AN OVERVIEW OF RANDOMIZED CONTROL TRIALS IN ORTHODONTICS

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Abstract
The comparison of technologies or alternative ways to accomplish the same aim, is inherently difficult. In orthodontics, technology covers a wide spectrum of areas: variations in treatment approach, appliances, wires, diagnostic procedures, and patient management techniques. Clinical trial methodology has been developed to minimize the effect of bias and to provide more objective answers to questions of comparative efficacy and benefits of particular treatments or procedures. The randomized controlled clinical trial (RCT) is now generally considered the strongest research design for the comparison of treatments. This article is intended to provide an overview of the RCT’s done in the field of orthodontics. They have been broadly classified and discussed under 4 headings- RCT’s in treatment techniques, biology and disorders, materials and devices and retaining devices.

Introduction
Clinical trials are always prospective studies, and can be classified as (1) uncontrolled, if there is no concurrent comparison group although historical controls may be used; (2) nonrandom controlled trial, if a concurrent comparison group is used but patients allocation to each group occurs by means of some nonrandom process (e.g., convenience or clinical judgment); and (3) randomized controlled trial (RCT), if subjects are randomly allocated into treatment and control groups.

Technology in orthodontics covers a wide spectrum of areas: variations in treatment approach, appliances, wires, diagnostic procedures, and patient management techniques. New developments or modifications of existing methods are frequently based on theoretical constructs or empirical evidence. Many of these technologies have later been deemed ineffective. The comparison of technologies, or alternative ways to accomplish the same aim, is inherently difficult. Until recently, comparisons in orthodontics have generally depended on case series or observational studies.

The Randomized clinical trial (RCT) is now generally considered the strongest research design for the comparison of treatment alternatives. The advantage of the RCT is that it is prospective with subjects and the data under some control by the investigator. The treatment or intervention is randomly allocated, so perceptions of the investigator on the value of a particular treatment should not influence treatment allocation, which could bias the results. The study is planned before the data is collected; hence it results in
a minimization of bias that is inherent in the retrospective study.

First step in conducting a RCT is to define a sample group from a group of population using inclusion and exclusion criteria. Adequate sample size is calculated. The treatment outcomes are clearly stated. Then the sample is allotted to control and experimental group, using selected randomization technique. Randomization is central to the mechanics of the trial, because by allocating patients randomly, patient characteristics are likely to be similar across the groups at the start. By keeping the groups balanced at baseline, the outcomes can be attributed to the intervention with minimal effects from other factors that may influence the treatments. Three frequently used methods of randomization are (1) Simple randomization is equivalent to coin tossing. (2) Block randomization assures that the number of subjects is closely balanced at periodic intervals (3) Blocked stratification guards against imbalances between the groups resulting in the prognostic factor(s) being more evenly distributed within the treatment groups.

The modern era of RCTs began in the early 1950s with the evaluation of streptomycin in patients with tuberculosis.

This article is intended to provide an overview of the RCT’s done in the field of orthodontics. Some articles failed to state in the title or abstract that the paper was reporting a clinical trial or those treatments were allocated randomly. So, those articles that were classified as RCT by Cochrane data bases and review articles were included in this overview. For convenience, RCT’s in orthodontics are broadly classified into 4 major topics,

1. RCT’s in treatment techniques
2. RCT’s in Biology and Disorders
3. RCT’s in Materials and Devices
4. RCT’s in retaining devices

**RCT’s in treatment techniques (Dentofacial orthopedics, Temporary anchorage devices, Expansion, Self Ligation etc)**

**RCT’s in Treatment of Class II malocclusion**

RCT’s on the treatment of Class II treatment were first conducted by Nelson and Webster at the University of Otago. Their inclusion criteria were Class II division 1 with bilateral Class II malocclusion. Treatment with Frankel, Harvold activator was compared with untreated controls. They found no evidence on mandibular size alteration, and the treatment effects were mostly vertical dimension increase.

During the early 1990s, three American orthodontic departments received around seven million dollars from the National Institute of Dental Research (NIDR) to run RCTs to study the effects of functional appliances and headgear on Class II malocclusions. These schools were the University of Pennsylvania, the University Florida, and the University North Carolina. Inclusion criteria of the RCT done in University of North Carolina were overjet greater than 7mm and 1 year pre-peak height velocity as judged by hand wrist radiograph. The subjects were randomly assigned to observation only, headgear, or functional appliance (modified bionator) and were monitored for 15 months. It was shown that headgear produces greater change in the maxilla (restricted forward movement of the maxilla), whereas functional appliance therapy produces greater mandibular change (increase in mandibular length), but there was considerable variation in the effect with both appliance systems. Children in all three groups were pooled together and continued into second phase of treatment, where all underwent comprehensive fixed appliance therapy. Results at end of second phase showed that, time in fixed appliances was shorter for children who underwent early treatment. Also, only small differences were noted in anteroposterior jaw position between the groups at the completion of treatment. The number of patients who required extraction of permanent teeth was greater in the early functional appliance group than in the headgear or control group. The option of orthognathic surgery was presented more often in the cases of children who did not undergo early treatment, but surgery was considered almost as frequently in the previous headgear group as in the controls, and less often in the patients previously treated with functional appliances.

Brin et al using the same sample showed that early growth modification reduces the severity of overjet in Class II malocclusion and might have a role in reducing the likelihood of external apical root resorption.

In a similarly designed RCT at University of Florida, children with Class II molars including subdivisions were randomly assigned to control, bionator, and headgear/biteplane treatments. Phase I results showed that both bionator and headgear treatments corrected Class II molar relationships. The skeletal changes, largely attributable to enhanced mandibular growth in both headgear and bionator subjects, were stable a year after the end of treatment, but dental movements relapsed. They also suggested that headgear may be superior to bionator/biteplane in achieving a Class II correction during early treatment. Results at the end
of phase 2 comprehensive treatment showed that there were no significant differences with respect to initial PAR or final PAR among the 3 treatment protocols. They did not support the hypothesis that different dentoalveolar outcomes are obtained between 2-phase and 1-phase treatment of Class II malocclusions.

In RCT done at University of Pennsylvania, children with bilateral distoclusion (unilateral Class I excluded) and a minimum ANB angle of 4.5° were assigned at random to treatment with either a headgear or a Frankel group. Ghafari et al showed that on average, the headgear has a distal effect on the maxilla and first molars; The Frankel FUNCTIONAL regulator restrains the growth of the maxilla and results in a retroclination of the maxillary incisors and a proclination of the mandibular incisors. The effects of both appliances on mandibular length were similar. A significant finding of the study is the increased maxillary intercanine distance and spacing among the maxillary anterior teeth with headgear treatment. Treatment in late childhood was as effective as that in mid childhood.

In a Multicenter RCT in United Kingdom, subjects with minimum of 7 mm overjet were randomly allocated to receive treatment with a Twin-block appliance or to an untreated, control group. After 15 months of observation, O’Brien showed that early treatment with the Twin-block appliance is effective in reducing overjet and severity of malocclusion but most of this correction was due to dentoalveolar change, but some was due to favorable skeletal change. Twin-block appliances resulted in an increase in self-concept and a reduction of negative social experiences. The subjects also reported treatment benefits that could be related to improved self-esteem. The second phase results are yet to be published; provisional results indicate that, at the end of phase 2 treatment, there were no differences between the patients who had early treatment and those who did not. In another multicentre RCT, Subjects with minimum of 7 mm overjet were randomly allocated to receive treatment with a Herbst or Twin-block appliance. Results showed that treatment with the Herbst appliance resulted in a lower failure-to-complete rate. O’Brien found that there were no differences in treatment time between appliances, but significantly more appointments were needed for repair of the Herbst appliance than for the Twin-block. There were no differences in skeletal and dental changes between the appliances. Because of the high cooperation rates of patients using it, the Herbst appliance could be the appliance of choice for treating adolescents with Class II Division 1 malocclusion.

RCT’s in Treatment of Class III

Facemask with or without rapid palatal expansion was compared. Subjects with Class III molar relationship were randomly assigned to 1 of 3 groups: facemask with palatal expansion, facemask without palatal expansion, and observation for 12 months. Vaughn et al found no significant differences between expansion and non expansion groups in any measured variable. This study demonstrated that facemask therapy with or without palatal expansion produced equivalent changes in the dentofacial complex that combined to improve the Class III malocclusion.

RCT’s in Distalization of molars

Bondemark and Karlsson using RCT methodology compared intraoral and extraoral appliances for distalization of maxillary molars and showed that intraoral appliance was more effective than the extraoral. Also, moderate anchorage loss was produced with intraoral appliance implying increased overjet whereas the extraoral appliance decreased overjet.

RCT’s in Temporary Anchorage Devices

Sandler and Benson using RCT methodology compared Midpalatal implants with Headgears for distalization of molars and demonstrated that all skeletal and dental points moved mesially more in the headgear group during treatment than in the implant group. The total number of visits was greater in the implant group, but the overall treatment times were almost identical. They concluded that Midpalatal implants are an acceptable technique for reinforcing anchorage in orthodontic patients.

Feldmann and Bondemark compared anchorage capacity of 4 anchorage systems namely onplant, orthosystem implant, headgear, and transpalatal bar. They found that stable anchorage was provided with the onplant and the orthosystem implant. Headgear anchorage was stable during the leveling/aligning phase but demonstrated anchorage loss at the end of the observation period. The transpalatal bar provided insufficient anchorage throughout the observation period.

Madhur Upadhyay quantified treatment effects of en-masse retraction of anterior teeth with mini-implants as anchor units and compared it with conventional anchorage. Anchorage loss, in both the horizontal and vertical directions, was noted in conventional anchorage, whereas space closure with mini-implants showed distalization and intrusion of molars. There was no difference in mean retraction time.

RCT’s in expansion

Thilander in his RCT compared grinding and expansion plates for correction of crossbite and suggested that removal of premature contacts of the
primary teeth is effective in preventing a posterior crossbite from being perpetuated to the mixed dentition. When grinding alone is not effective, using a removable expansion plate to expand will decrease the risk of a posterior crossbite from being perpetuated to the permanent dentition. Banded or bonded slow maxillary expansion were compared in an RCT by Mossaz-Joelson, and they found no difference in the expansion obtained when using either a bonded or banded slow maxillary expansion appliance. The banded appliance took longer to insert, and Oral hygiene was harder to maintain for patients in the bonded group. Comparing Quad helix and Expansion arch, McNally suggested that quadhelix and the expansion arch were equally effective in producing expansion. There was some evidence that the expansion arch was slightly more reliable for producing expansion since the data for quadhelix intercanine width increase are skewed. Petrén and Bondemark in his RCT compared Quad-helix, expansion plate, composite onlay, and untreated control. They said that if crossbite is planned to be corrected in the mixed dentition treatment with the quad-helix is an appropriate and successful method. Treatment with the expansion plate was unsuccessful in one third of the patients, and the reason was insufficient patient cooperation. Crossbite correction with composite onlay in the mixed dentition was not effective.

RCT's in correcting Anterior open bite
Erbay compared Fränkel's function regulator (FR-4) appliance on the treatment of Angle Class I skeletal anterior open bite malocclusion with untreated controls. The results indicate that a spontaneous downward and backward growth direction of the mandible observed in the control group could be changed to an upward and forward direction by FR-4 therapy.

Kiliaridis compared posterior bite blocks with posterior repelling magnet splints for correction of anterior open bite. Dental and skeletal vertical relation responded quickly to the magnet treatment. The open bite was generally closed in just under 4 months, especially in patients in early mixed dentition. Transverse problems, i.e. unilateral cross-bite, sometimes followed by scissor-bite on the opposite side were observed. The patients who wore acrylic posterior bite-blocks also showed improvement in the dental and skeletal vertical relationships, especially during the first months. This was followed by a 'plateau' period. No transverse problems were found in these patients.

Torres compared Removable appliance with a palatal crib with high-pull chin cup therapy in children with an Angle Class I anterior open bite. The results showed no significant differences in the level of molar eruption or in lower anterior face height, suggesting that the vertical control expected from the chin cup therapy did not occur. The dentoalveolar changes at the anterior region of the dental arches were mainly responsible for closure of the anterior open bite in patients treated in the mixed dentition.

RCT's in self ligation brackets
Scott compared the efficiency of mandibular tooth alignment and the clinical effectiveness of a self-ligating and a conventional preadjusted edgewise orthodontic bracket system. He found no significant difference in initial rate of alignment for either bracket system. Incisor root resorption was not clinically significant and did not differ between systems. Damon3 self-ligating brackets are no more efficient than conventional ligated preadjusted brackets during tooth alignment.

Fleming compared pain experience during Initial Alignment with a Self-ligating bracket system (SmartClip) and a Conventional appliance (Victory). He found that bracket type had no effect on subjective pain experience during the first week after initial placement of archwire. Significantly greater discomfort was experienced during archwire insertion and removal with the SmartClip appliance.

RCT's on canine lace backs
Active ligation, Power chain and NiTi coil spring for space closure were compared using RCT by Dixon, and showed that NiTi coil spring gave the most rapid rate of space closure; Power chain can be considered cheaper option as it is also effective. Slowest rate of closure was seen when active ligatures were used.

Two RCT's compared anchorage loss of molars during leveling with and without use of lacebacks. They showed contradictory results. Usmani showed no difference in anchorage loss of molars during leveling in the upper jaw with or without laceback ligatures. Irvine on the other hand, demonstrated a significant larger anchorage loss when laceback ligatures were used for leveling in the lower jaw.

RCT on sequelae of Extractions of lower primary canines to relieve crowding
Kau in a RCT done to assess extraction of deciduous canine as method to relieve crowding, randomly allocated subjects to a primary canine non-extraction or extraction group and were followed for 2 years. He showed that crowding reduced 1.27 mm in the non-extraction group and 6.03 mm in the extraction group. But arch perimeter decreased more in the extraction group by 2.73 mm by molars moving forward.
RCT on Orthodontic archwire sequence
Mandall\(^2\) compared three different wire sequence namely A = 0.016-inch nickel titanium (NiTi), 0.018 × 0.025-inch NiTi, and 0.019 × 0.025-inch stainless steel (SS); B = 0.016-inch NiTi, 0.016-inch SS, 0.020-inch SS, and 0.019 × 0.025-inch SS; and C = 0.016 × 0.022-inch copper (Cu) NiTi, 0.019 × 0.025-inch CuNiTi, and 0.019 × 0.025-inch SS. This trial showed that no archwire sequence tested was more effective than another, in terms of reported patient discomfort or upper incisor root resorption or time taken to reach working archwire. However, sequence B required statistically significantly more visits, before the working archwire was placed.

RCT on Ion implantation of TMA archwires
Kula\(^3\) conducted a split-mouth randomized clinical trial was used to determine whether ion implantation of b-titanium archwire would facilitate sliding space closure. 0.19 × 0.025-inch b-titanium archwires, ion-implanted on one half only, were placed. Nickel-titanium springs (150 g) were placed bilaterally to close the extraction spaces. He found that median rates of space closure were not significantly different between the ion-implanted and the unimplanted sides.

RCT on Gingival offset brackets
Thind\(^4\) compared the clinical bond failure rate of gingivally offset mandibular premolar brackets and standard mandibular premolar brackets, and showed that gingivally offset mandibular premolar brackets have a lower bond failure rate than standard mandibular premolar brackets.

RCT’s in Biology and Disorders

RCT’S on Treatment for Obstructive sleep apnea
Johnston\(^5\) compared mandibular advancement devices with placebo for correction of Obstructive Sleep Apnea and reported that mandibular advancement devices was more effective than placebo in reducing snoring, reported daytime sleepiness and morning tiredness but excessive salivation was the most common complaint.

Cooke and Battagel\(^6\) compared advanced and non advanced thermoplastic mandibular advancement devices and suggested that the advanced thermoplastic mandibular advancement device is effective in the treatment of snoring in two out of three non-apnoeic snorers; their sleeping partners derive benefits from this form of treatment.

Tan\(^7\) did RCT comparing Nasal continuous positive airway pressure vs. mandibular advancement device.

Nasal continuous positive airway pressure reduced the apnea-hypopnea index and day time sleepiness more than mandibular advancement device but the difference was not significant. And mandibular advancement device was better tolerated by the patients. With acceptable efficacy and better tolerability, mandibular advancement device is a suitable alternative treatment for obstructive sleep apnea.

RCT’s on Tempromandibular joint disorder
Keeling\(^8\) assessed symptoms and signs of temporomandibular disorders in children enrolled in a randomized controlled trial of early treatment for Class II malocclusion in University of Florida. He showed early treatment with bionators and headgear/bite planes did not place healthy children without these signs at risk for developing these signs. Only increasing age (for the development of sounds) and failure to achieve a Class 1 molar relation (for development of muscle pain) placed sign-free children at greater risk. This is in contrast to the current consensus that not achieving a specific gnathologic occlusal scheme does not increase the risk of having TMD signs. Subjects with TMJ pain at baseline were 7 times more likely to have pain at follow-up if they had been treated with a headgear/bite plane or observed than if they had been treated with a bionator. These data from children are in agreement with a review of the literature\(^9\) that recently concluded that adult anterior repositioning splint therapy appears to be superior to the flat-plane occlusal splint in eliminating palpatory tenderness of the TMJ.

Forssel\(^10\) in his review of occlusal treatments in temporomandibular disorders, found eight RCT’s. Based on these trials he concluded that occlusal splints might be of some benefit in the treatment of TMD but evidence for occlusal adjustment for management of temporomandibular disorders is lacking. Further 7 RCT’s were conducted to assess the effectiveness of intra-articular injection of hyaluronate. Reviewers found that long term effects (3 months) favor hyaluronate for the improvement of clinical signs and overall treatment of TMD, but mild and transient adverse reactions such as discomfort or pain at the injection site were reported.

RCT’s on Pain in Orthodontics
In a RCT comparing procedures recommended to reduce pain, Otasevic\(^11\) compared Bite-wafers where immediate mastication of the wafers for 10 minutes, and thereafter to bite on the wafers to prevent pain for the next 7 days, was compared with Reduced-mastication where patients were advised not to
masticate for 3 hours after placement of the fixed appliance and to avoid masticating hard food for 7 days. He found that more pain was reported by those using bite wafers than by those who avoided masticatory activity after placement of fixed appliances.

Bradley43 compared 400 mg of oral ibuprofen or 1 g of oral paracetamol an hour before and again 6 hours after separator placement for control of orthodontic pain. His trial found that a combination of preoperative and postoperative ibuprofen is more effective than paracetamol in the control of orthodontic pain.

**RCT’s in Retaining devices**

Rose44 compared the reliability of 0.0175-inch multistrand wire canine to canine retainers with resin composite reinforced with plasma-treated polyethylene ribbon retainers and reported that Ribbon reinforced retainer (five out of ten retainers failed) while the multi-strand wire retainer (one out of ten retainer failed)

Rowland45 and Hichens46 compared Hawley vs. vacuum formed retainers, their clinical effectiveness, cost-effectiveness and patient satisfaction. They reported that Vacuum formed retainers are more effective than Hawley retainers at holding the correction of the maxillary and mandibular labial segments. Vacuum formed retainers were more cost-effective than Hawley retainers from all perspectives. The majority of subjects showed a preference for Vacuum formed retainers compared with Hawley retainers.

### RCT’s in Materials and Devices

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**Conclusion**

Certainly, there are circumstances that would prohibit the use of an RCT, but the RCT still remains the strongest method for comparing the efficacy of treatments. The RCT is an unusually reliable method for learning from experience. Its success comes from structuring that experience so as to eliminate many of the sources of ambiguity apparent in other research designs.

**References**


42. Otasevic M, Naini FB, Daljit S. Gill. Prospective randomized clinical trial comparing the effects of a masticatory bite wafer and avoidance of hard food on pain associated with initial orthodontic tooth movement. Am J Orthod Dentofacial Orthop 2006;130:6.e9-6.e15


