniques have received increasing attention in recent years in an effort to reduce the duration of a course of orthodontic treatment. Various surgical techniques have been used; however, uncertainty exists in relation to the effectiveness of these procedures and the possible adverse effects related to them.

Objectives

To assess the effects of surgically assisted orthodontics on the duration and outcome of orthodontic treatment.

Search methods

We searched the following electronic databases: the Cochrane Oral Health Group's Trials Register (to 10 September 2014), the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2014, Issue 8), MEDLINE via OVID (1946 to 10 September 2014), EMBASE via OVID (1980 to 10 September 2014), LILACS via BIREME (1980 to 10 September 2014), metaRegister of Controlled Trials (to 10 September 2014), ClinicalTrials.gov (to 10 September 2014), and the World Health Organization (WHO) International Clinical Trials Registry Platform (to 10 September 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 electronic searches.

Selection criteria

Randomised controlled trials (RCTs) evaluating the effect of surgical adjunctive procedures for accelerating tooth movement compared with conventional treatment (no surgical adjunctive procedure).

Data collection and analysis

At least two review authors independently assessed the risk of bias in the trials and extracted data. We used the fixed-effect model and expressed results as mean differences (MD) with 95% confidence intervals (CI). We investigated heterogeneity with reference to both clinical and methodological factors.

Main results

We included four RCTs involving a total of 57 participants ranging in age from 11 to 33 years. The interventions evaluated were corticotomies to facilitate orthodontic space closure or alignment of an ectopic maxillary canine, with the effect of repeated surgical procedures assessed in one of these studies. The studies did not report directly on the primary outcome as prespecified in our protocol: duration of orthodontic treatment, number of visits during active treatment (scheduled and unscheduled) and duration of visits. The main outcome assessed within the trials was the rate of tooth movement, with periodontal effects assessed in one trial and pain assessed in one trial. A maximum of just three trials with small sample sizes were available for each comparison and outcome. We assessed all of the studies as being at unclear risk of bias.

Tooth movement was found to be slightly quicker with surgically assisted orthodontics in comparison with conventional treatment over periods of one month (MD 0.61 mm; 95% CI 0.49 to 0.72; P value < 0.001) and three months (MD 2.03 mm, 95% CI 1.52 to 2.54; P value < 0.001). Our results and conclusions should be interpreted with caution given the small number of included studies. Information on adverse events was sought; however, no data were reported in the included studies.

Authors' conclusions

This review found that there is limited research concerning the effectiveness of surgical interventions to accelerate orthodontic treatment, with no studies directly assessing our prespecified primary outcome. The available evidence is of low quality, which indicates that further research is likely to change the estimate of the effect. Based on measured outcomes in the short-term, these procedures do appear to show promise as a means of accelerating tooth movement. It is therefore possible that these procedures may prove useful; however, further prospective research comprising assessment of the entirety of treatment with longer follow-up is required to confirm any possible benefit.

PLAIN LANGUAGE SUMMARY

Surgical procedures for accelerating orthodontic treatment

Review question

Orthodontic treatment (use of braces) is lengthy, typically taking over 18 months to complete, with brace adjustments required every six weeks or so. Usually brace treatment is carried out without the use of surgery. However, special surgical procedures have been proposed to speed up orthodontic treatment. This review, produced through the Cochrane Oral Health Group, examines the merits and risks of surgical methods for speeding up orthodontic treatment compared to standard orthodontic treatment in adolescents and adults.

Background

Reduction of orthodontic treatment duration is highly desirable. Surgery has been advocated to speed up tooth movement and may work by stimulating cells adjacent to the teeth or by reducing the resistance presented by the supporting bone and mechanically shifting teeth. These procedures are relatively new and may carry additional risks compared to standard treatment.

Study characteristics

The evidence on which this review is based is up to date as of 10 September 2014. We found four relevant studies to include in this review. These studies involved 57 participants ranging in age from 11 to 33 years. All of the studies investigated the effects of surgical procedures on either the time taken to align a displaced tooth or to close gaps between teeth. None of these studies reported being funded by the orthodontic industry.

Key results

Slightly faster tooth movement was found with the surgical procedures, although this result is based on a relatively small number of participants. In addition, there were some problems inherent in the design and quality of all the studies. Therefore, further research is needed to confirm whether additional surgery is warranted to speed up tooth movement. The studies did not provide any information about negative side effects from the treatment.

Quality of the evidence

The quality of the evidence concerning the rate of tooth movement was judged to be low for assessments one month and three months after the procedure.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Patient or population: People requiring orthodontic tooth movement
Settings: University Clinic and Hospital
Intervention: Adjunctive surgical procedures
Comparison: Conventional treatment

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Conventional treatment	Surgical adjuncts				
Duration of orthodontic treatment, number of visits during active treatment (scheduled and unscheduled) and duration of visits	-	-				Not reported
Orthodontic tooth movement in mm (3 months)	The mean orthodontic movement in the control groups was 3.0 mm[1]	The mean orthodontic movement in the intervention groups was **2.03 mm higher** (1.52 to 2.54 higher)		31 (2 studies - both split-mouth)	⊕⊕◯◯ **low**[2]	Outcome also measured at 1 month in 3 split-mouth studies (42 participants): mean movement in intervention groups was **0.61 mm higher** (0.49 to 0.72 higher) - low quality evidence
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	See comment	See comment		13 (1 study, split-mouth)	⊕◯◯◯ **very low**[3]	Gingival and periodonal problems only were assesed in 1 study (Aboul-Ela 2011). No precise data were given, although no statistical difference (P value > 0.05) in plaque

resorption)			index, attachment loss, gingival recession and probing depth were found up to 4 months postoperatively. Gingival index scores were significantly higher ($P < 0.05$) on the operated side compared with the unoperated side after 4 months

*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% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval

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

[1] Based on the median of the mean orthodontic movement measurement in the two control groups (2.54 and 3.4 mm).
[2] Downgraded one level for risk of bias: blinding of participants and personnel unclear in Aboul-Ela 2011 and blinding of outcome assessment unclear in Leethanakul 2014. Also downgraded one level for indirectness.
[3] Downgraded one level for risk of bias in Aboul-Ela 2011. Also downgraded two levels for imprecision.

BACKGROUND

Approximately one-third of adolescents in the UK have an abnormal bite or malocclusion that might benefit from orthodontic (brace) treatment. The majority of comprehensive orthodontic treatment is undertaken with fixed appliances; treatment durations of 18 to 24 months are usual. Treatment tends to be more prolonged in certain scenarios; for example, in combined orthodontic-surgical cases (O'Brien 2009), in adults and in the management of ectopic canines (Fleming 2009). Shorter treatment times would offer benefits both to patients and providers, limiting cost and inconvenience, and would reduce the likelihood of iatrogenic consequences of treatment including root resorption and decalcification.

A range of surgical and non-surgical techniques to reduce the duration of orthodontic treatment have been proposed in recent years. These techniques include surgical adjuncts, vibratory stimulation, low-level laser therapy, customisation of appliances and routine avoidance of extractions. Surgical techniques geared towards reducing treatment times have been collectively described as 'surgically assisted orthodontics'. These procedures encompass four main approaches: distraction of the periodontal ligament; distraction of the dento-alveolus; alveolar decortication; and corticision. Each of these raise the possibility of dramatically reducing treatment times; however, they are relatively invasive and carry associated risks.

See Table 1 - 'Glossary of unfamiliar terms'.

Description of the condition

Orthodontic treatment is undertaken to address malocclusion. Approximately 35% of adolescents between 12 and 15 years in the UK are estimated to have a treatment need (Chestnutt 2006), with a further 8% within this age bracket already in treatment. There is also commonly a residual need for treatment in older age groups, with up to 34% of young adults complaining of irregular anterior teeth (Josefsson 2010); and an increasing demand for orthodontics in adulthood. Only 35% of adults in the United States were found to have aligned mandibular anterior teeth (Proffit 1998). Definitive correction of malocclusion typically involves upper and lower fixed appliances and may also involve extraction of teeth and occasionally orthognathic surgery. Treatment of this nature can be expected to take somewhere in the region of 18 to 24 months and usually involves re-activation of the appliance at intervals of between 4 and 10 weeks.

Successful interventions to reduce the duration of treatment would clearly be advantageous with time savings for both clinicians and patients, and a likely decrease in associated costs and inconvenience. In particular, acceleration of treatment may be advantageous in the presence of severe malocclusion or where prolonged treatment is likely, e.g. in situations where orthodontic treatment is combined with surgery in adult patients, and to effect mechanical eruption of ectopic canines. Patients with fixed appliances (braces) often have difficulty maintaining good oral hygiene, and this may lead to the development of white spot lesions due to demineralisation surrounding the attachments. Both demineralisation and root resorption are known to be time-dependent (Segal 2004). Hence, by limiting the duration of treatment it might be possible to reduce the prevalence of these adverse side effects.

Description of the intervention

Surgically assisted orthodontics may involve any one of the following procedures to accelerate treatment:

- Distraction of the periodontal ligament (PDL): a surgical procedure on interseptal bone to reduce resistance to movement.
- Distraction of the dento-alveolus: a surgical procedure involving separation of the dental segment from the jaw bone to allow distraction osteogenesis in the osteotomy site.
- Alveolar decortication: a surgical procedure involving intentional surgical insult to alveolar bone, designed to accelerate tooth movement. This approach has been modified by the addition of bioabsorbable grafts (Wilcko 2001).
- Corticision: this is a more conservative surgical procedure to divide cortices transmucosally without reflecting a mucoperiosteal flap.

These interventions are usually undertaken in conjunction with fixed appliance-based treatment, with the surgical procedure being carried out prior to, or near the beginning of, treatment.

How the intervention might work

The mode of action of surgically assisted orthodontics depends on the precise intervention undertaken. Distraction procedures may expedite tooth movement by facilitating movement of teeth at a known rate, while other surgical procedures to accelerate orthodontic treatment rely on triggering heightened osteoclastic activity by inducing regional accelerated phenomena (Wilcko 2001). These cellular mechanisms may result in a reduction in bone density, reducing the impediment to tooth movement (Teixeira 2010). When surgical adjuncts are used, it is standard practice to perform the procedure at the start of treatment with upregulation of inflammatory mediators facilitating tooth movement (Kim 2011). Assisted tooth movement during particular stages of treatment may be useful during particularly complex tooth movements; for example, retraction or mechanical eruption of maxillary canines. Consequently, it could be expected that overall treatment time would be reduced, with the potential to reduce costs and improve outcomes. However, the latter advantages are contingent on low surgical costs and the absence of surgical morbidity.

Why it is important to do this review

The duration of orthodontic treatment typically ranges from 18 to 24 months; consequently, there is a perpetual drive to reduce the duration of orthodontic treatment. An array of techniques and appliances, including surgically assisted orthodontics, vibratory stimulation, customisation of appliances and routine avoidance of extractions, have been proposed to achieve shorter treatment durations. Surgical techniques to accelerate treatment are a relatively recent development, having grown in popularity in recent years. While these procedures offer the possibility of dramatically reducing treatment times, the procedures are relatively invasive. The evidence concerning the effectiveness and potential harms of these approaches has not, however, been subjected to systematic review.

OBJECTIVES

To assess the effects of surgically assisted orthodontics on the duration and outcome of orthodontic treatment.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials.

Types of participants

Individuals of any age receiving orthodontic treatment with fixed appliances (braces) with adjunctive use of surgery to increase the rate of tooth movement. We excluded studies including participants treated with orthognathic surgery or involving participants with cleft lip or palate or other craniofacial deformity/syndrome.

Types of interventions

Active interventions: any form of orthodontic treatment with fixed appliances, including extraction and non-extraction treatment with or without interproximal reduction (tooth size reduction), incorporating surgically assisted orthodontics to increase the rate of tooth movement.
Control: any form of orthodontic treatment with fixed appliances, including extraction and non-extraction treatment with or without interproximal reduction, without use of surgically assisted orthodontics.

Types of outcome measures

Primary outcomes

- The duration of orthodontic treatment, number of visits during active treatment (scheduled and unscheduled) and duration of visits was to be assessed. Where data relating to the overall duration of treatment were not available, the rate of orthodontic tooth movement was recorded based on the time periods assessed in the primary studies.

Secondary outcomes

- 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)
- Patient-reported outcomes: impact of fixed appliances on daily life, quality of life and pain experience
- Patient satisfaction measured using validated questionnaires or scales
- Improvement in occlusion adjudged using Peer Assessment Rating (PAR) or other validated scale recorded at the completion of active orthodontic treatment
- Prolonged stability of treatment adjudged using an accepted scale

Search methods for identification of studies

To identify studies to be included or considered for this review, we developed detailed search strategies for each database searched. These were based on the search strategy we developed for MEDLINE and revised appropriately for each database (see Appendix 3).

Electronic searches

We searched the following databases:

- The Cochrane Oral Health Group's Trials Register (to 10 September 2014)(see Appendix 1);
- The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*, Issue 8, 2014)(see Appendix 2);
- MEDLINE via OVID (1946 to 10 September 2014)(see Appendix 3);
- EMBASE via OVID (1980 to 10 September 2014)(see Appendix 4);
- LILACS via BIREME (1980 to 10 September 2014)(see Appendix 5).

We combined the MEDLINE subject search with the Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomised trials: 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). The search of EMBASE was linked to the Cochrane Oral Health Group filter for identifying RCTs, and the LILACs subject search was linked to the filter developed by the Brazilian Cochrane Center.

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 in the following databases to identify ongoing trials (see Appendix 6 for details of the search strategy):

- metaRegister of Controlled Trials (mRCT) (to 10 September 2014);
- US National Institutes of Health Register (ClinicalTrials.gov)(to 10 September 2014);
- World Health Organization International Clinical Trials Registry Platform Search Portal (ICTRP) (to 10 September 2014).

Language

There were no language restrictions applied in the databases we searched.

Data collection and analysis

Selection of studies

Two review authors independently assessed the titles and abstracts of studies identified through the searches. We obtained full copies of all studies appearing to meet the inclusion criteria and those for which there were insufficient data in the title and abstract to make a clear decision. Two review authors assessed the full-text papers independently and resolved any disagreement on the eligibility of included studies through discussion with a third review author. From this group of studies, we recorded the studies that did not meet the inclusion criteria in the Characteristics of excluded studies section of the review and reported the reasons for exclusion.

Data extraction and management

We designed and piloted data extraction forms to record year of publication and country of origin, and details of the participants including demographic characteristics and criteria for inclusion. We entered study details into the Characteristics of included studies tables in Review Manager 5 (RevMan; RevMan 2011). Two review authors extracted data independently and in duplicate; any disagreements were resolved by consulting with a third review author. We extracted the following details if reported:

1. Trial methods: (a) method of allocation; (b) conduct of sample size calculation; (c) masking of participants, trialists and outcome assessors; (d) exclusion of participants after randomisation; and proportion of, and reasons for, losses 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.

If stated, we recorded the sources of funding. We used this information to aid assessment of heterogeneity and the external validity of any included trials.

Assessment of risk of bias in included studies

At least two review authors independently assessed risk of bias in the included 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 2011). We compared the assessments and resolved any disagreements through discussion. We assessed the following domains as at low, high or unclear risk of bias:

1. Sequence generation (selection bias);
2. Allocation concealment (selection bias);
3. Blinding of participants and personnel (performance bias), and outcome assessors (detection bias);
4. Incomplete outcome data addressed (attrition bias);
5. Selective outcome reporting (reporting bias);
6. Other bias.

We categorised and report 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 as 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 as 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 as at high risk of bias.

Measures of treatment effect

We calculated mean differences with 95% confidence intervals (CI) for continuous data. If dichotomous secondary outcomes are

found in updates of this review, we will calculate odds ratios (OR) to be obtained with 95% CI.

Unit of analysis issues

We anticipated that some of the included studies would present data from repeated or multiple site observations (or both) on participants, which may lead to unit of analysis errors. Where this arose, we followed the advice provided in section 9.3.4 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 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 2011).

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 Criteria for considering studies for this review. We assessed statistical heterogeneity using a Chi² test and the I² statistic where I² values of 30% to 60% indicate moderate to high heterogeneity, 50% to 90% substantial heterogeneity, and 75% to 100% very substantial ("considerable") heterogeneity. We considered heterogeneity to be significant when the P value was below 0.10 (Higgins 2003).

Assessment of reporting biases

If a sufficient number of studies assessing similar interventions are identified for inclusion in this review when it is updated, we will assess publication bias according to the recommendations on testing for funnel plot asymmetry as described in section 10.4.3.1 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). If asymmetry is identified we will attempt to assess other possible causes, exploring these in the discussion if appropriate.

Data synthesis

We pooled data where studies had similar participants, interventions and outcomes. We calculated a weighted treatment effect with the results expressed as mean differences (MD) and 95% CI for continuous outcomes. We would have used OR and 95% CI for dichotomous outcomes. We used fixed-effect models for meta-analyses.

In the presence of split-mouth design the inverse-variance method was used. The standard deviation (SD) of the difference was calculated using the formula: $\sqrt{(sd1^2+sd2^2-2*r*sd1*sd2)}$, where r = correlation coefficient between paired measurements. In the presence of sufficient information, the standard deviation was derived using calculated correlation coefficients, otherwise the calculation was based on the value of r = 0.5. Subsequently, the required standard error (SE) was calculated using $SE = SD/\sqrt{(n)}$.

Subgroup analysis and investigation of heterogeneity

If a sufficient number of studies are included in future updates of this review, and if moderate, substantial or considerable heterogeneity is identified (see Assessment of heterogeneity), we plan to carry out subgroup analyses according to type of surgery used and age category (adolescents versus adults).

Sensitivity analysis

If a sufficient number of studies are included in future updates of this review, we plan to carry out sensitivity analyses to assess the robustness of our review results. This will involve repeating the analyses but excluding studies with a high risk of bias.

Summary of results

We produced a 'Summary of findings' table to highlight results of the main outcomes (the primary outcomes and 'harms'). We assessed the quality of the body of evidence with reference to the overall risk of bias of the included studies, the directness of the evidence, the inconsistency of the results, the precision of the estimates, the risk of publication bias and the magnitude of the effect. We categorised the quality of the body of evidence for the primary outcomes as high, moderate, low or very low.

RESULTS

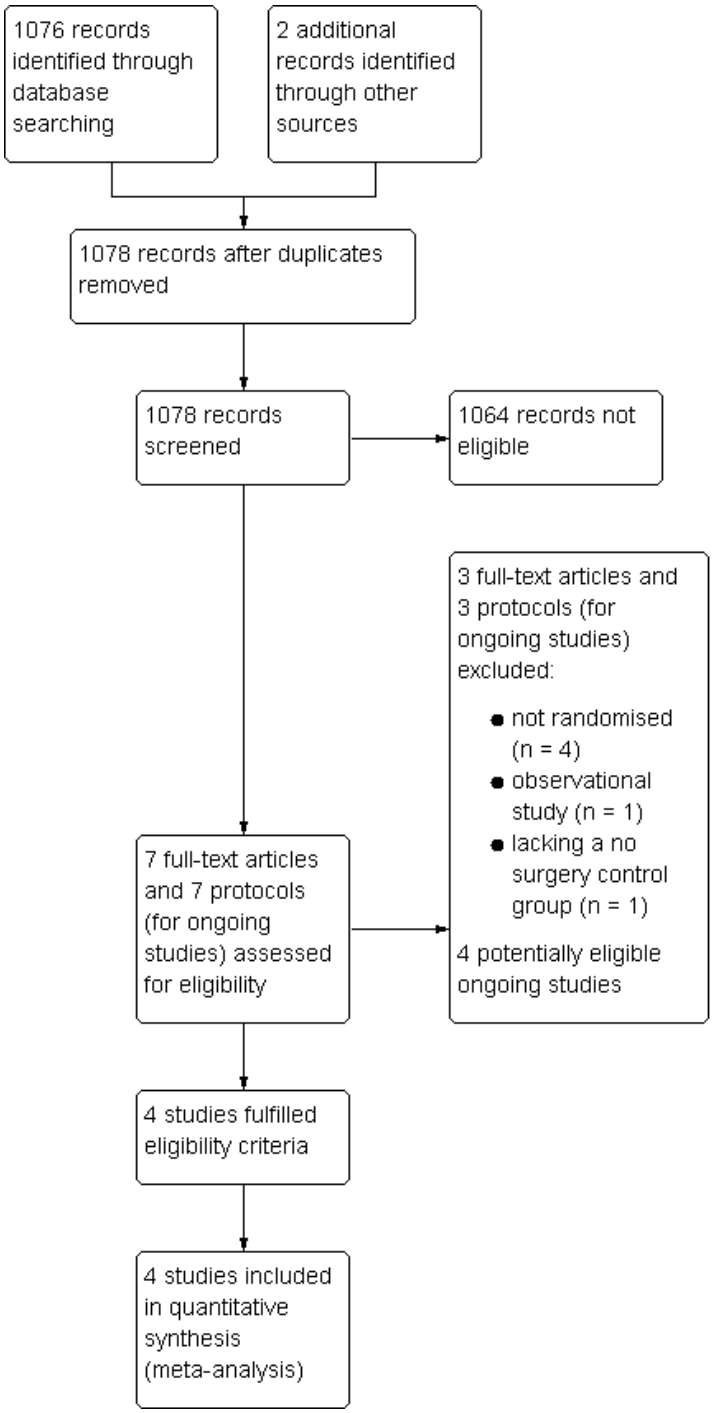
Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Results of the search

The electronic searches resulted in 1076 references with a further two references identified through other sources. We examined the titles and abstracts of these for eligibility and all of those not matching the inclusion criteria were eliminated. Fourteen potentially relevant studies were identified. We obtained full-text articles of seven studies and registry entries for seven ongoing studies and subjected them to further evaluation. After further assessment, we eliminated three of the completed studies and three of the ongoing studies (see Characteristics of excluded studies). We therefore had four studies to include and four studies are ongoing (Figure 1).

Figure 1. Study flow diagram



Included studies

We included four studies in this review (see Characteristics of included studies).

Characteristics of the trial settings and investigators

Three of the studies were carried out by consultants or specialists based in a university hospital (Aboul-Ela 2011; Alikhani 2013, Leethanakul 2014); the other included trial was undertaken in a practice setting (Fischer 2007). Study endpoints included the time to align ectopic maxillary canines (Fischer 2007), the time taken to retract a maxillary canine (Alikhani 2013; Leethanakul 2014), and the rate of space closure following extraction of maxillary first premolars during orthodontics (Aboul-Ela 2011). The latter involved follow-up to a maximum period of four months (Aboul-Ela 2011).

Characteristics of the participants

A total of 57 (15 male and 42 female) participants were included in the four studies overall. The mean age of participants in the study involving extraction space closure was 19.2 years (Aboul-Ela 2011). Adults only were included in the studies concerning the rate of canine retraction (Alikhani 2013; Leethanakul 2014); however, younger participants were the focus of the other study, with an age range of 11.1 to 12.9 years (Fischer 2007). Limited information was given in relation to clinical characteristics; however, subjects with Class I malocclusion treated without extraction were included in one study (Fischer 2007), while participants requiring maxillary first premolar extraction were included in the remaining studies (Aboul-Ela 2011; Alikhani 2013; Leethanakul 2014). Two of these studies were restricted to assessment of Class II division 1 incisor relationships (Aboul-Ela 2011; Alikhani 2013).

Characteristics of the interventions

Corticotomies were undertaken in the included studies to accelerate tooth movement, either to facilitate orthodontic space closure (Aboul-Ela 2011), or to accelerate alignment of an ectopic maxillary canine (Fischer 2007). To facilitate space closure following maxillary first premolar extraction, corticotomy was undertaken at the same time as extraction. By raising a full-thickness submarginal Luebke-Ochsenbein flap and using a Number 2 bur in a low-speed hand piece, corticotomy perforations were made from the lateral incisor to the first premolar (Aboul-Ela 2011). The flap was subsequently replaced and the maxillary archwire (0.016 x 0.022 inch stainless steel) ligated, with nickel-titanium closed-coil springs, applying 150 g on each side used for space closure from miniscrew implants to hooks on the maxillary canine brackets.

In the study concerning surgical uncovering of maxillary canines, following surgical exposure of the ectopic canine a supplementary corticotomy was undertaken with a series of circular holes made with a 1.5 mm round bur along the bone mesially and distally adjacent to the impacted tooth (Fischer 2007). These holes were spaced approximately 2 mm apart extending into the edentulous area into which the tooth was to be moved. Active orthodontic forces of approximately 60 g were subsequently placed after a two-week hiatus.

The study by Alikhani 2013 involved the use of repeated surgery. They described the use of micro-osteoperforations (MOPs) on three occasions throughout the course of treatment distal to the canines without elevation of a mucoperiosteal flap. Leethanakul 2014 used a more conservative surgical procedure with interseptal bone reduction performed from within the extraction socket without flap surgery. The extraction socket was deepened to the length of the canine apex, and the interseptal bone distal to the canine was reduced to 1 to 1.5 mm in thickness using round and cylindrical carbide burs. If present, the interradicular septal bone of the socket was also removed. The first premolar extraction socket was surgically widened in the buccopalatal dimension along the curvature of the root of the canine (Leethanakul 2014).

Control conditions

Conventional fixed appliance-based orthodontic treatment without surgical assistance was undertaken in all the included studies (Fischer 2007; Aboul-Ela 2011; Alikhani 2013; Leethanakul 2014).

Characteristics of the outcomes

Outcomes assessed included objective assessments primarily, with subjective pain experience considered in one study (Alikhani 2013).

Specific clinical outcomes included:

1. Rate of tooth movement: antero-posterior movement of the maxillary canines and first molars per unit time (Aboul-Ela 2011); and distance of movement of the maxillary canine per unit time (Fischer 2007; Alikhani 2013; Leethanakul 2014).

2. Periodontal health and inflammatory response: plaque index, gingival index, probing depth, attachment level, gingival recession and alveolar bone levels assessed with periapical radiography (Aboul-Ela 2011). Gingival crevicular fluid (GCF) was collected to evaluate the level of inflammatory response before orthodontic treatment, immediately before the start of canine retraction, and at each subsequent visit over the study period in one study (Alikhani 2013).

3. Pain experience: discomfort was assessed on the day of appliance placement, the day of canine retraction, and subsequently at 24

hours, 7 days and 28 days after canine retraction on a numeric rating scale (Alikhani 2013).

Follow-up was undertaken over one month in Alikhani 2013; over three months of canine retraction in Leethanakul 2014; over the period of orthodontic space closure (up to four months) in Aboul-Ela 2011; while a more prolonged follow-up until alignment of the tip of the ectopic canine was complete was undertaken in Fischer 2007.

Excluded studies

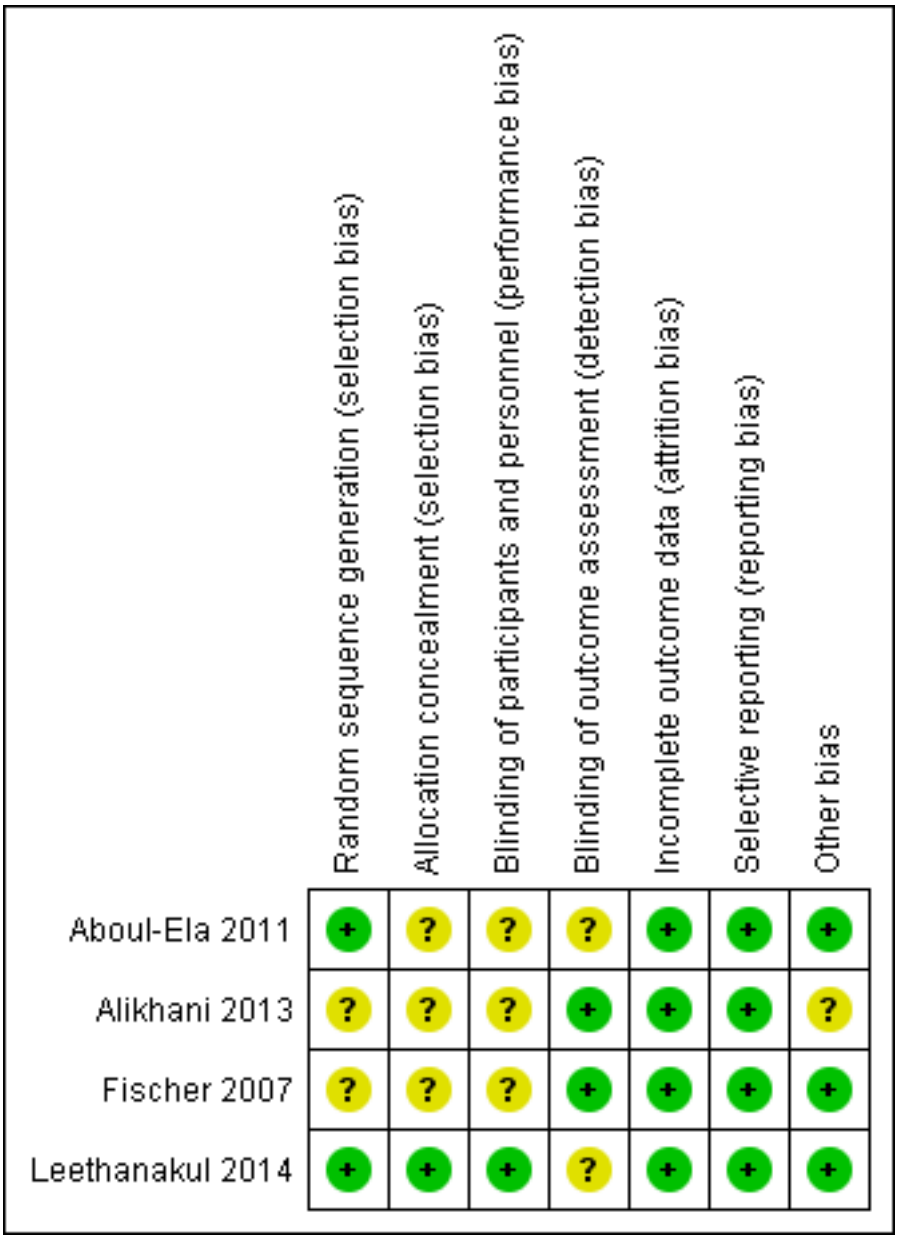
We excluded four studies: three were nonrandomised and one involved comparison of two surgical approaches without a negative control group (see Characteristics of excluded studies).

Risk of bias in included studies

No study fulfilled all of the criteria, across all of the domains, to permit a judgement of low risk of bias. In the overall rating of the risk of bias, all four studies were graded as having an unclear 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 table (Figure 2).

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



Allocation

The methods used to generate the allocation sequence and the method of concealing the sequence, such that participants and investigators enrolling participants could not foresee the upcoming assignment, are the most important and sensitive indicators for minimising bias in a clinical trial (Schulz 1995). In two studies the method of sequence generation was unclear (Fischer 2007; Alikhani 2013). Concealment of the allocation sequence was also not reported in three included studies (Fischer 2007; Aboul-Ela 2011; Alikhani 2013).

Blinding

Whilst the challenges of blinding participants and personnel to the interventions considered in this review are recognised, in only two studies was it stated that the outcome assessments were independent of the investigators (Fischer 2007; Alikhani 2013). In three of the studies it was unclear if foreknowledge of the allocated interventions by participants and personnel could have been prevented during the study (performance bias), therefore the judgement given for this domain was 'unclear' (Fischer 2007; Aboul-Ela 2011; Alikhani 2013).

In two studies it was unclear whether the outcome assessors were 'blinded' to the allocated interventions (detection bias); a judgement of 'unclear risk' of bias was given for this domain (Aboul-Ela 2011; Leethanakul 2014). This domain was judged to be at low risk of bias in the other included studies (Fischer 2007; Alikhani 2013).

Incomplete outcome data

In three included studies incomplete outcome data were reported and there were no losses to follow-up (Fischer 2007; Alikhani 2013; Leethanakul 2014). In Aboul-Ela 2011 two participants were lost to follow-up.

Selective reporting

Although study protocols were unavailable, in general the outcomes listed in the 'Methods' section were comparable to the reported results; therefore we assessed all four studies as being at low risk of reporting bias.

Other potential sources of bias

There did not appear to be any reason for concern about other potential sources of bias in three of the included studies; the risk of other bias was considered unclear in one study due to a possible conflict of interest (Alikhani 2013).

Effects of interventions

See: **Summary of findings for the main comparison** Surgical adjunctive procedures compared to conventional orthodontic treatment for tooth movement

Surgical adjuncts versus conventional treatment

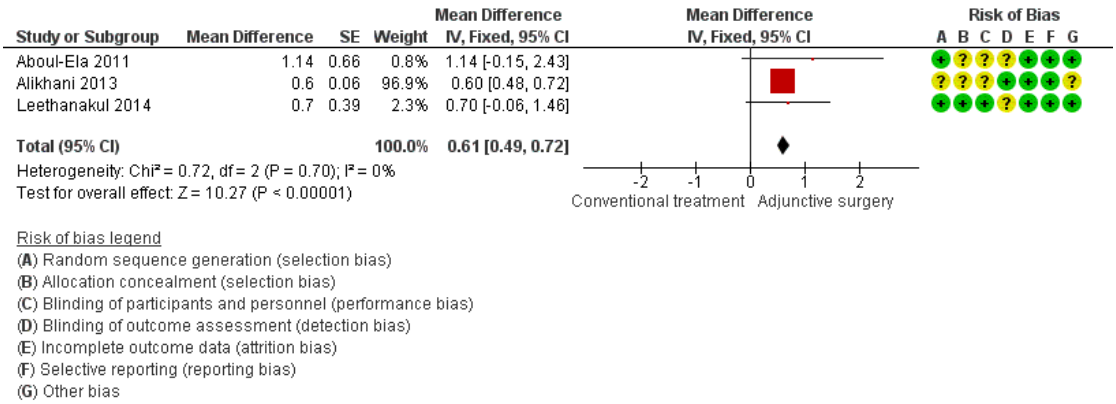
Primary outcomes

Our prespecified primary outcome (the duration of orthodontic treatment, number of visits during active treatment (scheduled and unscheduled) and duration of visits) was not measured directly in the included trials. We report below on a surrogate outcome - rate of tooth movement with values of 1 mm per month being typical.

1. Rate of tooth movement at one month

This comparison included three trials that assessed differences in tooth movement between surgical and conventional methods after one month of treatment. The pooled estimate of 0.61 mm (95% CI 0.49 to 0.72; P value < 0.001) indicates that the surgical intervention resulted in 0.61 mm more tooth movement during the first month; a statistically significant finding (Analysis 1.1; Figure 3).

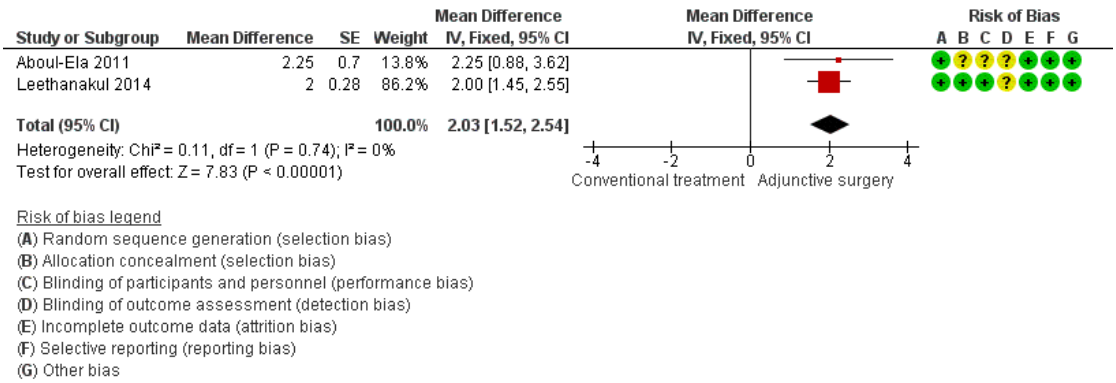
Figure 3. Forest plot of comparison: 1 Surgical adjunctive procedures versus conventional treatment, outcome: 1.1 Rate of tooth movement (1 month)



2. Rate of tooth movement at three months

This comparison included two trials that assessed differences in tooth movement between surgical and conventional methods after three months of treatment. The pooled estimate of 2.03 mm (95% CI 1.52 to 2.54; P value < 0.001) indicates that the surgical intervention resulted in 2.03 mm more tooth movement after three months of treatment; a statistically significant finding (Analysis 1.2; Figure 4).

Figure 4. Forest plot of comparison: 1 Surgical adjunctive procedures versus conventional treatment, outcome: 1.2 Rate of tooth movement (3 months)



The trial by Fischer 2007 involved comparison of the rate of tooth movement over a minimum period of 40 weeks; however, the results were reported as tooth movement in millimetres per week and, while the rate of tooth movement was reported as significantly higher for the corticotomy group compared to the conventional group (mean difference = 0.08 mm/week, 95% CI 0.05 to 0.11; P value < 0.001), changes at comparable time points were not given,

precluding direct comparison with follow-up of no more than 54 weeks in the corticotomy group and no less than 60 weeks in the control group.

Secondary outcomes

Our prespecified secondary outcomes of patient satisfaction, improvement in occlusion, and prolonged stability of treatment were not measured in the trials.

Harms arising during the course of orthodontic treatment: periodontal

Periodontal health was considered in just one study (Aboul-Ela 2011). In this study a full-thickness submarginal mucoperiosteal flap was raised with corticotomy perforations made at the time of extraction only (Aboul-Ela 2011). No statistical difference (P value > 0.05) in plaque index scores, attachment loss, gingival recession and probing depth values were found up to four months postoperatively. However, gingival index scores were significantly higher (P < 0.05) on the operated side compared with the unoperated side after four months.

Patient-reported outcomes: pain experience

Pain experience was compared between surgical and non-surgical cases in a single study (Alikhani 2013). Within 24 hours of appliance activation and canine retraction, both groups reported higher levels of discomfort compared with the levels before retraction; however, the difference between the control and experimental groups was not statistically significant (P > 0.5). Pain was reported for up to seven days, although no statistical difference between the groups was noted during that period (Alikhani 2013).

DISCUSSION

The use of surgical and non-surgical adjunctive procedures within orthodontics to accelerate treatment has become commonplace in recent years. In particular, treatment is known to be lengthier in adult patients and in the correction of specific occlusal problems, such as the management of ectopic canines and closure of extraction spaces. With any surgical procedure there are associated risks; on the basis of the present review there is limited evidence demonstrating a significant advantage of these procedures relative to the possible associated risks and potential complications. The optimal approach to comparing the effectiveness of surgical interventions to conventional treatments is the randomised controlled trial as the potential for bias and confounding variables can be kept to a minimum.

The objectives of this systematic review were to undertake a complete analysis of outcomes both from an objective viewpoint and with respect to patient reports. Outcomes assessed within the selected studies were primarily clinician-centred. In just one trial was subjective pain measured. Moreover, given that repeated surgical interventions are occasionally suggested, it is important that the effects of these repeated procedures on periodontal health be evaluated. It is therefore important that future studies consider patient-centred outcomes. It would also be important that investigators are consistent in relation to both the objective and subjective core outcomes that are assessed within future studies; and that investigators report studies consistently and transparently.

While we aimed to assess the effect of surgical adjunctive therapy on the duration of orthodontic treatment, pooled comparisons were only possible up to a maximum period of four months. In all the assessed studies space closure or the time taken to move individual teeth were used as surrogate measures of the overall effect of the surgical therapy. There is therefore a need for further research covering the entirety of treatment as it is possible that the possible benefit of surgical adjuncts may be diluted over a course of treatment, rendering it of little value.

The limited amount of evidence identified in this review may reflect the relative infancy of this approach to orthodontic treatment. There does, however, appear to be low quality evidence pointing to some potential value for these procedures, although we were unable to assess the prespecified primary outcome concerning the overall duration of treatment. A number of registered clinical trials were identified in this area; hopefully, results from these studies will be forthcoming before long. A further finding was that a range of surgical procedures were examined within the identified studies. An agreed surgical protocol has yet to emerge; for example, some studies recommended flapless procedures, while others recommended reflection of full-thickness mucoperiosteal flaps. As further research is published in this area, there will be evidence to inform the specifics of individual surgical procedures.

Summary of main results

We included four studies, all of which were assessed as having unclear risk of bias. A total of 57 participants were included overall; numbers were therefore very limited. The combined results and conclusions should therefore be interpreted with caution. Corticotomies were undertaken to accelerate tooth movement for separate indications: to facilitate space closure (Aboul-Ela 2011); to accelerate canine retraction (Alikhani 2013; Leethanakul 2014); or to align an ectopic maxillary canine (Fischer 2007). A range of surgical techniques were also used in the included studies with repeated surgery used in one trial (Alikhani 2013). The chief outcome assessed was the rate of tooth movement per unit time. Pain scores were also assessed in one study (Alikhani 2013).
Limited pooled data in relation to the rate of tooth movement indicated a potential benefit associated with adjunctive surgery to

accelerate orthodontic treatment. However, these results should be viewed with caution given the low number of participants considered. Moreover, the assessments were confined to a relatively short period at the beginning of orthodontic treatment; the potential impact of the surgical procedures may therefore be overstated.

Overall completeness and applicability of evidence

We planned to assess the impact of surgical adjunctive therapy on the overall duration of orthodontic treatment. However, meta-analysis was undertaken over a maximum period of three months. Surrogate measures of the overall effect of the surgical therapy were used in each trial. There is therefore a need for further research covering the entirety of treatment and measuring the overall duration of treatment, appointment duration and number of required visits. Little emphasis was placed on patient-reported measures and none on adverse effects of the surgical intervention, which were not measured in the studies included in this review. Moreover, a range of surgical protocols and conditions were assessed in the included studies. Further research concerning the relative merits of specific surgical protocols, single surgery versus repeated surgery, and in a range of orthodontic conditions is required.

Quality of the evidence

Limitations in study design and implementation

Although the overall design of the included studies was generally adequate, our assessments of risk of bias exposed limitations in the quality of the included studies. A number of methodological and reporting aspects required clarification. In particular there was poor reporting, with the methods used to generate the sequence to conceal the allocation, and the measures taken to blind investigators and participants requiring clarification in a number of studies (Table 2).

While it was possible to blind the outcome assessors in each of these studies, this was not universally reported. Independent post-operative evaluation could have helped to limit the effects of subjectivity in the assessment of these outcomes. Blinding of the investigators to the interventions is more complex; however, it is possible particularly when flapless surgical procedures are used. Nevertheless, blinding of operators was rarely reported.

Indirectness of the evidence

The objective of this review was to assess the effect of adjunctive surgical procedures on the duration of orthodontic treatment; ideally this would involve comparison of the time taken to complete a course of orthodontic treatment by conventional means and with adjunctive surgical procedures. However, no completed trials investigating the overall duration of treatment were found; surrogate measures of treatment efficiency including the rate of space closure, the rate of canine retraction, and the time taken to align an ectopic canine. These measures are likely to be indicative of the effect of the surgical procedures on the duration of orthodontic treatment; however, given that they constitute just one element of treatment, it is possible that use of these measures may overstate the impact of the procedures on the rate of tooth movement.

The included studies were undertaken predominantly on skeletally-mature individuals; it is therefore not possible to confirm the effectiveness of these procedures on adolescent populations. Furthermore, data relating to patient-preferred outcomes were very limited, with patient-centred outcomes largely overlooked and no assessment of the impact of the surgical procedure on quality of life. However, the research settings were representative with three studies undertaken in either hospital or university centres.

Inconsistency of results

The presence of clinical heterogeneity and the inability to extract much usable data made it difficult to further assess the consistency of the results between the studies.

Imprecision of results

The rather limited number of studies, of limited sample size and relatively short duration and examining various interventions, that were included in this review did not permit any substantive assessment of the degree of precision of effect.

Publication bias

Every effort was made to identify additional published and unpublished studies. Given that no more than three studies comparing similar interventions were found, funnel plot assessment of publication bias was not possible (Higgins 2011).

Potential biases in the review process

Efforts were made to limit bias in the review process by ensuring a comprehensive search for potentially eligible studies. The independent, duplicate assessments of eligibility of studies for inclusion in this review and the extraction of data limited the likelihood of additional bias.

Agreements and disagreements with other studies or reviews

While this review only considered randomised controlled trials, its findings concur with those of a recent systematic review and meta-

analysis that analysed randomised controlled trials, controlled clinical trials and case series involving more than five participants (Hoogeveen 2014). The authors of that review could only identify studies of low to moderate methodological quality and alluded to a temporary acceleration of tooth movement and no deleterious effects related to the procedures. The authors warned that the results be interpreted with caution in view of the limited level of evidence obtained allied to the short duration of follow-up. Other recent reviews have been carried out, focusing either exclusively on RCTs (Kalemaj 2015); or both on RCTs and controlled clinical trials (Long 2013; Gkantidis 2014). The review by Kalemaj 2015 suggested that surgically-assisted procedures may have a short-term effect, which may diminish over time. Overall, similar findings were found to those identified in the present review. Despite the inclusion of both surgical and non-surgical interventions within these reviews, no definitive conclusions were reached and a requirement for further research reported (Long 2013; Gkantidis 2014; Kalemaj 2015).

AUTHORS' CONCLUSIONS

Implications for practice

There is a limited amount of low quality evidence concerning the effectiveness of surgical interventions to accelerate orthodontic treatment. While significant inter-individual variation exists, a rate of tooth movement of 1 mm per month is considered representative during orthodontic space closure. Based on short-term research, these procedures do appear to show promise as a means of accelerating tooth movement, although no studies directly assessing the prespecified primary outcome were identified. It is therefore possible that these procedures may prove useful. However, further prospective research comprising assessment of the entirety of treatment with longer follow-up is required to confirm any possible benefit.

Implications for research

Designing and recruiting to a randomised controlled trial concerning the effectiveness of an elective, adjunctive surgical intervention is potentially problematic. For obvious reasons participants may be reluctant to be randomly allocated to an unproven surgical procedure. Nevertheless, there is a persistent need for more comprehensive trials assessing the effectiveness of adjunctive surgical procedures on the duration of orthodontic treatment.

A key limitation of the literature assessed was the brevity of the clinical trials, with research restricted to a short period at the beginning of treatment, often aiming to achieve a specific occlusal goal. Orthodontic treatment is a lengthy process encompassing a series of phases and a range of occlusal objectives. It is therefore important that the effectiveness of surgical adjuncts is measured throughout the complete course of treatment, as it is possible that any potential benefit of the procedure may dissipate over the course of treatment. While this does not necessarily invalidate the procedure, it suggests that the indications for surgical adjuncts may be more limited than the existing body of research currently suggests. A further consideration in future studies includes the assessment of the relative impact of single versus repeated procedures. Moreover, if repeated procedures are undertaken it is important that the periodontal effects are assessed.

Given that adjunctive procedures constitute the addition of a surgical procedure to an otherwise non-surgical course of treatment, it is important that both the possible adverse effects of treatment and the impact of the procedures on patient experiences be assessed. At present, most of the outcome measures used in clinical trials are not standardised patient-oriented outcome measurements. There is a pressing need for the development of an accepted set of patient-oriented outcomes within many specialties, including orthodontics. Addressing these measures during future studies will help to capture both the objective and subjective implications of surgical adjuncts and will facilitate meta-analysis by involving agreed, relevant and consistent outcomes.

Further trials should be robust, well-designed and reported in accordance with the CONSORT statement (http://www.consort-statement.org/) or the extensions of the CONSORT statement. They should also carefully consider the IDEAL recommendations for clinical trials evaluating surgical interventions (Ergina 2009; McCulloch 2009). Clear conduct and reporting will help with appraisal of study results, and accurate judgements about risk of bias and the overall quality of the evidence. Moreover, studies with unclear methodology have been shown to produce biased estimates of treatment effects (Schulz 1995).

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[author-defined order]*

Aboul-Ela 2011

Methods	Split-mouth randomised controlled trial Setting: Cairo University, Cairo, Egypt
Participants	N = 13 (5 male, 8 female) Mean age: 19 years SELECTION CRITERIA • No medical problems • No previous orthodontic treatment • Adequate oral hygiene • Healthy periodontium with probing depths of 3 mm or less, no loss of periodontal attachment or evidence of periodontal bone loss BASELINE CHARACTERISTICS: Class II division 1 incisor relationship
Interventions	After orthodontic alignment miniscrew implants (AbsoAnchor Dentos, Daegu, Korea; diameter, 1.3 mm; length, 8 mm), were placed bilaterally between the maxillary second premolar and the first molar in both groups INTERVENTION: on the corticotomy side the premolar was extracted, a full-thickness submarginal Luebke-Ochsenbein flap was raised and, using a Number 2 bur in a low-speed hand piece, corticotomy perforations were made from the lateral incisor to the first premolar region to a depth approximating the width of the buccal cortical bone. The flap was subsequently replaced and the maxillary archwire (0.016 x 0.022 inch stainless steel) ligated, with nickel-titanium closed-coil springs applying 150 g on each side used for space closure from the miniscrews to the canine hooks CONTROL: a premolar was extracted on the contralateral side 1 day prior to the corticotomy procedure
Outcomes	The following outcomes were assessed on a monthly basis over a 4-month period: • Antero-posterior movement in mm of the maxillary canines and first molars • Periodontal: plaque index, gingival index, probing depth, attachment level, and gingival health
Funding source	No funding declared
Declaration of interests	None
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Using a coin toss. Page 253: 'On the day before the corticotomy surgery, 1 maxillary premolar was extracted on a random basis

Aboul-Ela 2011 (*Continued*)

		(coin toss)' Comment: probably done
Allocation concealment (selection bias)	Unclear risk	There is no mention of allocation concealment. Page 253: 'On the day before the corticotomy surgery, 1 maxillary premolar was extracted on a random basis (coin toss) '. Authors were emailed to clarify, but no response was received Comment: the use a coin toss makes the next allocation unpredictable but the risk of selection bias related to allocation concealment remained unclear
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not feasible
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if assessment was blind. Authors were emailed to clarify, but no response was received
Incomplete outcome data (attrition bias) All outcomes	Low risk	Two subjects failed to complete with reasons given. Page 254: 'We started with 15 patients, but 2 patients were excluded from the study - 1 because of multiple missed appointments and the other because of poor oral hygiene.' Comment: given that failure to complete was reported with reasons given and that these represented less than 20% of the sample, we judged this as at a low risk of bias
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported Comment: we judged this as at a low risk of bias
Other bias	Low risk	Comment: the study appeared to be free of other forms of bias

Alikhani 2013

Methods	Split-mouth randomised controlled trial Setting: NYU graduate clinic, New York, USA
Participants	N = 20 (8 male, 12 female, 10 per group) Age range: 19.5 to 33.1 years, mean age 24.7 years for the control group and 26.8 years for the experimental group INCLUSION CRITERIA: age range: 18-45 years, Class II division 1 malocclusion, no systemic disease, no radiographic evidence of bone loss, history of periodontal therapy, or active periodontal disease, non-smokers, non-gingivitis or untreated caries, probing depth < 4 mm in all teeth, gingival index < 1, plaque index < 1 EXCLUSION CRITERIA: long-term use of antibiotics, phenytoin, cyclosporin, anti-inflammatory drugs, systemic corticosteroids, and calcium channel blockers Poor oral hygiene for more than 2 visits, extreme skeletal Class II malocclusion, overjet > 10 mm, Pg-N perpendicular > 18 mm, ANB > 7, SN-GoGn > 38
Interventions	Maxillary premolar extractions followed by initial alignment preceded the micro-osteoperforations (MOPs) or control space closure interventions EXPERIMENTAL: received MOPs on either the right or left side. Three MOPs were performed distal to the canines both before and during canine retraction using a disposable MOP device (PROPEL Orthodontics, Ossining, NY). A mucoperiostal flap was not raised, and neither anti-inflammatories or antibiotics were prescribed CONTROL: no MOPs. Canine retraction was achieved using calibrated 100 g nickel-titanium coil springs from a temporary anchorage device to a power arm on the canine bracket. Load deflection analysis for the 100 g spring showed that the force level remained relatively constant for decreases of 0.5 to 1.5 mm in the length of the spring after initial activation (data not shown)
Outcomes	• Distance of movement of maxillary canine in mm per unit time. The distance between the canine and the lateral incisor was assessed before and after canine retraction at 3 anatomical points: incisal, middle, and cervical thirds of the crowns. All cast measurements were made using an electric digital callipers (Orthopli Corp, Philadelphia, PA) with an accuracy of 0.01 mm • Gingival crevicular fluid (GCF) samples. GCF was collected to evaluate the level of inflammatory response before orthodontic treatment, immediately before the start of canine retraction, and at each subsequent visit, between 10 a.m. and 12 noon • Pain experience - discomfort was assessed on the day of appliance placement, the day of canine retraction, and subsequently at 24 hours, 7 days and 28 days after canine retraction with a numeric rating scale. Participants were instructed to choose a number (from 0 to 10) that best described their pain: 0 would mean "no pain" and 10 would mean "worst possible pain".
Funding source	No funding declared
Declaration of interests	NYU has filed a patent on microperforations. Propel Orthodontics Inc. licensed the patent and developed a tool for the procedure but did not participate in, or support, the study. NYU purchased the Propel tools used in this clinical trial
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Procedure was not specified. The authors state that participants were "randomly assigned to one of the study groups" (Page 640) Comment: authors were emailed for clarification but the risk of selection bias remained unclear (See Table 2)
Allocation concealment (selection bias)	Unclear risk	Allocation concealment was not reported. The authors state that participants were "randomly assigned to one of the study groups" (Page 640) Comment: authors were emailed for clarification but the risk of selection bias related to allocation concealment remained unclear
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding was not feasible. "The subjects and the residents administering the treatment were aware of the group assignment and therefore were not blinded." (Page 640) . It is unclear whether lack of blinding would affect the outcome
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Page 640: "The investigators performing the measurements and data analysis were blinded from the group assignments." Comment: probably done
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported Comment: we judged this as at a low risk of bias.
Other bias	Unclear risk	NYU has filed a patent on microperforations. Propel Orthodontics Inc. licensed the patent and developed a tool for the procedure but did not participate in or support the study. NYU purchased the Propel tools used in this clinical trial. It is unclear

		whether this association would affect the outcome

Fischer 2007

Methods	Split-mouth randomised controlled trial Setting: Unclear
Participants	N = 6 (2 male, 4 female) Age range = 11.1 to 12.9 years SELECTION CRITERIA: none given BASELINE CHARACTERISTICS: bilaterally ectopic canines requiring orthodontic alignment on a non-extraction basis
Interventions	Non-extraction treatment with preparation for surgical uncovering of both canines was undertaken. Simultaneous surgical exposure of both canines was performed for each patient by the same surgeon INTERVENTION: on the other canine an additional corticotomy procedure was performed involving a series of circular holes mesial and distal to the impacted tooth where possible. These holes were made with a 1.5 mm round bur spaced approximately 2 mm apart extending into the edentulous area into which the tooth was to be moved Attachments were placed on both teeth 2 weeks after the surgical procedure and traction applied with 60 g of force. Patients were seen at 4- to 6-week intervals initially; intervals were reduced to every 2 weeks to complete alignment. Patients were treated until the tips of both canines were fully aligned CONTROL: a conventional surgical exposure.
Outcomes	• Distance of movement of maxillary canine per unit time • Periodontal health: probing depth, alveolar bone levels assessed with periapical radiography
Funding source	No funding declared
Declaration of interests	None
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"By random selection, one canine had a conventional surgical uncovering procedure" (Page 418) Comment: authors were emailed for clarification but the risk of selection bias remained unclear

Fischer 2007 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	"By random selection, one canine had a conventional surgical uncovering procedure" (Page 418) Comment: authors were emailed for clarification but the risk of selection bias related to allocation concealment remained unclear
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding was not feasible. It is unclear whether lack of blinding would affect the outcome
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The orthodontist had no knowledge as to which canine had the corticotomy procedure. Upper study models were taken at this time to measure the distance from the incisal tip of each canine to its final position in the arch
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts were reported.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported Comment: we judged this as at a low risk of bias.
Other bias	Low risk	Comment: the study appeared to be free of other forms of bias

Leethanakul 2014

Methods	Split-mouth randomised controlled trial Setting: Orthodontic Clinic at the Dental Hospital, Prince of Songkla University, Songkhla, Thailand
Participants	N = 18, male (0), female (18) Mean age: 21.9 years (SD: 4.7 years). Age range: 18 to 25 years SELECTION CRITERIA: • Requiring maxillary first premolar extraction and bilateral maxillary canine distalization • Good oral hygiene • Probing depth values not exceeding 3 mm
Interventions	Alignment and levelling was undertaken until passive 0.016 X 0.022-inch stainless-steel archwires were in situ. Mini-implants were placed between the roots of the second premolars and first molars on both the left and right sides about 1 month before the

	surgical procedure INTERVENTION: extraction combined with interseptal bone reduction was performed on the experimental side. The surgical procedure was performed inside the extraction socket of the maxillary first premolar without flap surgery, deepening the socket to the length of the canine apex. The interseptal bone distal to the canine was reduced to 1 to 1. 5 mm in thickness using round and cylindrical carbide burs. If present, the interradicular septal bone of the socket was also removed. The first premolar extraction socket was surgically widened in the buccopalatal dimension along the curvature of the root of the canine CONTROL: traditional extraction of the first premolar without an adjunctive surgical procedure. A power arm fabricated from 0.021 X 0.025-inch stainless-steel archwire was attached to the mesial end of each canine bracket, with the height of the hook approximately the same as the vertical position of the mini-implant, and an elastomeric chain attached to the mini-implant was used to retract the canine. A lingual button was placed on the palatal surface of each canine and first molar. A force was applied on the palatal side by attaching an elastomeric chain between the buttons of the canine and first molar. Both the labial and palatal chains were adjusted to generate an approximately equal magnitude of force, producing a net force of 150 g
Outcomes	• Distance of movement of maxillary canine per unit time. Changes in angulation and rotational control were also assessed • Change in size of PDL space and extraction socket
Funding source	No funding declared
Declaration of interests	None
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	No details of randomisation procedures: "experimental side was allocated by randomisation" (page 40). Authors were emailed for clarification. Author response: "We allocated the experimental side from a pile of pre-shuffled cards. By order of entry, the card on the top of the pile would be opened to designate the experimental side of the subject." Comment: probably done
Allocation concealment (selection bias)	Low risk	Method of allocation concealment not described. Authors were emailed for clarification. Author response: "The surgeons were told by the researcher which side was to

		be experimental side. After that, the allocation data was concealed. The orthodontists treated the subject without knowing which side was experimental side." Comment: probably done
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Blinding was feasible as the procedure was flapless. No details of blinding were provided in the paper. Authors were emailed for clarification. Author response: "The surgeons were told by the researcher which side was to be experimental side. After that, the allocation data was concealed. The orthodontists treated the subject without knowing which side was experimental side. " Comment: probably done
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding of outcome assessors is not mentioned in the paper. Authors were emailed for clarification. Author response: "After finishing data collection, the concealed allocation information were disclosed for data input to the statistical software purpose. The statistician was not aware of the experimental allocation until the data collection process had finished." Comment: it appears that the data analyst was blinded to the respective groups but it remains unclear whether the outcome assessor was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts were reported.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported Comment: we judged this as at a low risk of bias.
Other bias	Low risk	Comment: the study appeared to be free of other forms of bias

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

Study	Reason for exclusion
Abed 2013	Non-randomised study. The study was split-mouth with the surgery performed on the side "which needed more distalization"
ChiCTR-ONRC-13004129	Study protocol evaluated: non-randomised study
IRCT2013082014415N1	Study protocol evaluated: non-randomised study. No comparator
Kharkar 2010	Comparison of two surgical adjunctive approaches without a negative control group
NCT01628575	Study protocol evaluated: Periodontally Accelerated Orthodontics - A Novel Technique For a Shortened Orthodontic Treatment With a Stable Result. A Clinical and Computerized Tomography Analysis Observational Model: Cohort, Time Perspective: Retrospective
Wu 2013	Non-randomised study. Participants agreeing to have the surgical procedure were assigned to the intervention group; those not providing consent were allocated to the control group

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

NCT01093352

Trial name or title	The Efficacy of Surgical Exposure With Alveolar-decortication vs. Conventional Surgical Exposure to Reduce Treatment Time for Orthodontic Alignment of Palatally Impacted Canines
Methods	Allocation: Randomised, Endpoint Classification: Safety/Efficacy Study, Intervention Model: Parallel Assignment, Masking: Double Blind (Subject, Outcomes Assessor), Primary Purpose: Treatment
Participants	30 **Inclusion criteria** • Patients at Birmingham Dental Hospital • Patients with a palatally impacted canine, awaiting surgical exposure • Patients with bilateral impacted canines may be included; in these cases both canines will be treated using the same surgical technique determined by allocation into either the test or control group • Informed consent gained **Exclusion criteria** • History of periodontal disease • Radiographical evidence of pathology associated with the impacted canine • Patients already participating in a research study
Interventions	This study aims to investigate the effect of alveolar-decortication in addition to surgical exposure, on the time taken to align palatally impacted canines. The alternative surgical technique will be compared to the conventional surgical exposure, by recording the time taken to subsequently align the tooth

NCT01093352 (*Continued*)

Outcomes	**Primary outcome:** rate of tooth movement **Secondary outcomes:** time for alignment; total orthodontic treatment time; duration of surgery; adverse effects of surgery
Starting date	2010-01-01
Contact information	PI Thomas Dietrich, DMD, MD, MPH Contact: Mary Bussell, BDS, MFDS Email: maryalicebussell@hotmail.com 0121 237 2817 School of Dentistry, University of Birmingham Birmingham B4 6NN United Kingdom
Notes	http://ichgcp.net/clinical-trials-registry/NCT01093352 Completion date: 2012-09-01

NCT01630473

Trial name or title	Clinical Comparison Between the Corticotomy-assisted Orthodontics and Conventional Orthodontics
Methods	Allocation: Non-Randomised, Endpoint Classification: Efficacy Study, Intervention Model: Parallel Assignment, Masking: Open Label, Primary Purpose: Treatment
Participants	**Inclusion criteria** • Voluntary participation • Legally adult age (> 18 years old) • Full permanent dentition (28 teeth excluding third molars) • Severe anterior teeth crowding • Thick periodontal biotype **Exclusion criteria** • Systemic diseases (i.e. diabetes, HIV) • Cigarette smoking • Under medications: bisphosphonates, anti-epileptic drugs, contraceptives, corticosteroids, estrogen, antihistamine drugs, calcitonin, vitamin D • Previous orthodontic treatment • Periodontal disease • Severe gingival recessions • Pregnancy • Previous root resorption
Interventions	After a periodontal full flap is dissected by using small round burs, vertical lines (2 mm depth corticotomy) parallel to each root of the teeth in the anterior segment (canines and incisors) are created 5 mm beyond the apex in the maxillary bones and interconnecting the lines at the apex by horizontal corticotomies. Marginal bone crest is not touched by the surgical procedure
Outcomes	**Primary outcome:** changes in tooth position **Secondary outcome:** periodontal parameters

NCT01630473 (*Continued*)

Starting date	2011-08-01
Contact information	PI Juan D Arango, DDS. Contact: Javier E Botero, PhD Phone: 057-4-219 6719 Email: drjavo@yahoo.com Faculty of Dentistry, Universidad de Antioquia, Medellin, Antioquia, 00000, Colombia
Notes	http://ichgcp.net/clinical-trials-registry/NCT01630473 Expected completion date 2013-08-01

NCT01720797

Trial name or title	Alveolar Microperforation for Inflammation-Enhanced Tooth Movement During Orthodontic Treatment
Methods	Efficacy Study, Intervention Model: Single Group Assignment, Masking: Single Blind (Outcomes Assessor)
Participants	**Inclusion criteria** • (15) Adolescent and adult subjects ages 18 to 55 years old, in good general health, with adult or mixed dentition, regardless of presence of third molars. • Healthy subjects (American Society of Anesthesiologists Class I) • Periodontal or gingivitis diseases must be addressed prior to study enrolment: Probing Depth < 5mm, Gingival Index < 1, Plaque Index = 1 • If any caries is present, patient will be referred to dentist for treatment and maintenance before beginning treatment • Able to understand English, follow simple instructions and sign informed consent **Exclusion criteria** • Subjects who have taken any local or systemic antibiotics, corticosteroids or periodontal medications in the previous six weeks • Subjects with extreme skeletal Class II: Overjet > 10mm, (Pogonion to Nasion Perpendicular line) Pg-Nper > 18 mm, A point Nasion B point (ANB) > 7, Sella Nasion line to Gonion Gnathion Line (SN-GoGN) > 38 degrees • Vulnerable subjects who unable to consent for themselves
Interventions	Minimally invasive micro-osteoperforation procedure to accelerate orthodontic tooth movement. Micro-osteoperforation (PROPEL) was to be conducted under local or topical anaesthesia after the appliance was placed. The procedure was to be randomised to either the left or right side in each subject. Following the procedure, chlorhexidine rinses were to begin twice a day for a week
Outcomes	**Primary outcome:** tooth movement **Secondary outcome:** radiographic changes
Starting date	2013-04-01
Contact information	Calogero Dolce, D.D.S, PhD University of Florida, Department of Orthodontics,

NCT01720797 (*Continued*)

	Gainesville, Florida, 32610, United States
Notes	Completion date 2015-06-01 http://ichgcp.net/clinical-trials-registry/NCT01720797

NCT01866345

Trial name or title	Randomised, Blinded, Controlled Clinical Trial of Surgically Facilitated Orthodontic Treatment
Methods	Allocation: Randomised, Intervention Model: Parallel Assignment, Masking: Single Blind (Outcomes Assessor), Primary Purpose: Treatment
Participants	**Inclusion criteria** • Adults (18 to 65 years old) who seek orthodontic treatment for proclination and/or de-crowding of mandibular anterior teeth **Exclusion criteria** • Bone-related diseases • Previous or current use of biphosphate therapy • Previous mucogingival surgery in the area • Genetic syndromes, craniofacial anomalies, or cleft lip and/or palate • History of previous orthodontic treatment less than 4 years ago • Smoking > 10 cigarettes/day • Medical history that contraindicates surgical treatment • People who are not cognitively able to give consent • Pregnancy
Interventions	Surgically facilitated orthodontic treatment in the mandibular anterior region
Outcomes	**Primary outcome:** Rate of orthodontic tooth movement **Secondary outcomes:** Incidence of mucogingival defects, incidence and magnitude of apical root resorption
Starting date	2013-06-01
Contact information	Investigator: Georgios A Kotsakis, DDS Contact: James E Hinrichs, DDS, MS Phone: 612-625-9107 Email: hinri001@umn.edu Advanced Education in Periodontology Clinic, Dental School, University of Minnesota, Minneapolis, Minnesota, 55455, United States
Notes	Not yet recruiting: http://ichgcp.net/clinical-trials-registry/NCT01866345

DATA AND ANALYSES

Comparison 1. Surgical adjunctive procedures versus conventional treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Rate of tooth movement (1 month)	3		Mean Difference (Fixed, 95% CI)	0.61 [0.49, 0.72]
2 Rate of tooth movement (3 months)	2		Mean Difference (Fixed, 95% CI)	2.03 [1.52, 2.54]

Analysis 1.1. Comparison 1 Surgical adjunctive procedures versus conventional treatment, Outcome 1 Rate of tooth movement (1 month).

Review: Surgical adjunctive procedures for accelerating orthodontic treatment

Comparison: 1 Surgical adjunctive procedures versus conventional treatment

Outcome: 1 Rate of tooth movement (1 month)

Study or subgroup	Mean Difference (SE)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Aboul-Ela 2011	1.14 (0.66)		0.8 %	1.14 [-0.15, 2.43]
Alikhani 2013	0.6 (0.06)		96.9 %	0.60 [0.48, 0.72]
Leethanakul 2014	0.7 (0.39)		2.3 %	0.70 [-0.06, 1.46]
Total (95% CI)			**100.0 %**	**0.61 [0.49, 0.72]**

Heterogeneity: $Chi^2 = 0.72$, df = 2 (P = 0.70); $I^2 = 0.0\%$

Test for overall effect: Z = 10.27 (P < 0.00001)

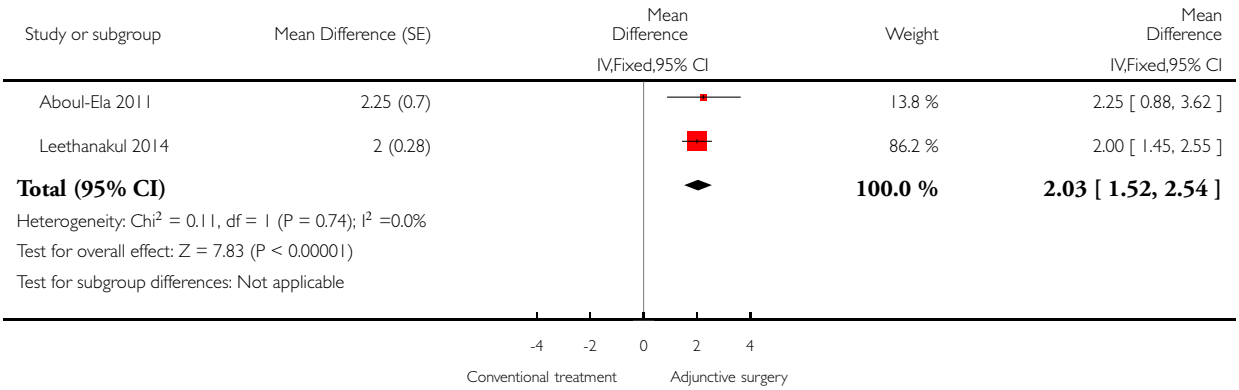
Test for subgroup differences: Not applicable

Analysis 1.2. Comparison 1 Surgical adjunctive procedures versus conventional treatment, Outcome 2 Rate of tooth movement (3 months).

Review: Surgical adjunctive procedures for accelerating orthodontic treatment

Comparison: 1 Surgical adjunctive procedures versus conventional treatment

Outcome: 2 Rate of tooth movement (3 months)



ADDITIONAL TABLES

Table 1. Glossary of unfamiliar terms

Term	Meaning
Alveolar decortication	A surgical procedure involving intentional surgical insult to alveolar bone, designed to accelerate tooth movement. This approach has been modified by the addition of bioabsorbable grafts (Wilcko 2001)
Corticision	A relatively conservative surgical procedure to divide cortices transmucosally without reflecting a mucoperiosteal flap
Distraction osteogenesis	Also known as osteodistraction. It is a surgical procedure used to correct skeletal deformities by lengthening bones at a known rate. This technique has been adapted to facilitate movement of tooth-bearing portions of bone. Variants of distraction osteogenesis include: • Distraction of the periodontal ligament (PDL): a surgical procedure on interseptal bone to reduce resistance to movement • Distraction of the dento-alveolus: a surgical procedure involving separation of the dental segment from the jaw bone to allow distraction osteogenesis in the osteotomy site
Ectopic canine	Abnormal position of a canine tooth; usually a maxillary canine
Iatrogenic	Condition caused or exacerbated by medical examination or treatment

Table 1. Glossary of unfamiliar terms (*Continued*)

Inflammatory mediators	Molecules released by immune cells when harmful chemicals are identified or following surgical intervention
Malocclusion	Deviation from the normal occlusion with incorrect bite, dental malalignment or a combination of these
Osteoclastic activity	Processes of cells which break down bone and are instrumental in bone remodelling and tooth movement

Table 2. Email contact with trial authors

Author	Email address	Date	Request
Dr. El-Mangoury (Aboul-Ela 2011)	mangoury@usa.net	16/11/2013	We would be grateful if you could possibly provide further information on the following: 1. You mention randomisation via a coin toss. Did you use any mechanisms to balance between left and right sides the allocation of the interventions? 2. We understand that blinding the investigator/patient was not feasible. Was the assessment of the outcome on the dental casts blind?
Dr. Fischer (Fischer 2007)	tfdmd@mac.com	16/11/2013	You discuss randomisation: "By random selection, one canine had a conventional surgical uncovering procedure". Did you use any particular methods to generate your random allocation or did you sequentially assign the interventions (Right-left, Left-right etc). Did you use any methods for allocation concealment?
Dr. Teixeira (Alikhani 2013)	cristina.teixeira@nyu.edu	1/12/2013	We would be grateful if you could possibly provide further information on the following so we can properly assess your trial: 1. Randomisation: you mention that: "randomly assigned to one of the study groups". Could you possibly provide further details on how you actually prepared and implemented randomisation to the control or intervention group? Did you use any mechanisms such as restrictions to balance between left and right sides during the allocation the MOPs? You also state that: "The patients were divided randomly into 2 groups with similar severities of malocclusion (P . 0.05) (Table III)". I assume you used stratification to assure balance on baseline characteristics between treatment groups? How many strata and which ones did you use? How did you implement allocation concealment? 2. We understand that blinding the investigator/patient was not feasible. Do you think this has an im-

Table 2. Email contact with trial authors (*Continued*)

			pact on follow-up? How did you assure blinding during outcome assessment? 3. We would be grateful if you could possibly provide us with the mean values and standard deviations for space closure per treatment group You used a split mouth approach for 10 patients, if I understood correctly, and for the other 10 patients a parallel approach. Could you possibly provide us also with the mean (SD) per quadrant and-the mean difference between the maxillary quadrants and the associated standard deviation as those values are not retrievable from the graphs and it is important that we have the correct numbers? We would need the SD of mean difference between quadrants as there is correlation for within patient measurements which is not estimable if you only supply the SDs per quadrant 9/12/2013: Reminder email: ct40@nyu.edu, ma343@nyu.edu, mani.alikhani@nyu.edu, cristina.teixeira@nyu.edu
Dr Leethanakul (Leethanakul 2014)	nokleethanakul@yahoo.com	18/9/2014	I would just like to clarify a couple of points. 1. How did you randomise participants to each group? Did you for example use coin toss, date of birth or a computer programme? 2. Was group allocation concealed from the treating clinician? 3. Were operators or data assessor a kept blind to group allocation?

APPENDICES

Appendix 1. Cochrane Oral Health Group Trials Register search strategy

#1 (((tooth or teeth) AND move*):ti,ab) AND (INREGISTER) [REFERENCE] [STANDARD]
#2 (orthodontic*:ti,ab) AND (INREGISTER) [REFERENCE] [STANDARD]
#3 (#1 or #2) AND (INREGISTER) [REFERENCE] [STANDARD]
#4 ((distract* and ("periodontal ligament*" or PDL* or dento-alveolus or "dento alveolus" or dentoalveolus)):ti,ab) AND (INREGISTER) [REFERENCE] [STANDARD]
#5 ((surg* and "interseptal bone"):ti,ab) AND (INREGISTER) [REFERENCE] [STANDARD]
#6 ((decorticat* or corticision or corticotom*):ti,ab) AND (INREGISTER) [REFERENCE] [STANDARD]
#7 ((periodont* and accelerat*):ti,ab) AND (INREGISTER) [REFERENCE] [STANDARD]
#8 ((alveolar and (reshap* or augment* or distract*)):ti,ab) AND (INREGISTER) [REFERENCE] [STANDARD]
#9 ((surgery or surgical or "distraction osteogenesis"):ti,ab) AND (INREGISTER) [REFERENCE] [STANDARD]
#10 (#4 or #5 or #6 or #7 or #8 or #9) AND (INREGISTER) [REFERENCE] [STANDARD]
#11 (#3 and #10) AND (INREGISTER) [REFERENCE] [STANDARD]

Appendix 2. Cochrane Central Register of Controlled Trials search strategy

#1 [mh "Orthodontics, corrective"]
#2 orthodontic*
#3 ((tooth or teeth) and move*)
#4 #1 or #2 or #3
#5 (distract* and ("periodontal ligament*" or PDL* or dento-alveolus or "dento alveolus" or dentoalveolus))
#6 (surg* and "interseptal bone")
#7 (decorticat* or corticision or corticotom*)
#8 (periodont* near/3 accelerat*)
#9 (alveolar near/5 (reshap* or augment* or distract* or surg*))
#10 [mh ^"Distraction osteogenesis"]
#11 [mh ^"Oral surgical procedures"]
#12 (surgery or surgical)
#13 #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12#11 #4 and #13

Appendix 3. MEDLINE via OVID search strategy

1. exp Orthodontics, Corrective/
2. orthodontic$.ti,ab.
3. ((tooth or teeth) and move$).ti,ab.
4. or/1-3
5. (distract$ and ("periodontal ligament$" or PDL$ or dento-alveolus or "dento alveolus" or dentoalveolus)).ti,ab.
6. (surg$ and "interseptal bone").ti,ab.
7. (decorticat$ or corticision or corticotom$).ti,ab.
8. (periodont$ adj3 accelerat$).ti,ab.
9. (alveolar adj5 (reshap$ or augment$ or distract$ or surg$ or piezocision or fiberotom$)).ti,ab.
10. Distraction osteogenesis/
11. Oral surgical procedures/
12. (surgery or surgical).ti,ab.
13. or/5-12
14. 4 and 13

The above subject search was linked to the Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomized 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 via OVID search strategy

1. exp Orthodontics/
2. orthodontic$.ti,ab.
3. ((tooth or teeth) and move$).ti,ab.
4. or/1-3
5. (distract$ and ("periodontal ligament$" or PDL$ or dento-alveolus or "dento alveolus" or dentoalveolus)).ti,ab.
6. (surg$ and "interseptal bone").ti,ab.
7. (decorticat$ or corticision or corticotom$).ti,ab.
8. (periodont$ adj3 accelerat$).ti,ab.
9. (alveolar adj5 (reshap$ or augment$ or distract$)).ti,ab.
10. Distraction osteogenesis/
11. Oral surgery/
12. (surgery or surgical or "distraction osteogenesis").ti,ab.
13. or/5-12
14. 4 and 13

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 via BIREME Virtual Health Library search strategy

Mh Osteogenesis, Distraction or mh Oral Surgical Procedures or surgery or surgical or cirúrgicos or quirúrgicos or decortica$ or corticision or cortico$ or distrac$ or (periodon$ and acceler$) or (alveolar and reshap$) or (alveolar and remodel$) or (alveolar and augment) or (alveolar and aument$) [Words]
Mh Orthodontics or orthodontic$ or ortodoncia or ortodontia [Words]
The above subject search was linked to the Brazilian Cochrane Center filter for identifying randomised controlled trials in 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)))

Appendix 6. Trials registries search strategy

Meta Register of Controlled Trials Search Strategy; US National Institutes of Health Trials Register (ClinicalTrials.gov) Search Strategy; WHO International Trials Registry Platform Search Strategy
Search terms used: orthodontic and accelerating; orthodontic and acceleration; orthodontic and accelerate

CONTRIBUTIONS OF AUTHORS

- Running searches: Cochrane Oral Health Group
- Identifying relevant titles and abstracts from searches: Padhraig S Fleming (PSF), Nikolaos Pandis (NP), Zbys Fedorowicz (ZF)
- Obtaining copies of trials: PSF, NP, ZF
- Selection of trials: PSF, NP
- Extracting data from trials: PSF, NP
- Entering data into RevMan: NP, PSF
- Carrying out 'Risk of bias' assessment: PSF, Ama Johal (AJ)
- Carrying out analysis: NP, PSF
- Interpreting the data: PSF, NP, ZF, Ahmed El-Angbawi (AE)
- Drafting the final review: PSF, NP, ZF

DECLARATIONS OF INTEREST

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

Padhraig S Fleming: none known

Nikolaos Pandis: none known

Ama Johal: none known

Ahmed El-Angbawi: none known

Zbys Fedorowicz: none known

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- Cochrane Oral Health Group Global Alliance, Other.

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- School of Dentistry, The University of Manchester, UK.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In view of the absence of data concerning the overall duration of orthodontic treatment, we used surrogate measures of the duration of treatment including the rate of tooth movement over a defined period.

We changed the presentation order of the secondary outcomes.

INDEX TERMS

Medical Subject Headings (MeSH)

Alveolar Process [surgery]; Cuspid; Malocclusion [therapy]; Orthodontics, Corrective [*methods]; Osteogenesis, Distraction [methods]; Randomized Controlled Trials as Topic; Reoperation; Time Factors; Tooth Movement [methods; statistics & numerical data]

MeSH check words

Adolescent; Adult; Child; Humans