Optimal force magnitude for bodily orthodontic tooth movement with fixed appliances: A systematic review

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Introduction: There is a high degree of uncertainty regarding the appropriate force level that should be applied during orthodontic tooth movement (OTM). As a result, orthodontic treatments may take longer than necessary, leading to unwanted side effects. This review aimed to identify an optimal force range with the rate of OTM as the primary outcome. External apical root resorption and pain were evaluated as secondary outcomes, and the influence of growth was examined. **Methods:** Five electronic databases were searched (MEDLINE [via PubMed], Embase [via OVID], Cochrane Library, CINAHL, and Web of Science) with no publication date or language restrictions. Inclusion eligibility screening, quality assessment, and data extraction were performed by 3 investigators. Each retrieved record was assessed by 2 observers independently. Only randomized controlled trials and randomized split-mouth studies were included. **Results:** A total of 12 articles satisfied the inclusion criteria—two randomized controlled trials and 10 randomized split-mouth studies. Only 1 study showed a low risk of bias, whereas the remaining 11 were unclear. The qualitative analysis showed that forces between 50 cN and 250 cN produced a similar OTM rate; forces >250 cN yielded a slightly higher rate but were accompanied by adverse effects. Because of considerable heterogeneity in methodology, clinical diversity with varying forces between 18 cN and 360 cN, and poor statistical reporting, a meta-analysis was deemed inappropriate. **Conclusions:** Forces between 50 cN and 100 cN seem optimal for OTM, patient comfort and potentially exhibit fewer side effects. Nevertheless, careful data interpretation is necessary because of the lack of strong evidence. Protocol registration: PROSPERO CRD42016039985. (Am J Orthod Dentofacial Orthop 2019;156:582-92)

An optimal force magnitude for orthodontic tooth movement (OTM) has been described as the lightest force providing a maximum or a near-maximum response.[1] This would mean that with an appropriate orthodontic force, a tooth could be moved through the alveolar bone, as a result of remodeling of the periodontal ligament (PDL) and the bone per se.[2] However, if the force level were to be set higher, the risk of side effects, such as external apical root resorption (EARR), uncontrolled tipping, and increased hyalinization, most likely would be enhanced, always at the expense of patient comfort and clinical efficiency.[3-5]

Hyalinization is with undoubtedly inevitable in OTM. However, if the force magnitude against the tooth is great enough to completely cut off the blood supply to an area within the PDL, then it de facto becomes avascular. The larger the hyalinized area, the longer the delay in initiation of OTM, as differentiation of osteoclasts within the PDL is not possible, and thus, the process of undermining resorption cannot take place until a much later stage.[1]

Even though the exact biological mechanisms that determine OTM are not yet fully elucidated, force magnitude has an important role to play. Other factors, including orthodontic force duration, growth, medication intake, and individual environmental and genetic variability are also of significant substance.[6-8]

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Therefore, OTM is a highly complex process, a fact that is frequently forgotten in an era of accelerated orthodontics.

In the past, there has been considerable interest in comparing orthodontic force magnitudes, especially in animals.[7-9] Regardless, interspecies differences seem to apply for the regulation of various genes in animals and humans, which could be critical for the translation of animal findings into clinical applications. Hence, simple extrapolation of preclinical data toward the human setting is not always possible.

The only previous systematic review on this topic published in 2003, concluded that there was no evidence regarding an optimal force level for OTM.[5] However, it did not meet the current standards for systematic reviews and included both animal and human studies. In addition, the included studies were not of high quality and showed clinical and methodological heterogeneity. Since then, further human randomized studies have been published, and thus, the present systematic review provides an update of the previous one but with a focus on human studies.

This review aimed to identify an optimal force range by comparing the rate of tooth movement in humans undergoing orthodontic treatment with full fixed appliances using different quantified force magnitudes. The rate of OTM was evaluated as a primary outcome, whereas EARR and pain were assessed as secondary outcomes. The influence of growth was also examined.

MATERIAL AND METHODS

Protocol and registration

This systematic review was registered at PROSPERO under the unique ID number CRD42016039985 and reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[10] Details of the protocol can be found at: www.crd.york.ac.uk/prospero.

Eligibility criteria

A PICOS question was formulated to aid the selection of eligible studies. The eligibility criteria were as follows:

1. Population: human subjects with a permanent dentition of any sex and ethnicity.
2. Intervention: orthodontic treatment with fixed appliances, using a quantified force (as determined per study) applied bodily in a mesiodistal direction.
3. Control: no treatment or intervention with a different quantified force (as determined per study) applied bodily in a mesiodistal direction.
4. Outcome: rate of OTM was examined as a primary outcome, EARR and pain were assessed as secondary outcomes, and the influence of growth was also evaluated.
5. Study design: randomized controlled trials (RCTs) and randomized split-mouth studies.

Studies concerning accelerated orthodontics and the use of drugs influencing OTM or bone metabolism were excluded. Studies were also excluded when subjects had craniofacial anomalies or an active periodontal disease or had previously undergone an orthodontic treatment.

Information sources and search strategy

A comprehensive search strategy was performed in the following electronic databases in collaboration with an experienced health science librarian on July 3, 2016: MEDLINE (via PubMed), Embase (via OVID), Cochrane Library, CINAHL and Web of Science. Grey literature was not included in our search.

The search strategy was limited to humans, with no language or publication date restrictions. The search terms were developed for MEDLINE and modified accordingly for the aforementioned databases. Table I illustrates the details of the MEDLINE and Embase searches.

Study selection

Three investigators were involved in the study selection process (A.K., C.T., and F.W.). Each retrieved record was assessed by 2 observers. The selection process was carried out using Covidence (Veritas Health Innovation, Melbourne, Australia. Available at https://www.covidence.org), a Web-based software platform that streamlines the production of systematic reviews. The first screening was on title and abstract. Titles and abstracts that did not meet the predefined eligibility criteria were excluded, and the resulting articles were carefully evaluated and judged based on their full texts by all authors. Furthermore, the reference lists of the selected studies were hand-searched to identify any additional relevant studies. Authors were contacted if information was lacking or unclear. All doubts and disagreements were resolved in consensus by all investigators, and the corresponding authors were contacted when additional or clarifying information was needed.

Data items and collection

A customized data extraction form was developed on Covidence to record the following:

Table I. MEDLINE and Embase search strategies http://www.ncbi.nlm.nih.gov/pubmed/advanced

Search group	*MEDLINE search term*
1	"Tooth Movement"[Mesh]) OR Tooth Mov*[tiab]
2	("Stress, Mechanical"[Mesh] OR "Dental Stress Analysis"[Mesh] OR "Biomechanical Phenomena"[Mesh] OR "Pressure"[Mesh:NoExp] OR Force*[tiab] OR Pressure*[tiab] OR Stress*[tiab])
3	#1 AND #2 ("Tooth Movement"[Mesh]) OR Tooth Movement[tiab]) AND ("Stress, Mechanical"[Mesh] OR "Dental Stress Analysis"[Mesh] OR "Biomechanical Phenomena"[Mesh] OR "Pressure"[Mesh:NoExp] OR Force*[tiab] OR Pressure*[tiab] OR Stress*[tiab])
4	(Orthodont*[tw] AND ("Tooth Movement"[Mesh] OR movement[Mesh] OR "Orthodontic Space Closure"[Mesh] OR ((Tooth[tiab] OR teeth[tiab] OR dental[tiab] OR "Tooth"[Mesh:NoExp] OR "Bicuspid"[Mesh] OR "Cuspid"[Mesh] OR "Incisor"[Mesh] OR "Molar"[Mesh] OR Bicuspid*[tiab] OR Cuspid*[tiab] OR Incisor*[tiab] OR Molar*[tiab] OR canine*[tiab] OR premolar*[tiab]) AND (Mov*[tiab] OR displacement*[tiab] OR shift*[tiab])))) AND ("Stress, Mechanical"[Mesh] OR "Dental Stress Analysis"[Mesh] OR "Biomechanical Phenomena"[Mesh] OR "Pressure"[Mesh:NoExp] OR Force*[tiab] OR Pressure*[tiab] OR Stress*[tiab]))
5	#3 OR #4 (("Tooth Movement"[Mesh]) OR Tooth Movement[tiab]) AND ("Stress, Mechanical"[Mesh] OR "Dental Stress Analysis"[Mesh] OR "Biomechanical Phenomena"[Mesh] OR "Pressure"[Mesh:NoExp] OR Force*[tiab] OR Pressure*[tiab] OR Stress*[tiab])) OR ((Orthodont*[tw] AND ("Tooth Movement"[Mesh] OR movement[Mesh] OR "Orthodontic Space Closure"[Mesh] OR ((Tooth[tiab] OR teeth[tiab] OR dental[tiab] OR "Tooth"[Mesh:NoExp] OR "Bicuspid"[Mesh] OR "Cuspid"[Mesh] OR "Incisor"[Mesh] OR "Molar"[Mesh] OR Bicuspid*[tiab] OR Cuspid*[tiab] OR Incisor*[tiab] OR Molar*[tiab] OR canine*[tiab] OR premolar*[tiab]) AND (Mov*[tiab] OR displacement*[tiab] OR shift*[tiab])))) AND ("Stress, Mechanical"[Mesh] OR "Dental Stress Analysis"[Mesh] OR "Biomechanical Phenomena"[Mesh] OR "Pressure"[Mesh:NoExp] OR Force*[tiab] OR Pressure*[tiab] OR Stress*[tiab]))))
6	(animals[mesh] NOT humans[mesh])
7	#5 NOT #6 (("Tooth Movement"[Mesh]) OR Tooth Movement[tiab]) AND ("Stress, Mechanical"[Mesh] OR "Dental Stress Analysis"[Mesh] OR "Biomechanical Phenomena"[Mesh] OR "Pressure"[Mesh:NoExp] OR Force*[tiab] OR Pressure*[tiab] OR Stress*[tiab])) OR ((Orthodont*[tw] AND ("Tooth Movement"[Mesh] OR movement[Mesh] OR "Orthodontic Space Closure"[Mesh] OR ((Tooth[tiab] OR teeth[tiab] OR dental[tiab] OR "Tooth"[Mesh:NoExp] OR "Bicuspid"[Mesh] OR "Cuspid"[Mesh] OR "Incisor"[Mesh] OR "Molar"[Mesh] OR Bicuspid*[tiab] OR Cuspid*[tiab] OR Incisor*[tiab] OR Molar*[tiab] OR canine*[tiab] OR premolar*[tiab]) AND (Mov*[tiab] OR displacement*[tiab] OR shift*[tiab])))) AND ("Stress, Mechanical"[Mesh] OR "Dental Stress Analysis"[Mesh] OR "Biomechanical Phenomena"[Mesh] OR "Pressure"[Mesh:NoExp] OR Force*[tiab] OR Pressure*[tiab] OR Stress*[tiab])))) NOT ((animals[mesh] NOT humans[mesh]))
Search group	*Embase search term*
1	exp orthodontics/
2	orthodontic$.ti,ab,kw.
3	((tooth or teeth or Bicuspid* or Cuspid* or Incisor* or Molar* or canine* or premolar*) and mov$).ti,ab,kw.
4	1 OR 2
5	3 AND 4
6	mechanical stress/or biomechanics/or "pressure and tension"/or pressure/or (Force* or Pressure* or Stress*).ti,ab,kw.
7	5 AND 6
8	1 OR 2 OR 3
9	8 AND 6

1. Study identification (authors, publication year, setting, and country)
2. Study design
3. Sample characteristics (inclusion and exclusion criteria, sample size, sex, mean age, and growth status)
4. Intervention and control group details (initial force magnitude in cN, site of force application, type of appliance used for force application and reactivation of the appliance, method of measuring force magnitude and tooth movement, duration of the experiment and the amount of OTM)
5. Outcome (OTM rate, EARR, and pain)

The rate of OTM was defined as millimeters per week, EARR was determined per study either in millimeters or as a score (range, 0-3), and pain was also defined as a score (range, 0-100) based on the visual analog scale.

Before data extraction, our customized form was pilot-tested on 10 articles to identify data that were potentially missing from the form and adapted accordingly.

Risk of bias assessment in individual studies

The risk of bias (high, unclear, low) for the RCTs and randomized split-mouth studies was evaluated by pairs of observers on Covidence using the Cochrane Collaboration risk of bias tool, as described in the *Cochrane Handbook for Systematic Reviews of Interventions.*[11] Seven criteria were analyzed to grade the risk of bias for each study, including random sequence generation,

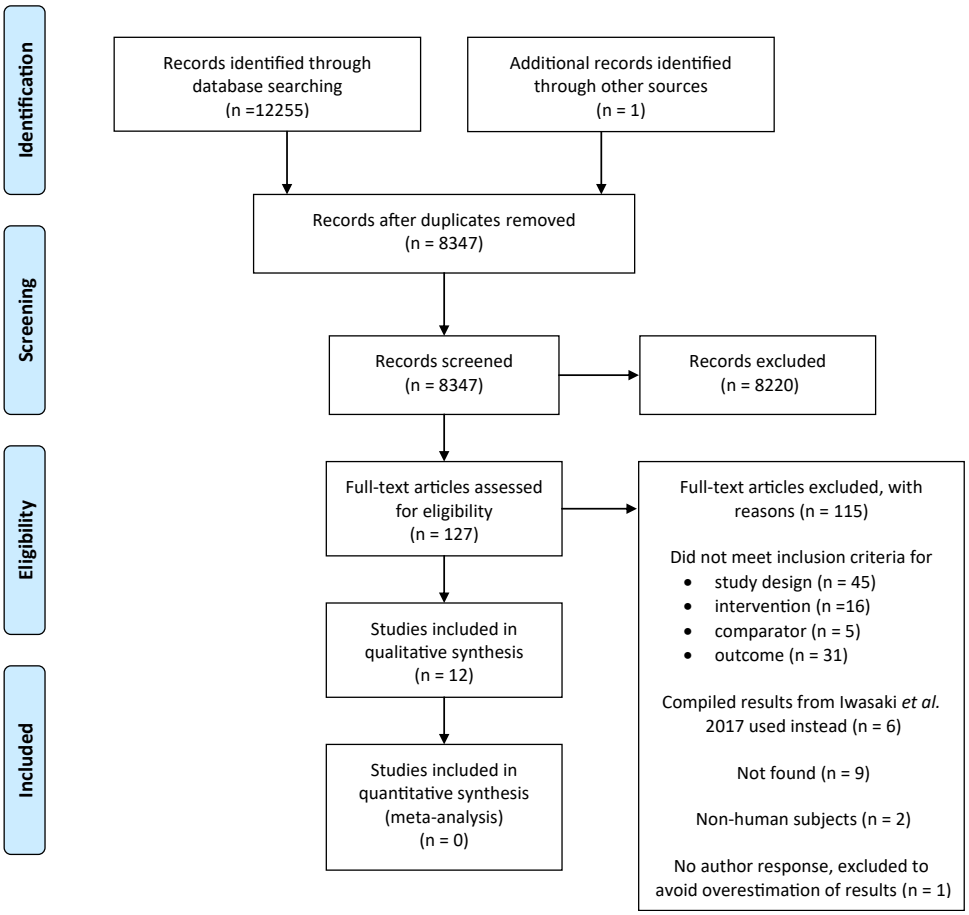

Fig 1. PRISMA flow diagram.

allocation concealment, blinding of participants and personnel, blinding of assessors, incomplete outcome data, selective reporting of outcomes, and other potential sources of bias. In case of disagreement, the third investigator assessed the paper, and all disagreements were resolved between the 3 observers.

RESULTS

Study selection and characteristics

A total of 12,255 articles were identified by database searching, and 1 article was included by hand search. After duplicate removal, 8347 studies underwent title and abstract screening, 127 studies underwent full-text screening, and 115 articles were excluded. Among these 115 articles, 6 were excluded upon author recommendation,[12-17] and 1 article from the same author group was included instead. This article comprised the compiled results of the 6 articles previously described.[18] Another article was excluded[19] to avoid result overestimation, as the author failed to reply to an e-mail regarding the sample size used. A remaining total of 12 articles, two RCTs,[20,21] and 10 randomized split-mouth studies,[18,22-30] met the inclusion criteria of this review and were used in the final qualitative analysis. The selection process is summarized in Figure 1, and the main characteristics of the included studies are shown in Table II.

Risk of bias within studies

All included studies were assessed for risk of bias (Fig 2). One RCT[20] showed an unambiguous low risk of bias, whereas the remaining studies had an unclear risk of bias.[18,21-27,29,30] Tests for the risk of bias across studies were not undertaken.

Results of individual studies

The outcomes of all individual studies are summarized in Tables III and IV. Because of considerable heterogeneity in methodology, clinical diversity, and poor statistical reporting, data synthesis was not possible,

Table II. Main characteristics of the included studies

Study, setting and country, and method	*Sample size, sex, age (SD)*	*Intervention: force (cN), appliance used and reactivation (if applicable)*	*Control/intervention force (cN), appliance used and reactivation (if applicable)*	*Site (jaw, side, tooth moved)*	*Method for measuring force and OTM*	*Outcome*	*Study duration, wk (SD)*
Megat Abdul Wahab et al[23] (2014) academic, Malaysia Split mouth RCT	n = 19 sex: 14 F, 5 M, age: 16-28	100 cN NiTi spring reactivation: NA	150 cN NiTi spring reactivation: NA	Max R or L Canine	Force: correx gauge OTM: digital caliper	Rate of OTM	5
Ariffin et al[25] (2013) academic, Malaysia Split-mouth RCT	n = 12 sex: NM age: 19.7 (5.0)	100 cN NiTi spring reactivation: NA	150 cN NiTi spring reactivation: NA	Max R or L Canine	Force: correx gauge OTM: digital caliper	Rate of OTM	5
Bokas and Woods[26] (2006) academic, Australia Split-mouth RCT	n = 12 sex: 6 F, 6 M age: 13-14.5	200 cN NiTi spring reactivation: 28 d	200 cN EC reactivation: 28 d	Max R or L Canine	Force: NiTi spring and EC activated from passive position to 9 mm and 20 mm, respectively (following the manufacturer's recommendation). Confirmed intraorally 3 times using a customized caliper OTM: space closure assessed on digital dental casts. Also confirmed directly on the study models with a needle point and digital calipers	Rate of OTM	8, 12, 16
Falkensammer et al[20] (2014) academic, Austria Parallel-group RCT	n = 12 sex: 8 F, 4 M age: 26.6 (13.5)	200 cN Superelastic coil spring reactivation: NA	No control	Man R or L 2nd molar	Force: NA OTM: Measured using defined landmarks on scanned dental casts	Rate of OTM	16
Keng et al[27] (2012) private practice & academic, New Zealand Split-mouth RCT	n = 12 sex: 6 F, 6 M age: 13.3-20.1	150 cN TMA T-loop reactivation: at 3 mm (if necessary)	150 cN NiTi T-loop reactivation: at 3 mm (if necessary)	Max R or L Canine	Force: both closing loops activated by 3 mm, as measured by a dial caliper OTM: rate of space closure based on the amount of space closure achieved per month as measured on the upper dental casts	Rate of OTM	8-24
Luppanapornlarp et al[28] (2010) academic, Thailand Split-mouth RCT	n = 16 sex: 14 F, 2 M age: 18-24	50 cN NiTi spring reactivation: NA	150 cN NiTi spring reactivation: NA	Max R or L Canine	Force: calibrated orthodontic force gauge OTM: on dental casts using a measuring microscope	Rate of OTM Pain	8

Table II. Continued

Study, setting and country, and method	*Sample size, sex, age (SD)*	*Intervention: force (cN), appliance used and reactivation (if applicable)*	*Control/intervention force (cN), appliance used and reactivation (if applicable)*	*Site (jaw, side, tooth moved)*	*Method for measuring force and OTM*	*Outcome*	*Study duration, wk (SD)*
Megat Abdul Wahab et al[22] (2013) academic, Malaysia Split-mouth RCT	n = 12 sex: F age: 24.7 (3.0)	100 cN NiTi spring reactivation: NA	150 cN NiTi spring reactivation: NA	Max R or L Canine	Force: correx gauge OTM: digital caliper	Rate of OTM EARR	5
Norman et al[21] (2016) academic, UK Parallel-group RCT	n = 15 sex: 8 F, 7 M age: 16.3 (3.1) n = 15 sex: 9 F, 6 M age: 16.0 (2.0)	200 cN NiTi spring reactivation: as necessary	226.8 cN SS spring reactivation: as necessary	Max/Man R and/or L Canine	Force: both stretched not more than twice their length (according to manufacturer's recommendations) OTM: digital calipers	Rate of OTM	NA
Samuels et al[29] (1998) academic, UK Split-mouth RCT	n = 18 sex: 12 F, 6 M age: 9.8-24.1	100 cN NiTi spring reactivation: NA	200 cN NiTi spring reactivation: NA	Max or Man R or L Canine	Force: springs stretched between 3 mm and 15 mm (according to manufacturer's recommendations) OTM: measured using defined landmarks on a dental cast with a Reflex microscope	Rate of OTM	27
Wahab et al[24] (2015) academic, Malaysia Split-mouth RCT	n = 19 sex: 13 F, 6 M age: 21.3 (3.3)	100 cN NiTi spring reactivation: NA	150 cN NiTi spring reactivation: NA	Max R or L Canine	Force: correx gauge OTM: digital caliper	Rate of OTM EARR	5
Yee et al[30] (2009) academic, Australia Split-mouth RCT	n = 14 sex: 9 F, 5 M age: 13.0-19.5	50 cN NiTi spring reactivation: not needed	300 cN NiTi spring reactivation: not needed	Max R or L Canine	Force: elongation 200% and 500% of its activation OTM: intraoral and maxillary cast measurements	Rate of OTM	12
Iwasaki et al[18] (2017) academic, United States Split-mouth RCT	n = 56 sex: G: 19 F, 17 M NG: 8 F, 2 M age: G 13.5 (1.7) NG 19.2 (5.3)	Intervention 1: 18 cN NiTi spring; reactivation: NA Intervention 2: 60 cN NiTi spring; reactivation: NA Intervention 3: 120 cN NiTi spring; reactivation: NA Intervention 4: 240 cN NiTi spring; reactivation: NA Intervention 5: 360 cN NiTi spring; reactivation: NA		Max R or L Canine	force: NA OTM: 3D measurement on dental cast	Rate of OTM	12 (8)

F, Females; *M*, males; *NA*, not available; *NiTi*, nickel titanium; *EC*, elastomeric chain; *TMA*, beta titanium; *SS*, stainless steel; *NM*, not mentioned; *Max*: maxilla; *Man*, mandible; *R*, right; *L*, left; *NG*, nongrower; *G*, grower.

Fig 2. Risk of bias summary outlining judgment of risk of bias items for studies included in the qualitative synthesis.

and thus, a meta-analysis was considered inappropriate.

Rate of OTM

The rate of OTM was measured in all studies[18,20-30] (Table III), and the force magnitude used varied between 18 cN and 360 cN. For ease of description, the forces were categorized in 4 groups: low (<100 cN), moderate (100 cN-150 cN), high (150 cN-250 cN), and very high (250 cN-400 cN). The rate of OTM ranged between 0.23 and 0.44 mm/wk for the low force group, 0.16 and 0.47 mm/wk for the moderate force group, 0.1 and 0.46 mm/wk for the high force group, and 0.34 and 0.49 mm/wk for the very high force group.

Four studies[22-25] that compared 100 cN with 150 cN forces favored the higher range; however, of these, only in 2 studies,[22,25] the difference in the rate of OTM was found to be statistically significant ($P < 0.05$). Iwasaki

Table III. Results of individual studies for the rate of OTM

Study	*Force (cN) and appliance used*	*Amount OTM, mm (SD)*	*Rate OTM (mm/week)*	P *value*
Abdul Wahab et al[23] (2014)	100 cN, NiTi spring	NA	0.30 (0.09)	>0.05
	150 cN, NiTi spring		0.40 (0.10)	
Ariffin et al[25] (2013)	100 cN, NiTi spring	1.85 (0.27)	0.37 (0.05)	<0.05
	150 cN, NiTi spring	2.36 (0.28)	0.47 (0.05)	
Bokas and Woods[26] (2006)	200 cN, NiTi spring	NA	0.46	0.011
	200 cN, EC		0.42	
Falkensammer et al[20] (2014)	200 cN, Superelastic coil spring	1.6 (0.4)	0.1 (0.02)	0.16
Iwasaki et al[18] (2017)	18 cN, NiTi spring	2.82 (1.20)	0.23 (0.10)	0.01
	60 cN, NiTi spring	3.36 (1.70)	0.33 (0.14)	
	120 cN, NiTi spring	5.38 (0.99)	0.44 (0.08)	
	240 cN, NiTi spring	5.47 (1.39)	0.45 (0.11)	
	360 cN, NiTi spring	5.96 (1.80)	0.49 (0.15)	
Keng et al[27] (2012)	150 cN, TMA T-loop	NA	0.21 (0.08)	0.07
	150 cN, NiTi T-loop		0.22 (0.11)	
Luppanapornlarp et al[28] (2010)	50 cN, NiTi spring	1.13 (0.63)	0.14 (0.08)	>0.05
	150 cN, NiTi spring	1.28 (0.70)	0.16 (0.09)	
Megat Abdul Wahab et al[22] (2013)	100 cN, NiTi spring	1.57 (0.44)	0.30 (0.09)	0.04
	150 cN, NiTi spring	2.10 (0.50)	0.40 (0.10)	
Norman et al[21] (2016)	200 cN, NiTi spring	3.42 (1.79)	0.14 (0.06)	0.76
	226.8 cN, SS spring	3.25 (1.28)	0.21 (0.09)	
Samuels et al[29] (1998)	100 cN, NiTi spring	NA	0.16	0.000
	200 cN, NiTi spring		0.24	
Wahab et al[24] (2015)	100 cN, NiTi spring	1.24 (0.29)	0.46 (0.04)	>0.05
	150 cN, NiTi spring	1.36 (0.39)	0.47 (0.05)	
Yee et al[30] (2009)	50 cN, NiTi spring	1.69 (0.58)	0.14 (0.04)	<0.001
	300 cN, NiTi spring	4.10 (1.68)	0.34 (0.14)	

NiTi, Nickel titanium; *NA*, not available; *EC*, elastomeric chain; *TMA*, beta titanium; *SS*, stainless steel.

et al[18] assessed 5 different force magnitudes (ie, 18, 60, 120, 240, and 360 cN), showing an optimal force range between 120 cN and 240 cN, as well as more distopalatal rotations with forces of 360 cN. One study[28] compared 50 cN with 150 cN and found no significant difference in the rate of OTM between the experimental groups ($P > 0.05$). Another study[29] examined the difference between the rates of space closure for 150 cN and 200 cN and noted no significant difference. However, Yee et al,[30] reported that the initial OTM was not related to force magnitude. Nevertheless, during the later periods of the study, higher rates of OTM, as well as increased anchorage loss and loss of rotation canine control were observed at the 300 cN vs 50 cN ($P < 0.05$).

The remaining studies compared the same forces or a very similar range of force magnitudes and used different materials for applying the force[21,26,27] or used extracorporeal shock-wave therapy in 1 group.[20]

The influence of growth on the rate of OTM was only evaluated by Iwasaki et al,[12] who found that the overall speed of tooth movement was 1.5-fold faster in growing subjects compared with nongrowing subjects ($P = 0.001$).

EARR

EARR was examined in 2 studies from the same author group.[22,24] Abdul Wahab et al[23] used the methods reported by Liou and Huang (score range, 0-3) to assess apical and lateral root resorption (RR) on periapical radiographs taken at baseline, 5 weeks, and 6 months after maxillary canine retraction. No RR was detected around the canines of either the test or control teeth between the 100 cN and 150 cN forces. In the study by Wahab et al,[24] periapical radiographs of maxillary canines were taken before orthodontic appliance placement (R1), before canine retraction (R2), and 5 weeks after canine retraction (R3). The tooth lengths were subsequently measured on the radiographs in millimeters using digital calipers, and EARR was calculated from the difference between the tooth lengths at the 3 radiographic time points. In addition, they found no sign of EARR at R1, minimal signs of EARR at R2, and at R3, the 150 cN force showed more pronounced EARR (1.42 ± 0.13, standard deviation [SD]) compared with the 100 cN force (0.89 ± 0.04, SD), although the difference was not statistically significant ($P > 0.05$).

Table IV. Results of Luppanapornlarp et al. for pain (VAS)

	1 hour	*24 hours*	*1 week*	*1 month*	*2 months*
Force	Mean ± SD (mm)	Mean ± SD (mm)	Mean ± SD (mm)	Mean ± SD (mm)	Mean ± SD (mm)
50 cN	12.24 ± 15.33	20.24 ± 24.11	8.05 ± 12.18	9.44 ± 19.06	10.97 ± 18.50
150 cN	18.84 ± 18.19	35.15 ± 16.89	8.09 ± 10.84	10.45 ± 16.79	15.03 ± 22.02

Pain

Pain was assessed in the study by Luppanapornlarp et al,[28] (Table IV), who found a significant difference between the 50 cN and 150 cN groups at 24 hours (P <0.01). However, the pain intensity was reduced toward the end of the experiment. Overall, the 50 cN group showed less pain than the 150 cN group throughout the study period of 2 months.

Additional analysis

A meta-analysis was considered for the studies comparing low (<100 cN) to high (>150 cN) forces. There were 7 split-mouth design studies[18,19,22-25,28,30] that met these criteria, and the opportunity to perform a meta-analysis was examined. Quantitative analysis requires information regarding the precision of the overall outcome (ie, the difference in the rate of OTM between the given forces). In a split-mouth design setup, the SD of the difference in the rate of OTM cannot be calculated from the SD reported for the rate of OTM of individual forces, as tooth movement is correlated within patients. Therefore, at least 1 of the following should have been reported in a study to be considered for a meta-analysis: (1) the P value of the difference in the rate of OTM; (2) a 95% confidence interval for that difference; or (3) the SD or standard error of the difference. Of the 7 split-mouth design studies, only 1 met these criteria.[22] Attempts made to contact the authors regarding the missing information, where possible, were unsuccessful. Thus, with 6 of 7 studies lacking statistical precision, a meta-analysis was deemed inappropriate.

DISCUSSION

Summary of evidence

There has been considerable interest in the past in comparing orthodontic force magnitudes, with a previously published systematic review[5] indicating that the evidence is insufficient regarding an optimal force range. Fifteen years later, upon deciding to update the previously published review, 12 human studies were identified (10 randomized split-mouth designs[18,22-30] and 2 RCTs[20,21]). The rate of OTM was measured in all 12 studies,[18,20-30] whereas the influence of growth was assessed in 1 article.[18] In addition, EARR[22,24] was investigated in 2 studies, and pain was examined in 1 study.[28]

In the 2003 review,[5] 12 different human studies were included from the current systematic review. This difference can be attributed to our strict inclusion criteria that were set with a limitation to RCTs and randomized split-mouth studies. Even though split-mouth studies are known to exhibit a carry-across effect, the risk was assessed as unlikely for this type of orthodontic clinical trials and, therefore, were included in this review.

It must be noted that force magnitude from a mechanobiological point of view should be clearly expressed as a pressure unit in Pa rather than cN. Once stress is applied on a tooth and distributed per unit area, the tooth moves within its socket, leading to PDL strain at a cellular level. However, it is feasibly impossible to measure stress and strain within the PDL of a loaded tooth. Therefore, forces applied directly to the tooth are measured instead.[2,5]

The force magnitudes used in the included studies were applied to canines, with the exception of 1 study.[20] In the study of Falkensammer et al,[20] the mandibular second molar was mesialized with a 200 cN force and was included in our review as it fulfilled our eligibility criteria. The forces in all included studies ranged between 18 cN and 360 cN, and according to the qualitative analysis, forces between 50 cN and 250 cN produced a similar rate of OTM (0.1 mm/wk-0.47 mm/wk), whereas, forces >250 cN produced a higher rate of OTM (0.34 mm/wk-0.49 mm/wk). The studies that used high or very high forces in 1 of their intervention groups[18,28,30] reported more unwanted side effects, such as loss of canine rotation control, anchorage loss, and pain. However, the strength of evidence regarding the primary outcome was considered weak to moderate, as most articles had an unclear status for allocation concealment, blinding of participants and personnel, and blinding of outcome assessment (Fig 2). Furthermore, a positive correlation was found between growth and the rate of OTM. Iwasaki et al[18] reported a 1.5-fold difference between growers and nongrowers, although the evidence was regarded as weak because of the unclear risk of selection, performance, and detection bias.

Regarding the study of Falkensammer et al,[20] one might speculate that a 200 cN force may not be sufficient for bodily movement of a mandibular molar given that its root surface area is much larger than that of a

canine. The rate of OTM in this study was 0.1 ± 0.02 mm/wk, which is relatively low compared with the other included studies using a 200 cN force on canines with the rate of OTM ranging from 0.14 to 0.46 mm/wk.

With respect to the secondary outcomes of this systematic review, Megat Abdul Wahab et al[22] did not detect any EARR when comparing 100 cN with 150 cN in the study of 2013 and found no statistically significant difference in the study of 2015.[24] Megat Abdul Wahab et al[22] tried measuring lateral RR; however, this cannot be performed based on a periapical radiograph. Regarding pain, Luppanapornlarp et al[28] showed that the lower force group (50 cN) had less pain than the higher force group (150 cN) throughout the experiment. Nonetheless, the strength of evidence for both secondary outcomes was considered weak as the number of articles reporting on EARR and pain was insufficient to lead to a solid conclusion.

In consideration of the above-mentioned findings, practitioners must keep in mind that patient comfort should prevail during orthodontic treatment and that lack of evidence regarding an optimal force range does not give clinicians carte blanche to use high forces, which could eventually lead to unwanted side effects such as pain, EARR, and tipping of teeth during OTM.

It is widely accepted that the rate of OTM is influenced by several variables and that significant differences can exist with identical experimental settings, which are largely independent of force magnitude.[7,8] Therefore, unraveling major factors that contribute to the rate of OTM is important and could eventually lead to a more personalized orthodontic treatment.

Limitations

One of the main limitations at outcome level is the unclear risk of bias detected in 11 of 12 studies, making it difficult to draw a conclusion regarding an optimal force range. Moreover, we had hoped to analyze the influence of growth on the rate of OTM, as well as the effect of force magnitude on EARR and pain. However, only 1 study reported on the influence of growth,[18] 2 studies on EARR,[22,24] and 1 on pain.[28] All of these studies had an unclear risk of bias, and thus, no sound conclusion could be made. Another limitation of this systematic review is the inability to perform a meta-analysis because of statistical imprecision of the considered articles.

Inclusion of split-mouth studies could also be perceived as a study limitation. Nevertheless, their exclusion could have potentially led to the loss of important data, as research regarding an optimal force magnitude for OTM is scarce. This type of study design has received increased popularity in the past decades, as a smaller sample size is required compared with a parallel-group design,[31] thereby making a clinical trial easier to conduct.

Furthermore, the different appliances used for tooth movement in the included studies could have influenced the rate of OTM, leading to a confounding effect and a potential limitation at outcome level.

CONCLUSIONS

Based on this systematic review, we concluded the following:

1. There is weak to moderate evidence showing that forces ranging between 50 cN and 100 cN are optimal for the rate of OTM, patient comfort, and potentially exhibit fewer side effects.
2. No sound conclusions can be drawn regarding EARR and pain because of the limited amount of evidence.
3. Weak, but statistically significant evidence, suggests that growth increases the rate of OTM.

Based on the results of this systematic review, more robust and well-designed RCTs are needed to enable a future meta-analysis to identify an optimal force range.

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