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Review Article

Whether adequate attention given to confounding factors affecting tooth movement in canine retraction studies? - A literature review with systematic criteria

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***ABSTRACT*:**
Background: The commonly used models to evaluate orthodontic tooth movement(OTM)in humans are canine retraction, lower anterior de-crowding, premolar buccal/apical movement, incisor apical movement, en-mass retraction, mesial/distal movement of molars and dental expansion.In therapeutic extraction cases, closure of first premolar space is a major step; hence earlier researchers have focused their attention on canine retraction to evaluate OTM. **Objective:** Studying OTM by considering as much as possible key factors that might have an effect on OTM is important and hence this review aimed to discuss whether the well-studied confounding variables had been considered when evaluating tooth movement in canine retraction studies. **Method-Data source:** Literature search had been carried out in the PubMed and Cochrane central library database using an appropriate search strategy together with hand searching. **Study selection:** A total of 47 articles were scrutinized from 418 clinical trials that met the stringent inclusion and exclusion criteria. **Data extraction**: Two authors independently extracted the data from each article with a pre-defined data field and the extracted data was finalized by the third author. **Results:** There is a presence of heterogeneity among the studies. Few studies have given adequate attention to well-studied confounding variables. **Conclusion**: The present review reveals that the factors that influence the tooth movement are vast and hence the outcomes of these studies should be viewed cautiously.
Key words: Confounding factors, OTM, Canine retraction.

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INTRODUCTION:

Orthodontic tooth movement (OTM) is a multifactorial event and individual variation in these factors might alter OTM.OTM varies depending upon the magnitude, duration and frequency of the applied force as well as the individual biological response of periodontal ligament and bone. Hence in the past, due importance was given to the type of force and the force generating mechanics, later at the beginning of twentieth-century histological studies conducted by Oppenheim[1]gave an in-depth knowledge about the biological response for a given orthodontic force. Various studies[1-5] had been carried out to explore about optimal orthodontic force and to understand the relationship between orthodontic force and rate of tooth movement.[6] Yijin Ren et al.,[7] based on their systematic review concluded that there is no evidence to recommend a force as optimal in clinical orthodontics

Iwasaki et al.,[8] and Derandellier et al.,[9] studied stresses in addition to forces. Even with standardized force/stress there exists a variability in the rate of tooth movement in human. Parallel to these studies, investigators are attempting to accelerate the rate of tooth movement with less or no iatrogenic effect on the tooth and surrounding structures using different adjuvant and thereby reducing the overall treatment duration.OTM research is under paradigm shift from the mechanical perspective to the biologic and genetic perspective and that warrants the need to study the individual-specific characteristics that might affect the biological response that initiates the bone modeling thereby tooth movement when orthodontic force are being applied. Recent studies focus on not only

evaluation but also correlate the tooth movement with biomarkers in gingival crevicular fluid (GCF) and genetic data in orthodontic patients.
Considering as much as possible key factors that might have an effect on OTM is necessary for evaluating OTM. In humans, OTM can be studied using various models and they are studied either in the single tooth or multiple teeth. When studying single tooth movement, canine retraction can be considered as an ideal model as this is routinely done in clinical practice in maximum anchorage cases, it is the most significant part of orthodontic treatment in the therapeutic extraction of first premolar cases. Besides this Force/stress calculation based on root surface area is not cumbersome in this model.

Objective:
To examine "Whether the adequate attention is given to well-studied confounding factors affecting tooth movement in canine retraction studies?" we reviewed clinical trials that assessed canine movement using different mechanical appliances with and without adjuvants

MATERIALS AND METHODS:

Eligibility criteria:

The Inclusion criteria for the articles were:
Population- Humans, Age- must be specified, Sex- must mention, sample size > 5,canine retraction mechanics- either arch/sliding/loop mechanism with or without adjuvant, force- amount must be specified, primary or secondary outcome should be - rate/speed/velocity of tooth movement and the method utilized to calculate tooth movement must be mentioned, site of the studymust be specified, type of study – clinical trials.

The Exclusion criteria for the articles were:
Animal studies/Computer simulated studies/FEM studies/canine distraction device study/ systematic review/overview/ Comments and letters /lingual orthodontics/Impacted canines/highly placed / canine in cross bite/Case report/ periodontal disease/ canine retraction studied in patients under medication/ if canine retraction measurement or value not mentioned.

Information source:
An electronic Literature search was conducted in PubMed and Cochrane central library from 1965/01/01 to 2018/05/31 in addition to electronic search, a manual search of articles had also been done during the same period of time. Only English language literatures are included in this review and no translation of articles of other languages has been done.

Search strategy details:
Using Boolean operators and free text terms the search strategy was finalized and applied to the following database:

PubMed- (canine retraction) OR rate of canine movement) OR GCF during canine retraction) OR bone density of maxillary arch) OR bone density of mandibular arch) AND humans) NOT animals) NOT osteoporosis) NOT bisphosphonate) NOT systemic bone disease) NOT systemic inflammatory disease) NOT diabetes) NOT periodontitis) NOT peri-implantitis

Cochrane central library –1.canine retraction and rate of canine movement :ti,ab,kw (Word variations have been searched),2.GCF and canine retraction, 3.bone density and canine retraction.

Study selection:
After removing the duplicates and non-English language literatures, preliminary screening was done by going through the title and abstract. Inappropriate articles were removed at this stage and the remaining articles were independently and manually assessed for eligibility based on the inclusion and exclusion by going through the full text by two reviewers LPS and BV and the conflicts were resolved by the third reviewer RK. The study selection process has been summarised using the PRISMA flow diagram **(Figure 1)**

Data collection and Data items:
After removing articles that did not fit into inclusion and exclusion criteria, the primary data extraction was done based on the following study characteristics Sample size, Age in years, Sex, Retraction mechanics, Force, Site of study, GCF, Oral hygiene regime/monitoring, Methods to measure OTM, Anchorage, Occlusal interference consideration and Genetic data (**Annexure-1**). From this primary data, details of well-studied confounding variables (**Table I)**and associated outcomes (**Table II)**were collected by two review authors using a custom-made questionnaire and the third author checked the extracted data.

Well-studied confounding variables (Table: I)

1. Age- Whether the study sample consists of the same age group or the authors compared different age group?
2. Sex-Did the authors study either specific sex or both sex divided equally without combining the results of both genders?
3. Site- Whether the study conducted in the single arch? If no whether the arches have been evaluated separately?
4. Force/stress- Did the authors described the mechanics and amount of force or stress applied?
5. Anchorage: Did the authors explained and executed proper anchorage measures?
6. Occlusal interference: Whether the author discussed and mentioned about occlusal interference?

Associate outcomes (Table: I)

1. GCF: Did the authors evaluate biomarkers in GCF- if yes; have they correlated with the tooth movement?
2. Genetic data: Did the authors evaluate Genetic data - if yes, have they correlated with the tooth movement?
3. Pain: Did the authors evaluate Pain?
4. Resorption: Did the authors evaluate Root resorption?

Iwasaki et al.,[10]quoted in his study that the study group and method used to measure tooth movement were same as his previous study.[8] But the parameters evaluated were different hence this study will not be considered as duplication and extraction of data for the following data field namely sample size, sex, age distribution, study period, mechanics of force application, stress, oral hygiene regime and assessment of gingival/ periodontal health, occlusal interference, anchorage, site of study and methods to measure OTM will be done only in Iwasaki et al[8]. No conflicts raised in this stage.

RESULTS:

After analyzing the data from Table-I, Table-II and Annexure-1, the results were synthesized as follows

Sex:

Except for 2 studies, the remaining studies mentioned the number of male and female patients. Among the 2 studies, one of them has mentioned as "both gender" while has given the percentage value instead of a number of patients. 5 studies included an equal number of male and female patients. In 3 studies they included only female patients.

Age distribution:

Age was mentioned in all the studies either as range or as mean. Grower vs. non growers was compared in 1 study, comparative evaluation of adolescents vs. adults was reported in 2 studies, only mean age has been mentioned in 3 studies, patients with above 30 years age has been included in 2 studies, remaining studies included patients within the age group of 10-30 years.

Expression of levels of biomarkers in GCF:

12 studies have evaluated biomarkers in GCF which included interleukin 1 beta (N=7), Matrix metalloproteinase MMP 9 and Receptor activator nuclear factor kappa ligand RANKL (N=1), interleukin-6 (N=1), Alkaline phosphatase ALP (N=1), Chondrotin sulphate CS (N=1), Tartrate resistant acid phosphatase TRAP (N=1) while the remaining 35 studies did not evaluate biomarkers in GCF.

Mechanics of force application:

The canineretraction was initiated in the studies using loop (N=4), Nickel titanium coil spring (N=24), sentalloy coil spring (N=2), elastomeric chain (N=4). Some studies had done comparative studies which included drum spring vs. push coil spring(1), Nickel titanium coil spring vs. rickets retraction loop(1), hybrid spring vs. PG spring(1), nickel titanium loop vs. TMA loop(1), PG retraction spring vs. elastomeric chain (1), using both loop and nickel titanium coil spring(N=7), in 1 study loop mechanics was used in phase I and niti coil spring was used in phase II

Amount of force applied:

50 gram force was used in three studies(N=3), followed by 100 gram employed in 5 studies(N=5), 150 gram(N=15),120 gram(N=1), 120-150 gram(N=1), 200 gram(N=2), 396 gram(N=2), 50 cN(N=1), 124cN(N=1),8 ounce(N=1), 1 N (N=1). comparative Studies were done which included 5N vs. 1N(N=1), 70 grams vs. 120 grams(N=1), 80 grams vs. 60 grams(N=1), 50 grams vs. 150 grams(N=1),100 grams vs. 150 grams(N=1), 300 grams vs. 50 grams(N=1), 160 grams vs. 380grams(N=1), 100 grams vs. 100 grams(N=1).

Stress applied:

Assigned stress (achieved by desired force) 4kPa vs. 13kPa (N=1), one side receives 13kPa other side receives either 4kPa or 26kPa or 52 kPa (N=1), one side 26kPa other side 8 subjects or 52 kPa while 2 subjects receives13kPa (N=1), 2 different stress using incomplete block design 4kPa , 13kPa, 26kPa, 52 kPa, 78kPa(N=3)

Oral hygiene regime (OHR) and monitoring of gingival/ periodontal health:

30 studies neither mentioned the OHR nor monitored the gingival health. 5 studies either mentioned oral OHR or monitored the gingival health. 12 studies mentioned OHR and monitored the gingival health.

Occlusal interference:

4 studies discussed and mentioned about the occlusal interference, in 26 studies where canine retraction was initiated using friction mechanics, the authors mentioned that retraction has been initiated after leveling and aligning, 7 studies did not mention about this issue.

Method of canine movement assessment:

Three studies (N=3) did not mention the method of assessment. studies assessed canine movement as the space open between lateral incisor and canine(N=2), using slit laser 3d surface scanning and analysis using mid-palatal implant as reference(N=3), with the use of 3D model and CAD software (N=3), as scanned image of dental cast(1), direct intraoral measurement using digital Venire calliper (N=4), direct intraoral measurement using flexible millimetre scale (N=1), using basilar and lateral cephalogram (N=1), with the help of study model and digital Vernier calliper (N=9), using both model and lateral cephalogram (N=4), using study model and acrylic template (N=3), direct intraoral and study model-(N=1), using 3-axis measuring microscope on study model (N-=8), 45 degree oblique cephalogram(N=2), using only lateral cephalogram (N=3) Out of 47 study articles

Among the 6 well-studied confounding variables, 5 variables had been considered by 3 studies followed by 4 variables had been taken into account by 18 studies, 3 variables were looked by 22 studies, and 2 variables had been considered by 4 studies, while no study had considered all the 6 variables.

Table I- Well studied confounding variables

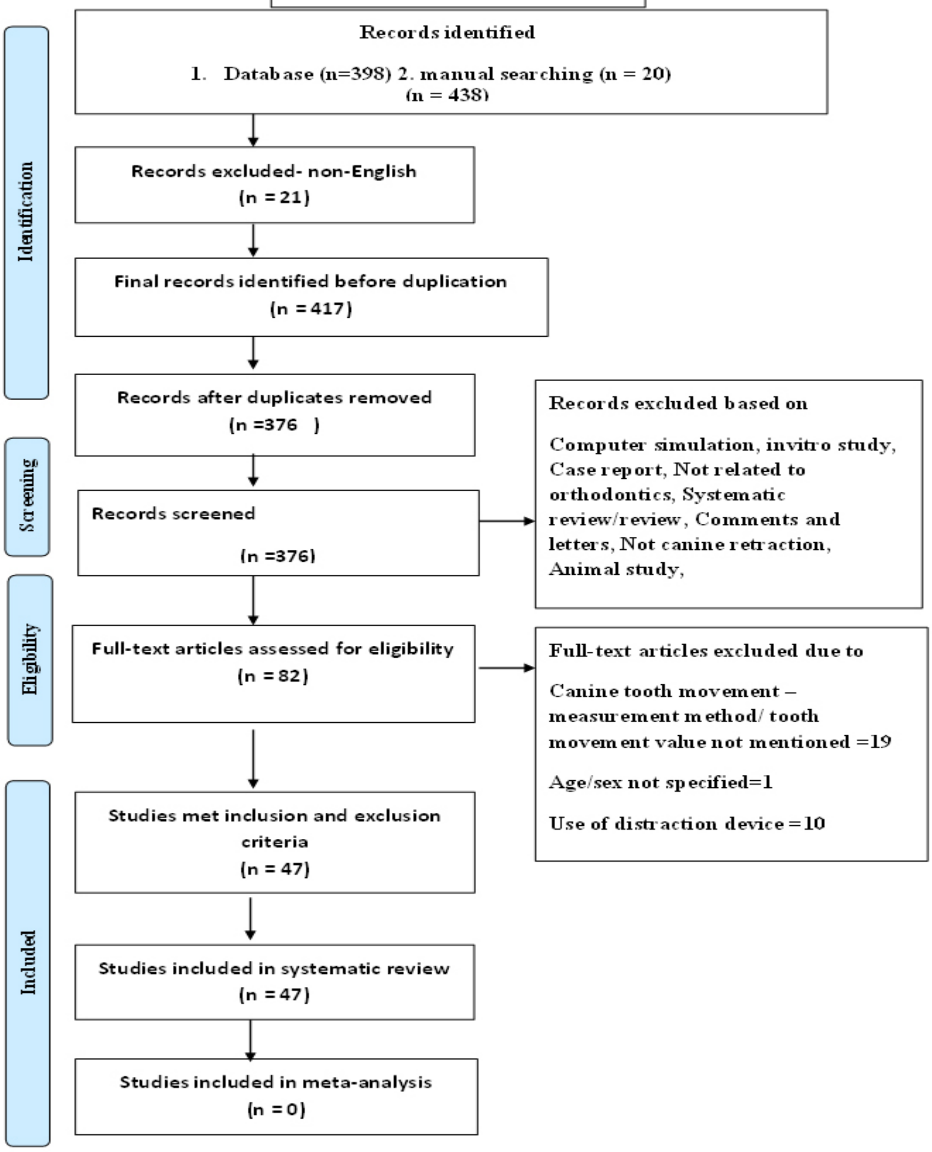
No	Author	**Age** Whether study sample consist of same age group or the authors compared different age group?	**Sex** Did the authors study either specific sex or both sex divided equally without combining the results of both gender?	**Site** Whether the study conducted in single arch? If no whether the arches have been evaluated separately?	**Force/stress** Did the authors described about the mechanics and amount of force or stress applied?	**Anchorage** Did the authors explain and execute proper anchorage measures?	**Occlusal interference** Did the authors discuss and mention about Occlusal interference?
1.	Yamasaki et al.,[46] Phase II/Phase III	Yes/No	No/No	Yes/Yes	Yes/Yes	Yes/Yes	No/No
2.	Ziegler et al.,[47]	No	No	Yes	Yes	Yes	No
3.	Lotzofet al.,[48]	Yes	No	Yes	Yes	No	No
4.	Darendeliler et al.,[9]	Yes	No	Yes	Yes	No	Yes
5.	Iwasaki et al.,[8]	Yes	No	Yes	Yes	Yes	No
6.	Iwasaki et al.,[10]	Yes	No	Yes	Yes	Yes	No
7.	Cruz et al.,[49]	Yes	No	Yes	Yes	Yes	No
8.	Hayashi et al.,[50]	No	No	Yes	Yes	Yes	No
9.	Iwasaki et al.,[27]	Yes	No	Yes	Yes	Yes	No
10.	Batraet al.,[24]	No	Yes	Yes	Yes	No	No
11.	Herman et al.,[51]	No	No	Yes	Yes	Yes	No
12.	Iwasaki et al.,[20]	No	Yes	Yes	Yes	Yes	No
13.	Limpanichkulet al.,[52]	No	No	Yes	Yes	Yes	No
14.	Sueriet al.,[31]	Yes	No	Yes	No	No	No
15.	Deguchiet al.,[53]	No	No	Yes	Yes	Yes	No
16.	Hayashi et al.,[54]	No	No	Yes	Yes	Yes	No
17.	Thiruvenkatachari et al.,[55]	No	No	Yes	Yes	No	No
18.	Martins et al.,[56]	Yes	No	Yes	Yes	No	No
19.	Martins et al,[57]	No	No	Yes	Yes	No	No
20.	Iwasaki et al.,[21]	Yes	No	Yes	Yes	Yes	No
21.	Yee et al.,[18]	Yes	No	Yes	Yes	No	No
22.	Burrow et al.,[58]	No	No	Yes	Yes	Yes	No
23.	Luppanapornlarp et al.,[28]	Yes	No	Yes	Yes	Yes	No
24.	Showkatbakhshet al.,[59]	Yes	Yes	Yes	Yes	Yes	No
25.	Aboul-elaet al.,[60]	No	No	Yes	Yes	Yes	No
26.	Kenget al.,[61]	No	Yes	Yes	Yes	Yes	No
27.	Mezomoet al.,[62]	No	No	Yes	Yes	Yes	No
28.	Wahabet al.,[29]	No	No	Yes	Yes	Yes	No
29.	Dholakiaet al.,[63]	No	No	Yes	Yes	No	No
30.	Doshi-mehtaet al.,[64]	No	No	Yes	Yes	Yes	No
31.	Oz et al.,[65]	Yes	No	Yes	Yes	Yes	No
32.	Alikhani et al.,[22]	Yes	No	Yes	Yes	Yes	Yes
33.	Inseeet al.,[26]	No	No	Yes	Yes	Yes	No
34.	Iskaslanet al.,[66]	Yes	No	Yes	Yes	No	No
35.	Al-naoum et al.,[67]	No	Yes	Yes	Yes	Yes	No
36.	Leethankulet al.,[68]	N	Yes	Yes	Yes	Yes	No
37.	Nickel et al.,[69]	Yes	No	Yes	Yes	Yes	No
38.	Rajasekaran et al.,[70]	No	No	Yes	Yes	Yes	No
39.	Li et al.,[71]	Yes	No	Yes	Yes	No	No
40.	Ekizeret al.,[25]	No	No	Yes	Yes	Yes	No
41.	Ozkan et al.,[72]	Yes	No	Yes	Yes	Yes	No
42.	Sabuncuogluet al.,[73]	No	No	Yes	Yes	Yes	No
43.	Yassaeiet al.,[30]	No	Yes	Yes	Yes	Yes	No
44.	Iwasaki et al.,[32]	Yes	No	Yes	Yes	Yes	No
45.	Qamruddinet al.,[74]	No	Yes	Yes	Yes	No	No
46.	Alikhaniet al.,[23]	Yes	No	Yes	Yes	Yes	Yes
47.	Alkebsiet al.,[75]	No	No	Yes	Yes	Yes	Yes

Table II: Associated outcomes

No	Author	Evaluation of biomarkers in GCF	Correlation the GCF data with the tooth movement	Evaluation of Genetic data	Correlation the gene data with the tooth movement	Evaluation of Pain	Evaluation of Root resorption
1.	Alikhani et al.,[22]	Yes	Yes	No	No	Yes	No
2.	Alikhani et al.,[23]	Yes	Yes	No	No	Yes	No
3.	Alkebsi et al.,[75]	No	No	No	No	Yes	Yes
4.	Al-naoum et al.,[67]	No	No	No	No	Yes	No
5.	Batraet al.,[24]	Yes	Yes	No	No	No	No
6.	Deguchi et al.,[53]	No	No	No	No	No	Yes
7.	Doshi-Mehta et al.,[64]	No	No	No	No	Yes	No
8.	Ekizer et al.,[25]	Yes	Yes	No	No	No	No
9.	Herman et al.,[51]	No	No	No	No	Yes	No
10.	Insee et al.,[26]	Yes	Yes	No	No	Yes	No
11.	Iwasaki et al.,[10]	Yes	Yes	No	No	No	No
12.	Iwasaki et al.,[27]	Yes	Yes	No	No	No	No
13.	Iwasaki et al.,[20]	Yes	Yes	Yes	Yes	No	No
14.	Iwasaki et al.,[21]	Yes	Yes	Yes	Yes	No	No
15.	Luppanapornlarp et al.,[28]	Yes	Yes	No	No	Yes	No
16.	Wahab et al.,[29]	Yes	Yes	No	No	No	Yes
17.	Yassaei et al.,[30]	Yes	Yes	No	No	No	No

GCF-Gingival crevicular fluid

Figure: 1- PRISMA flow diagram



DISCUSSION

Since OTM is a multifactorial event when studying OTM utmost care should be taken to control the variables that might alter the OTM. In the literature, the influence of the following variables in altering the tooth movement has been well-studied age, sex, site of the study, force/stress applied, occlusal interference and anchorage consideration.[11-18]

In addition to these variables, In recent years tooth movement researchers started to consider other biological variables such as genetic influence and expression of biomarkers in the GCF. Some authors[17,19] have suggested including bone density in tooth movement research model.

Hence it is evident now that it is necessary to control the variables as much as possible and failed to do so will affect the results.

In this review,there exists a variation across the studies while considering the confounding factors in their study protocol. Since genetic informationis being explored in recent years only, most of the studies have not considered this variable except in 2 studies, [20,21]where their aim of the study is to find the correlation between gene polymorphism and velocity of tooth movement.

Similarly, the individual's response to the applied orthodontic force was studied indirectly by evaluating the levels of expression of biomarkers in the GCF are under research for quite some time in orthodontics. In this review, only the studies[10, 20- 30] with their aim to evaluate biomarkers in GCF and to correlate it with tooth movement had considered this factor and not all the studies have done this.

Force is an important factor and in all the studies included in this review the mechanics used to retract canines has been described. Even though we know that certain type of mechanics results in a certain type of force, we didn't define the type of force by assumption since the authors have not reported it.

Except for one study,[31] all the studies have mentioned the amount of force. The author compared the efficacy of Niti closed coil spring over lace back and though the author mentioned the amount of force generated by Niti closed coil spring did not report the amount of force generated by lace back.

Except for few studies[9,23,32] in which either the authors particularly selected and grouped patients as either growers and non-growers or adults and adolescentsof certain age group and compared the results and studied the effect of age on the tooth movement, remaining studies combined the patients of different age groups. Since the effect of age directly confounds the tooth movement, care should be given by selecting the appropriate patient sample.

In orthodontics analysis of cervical vertebra maturation and hand-wrist radiograph, have been used to identify the growth status of an individual.[33-36]

Apart from the above mentioned methods authors have also used dental age and chronological age to identify the growth status of an individual.[37-39] However recent studies revealed that these methods are not reliable.[40-42] Recently biomarkers from GCF have been identified to represent growth status of an individual.[43-45]

Many articles have not mentioned the inter-arch occlusal interference. Most of the studies mentioned that canine retraction started after leveling aligning but failed to mention that whether monitoring has been done for occlusal interference during the canine retraction. To overcome this issue probably certain studies selected patients with large overjet.

This review revealed that both manual and computer-assisted methods were utilized for assessment of tooth movement in the studies. Each method hasits own advantages and disadvantages. When it comes totwo-dimensional analysis manual methods are preferable whereas for three-dimensional analysis computer-assisted method may be employed. Inter-operator error will be minimized when the computer-aided analysis is used however availability and cost might be a hindrance for the present scenario to incorporate computer-aided analysis in routine studies.

Results from Table I &II gave us some more clarity about how well the confounding variables were handled by the authors. We do accept that the variables affecting the rate of tooth movement is a vast subject and it is impossible to control all the factors that affect OTM while assessing the rate of tooth movement. By adhering to a well-framedinclusion and exclusion criteria which addresses all the known variables might help in controlling the same. Research in this area will add further knowledge about the confounders and how to control it in the future.

CONCLUSIONS:

In this review of the 47 study articles

1. Only 3 studies considered adequate confounding factors that might influence the outcome of the tooth movement.
2. Out of these 3studies1 study had considered the associated outcome of OTM in addition to well-studied confounding variables.
3. 2 studies have explored the genetic influence on tooth movement.

The present review reveals that the factors that influence the tooth movement are vast and hence the outcomes of these studies should be viewed cautiously.

REFERENCES:

1. Oppenheim A. Human tissue response to orthodontic intervention of short and long duration. Am J Orthod Oral Surg.1942;28:263–301.
2. Storey E, Smith R. Force in orthodontics and its relation to tooth movement. Aust Dent J.1952;56:11–18.
3. Boester CH, Johnston LE. A clinical investigation of the concepts of differential and optimal force in canine retraction. Angle Orthod. 1974 Apr;44(2):113-9.
4. Schwarz AM. Tissue changes incident to orthodontic tooth movement.Int J Orthod.1932;18:331–352.
5. Reitan K. Clinical and histologic observations on tooth movement during and after orthodontic treatment. Am J Orthod.1967;53:721–745
6. Quinn RS, Yoshikawa DK. A reassessment of force magnitude in orthodontics. Am J Orthod. 1985 Sep;88(3):252-60.

7. Ren Y, Maltha JC, Kuijpers-Jagtman AM. Optimum force magnitude for orthodontic tooth movement: a systematic literature review. Angle Orthod. 2003 Feb;73(1):86-92.
8. Iwasaki L. R., J. E. Haack, J. C. Nickel, and J. Morton, 'Human Tooth Movement in Response to Continuous Stress of Low Magnitude', Am J Orthod Dentofacial Orthop 2000;117:175-83
9. Darendeliler MA, Darendeliler H, Uner O. The drum spring (DS) retractor: constant and continuous force for canine retraction. Eur J Orthod. 1997 Apr;19(2):115-30.
10. Iwasaki L. R., J. E. Haack, J. C. Nickel, R. A. Reinhardt, and T. M. Petro, 'Human Interleukin-1 Beta and Interleukin-1 Receptor Antagonist Secretion and Velocity of Tooth Movement'. Arch Oral Biol. 2001 Feb;46(2):185-9.
11. Vujačić Amila, Konić Aleksandra, Pavlović Jasna, Todorović Vera, Vukićević Vladanka, Jevremović Danimir et al., Differences in IL-1β and IL-6 levels in the gingival crevicular fluid during acute phase of orthodontic tooth movement between juveniles and young adults, Vojnosanit Pregl 2017; 74(3): 219–226.
12. Kawasaki K, Takahashi T, Yamaguchi M, Kasai K: Effects of aging on RANKL and OPG levels in gingival crevicular fluid during orthodontic tooth movement. Orthod Craniofacial Res 9, 2006; 137–142.
13. Dudic A, Giannopoulou C, Kiliaridis S. Factors related to the rate of orthodontically induced tooth movement. Am J Orthod Dentofacial Orthop. 2013 May;143(5):616-21.
14. Chibebe PC, Starobinas N, Pallos D. Juveniles versus adults: differences in PGE2 levels in the gingival crevicular fluid during orthodontic tooth movement. Braz Oral Res. 2010 Jan-Mar;24(1):108-13.
15. Sandhu SS, Sandhu J. Orthodontic pain: an interaction between age and sex in early and middle adolescence. Angle Orthod. 2013 Nov;83(6):966-72.
16. Chisari JR, McGorray SP, Nair M, Wheeler TT. Variables affecting orthodontic tooth movement with clear aligners. Am J Orthod Dentofacial Orthop. 2014 Apr;145(4 Suppl):S82-91.
17. Shirazi M, Soudi A, Baghaeian P, Farajzadeh Jalali Y. Analyzing the Crystal Structure of Alveolar Bone and its Impact on the Rate of Tooth Movement, Iran J Ortho. 2017 ;12(2):e7590
18. Yee JA, Türk T, Elekdağ-Türk S, Cheng LL, Darendeliler MA. Rate of tooth movement under heavy and light continuous orthodontic forces. Am J Orthod Dentofacial Orthop. 2009 Aug;136(2):150.e1-9; discussion 150-1.
19. Iwasaki L.R., L.D. Crouch, and J.C. Nickel Genetic Factors and Tooth Movement. Semin Orthod 2008;14:135-145.
20. Iwasaki Laura R., Colin S. Gibson, Larry D. Crouch, David B. Marx, Janardan P. Pandey, and Jeffrey C. Nickel, 'Speed of Tooth Movement Is Related to Stress and IL-1 Gene Polymorphisms', Am J Orthod Dentofacial Orthop 2006;130:698.e1-698.e9
21. Iwasaki L. R., J. R. Chandler, D. B. Marx, J. P. Pandey, and J. C. Nickel, 'IL-1 Gene Polymorphisms, Secretion in Gingival Crevicular Fluid, and Speed of Human Orthodontic Tooth Movement', Orthod Craniofac Res 2009;12:129–140
22. Alikhani M, Raptis M, Zoldan B, Sangsuwon C, Lee YB, Alyami B, et al. Effect of micro-osteoperforations on the rate of tooth movement. Am J Orthod Dentofacial Orthop. 2013 Nov;144(5):639-48.
23. Alikhani M, Chou MY, Khoo E, Alansari S, Kwal R, Elfersi T, et al. Age-dependent biologic response to orthodontic forces. Am J Orthod Dentofacial Orthop. 2018 May;153(5):632-644.
24. Batra P, Kharbanda O, Duggal R, Singh N, Parkash H. Alkaline phosphatase activity in gingival crevicular fluid during canine retraction. Orthod Craniofac Res. 2006 Feb;9(1):44-51.
25. Ekizer A, Türker G, Uysal T, Güray E, Taşdemir Z. Light emitting diode mediated photobiomodulation therapy improves orthodontic tooth movement and miniscrew stability: A randomized controlled clinical trial. Lasers Surg Med. 2016 Dec;48(10):936-943.
26. Insee K1, Pothacharoen P, Kongtawelert P, Ongchai S, Jotikasthira D, Krisanaprakornkit. Comparisons of the chondroitin sulphate levels in orthodontically moved canines and the clinical outcomes between two different force magnitudes. Eur J Orthod. 2014 Feb;36(1):39-46.
27. Iwasaki Laura R., Larry D. Crouch, Albert Tutor, Scott Gibson, Navin Hukmani, David B. Marx, et al., 'Tooth Movement and Cytokines in Gingival Crevicular Fluid and Whole Blood in Growing and Adult Subjects', Am J Orthod Dentofacial Orthop 2005;128:483-91
28. Luppanapornlarp S, Kajii TS, Surarit R, Iida J. Interleukin-1beta levels, pain intensity, and tooth movement using two different magnitudes of continuous orthodontic force. Eur J Orthod. 2010 Oct;32(5):596-601.
29. Wahab RMA, Dasor MM, Senafi S, Abdullah AAA, Jemain AA, Kasim NA et al. Crevicular tartrate resistant acid phosphatase activity and rate of tooth movement under different continuous force applications. African Journal of Pharmacy and Pharmacology. 2011 Nov 29;5(20):2213-2219.
30. Yassaei S, Aghili H, Afshari JT, Bagherpour A, Eslami F. Effects of diode laser (980 nm) on orthodontic tooth movement and interleukin 6 levels in gingival crevicular fluid in female subjects. Lasers Med Sci. 2016 Dec;31(9):1751-1759.
31. Sueri MY, Turk T. Effectiveness of laceback ligatures on maxillary canine retraction. Angle Orthod. 2006 Nov;76(6):1010-4.
32. Iwasaki L. R., Y. Liu, H. Liu, and J. C. Nickel, 'Speed of Human Tooth Movement in Growers and Non-Growers: Selection of Applied Stress Matters', *Orthod Craniofac Res.* 2017;20(Suppl. 1):63–67.
33. Baccetti T, Franchi L, McNamara JA Jr. An improved version of the cervical vertebral maturation (CVM) method for the assessment of mandibular growth. Angle Orthod. 2002 Aug;72(4):316-23.
34. Franchi L, Baccetti T, McNamara JA Jr. Mandibular growth as related to cervical vertebral maturation and body height. Am J Orthod Dentofacial Orthop. 2000 Sep;118(3):335-40.
35. Björk A, Helm S. Prediction of the age of maximum puberal growth in body height. Angle Orthod. 1967 Apr;37(2):134-43.
36. Greulich W. W. and S. I. Pyle, Radiographic Atlas of Skeletal Development of the Hand and Wrist, Stanford University Press, Stanford, Calif, USA, 2nd edition, 1959.
37. Franchi L, Baccetti T, De Toffol L, Polimeni A, Cozza P. Phases of the dentition for the assessment of skeletal maturity: a diagnostic performance study. Am J Orthod Dentofacial Orthop. 2008 Mar;133(3):395-400
38. Baccetti T, Franchi L, De Toffol L, Ghiozzi B, Cozza P. The diagnostic performance of chronologic age in the assessment of skeletal maturity. Prog Orthod. 2006;7(2):176-88.
39. Fishman LS. Chronological versus skeletal age, an evaluation of craniofacial growth. Angle Orthod. 1979 Jul;49(3):181-9.
40. Perinetti G, Baccetti T, Di Leonardo B, Di Lenarda R, Contardo L. Dentition phase and chronological age in relation to gingival crevicular fluid alkaline phosphatase activity in growing subjects. Prog Orthod. 2011 Nov;12(2):100-6.
41. Beit P, Peltomäki T, Schätzle M, Signorelli L, Patcas R. Evaluating the agreement of skeletal age assessment based on hand-wrist and cervical vertebrae radiography. Am J Orthod Dentofacial Orthop. 2013 Dec;144(6):838-47.
42. Perinetti G, Contardo L. Dental maturation is not a reliable indicator of the pubertal growth spurt. Am J Orthod Dentofacial Orthop. 2016 Jul;150(1):4-6.
43. Perinetti G and L. Contardo, "Gingival crevicular fluid alkaline phosphatase activity in relation to pubertal growth spurt and dental maturation: a multiple regression study," South European Journal of Orthodontics and Dentofacial Research, vol. 3, no. 1, pp. 6–11, 2016.
44. Perinetti G, Baccetti T, Contardo L, Di Lenarda R. Gingival crevicular fluid alkaline phosphatase activity as a non-invasive biomarker of skeletal maturation. Orthod Craniofac Res. 2011 Feb;14(1):44-50.

45. Szulc P, Seeman E, Delmas PD. Biochemical measurements of bone turnover in children and adolescents. Osteoporos Int. 2000;11(4):281-94.
46. Yamasaki K, Shibata Y, Imai S, Tani Y, Shibasaki Y, Fukuhara T. Clinical application of prostaglandin E1 (PGE1) upon orthodontic tooth movement. Am J Orthod. 1984 Jun;85(6):508-18
47. Ziegler P, Ingervall B. A clinical study of maxillary canine retraction with a retraction spring and with sliding mechanics. Am J Orthod Dentofacial Orthop.1989 Feb;95(2):99-106.
48. Lotzof LP, Fine HA, Cisneros GJ. Canine retraction: a comparison of two preadjusted bracket systems. Am J Orthod Dentofacial Orthop. 1996 Aug;110(2):191-6.
49. Cruz DR, Kohara EK, Ribeiro MS, Wetter NU. Effects of low-intensity laser therapy on the orthodontic movement velocity of human teeth: a preliminary study.Lasers Surg Med. 2004;35(2):117-20.
50. Hayashi K, Uechi J, Murata M, Mizoguchi I. Comparison of maxillary canine retraction with sliding mechanics and a retraction spring: a three-dimensional analysis based on a midpalatal orthodontic implant. Eur J Orthod. 2004 Dec;26(6):585-9
51. Herman RJ, Currier GF, Miyake A. Mini-implant anchorage for maxillary canine retraction: a pilot study. Am J Orthod Dentofacial Orthop. 2006 Aug;130(2):228-35.
52. Limpanichkul W, Godfrey K, Srisuk N, Rattanayatikul C. Effects of low-level laser therapy on the rate of orthodontic tooth movement. Orthod Craniofac Res. 2006 Feb;9(1):38-43.
53. Deguchi T, Imai M, Sugawara Y, Ando R, Kushima K, Takano-Yamamoto T. Clinical evaluation of a low-friction attachment device during canine retraction. Angle Orthod. 2007 Nov;77(6):968-72.
54. Hayashi K, Uechi J, Lee SP, Mizoguchi I. Three-dimensional analysis of orthodontic tooth movement based on XYZ and finite helical axis systems. Eur J Orthod. 2007 Dec;29(6):589-95.
55. Thiruvenkatachari B, Ammayappan P, Kandaswamy R. Comparison of rate of canine retraction with conventional molar anchorage and titanium implant anchorage. Am J Orthod Dentofacial Orthop. 2008 Jul;134(1):30-5.
56. Martins RP, Buschang PH, Gandini LG Jr. Group A T-loop for differential moment mechanics: an implant study. Am J Orthod Dentofacial Orthop. 2009 Feb;135(2):182-9.
57. Martins RP, Buschang PH, Gandini LG Jr, Rossouw PE. Changes over time in canine retraction: an implant study. Am J Orthod Dentofacial Orthop. 2009 Jul;136(1):87-93.
58. Burrow SJ. Canine retraction rate with self-ligating brackets vs. conventional edgewise brackets. Angle Orthod. 2010 Jul;80(4):438-45.
59. Showkatbakhsh R, Jamilian A, Showkatbakhsh M. The effect of pulsed electromagnetic fields on the acceleration of tooth movement. World J Orthod. 2010 Winter;11(4):e52-6.
60. Aboul-Ela SM, El-Beialy AR, El-Sayed KM, Selim EM, El-Mangoury NH, Mostafa YA. Miniscrew implant-supported maxillary canine retraction with and without corticotomy-facilitated orthodontics. Am J Orthod Dentofacial Orthop. 2011 Feb;139(2):252-9.
61. Keng FY1, Quick AN, Swain MV, Herbison P. A comparison of space closure rates between preactivated nickel-titanium and titanium-molybdenum alloy T-loops: a randomized controlled clinical trial. Eur J Orthod. 2012 Feb;34(1):33-8.
62. Mezomo M, de Lima ES, de Menezes LM, Weissheimer A, Allgayer S. Maxillary canine retraction with self-ligating and conventional brackets. Angle Orthod. 2011 Mar;81(2):292-7.
63. Dholakia KD, Bhat SR. Clinical efficiency of nonconventional elastomeric ligatures in the canine retraction phase of preadjusted edgewise appliance therapy: an in-vivo study. Am J Orthod Dentofacial Orthop. 2012 Jun;141(6):715-22.
64. Doshi-Mehta G, Bhad-Patil WA. Efficacy of low-intensity laser therapy in reducing treatment time and orthodontic pain: a clinical investigation. Am J Orthod Dentofacial Orthop. 2012 Mar;141(3):289-97.
65. Oz AA, Arici N, Arici S. The clinical and laboratory effects of bracket type during canine distalization with sliding mechanics. Angle Orthod. 2012 Mar;82(2):326-32.
66. Işik Aslan B., B. Baloştuncer, and M. Dinçer, 'Are There Differences on Tooth Movement between Different Sectional Canine Retractors?' J Orofac Orthop 2013; 74:226-235.
67. Al-Naoum F, Hajeer MY, Al-Jundi A. Does alveolar corticotomy accelerate orthodontic tooth movement when retracting upper canines? A split-mouth design randomized controlled trial. J Oral Maxillofac Surg. 2014 Oct;72(10):1880-9
68. Leethanakul C, Kanokkulchai S, Pongpanich S, Leepong N, Charoemratrote C. Interseptal bone reduction on the rate of maxillary canine retraction. Angle Orthod. 2014 Sep;84(5):839-45.
69. Nickel JC, Liu H, Marx DB, Iwasaki LR. Effects of mechanical stress and growth on the velocity of tooth movement. Am J Orthod Dentofacial Orthop. 2014 Apr;145(4 Suppl):S74-81.
70. Rajasekaran UB, Krishna Nayak US. Effect of prostaglandin E1 versus corticotomy on orthodontic tooth movement: an in vivo study. Indian J Dent Res. 2014 Nov-Dec;25(6):717-21.
71. Li S, Xia Z, Liu SS, Eckert G, Chen J. Three-dimensional canine displacement patterns in response to translation and controlled tipping retraction strategies. Angle Orthod. 2015 Jan;85(1):18-25.
72. Ozkan S, Bayram M. Comparison of direct and indirect skeletal anchorage systems combined with 2 canine retraction techniques. Am J Orthod Dentofacial Orthop. 2016 Nov;150(5):763-770.
73. Sabuncuoglu FA, Ersahan S. Changes in human pulp blood flow during canine retraction. Acta Odontol Scand. 2016 Aug;74(6):436-42.
74. Qamruddin I, Alam MK, Mahroof V, Fida M, Khamis MF, Husein A. Effects of low-level laser irradiation on the rate of orthodontic tooth movement and associated pain with self-ligating brackets. Am J Orthod Dentofacial Orthop. 2017 Nov;152(5):622-630.
75. Alkebsi A, Al-Maaitah E, Al-Shorman H, Abu Alhaija E. Three-dimensional assessment of the effect of micro-osteoperforations on the rate of tooth movement during canine retraction in adults with Class II malocclusion: A randomized controlled clinical trial. Am J Orthod Dentofacial Orthop. 2018 Jun;153(6):771-785.

Annexure: I Study characteristics

No	Author	Sample size	Age in years	Sex	Retraction mechanics	Force		Site of study	GCF	OHR/ MON	Methods to measure OTM	Anchorage	Occlusal interference consideration	Genet- ic data
						Amount	Recalibr-ation							
1.	Yamasaki et al.,[46]	Phase II-8 Phase III-8	11.07-14.05 10.03-26.09	M-2 F-6 M-2 F-6	Contraction spring Open coil	150g 150g	Done Done	Max, Man Max, Man	NS NS	NM NM	Direct intra oral Direct intra oral	HG or HA or both HG or HA or both	No/No	NS NS
2.	Ziegler et al.,[47]	21	10-27	M-5 F-16	Retraction spring Vs sliding mechanics	160/ 380 g	Done	Max	NS	NM	Study models	TPA+HG	NO	NS
3.	lotzofet al.,[48]	12	12-15	M-5 F-7	Tip edge bracket Vs A company st wire bracket	200g	Done	Max	NS	NM	Study models	NM	No	NS
4.	Darendeliler et al.,[9]	15	G1-11.08-14.04 G2-18.08-21.06	G1-M-3, F-5 G2-M-3, F-4	Drum spring vs PC retractor	50g	Not done	Max	NS	NM/Yes	Direct intra oral And Lateral and basilar cephalometric X-ray	NM	Yes	NS
5.	Iwasaki et al.,[8]	7	12.03-16.03	M-2 F-5	Custom design spring	18g Vs 60g	Done	Max	NS	Yes/Yes	Model- using 3-axis microscope	TPA+HA	No	NS
6.	Iwasaki et al.,[10]	7	12.03-16.03	M-2 F-5	Custom design spring	18g Vs 60g	Done	Max, Man	IL_1 beta and L-1RA	Yes/Yes	Model- using 3-axis microscope	TPA+HA	No	NS
7.	Cruz et al.,[49]	11	12-18	Both gender	Niti coil spring	150 g	Done	Max	NS	NM	Direct intraoral	TPA+HA	No	NS
8.	Hayashi et al.,[50]	8	19.04-29.02	M-3 F-5	Retraction spring vs sliding mechanics	1N	Done	Max	NS	NM	3d surface scanning	TAD	No	NM
9.	Iwasaki et al.,[27]	10	10.05-30.11	M-3 F-7	Custom design	13 kPa Vs 4, 26, or 52 kPa	Done	Max, Man	IL_1 beta and IL-1RA	Yes/Yes	Model- using 3-axis Microscope,	TPA+HA	No	NS
10.	Batraet al.,[24]	10	12- 21	F-10	Sentalloy spring	100g	Done	Max	Alp	Yes/NM	Direct intraoral	NM	No	NS
11.	Herman et al.,[51]	16	11.04-22.06	M-6 F-10	Niti coil spring	150g	NM	Max	NS	NM	Study model, OPG, photographs,	TAD	No	NS
12.	Iwasaki et al.,[20]	10	11.02-18.08	M-5 F-5	Custom design spring	13, 26, or 52 kPa	Done	Max, Man	IL_1 beta and IL-1RA	Yes/Yes	Model- using 3-axis microscope	TPA+HA	No	IL-1 gene cluster polymorphisms
13.	Limpanichkulet al.,[52]	12	17.07-24.03	M-4 F-8	Niti coil spring	150 g	Done	Max	NS	NM	model using a stereo microscope	Molar stops	No	NS
14.	Sueriet al.,[31]	15	12-18	M-3 F-12	Niti coil springVs lace backs	Niti coil spring-150g Force not mentioned for lace backs	Done	Max	NS	NM	lateral cephalometric and submento vertical radiographs	NM	No	NM
15.	Deguchiet al.,[53]	30	14- 27	M-6 F-24	Closed coil spring	50g Vs 100g Vs 150g	Done	Max	NS	NM	Direct intraoral and IOPA	HA +HG	No	NS
16.	Hayashi et al.,[54]	10	19.04-29.02	M-6 F-4	Niti coil spring	0.5N Vs 1N	Done	Max	NS	NM	3D surface scanning using laser beam	TAD	No	NM
17.	Thiruvenkatachariet al.,[55]	12	16-22	M-4 F-8	Niti coil spring	100g	Done	10 cases-Max, Man, 2 case-only	NS	NM	Superimposition of radiographs	Combined Skeletal and dental	No	NS

								max						
18.	Martins et al.,56	10	14.10-19.10	M-4 F-6	TMA T loop	396 gF horizontally 35.4 gF vertically	NM	Max, Man	NS	NM	Superimposition of radiographs	TPA+ Lingual arch	No	NS
19.	Martins et al.,57	11	14.10-22	M-3 F-7	TMA T loop	396 gF horizontally 35.4 gF vertically	Done	Max, Man	NS	NM	Superimposition of radiographs	TPA+ Lingual arch	No	NS
20.	Iwasaki et al.,[21]	33	10.11-18.05	M-12 F-21	Custom design spring	4, 13, 26, 52, or 78 kPa	Done	Max	IL_1 beta and IL-1RA	Yes/Yes	Model- using 3-axis microscope	TPA+ HA	No	IL-1 gene cluster polymorphisms
21.	Yee et al.,[18]	14	13.0-19.5	M-5 F-9	Niti coil spring	300g Vs 50g	Not done	Max	NS	Yes/NM	direct intra oral and digitalised models	NM	No	NS
22.	Burrow et al.,[58]	43	11.03-27.06	M-44% F-56%	Sentalloy spring	150 g	NM	Max	NS	NM	Direct intraoral	NM	No	NS
23.	luppanapornlarpet al.,[28]	16	18–24	M-2 F-14	Niti coil spring	50g Vs 150 g	Done	Max	IL-1 b	Yes/Yes	Model-microscope	TPA	No	NS
24.	Showkatbakhshet al.,[59]	10	19.09-26.03	M-5 F-5	closed coil spring	50g	Done	Max	NS	NM	Study Model	Tip back and molar stop	No	NS
25.	Aboul-Ela et al.,[60]	13	mean age – 19	M-5 F-8	Niti coil spring	150gms	NM	Max	NS	NM/Yes	Study model	TAD	No	NS
26.	Keng et al.,[61]	12	13.03 – 20.01	M-6 F-6	Niti T loop vs TMA T- loop	150g	Done	Max	NS	NM	Study model	TAD & HA	No	NS
27.	Mezomoet al.,[62]	15	12- 26	M-5 F-10	Echain	150g	NM	Max	NS	NM	Study model and lateral cephalogram	1st molar and 2nd premolar ligated	No	NM
28.	Wahabet al.,[29]	12	14- 24	M-1 F-11	Niti coil spring	100g Vs 150 g	Done	Max	TRAP	Yes/Yes	study model and IOPA	HA	No	NS
29.	Dholakiaet al.,[63]	20	14.11-21.07	M-8 F-12	Echain	8 oz	Done	Max, Man	NS	NM	Study Model	NM	No	NS
30.	Doshi-Mehta et al.,[64]	20	12-23	M-8 F-12	Niti coil spring	150g	Done	Max, Man	NS	NM	Study Model	TPA	No	NS
31.	Oz et al.,[65]	19	12.07-15.03	M-5 F-14	Niti coil spring	200g	Done	Max, Man	NS	NM	Radiographic superimposition	TAD	No	NS
32.	Alikhaniet al.,[22]	20	19.05 - 33.01	ControlM-3 F-7 Exp M-5 F-5	Niti coil spring	100g	Done	Max	cytokines	NM	Study Model	TAD	Yes	NS
33.	Inseeet al.,[26]	16	12.03–22.5	M-6 F-10	Niti coil spring	70g Vs 120g	Done	Max	CS	Yes/Yes	Study Model	TPA+TAD	No	NS
34.	Iskaslanet al.,[66]	16	12.11-16.01	M-7 F-9	Hybrid retracts. Vs PG retract spring	100g	Done	Max, Man	NS	NM	Study Model &lateral cephalogram	NM	No	NS
35.	Al-Naoumet al.[67]	30	15-24	M-15 F-15	Niti coil spring	120g	Done	Max	NS	NM	Direct intra oral	TPA	No	NS
36.	leethankul et al.,[68]	18	18–25	F-18	Echain	150g	Done	Max	NS	NM	study models, and lateral cephalograms	TAD	No	NS
37.	Nickel et al.,[69]	41	10.01-30.09	M-17 F-24	Custom design spring	4, 13, 26, 52, or 78 kPa	Done	Max	NS	Yes/Yes	Study Model	HA	No	NS
38.	Rajasekaranet al.,[70]	32	mean age - 20.05	M-17 F-15	Niti coil spring	100g	NM	Max	NS	NM	Study Model	NM	No	NS
39.	Li et al.,[71]	21	Mean age – 21	M-9 F-12	T-loops	124.4 +/-3.3 cN	Done	Max	NS	NM	3D laser scanner	NM	No	NS

40.	Ekizer et al.,[25]	20	13.11-9	M-7 F-13	Niti coil spring	150-g	Done	Max	IL-1b	NM	3D laser scanner	TAD	No	NS
41.	Ozkanet al.,[72]	36	14.04-19	M-17 F-19	Reverse closing loop VsLadanyi spring	120g-150g	NM	Max	NS	NM	Study model and Lateral cephalogram	TAD+HA	No	NS
42.	Sabuncuogluet al.,[73]	24	19–25	M-10 F-14	Niti coil spring	100g	Done	Max	NS	NM	**NM**	TAD	No	NS
43.	Yassaei et al.,[30]	11	14-25	F-11	Niti coil spring	150g	Done	Max	IL-6	Yes/NM	Study model	TPA	No	NS
44.	Iwasaki et al.,[32]	46	G-11.10-15 NG-13.11-24.05	G-M-17 F-19 NG-M-2 F-8	Custom design spring	4, 13, 26, 52 or 78 kPa	Done	Max	NS	Yes/Yes	Model- using 3-axis measuring microscope	TPA+HA	No	NS
45.	Qamruddinet al.,[74]	22	12-25	M-11 F-11	Niti coil spring	150g	Done	max	NS	NM	CAD/CAM scanner	NM	No	NS
46.	Alikhaniet al.,[23]	18	ADO 11-14 ADU 21-45	ADO F-5 M-4 ADU M-3 F-6	Niti coil spring	50cN	Done	Max	Cytokines	NM	Study model	Group consolidation	Yes	NS
47.	Alkebsiet al.,[75]	32	16.07-21.07	M-8 F-24	Niti coil spring	150g	Done	Max	NS	Yes/Yes	3D digital models	TAD	Yes	NS

GCF-Gingival crevicular fluid, Max-Maxilla, Man-Mandible, g-Grams, Oz-ounce,cN-centric newton, Kpa-kilopascal, Niti-nickel titanium, M-Male, F-Female, NS-not studied, NM-Not mentioned, IL-1a-Interluikin1 Alpha, IL-1b-Interluikin1 Beta, IL-1RA- Interluikin1 receptor antagonist, TRAP-Tartrate resistant acid phosphatase, CS- chondroitin sulphate, ALP-Alkaline phosphatase, TNF-Tumour necrosis factor, RANKL-Receptor activator nuclear factor kappa ligand, MMP- Matrix metalloproteinase, TAD-Temporary anchorage device, TPA-Transpalatal arch, HA-Nance holding arch, HG-Head gear, OHR/ MON-Oral hygiene regime/Monitoring, ADO-Adolescents, ADU-Adults , CAD/CAM-computer aided design/computer aided manufacturing, IOPA-intraoral periapical radiograph, OPG-orthopantamogram, 3D-Three dimension, OTM-Orthodontic tooth movement.

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