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**Systematic Review**

# Extraction of premolars in orthodontic treatment does not negatively affect upper airway volume and minimum cross-sectional area: a systematic review with meta-analysis

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## Abstract

**Background:** Extraction of premolars is usually prescribed for the orthodontic treatment of cases with inadequate space within the dental arch or when anterior teeth retraction is indicated; however, it has been advocated that this treatment approach could negatively influence the airways.

**Objective:** To identify and critically appraise studies of premolar extractions during orthodontic treatment on upper airway dimensions. **Search methods:** Electronic unrestricted searches in nine databases until October 2024. **Selection criteria:** Clinical studies on humans comparing comprehensive orthodontic treatment with versus without the extraction of premolars using cone-beam computed tomography to assess upper airway volume or minimum cross-sectional area (minCSA). **Data collection and analysis:** After duplicate study selection, data extraction, and risk-of-bias assessment according to Cochrane, random-effects meta-analyses of Mean Differences (MD) with their 95% confidence intervals (CI) were performed, followed by subgroup/meta-regression analyses and assessment of the quality of evidence.

**Results:** Twelve papers corresponding to 11 unique retrospective non-randomized studies were included, covering 891 patients (35.8% male; 20.0 years-old on average). No statistically significant differences in the effect of orthodontic treatment on the volume of the nasopharynx, palatopharynx, glossopharynx, oropharynx or oral cavity were seen between patients treated with versus without premolar extractions ($P > .05$). Similarly, no significant differences were seen between extraction and non-extraction patients in terms of minCSA of the nasopharynx, palatopharynx, or glossopharynx ($P > .05$). On the contrary, patients treated with premolar extractions showed increased minCSA of the oropharynx compared to those treated without premolar extractions (4 studies; MD = 23.00 $mm^2$; 95% CI = 10.74–35.26 $mm^2$; $P = .009$). No significant effects from patient age, sex, or equivalence of the extraction/non-extraction groups were found, while the strength of evidence was moderate in all cases due to the inclusion of non-randomized studies with high risk of bias.

**Conclusions:** Limited evidence of moderate strength indicates that, on average, premolar extractions during comprehensive orthodontic treatment have little to no effect on the volume and minCSA of the airways.

**Registration:** CRD42024621355

**Keywords:** orthodontic treatment; tooth extraction; airways; systematic review; meta-analysis

## Introduction

The interplay between form and function has long been the subject of discussions in the field of orthodontics and dentofacial orthopedics, especially when it comes to breathing. Patients with sleep disordered breathing, and specifically Obstructive Sleep Apnea (OSA), tend to show distinct craniofacial traits, including short and steep cranial base, increased mandibular plane to hyoid bone distance, greater anterior and posterior face height, more skeletal Class II, shorter and retrognathic jaws, more vertical craniofacial configuration, increased soft palate length and thickness, and greater uvula length and thickness compared to patients without OSA [1–5].

Skeletal malocclusions as well as their treatment have been associated with the size and morphology of the upper airways—even though this does not necessarily translate to differences in breathing. Patients with skeletal Class II craniofacial patterns seem to have on average decreased upper airway volume (mainly at the oro-, palato, and the glossopharynx compartments), while skeletal Class III patients seem to have increased upper airway volume (mainly at the oropharynx, the intraoral cavity, and the hypopharynx) compared to Class I patients [6]. Additionally, hyperdivergent patients seem to have on average decreased airway volume at the oropharynx compared to normodivergent patients [6].

Regarding several dentofacial orthopedic treatment protocols for Class II, Class III, or transverse discrepancies (mandibular advancement, maxillary extraoral traction, maxillary protraction, or rapid maxillary expansion), these have been shown to positively influence the size of the upper airways of growing children [7–11]. Subsequently, these results were interpreted as signs that the orthodontist might be in a position to indirectly influence the breathing capacity of growing children, even though the morphological assessment of the airways with radiographic imaging or even computational fluid dynamics simulation [12] does not assess the actual breathing function and does not necessarily correlate well with functional measurements of breathing [13, 14].

Contrary to the assumption that dentofacial orthopedics might be able to positively influence the anatomic and functional parameters of the upper airways, a question arises as to whether certain orthodontic therapeutic protocols might exert a negative influence on the morphology of the upper airways or even the breathing capacity. This concept is discussed mostly, but not exclusively, on the basis of tooth extractions performed in conjunction with orthodontic treatment with fixed appliances. According to this concept, extraction of teeth and subsequent retraction of the anterior teeth limits the antero-posterior dimension of the dental arch and the space available for the tongue, which further restricts the upper airways and can supposedly exacerbate the risk for OSA. It is important to note though that this notion is supported mostly by anecdotal evidence, subjective opinion pieces, or individual uncontrolled clinical studies of poor design and low internal validity [15–17]. A recent white paper from the American Association of Orthodontists stated that existing evidence does not support the notion that arch constriction or retraction of the anterior teeth facilitated by dental extractions has a detrimental effect on respiratory function [18]. Finally, a study assessing the electronic medical and dental health records in the United States reported that the absence of four premolars and, therefore, a presumed indicator of past 'extraction during orthodontic treatment' cannot be supported as a significant cause of OSA [19]. This is also confirmed by a recent large cross-sectional study finding no association between sleep disordered breathing/sleep disruption and absence of four first premolars [20].

Previous studies on the subject have used either two-dimensional lateral cephalograms or three-dimensional imaging (mostly cone-beam computerized tomography [CBCT]) to assess the upper airways before and after orthodontic treatment with or without extractions. Even though CBCT does not provide information on the pharyngeal neuromuscular tone, susceptibility to collapse, or actual function of the airway and should not be used to diagnose breathing disorders, it still offers considerable advantages to the lateral cephalogram in terms of visualizing the upper airway volume and minCSA, which could be useful for diagnostic purposes [21]. The existing systematic reviews comparing extraction versus non-extraction patients assessed with CBCT are prone to language bias due to excluding non-English studies [22], did not follow Cochrane's guidelines on critically appraising the internal validity of included studies [22–25], or did not perform meta-analysis [22, 23, 25]. Therefore, it was judged that a new review on the subject is justified. This systematic review aims to identify and critically appraise the evidence from clinical studies in human subjects on the effect of premolar extractions, as part of comprehensive orthodontic treatment, on the upper airway volume and minCSA through CBCT assessment. The null hypothesis was that there is no difference in upper airway volume and minCSA between patients treated with and those treated without bilateral premolar extractions during fixed-appliance treatment.

## Materials and methods

### Protocol and registration

The protocol for this review was prepared a priori, was registered in PROSPERO (CRD42024621355), and all changes to the protocol were noted (Supplementary Appendix 1). This conduct and reporting of this systematic review is based on the Cochrane Handbook [26] and the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement [27], respectively.

### Eligibility criteria

Any clinical study on systemically healthy and non-syndromic human patients of any age, sex and ethnicity with any kind of dental and skeletal malocclusion was considered eligible for inclusion in this systematic review. Based on the nature of the research question, the ideal study design to include was parallel randomized clinical trials. However, as previous reviews on orthodontic extractions indicated that very few randomized trials exist [24, 28], non-randomized comparative prospective and retrospective before-and-after (cohort) studies were also included. Excluded were case series/reports, animal studies, non-clinical studies, studies without comprehensive orthodontic treatment, studies on patients with systemic diseases (including clefts), studies not using CBCT, studies not reporting the outcomes of interest, and studies that did not include a non-extraction fixed-appliance control group. Any clinical setting was included to increase the generalizability of the review's results.

### Information sources and search

We searched nine electronic databases without restrictions for publication language, year and type from inception up to October 31st, 2024 (Supplementary Appendix 2). The reference lists and citation lists through Google Scholar of eligible articles and existing systematic reviews were reviewed to identify any additional studies.

### Selection process

Initially, studies being obviously not relevant to the review's scope were eliminated based on their title and abstract. Subsequently, the remaining full texts were checked against the review's criteria. Study selection was performed independently and in duplicate by two authors (SNP and MZ) and any disagreements were resolved through discussion with a third author (AKP).

### Data collection process and items

A pre-piloted collection form was used for data extraction, which covered (a) study characteristics, including the primary author with the year of publication, study design, clinical setting, and country; (b) patient characteristics, comprising number of patients, age, and sex; (c) whether any matching between extraction/non-extraction groups was made; (d) the skeletal maturation stage of included patients; (e) the malocclusions of included patients; (f) whether any airway-related eligibility criteria were used for patient selection (including Body Mass Index [BMI] [29]); (g) which premolars were extracted; (h) whether any anchorage management was reported; and (i) the voxel size of the used CBCT imaging. Data extraction was independently and in duplication by two authors (SNP and MZ), while a third author (AKP) resolved any existing disparities.

### Risk of bias of individual studies

The risk of bias of included randomized trials and non-randomized comparative clinical studies was assessed with Cochrane's ROB 2.0 [30] and ROBINS-I tools [31], respectively. All assessments were performed by two authors independently (MZ and AKP), with discrepancies resolved through discussion with a third author (SNP).

### Effect measures and data synthesis

Pairwise meta-analysis of mean differences (MD) and their 95% confidence intervals (CI) was used to pool data from ≥ 2 similar studies reporting on the same outcome. Regardless of how the authors of original studies named them, all reported outcomes were categorized according to widely accepted anatomical landmarks that delineate each upper airway compartment (Supplementary Appendix 3). Even though all compartments were included and reported, the volume and minCSA of the oropharynx and its separate constituent compartments of the palatopharynx and the glossopharynx were adopted as the main outcomes of this review, due to their critical role in breathing disorders [32, 33]. As several malocclusion-related or treatment-related characteristics might influence airway dimensions [6, 8, 9, 12, 29, 34], effects of comprehensive orthodontic treatment were expected to vary among studies, and a random-effects model was deemed a priori more appropriate to capture this variability and calculate the average distribution of treatment effects across studies [35]. A novel restricted maximum likelihood variance estimator was chosen in all instances [36] and the Knapp & Hartung adjustment [37] was used for meta-analyses with ≥ 3 studies. Heterogeneity between studies was assessed through visual inspection of a contour-enhanced forest plot (Supplementary Appendix 1) [38], through estimation of tau (absolute heterogeneity) and $I^2$ (relative inconsistency), together with their 95% uncertainty intervals. Ninety-five percent predictions were calculated, which incorporate identified heterogeneity and assist in the interpretation of the meta-analytical estimates by providing a range of expected effects across various future clinical settings [39]. Random-effects meta-regressions and subgroup analyses were performed according to mean age, included age group (underage, adult, mixed), and % of male patients in the study. In order to address the baseline equivalence of the extraction/non-extraction patients, standardized mean differences (SMD; Cohen's d) for baseline (pretreatment) upper airway dimensions were calculated. Additionally, extraction versus non-extraction comparisons from non-randomized studies are bound to be wrought by confounding by indication (i.e. more severe cases allocated to extraction treatment) and baseline severity is associated with treatment duration [40]. As such, SMDs for treatment duration between extraction/non-extraction patients were calculated as a proxy for baseline malocclusion severity. SMDs for baseline airway dimensions and treatment duration were used to run meta-regression or sensitivity analysis (using an arbitrary cutoff of SMD < 0.5 indicating equivalence). All analyses were conducted in R 4.2.2. (R Foundation for Statistical Computing, Vienna, Austria) by one author (SNP), with open dataset [41], alpha set at 0.05 and a two-sided P-value.

### Reporting bias assessment and certainty assessment

Hints of reporting biases (including the possibility of publication bias) were planned to be assessed through contour-enhanced funnel plots and formally with Thompson's test. The Grades of Recommendations, Assessment, Development, and Evaluation (GRADE) approach was employed [42] to gauge the certainty around the results of meta-analyses and findings were presented with a revised summary of findings table [43].

## Results

### Study selection

The initial electronic database search yielded 1202 records and one additional was identified through manual searching (Fig. 1). After eliminating 258 duplicates, 944 records were left for further evaluation and were assessed against the eligibility criteria (Supplementary Appendix 4). Ultimately, 12 publications [44–55], corresponding to 11 distinct clinical studies, were included in the quantitative synthesis (as one study was reported in two papers [54, 55]). Most of the included studies (7/11; 64%) were published as papers in peer-reviewed journals, while the remaining four (36%) were published as dissertation/thesis [45, 47, 51, 52]. All studies were in English, except for one paper published in a Chinese journal [49].

### Study characteristics

The characteristics of included studies are summarized in Table 1. All 11 included studies were retrospective non-randomized before-and-after (cohort) studies and were conducted in university clinics or private practices from just three different countries (Australia, China, and United States of America). In total, 891 patients were included in the 11 studies (mean 81 patients/study from the 11 studies reporting sample size), with 36% being male (319/891; from the 11 studies reporting sex) while the average age was 19.9 years (from the 10 studies reporting on age). Among the 11 studies, 2/11 included underage samples [44, 47], 3/11 included adult samples [48, 50, 53], 3/11 included mixed underage/adult samples [45, 51, 52], and 3/11 did not report the age range of their sample [46, 49, 54]. Matching of the extraction and non-extraction patients was done in only about half the studies (6/11; 55%), but not always for all confounders that could potentially affect airway dimensions. Skeletal maturation was reported only in one study [51], which used the cervical vertebral maturation method. Various types of malocclusions were included within the identified studies defined either as skeletal/dental Classes I-III, crowding, sagittal/vertical skeletal configuration, or dentoalveolar inclination. Breathing disorders or upper airway anomalies were explicitly ruled out in only 45% (5/11) of the included studies. In the extraction group, either two maxillary or four premolars were extracted, and the 1st premolars were extracted more often than the 2nd premolars (even though this was only partially reported). In all studies fixed appliances were used for comprehensive orthodontic treatment, except for one study

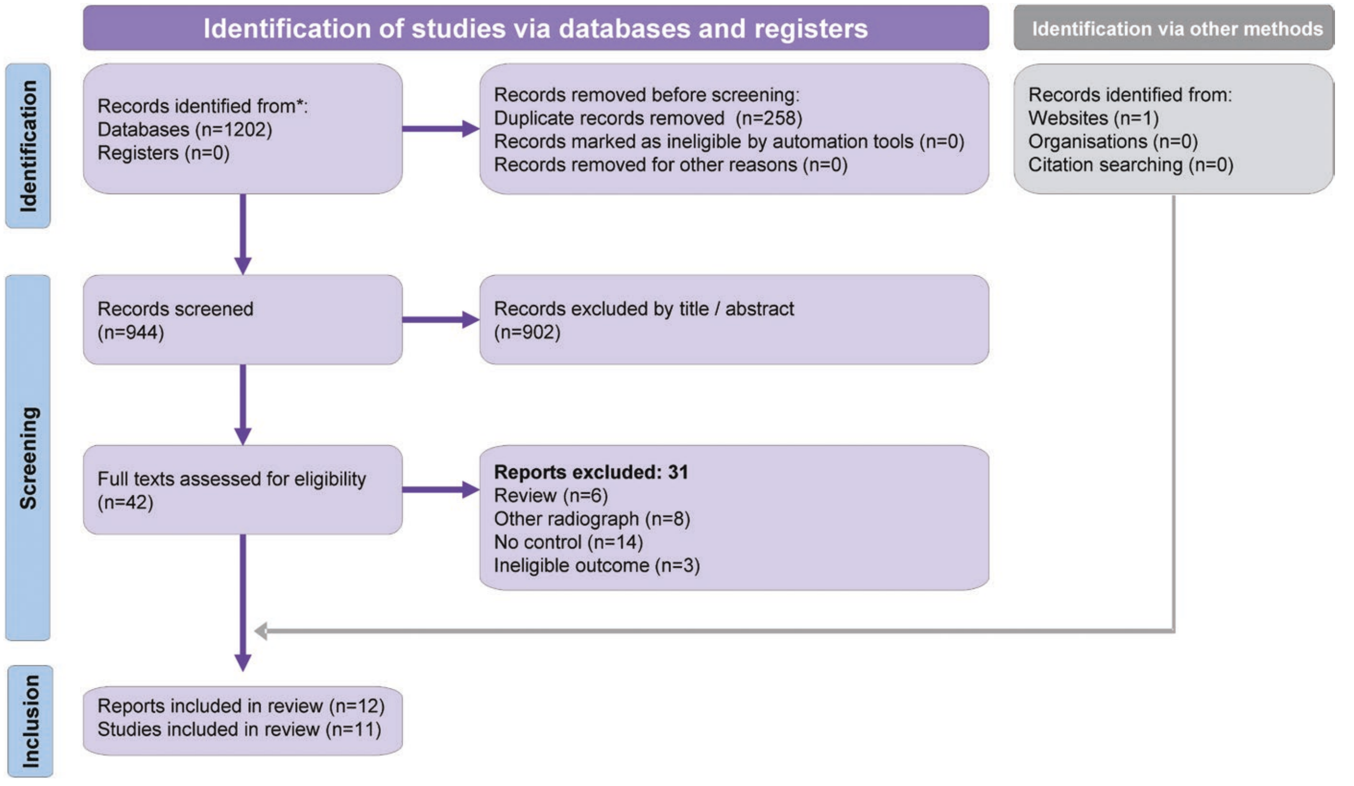


**Figure 1.** PRISMA flow diagram for the identification and selection of eligible studies.

[50], where 7% of the patients were treated with aligners. CBCT voxel size was reported in 8/11 studies and ranged between 0.3 and 0.4 mm.

## Risk of bias of included studies

The risk of bias for the included non-randomized studies was assessed with the ROBINS-I tool (Table 2). The most problematic domains were the selection of patients into the study (critical in 100% of the studies), followed by confounding (critical in 55% and serious in 27% of the studies), while it was unclear in all studies if blinding of the outcome measurement was undertaken.

## Data synthesis

All eleven included studies reported data on treatment-related (post- minus pretreatment) volumetric changes of at least one upper airway compartment (or combinations of two compartments). One study [51] included its full data in a table, which was extracted and re-analyzed for this review (Supplementary Appendix 5). Existing evidence indicated that overall no statistically significant differences ($P > .05$ in all instances) were observed between extraction and non-extraction patients for volume of (i) the nasopharynx (4 studies; MD = –74.72 $mm^3$; 95% CI = –236.34 to 86.90 $mm^3$; P = .24; Appendix 6); (ii) the palatopharynx (7 studies; MD = –351.57 $mm^3$; 95% CI = –993.31 to 290.17 $mm^3$; P = .23; Fig. 2A); (iii) the oral cavity (1 study; MD = –1421.92 $mm^3$; 95% CI = 04596.76 to 1752.92 $mm^3$; P = .38; Appendix 7); (iv) the oropharynx (6 studies; MD = 286.47 $mm^3$; 95% CI = –1171.66 to 1744.60 $mm^3$; P = 0.64; Fig. 2B); (v) the glossopharynx (4 studies; MD = 165.07 $mm^3$; 95% CI = –1142.45 to 1472.58 $mm^3$; P = .71; Fig. 2C); (vi) the naso- & oropharynx combined (1 study; MD = 337.80 $mm^3$; 95% CI = –1859.48 to 2535.08 $mm^3$; P = .76; Appendix 8); and (vii) the glosso- & hypopharynx (2 studies; MD = –527.52 $mm^3$; 95% CI = –1617.53 to 562.48 $mm^3$; P = .34; Appendix 9).

Data on treatment-related changes in the minCSA of different airway compartments were reported from 9 of the 11 included studies, as two studies [45, 54] did not report such data. Existing evidence indicated that overall no statistically significant differences ($P > .05$ in all instances) were observed between extraction and non-extraction patients for the minCSA of (i) the nasopharynx (2 studies; MD = –16.56 $mm^2$; 95% CI = –51.91 to 18.80 $mm^2$; P = .36; Appendix 10); (ii) the palatopharynx (4 studies; MD = –19.62 $mm^2$; 95% CI = –43.74 to 4.51 $mm^2$; P = .08; Fig. 3A); (iii) the glossopharynx (2 studies; MD = –1.73 $mm^2$; 95% CI = –33.80 to 30.34 $mm^2$; P = .92; Fig. 3C); (iv) the glosso- & hypopharynx combined (2 studies; MD = –10.61 $mm^2$; 95% CI = –45.93 to 24.71 $mm^2$; P = .56; Appendix 11); and (v) the naso- & palatopharynx (2 studies; MD = 4.27 $mm^2$; 95% CI = –19.18 to 27.72 $mm^2$; P = .72; Appendix 12). On the contrary statistically significant differences were seen for the minCSA of the oropharynx, where patients treated with premolar extractions showed significantly greater minCSA than patients treated without premolar extractions (4 studies; MD = 23.00 $mm^2$; 95% CI = 10.74 to 35.26 $mm^2$; P = .009; Fig. 3B). However, in all instances the differences between extraction versus non-extraction treatment were of very small magnitude (small effect) and therefore are bound to be of little clinical relevance.

Between-study heterogeneity was for the most part small to moderate (Table 3), with a couple of exceptions like the minCSA for the nasopharynx (Supplementary Appendix 10) and the minCSA for the glosso- & hypopharynx (Supplementary Appendix 11), where only two studies with

**Table 1.** Characteristics of included studies.

| Study | Design; country; setting | Patients (M/F) | Age* | Matching | Malocclusion characteristics | Breathing/airways characteristics | Extraction | Appliance; anchorage | CBCT voxel size |
|---|---|---|---|---|---|---|---|---|---|
| Chen 2018 [49] | rNRS; Uni; CHN | EX: 25 (10/15)<br>NEX: 25 (10/15) | EX: 12.2 (NR)<br>NEX: 12.4 (NR) | - | Dental Cl. I; no-mild crowding; ANB 0-4°; average angle/growth type; 1s-SN > 110°; 1i-ML > 99° | No snoring/obstructive sleep apnea/adenoid-/tonsillectomy; normal BMI | 4 × 1st PMs | FA; headgear | NR |
| Feizi 2021 [51] | rNRS; Pract; USA | EX: 9 (4/5)<br>NEX: 18 (8/10) | EX: 19.2 (11.0–46.0)<br>NEX: 13.1 (11.0–17.0) | - | Dental Class II (≥ 1/2 cusp); no agenesis (excluding M2/M3); no craniofacial anomaly | - | 4x PMs | FA | 0.3 mm |
| Guo 2022 [53] | rNRS; Uni; CHN | EX: 120 (0/120)<br>NEX: 40 (0/40) | EX: 25.1 (20.0–25.0)<br>NEX: 26.4 (20.0–25.0) | Age; skeletal type | Skeletal Class I-II/1 (ANB > 0°, SN-ML > 28°); no Cl. II/2; mild-moderate crowding | BMI < 27 kg/m²; no breathing disorder | 4 × 1st PMs | FA; MX anterior retraction ≥3 mm | 0.3 mm |
| Joy 2020 [50] | rNRS; Uni; USA | EX: 41 (20/21)<br>NEX: 42 (22/20) | EX: 26.1 (18.0-NR)<br>NEX: 26.0 (18.0-NR) | Age; sex | Cl. I-III; any crowding | - | 2x MX or 4x PMs | FA/AL; | 0.3 mm |
| Leslie 2014 [47] | rNRS; Uni; USA | EX: 64 (23/41)<br>NEX: 90 (42/48) | EX/NEX: NR (NR-18.0) | - | - | - | 4x PMs | FA | 0.4 mm |
| Mladenovic 2024$_{coll}$ [54, 55] | rNRS; Pract; AUS | EX: 54 (18/36)<br>NEX: 59 (24/35) | EX/NEX: 15.0 (NR) | Crowding | Skeletal Cl. I-II; any crowding; no craniofacial deformities | - | 2x MX or 4 × 2nd PMs | FA | 0.3 mm |
| Mostanghi 2021 [52] | rNRS; Pract; USA | EX: 20 (7/13)<br>NEX: 20 (5/15) | EX: 24.9 (18.5–38.3)<br>NEX: 26.2 (16.0–42.6) | Age; sex; treatment duration | Crowding or bimaxillary dentoalveolar protrusion; no impactions | No reported obstructive sleep apnea | 2x MX or 4x PMs | FA | 0.3 mm |
| Pliska 2016 [48] | rNRS; Uni; USA | EX: 26 (8/18)<br>NEX: 48 (17/31) | EX: 27.4 (18.0-NR)<br>NEX: 31.9 (18.0-NR) | - | Cl. I-II (ANB ≥ 0°); no agenesis | - | ≥2x PMs | FA | NR |
| Shannon 2012 [45] | rNRS; Pract; USA | EX: 27 (11/16)<br>NEX: 61 (30/31) | EX: 13.5 (9.0–22.0)<br>NEX: 13.2 (10.0–22.0) | - | No agenesis; no craniofacial anomaly | - | 4x PMs | FA | NR |
| Stefanovic 2023 [46] | rNRS; Uni; USA | EX: 31 (15/16)<br>NEX: 31 (15/16) | EX: 13.0 (NR)<br>NEX: 12.9 (NR) | Age; sex | Cl. I-III | No breathing disorder | 4 × 1st PMs | FA | 0.38 mm |
| Valiathan 2010 [44] | rNRS; Uni; USA | EX: 20 (10/10)<br>NEX: 20 (10/10) | EX: 13.6 (11.3–15.6)<br>NEX: 13.7 (11.3–15.6) | Age, gender, height, ethnicity, weight, BMI, and skeletal features, and oropharynx volume | Cl. I; no craniofacial deformities | No pharyngeal pathology and/or nasal obstruction, snoring, obstructive sleep apnea, adenoid- or tonsillectomy. | 4x PMs | FA | 0.38 mm |

AL, aligner; BMI, body mass index; CBCT, cone-bean computerized tomography; Cl., Angle's Class; coll, collated multiple reports; CVM, cervical vertebrae maturation; EX, extraction group; FA, fixed appliance; M2/M3, 2nd/3rd molar; MX, maxillary; NEX, non-extraction group; NR, not reported; PM, premolar; Pract, private practice; rNRS, retrospective non-randomized study.

**Table 2.** Risk of bias of included studies with the ROBINS-I tool.

| Domain | Chen 2018 | Feizi 2021 | Guo 2022 | Joy 2020 | Leslie 2014 | Mladenovic 2024 | Mostanghi 2021 | Pliska 2016 | Shannon 2012 | Stefanovic 2023 | Valiathan 2010 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Confounding (crowding, skeletal pattern, amount of retraction, age, sex, BMI) | Critical | Critical | Moderate | Moderate | Critical | Serious | Critical | Serious | Critical | Critical | Serious |
| Selection of participants into the study | Critical | Critical | Critical | Critical | Critical | Critical | Critical | Critical | Critical | Critical | Critical |
| Classification interventions | Low | Low | Low | Low | Low | Low | Low | Low | Low | Low | Low |
| Deviations from intended interventions | Low | Low | Low | Low | Low | Low | Low | Low | Low | Low | Low |
| Missing data (prerequisite the presence of data for inclusion in the study) | Low | Low | Low | Low | Low | Low | Low | Low | Low | Low | Low |
| Measurement of outcomes (blinding) | Unclear | Unclear | Unclear | Unclear | Unclear | Unclear | Unclear | Unclear | Unclear | Unclear | Unclear |
| Selection of reported results (selective reporting) | Low | Low | Low | Low | Low | Low | Low | Low | Low | Low | Low |

BMI, body mass index.

varying results were included. The impact of observed heterogeneity can also be gauged by the random-effects predictions, which in all cases included both negative and positive values. This means that orthodontic treatment with premolar extractions in a future patient cannot be associated with certainty with either greater or smaller airway volume and or minCSA.

The strength of clinical recommendations that can be drawn for the review's main outcomes is in all instances moderate, due to the inclusion of non-randomized studies with methodological limitations and high risk of bias (Table 4).

Similarity of the compared extraction versus non-extraction groups within each study according to baseline (pretreatment) airway dimensions and treatment duration was assessed by calculating the SMDs for these variables (Supplementary Appendix 13). No significant differences were mostly seen for baseline airway dimensions ($P > .05$, except for one instance of a single study), indicating that the compared extraction and non-extraction groups were mostly similar in airway dimensions. The complete opposite was seen for treatment duration, where in all instances orthodontic treatment in the extraction group took significantly longer than in the non-extraction group ($P < .05$ in all instances; effect moderate to very large). This indicates that the included studies did not assess borderline extraction/non-extraction cases but included extraction cases that were considerably different (presumably more severe) than non-extraction cases.

Subgroup analyses, meta-regressions, and sensitivity analyses were conducted for the two meta-analyses including at least 5 studies (Supplementary Appendix 14-15). No significant results were found according to (i) patient sex (as % of male patient in the study sample); (ii) mean age; (iii) inclusion of underage, adult, or mixed patient samples; (iv) extraction/non-extraction difference in treatment duration; and (iv) baseline upper airway volume differences between extraction/non-extraction patients (Supplementary Appendix 14). Finally, several additional analyses were planned in the protocol but could ultimately not be performed due to the limited material that was available (Supplementary Appendix 1).

## Discussion

### Evidence in context

This systematic review summarizes evidence from clinical studies comparing comprehensive orthodontic treatment with versus without premolar extractions using CBCT to assess any possible changes in the pharyngeal volume and or minCSA. Data from 11 studies and a total of 891 growing or adult patients indicated that there are overall little to no differences in treatment-related changes in the pharyngeal volume and or minCSA between patients treated with versus without premolar extractions. The only exception was the minCSA of the oropharynx, where significantly greater minCSA was seen for patients treated with extractions compared to patients without extractions ($P < .05$): however, this was of little clinical relevance compared to the natural variability of the upper airway size.

The growth of the upper airway seems to coincide with somatic growth as both the pharyngeal volume and minCSA gradually increase in both sexes from the age of 8 years until the age of 18 years, while the minCSA in males shows maximum peak growth after the age of 13 years [56]. Similarly, comparisons of three-dimensional pharyngeal airway dimensional parameters such as volume, mean CSA, minCSA, linear width, depth, and length in adults and children at various dental developmental stages showed that there is a positive correlation with age, meaning they increased with time, while the shape of the pharynx becomes more elliptical mediolateral (increased width relative to the anteroposterior depth) with adulthood [57]. The greatest rate of growth in pharyngeal dimensions was noted when children were in the primary dentition (0–5 years) and the permanent dentition (12–16 years)

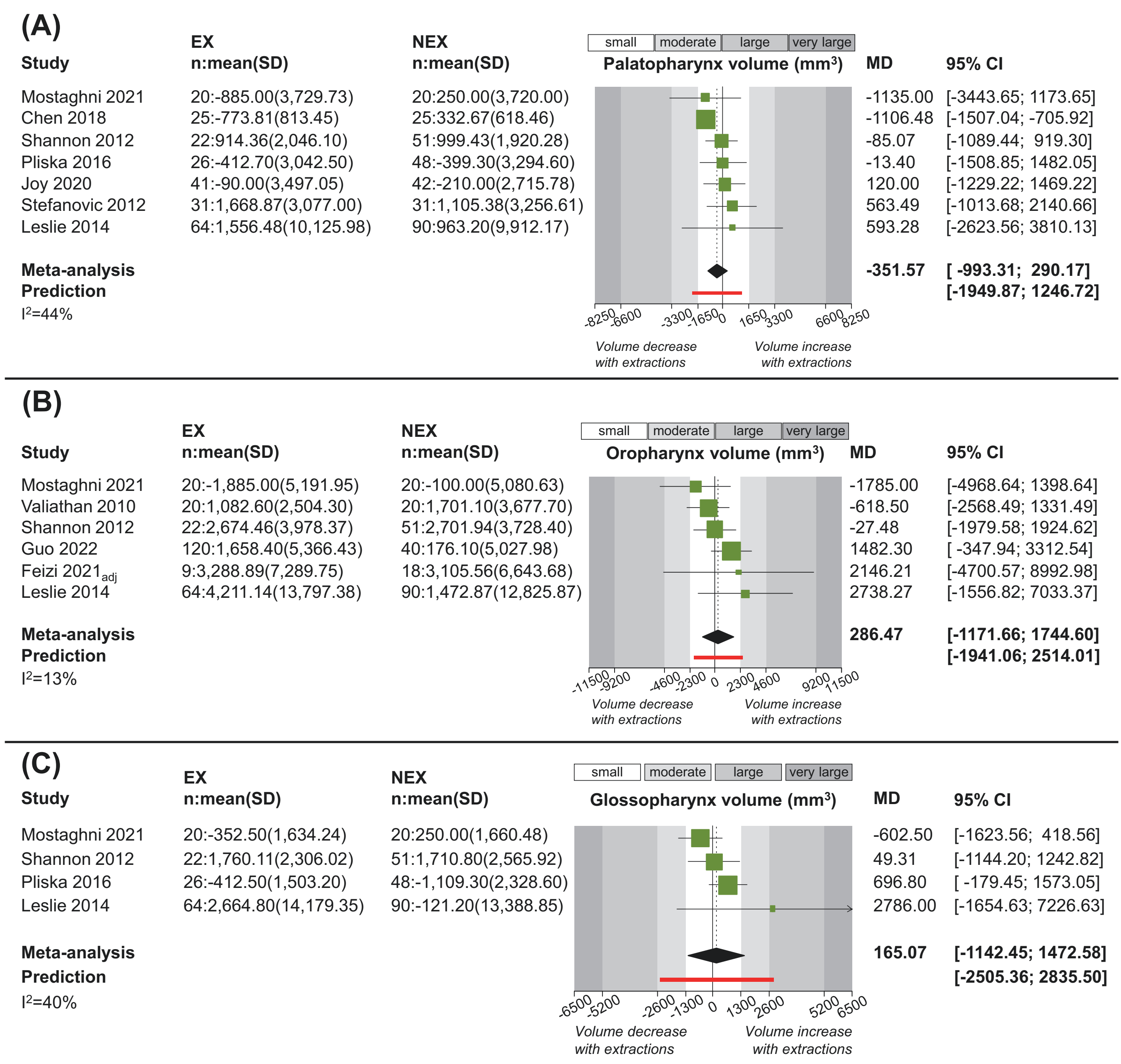


**Figure 2.** Random-effects meta-analyses comparing extraction and non-extraction comprehensive orthodontic treatment in terms of volume of the (A) palatopharynx, (B) oropharynx, and (C) glossopharynx. adj, adjusted-for-confounders estimates used; CI, confidence interval; EX, extraction treatment; MD, mean difference; n, number of patients; NEX, non-extraction treatment; SD, standard deviation.

stages [57]. The mode of growth was similar amongst male and female patients, while the only difference was that the pharyngeal length was greater in adult male versus adult female patients [57] with this finding being attributed to the pubertal vocal remodeling in males [58].

One of the findings of the present meta-analysis was an increase in the minCSA of the oropharynx in the extraction group. This finding could be mostly attributed to the above evidence regarding the evolution of upper airway dimensions during craniofacial growth until adulthood and the fact that orthodontic treatment usually is performed during this developmental stage rather to orthodontic treatment itself. The meta-analysis was based on four studies [44, 47, 53]: two with underage patients [44, 47], one with adult patients [53], and one with mixed underage/adult patients (but where age was taken into account through re-analysis [Appendix 5]). Explorative analysis of the baseline minCSA of the oropharynx differences between extraction/non-extraction groups showed similarity (4 studies; SMD = 0.09; 95% CI = –0.24 to 0.42; P = .60). On the other hand, treatment duration differed significantly between extraction/non-extraction groups (4 studies; SMD = 1.16; 95% CI = 0.80 to 1.52; P < .001). This indicates that more time might have passed and presumably more growth for the extraction than for the non-extraction patients, which might explain the greater increase in minCSA during treatment for the former than the later. On the other hand, the one study on adult patients [53] still showed a greater oropharynx minCSA for

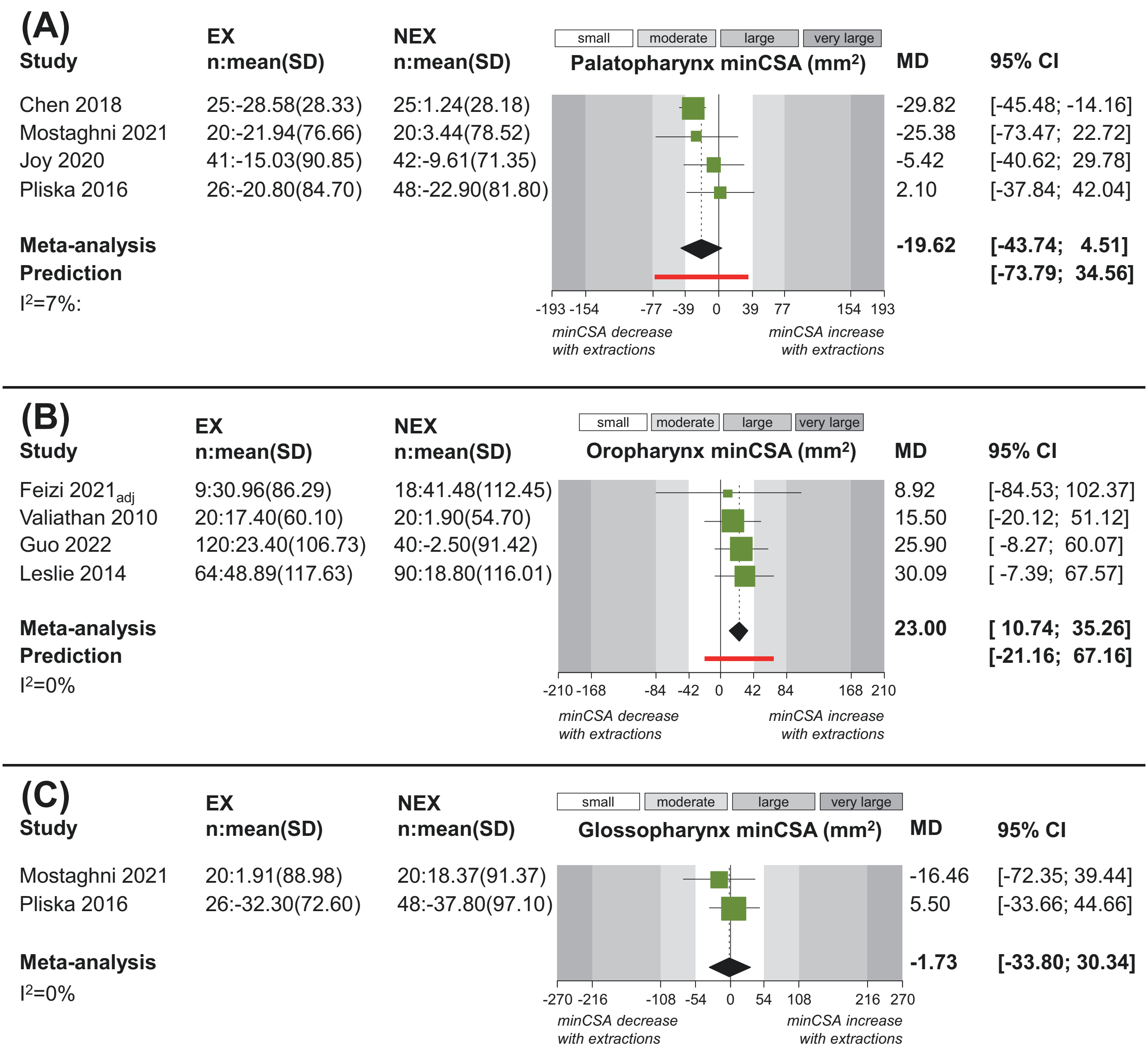


**Figure 3.** Random-effects meta-analyses comparing extraction and non-extraction comprehensive orthodontic treatment in terms of minimum cross-sectional area of the (A) palatopharynx, (B) oropharynx, and (C) glossopharynx. adj, adjusted-for-confounders estimates used; CI, confidence interval; EX, extraction treatment; MD, mean difference; minCSA, minimum cross-sectional area; n, number of patients; NEX, non-extraction treatment; SD, standard deviation.

extraction patients (MD = 25.90 mm$^2$). Therefore, the observed significantly greater minCSA for extraction patients cannot be fully explained by the differential growth potential.

An association between upper airway dimensions and OSA severity assessed through polysomnography has been identified in children with Class II malocclusion with the differences being mainly observed in the oropharyngeal and hypopharyngeal compartments and the values being consistently reduced in children suffering from OSA [59]. More specifically, children with OSA exhibited reduced values in the minCSA of the oropharynx and hypopharynx, reduced linear depth (antero-posteriorly) at the level of the oropharyngeal minCSA, and increased oropharyngeal length [59]. Amongst the various upper airway dimensional parameters tested against OSA presence, the minCSA of the oropharynx, minCSA of the hypopharynx and oropharyngeal length were identified as significant predictors of OSA while the minCSA of the oropharynx was the only significant predictor for OSA severity [59].

OSA pathophysiology is attributed to factors not only related to narrow upper airways, but also aberrations in neuromotor tone, as solely anatomic factors (such as discrepancies in craniofacial skeletal development/pattern, obesity, or adenotonsillar hypertrophy) cannot always predict the presence of OSA [60]. Postnatal environmental changes and functional demands throughout life related to hypoxia, hypercapnia, increased physical activity through exercise, injury, stress, pharmacological interventions, or respiratory gas changes during early development play a crucial role in causing permanent alterations in the neural control

**Table 3.** Meta-analyses performed.

| Outcome | Studies (Patients) | MD (95% CI) | P | tau2 (95% CI) | $I^2$ (95% CI) | Prediction |
|---|---|---|---|---|---|---|
| Volume: nasopharynx ($mm^3$) | 4 (269) | −74.72 (−236.34, 86.90) | .24 | 0 (0, > 100) | 0% (0%, 85%) | −479.13, 329.70 |
| Volume: palatopharynx ($mm^3$) | 7 (536) | −351.57 (−993.31, 290.17) | .23 | 280654.65 (0, > 999999.99) | 44% (0%, 76.4%) | −1949.87, 1246.72 |
| Volume: oral cavity ($mm^3$) | 1 (113) | −1421.92 (−4596.76, 1752.92) | .38 | - | - | - |
| Volume: oropharynx ($mm^3$) | 6 (494) | 286.47 (−1171.66, 1744.60) | .64 | 310109.09 (0, > 310109.09) | 13% (0%, 78%) | −1941.06, 2514.01 |
| Volume: glossopharynx ($mm^3$) | 4 (341) | 165.07 (−1142.45, 1472.58) | .71 | 224825.73 (0, > 999999.99) | 40% (0%, 79%) | −2505.36, 2835.50 |
| Volume: naso- & oropharynx ($mm^3$) | 1 (74) | 337.80 (−1859.48, 2535.08) | .76 | - | - | - |
| Volume: glosso- & hypopharynx ($mm^3$) | 2 (133) | −527.52 (−1617.53, 562.48) | .34 | 449083.89 (-) | 66% (-) | - |
| minCSA: nasopharynx ($mm^2$) | 2 (133) | −16.56 (−51.91, 18.80) | .36 | 539.91 (-) | 81% (-) | - |
| minCSA: palatopharynx ($mm^2$) | 4 (247) | −19.62 (−43.74, 4.51) | .08 | 80.83 (0, > 808.30) | 7% (0%, 86%) | −73.79, 34.56 |
| minCSA: oropharynx ($mm^2$) | 4 (381) | 23.00 (10.74, 35.26) | .009 | 0 (0, > 100) | 0% (0%, 85%) | −21.16, 67.16 |
| minCSA: glossopharynx ($mm^2$) | 2 (114) | −1.73 (−33.80, 30.34) | .92 | 0 (-) | 0% (-) | - |
| minCSA: glosso- & hypopharynx ($mm^2$) | 2 (133) | −10.61 (−45.93, 24.71) | .56 | 500.78 (-) | 75% (-) | - |
| minCSA: naso- & palatopharynx ($mm^2$) | 2 (136) | 4.27 (−19.18, 27.72) | .72 | 0 (-) | 0% (-) | - |

CI, confidence interval; MD, mean difference; minCSA, minimum cross sectional anchorage.

system by inducing changes in cellular and synaptic levels [61]. Subsequently, these environmental influences during important pre- and postnatal maturation stages establish developmental plasticity, which refers to persistent changes in the structure and/or function of the respiratory control neural network, depicting adaptations beyond the patients' genetic blueprint [62] that could even be triggered by maternal psychological stress or habits such as smoking [63]. Thus, it is worth noting and recognizing that major factors beyond the scope of orthodontics are related to the developmental and functional parameters and characteristics of the upper airways.

The relationship of orthodontic treatment and functional breathing assessments remains inconclusive. An unpublished randomized cross-over trial simulating arch constriction (similar to post-extraction space closure and retraction) by using vacuum-formed retainers with 5 mm acrylic added to the lingual aspects of the dentition found no significant effects on breathing, as seen through the oxygen desaturation or the respiratory events index [64]. Similarly, a retrospective study of extraction versus non-extraction patients using subjective questionnaires of patient-reported sleep quality/OSA risk [65] indicated that no differences existed between normodivergent extraction patients, hyperdivergent extraction patients, and normodivergent non-extraction patients. This is further confirmed by two large national health records studies that failed to find an association between diagnosis of OSA/sleep disordered breathing and absence of four premolars (taken as proxy for history of past extraction-based orthodontic treatment) [19, 20]. On the other hand, an unpublished prospective uncontrolled cohort study indicated that changes in maxillary dental arch length and maxillary intercanine width correlated significantly with the change in the Apnea-Hypopnea Index (AHI) [66]. It is, however, important to note that the present study was observational and without a control group and included both underage and adult patients. A wide range of dental movements were performed, including (i) upper incisor retroclination/proclination (−17° to 17°) and (ii) upper incisor retraction/protraction (−5.4 to 3.4 mm). Most importantly, only correlations were provided and no actual effect measures, while no differentiation between health and OSA before and after treatment was made. A retrospective study on four 1st premolar extractions with large incisor retraction under maximum anchorage in adult patients with bimaxillary protrusion found that the amount of upper incisor incisal edge retraction correlated with retraction of the hyoid in the horizontal direction and decrease in the average cross-sectional area of the hypopharynx [16]. However, in this study the upper incisors were significantly retracted (mean retraction of the incisor tip 7.6 mm [95% CI: 7.0 to 8.2 mm]; mean retraction of the incisor apex 3.9 mm [95% CI 3.2 to 4.7 mm]), which is not representative of the average premolar extraction case. Furthermore, the average cross-sectional area was measured and not the minCSA while no functional assessment of breathing or formal diagnosis of breathing disorders were performed. Another study on post-adolescent patients (mean age 21.2 years) with bimaxillary protrusion treated with 1st premolars' extractions and large incisor retraction with maximum anchorage (mean retraction of the incisor tip 6.8 mm [95% CI: 5.9 to 7.7 mm]) found that the amount of retraction of the lower incisor tip correlated with decreases in lateral cephalometric measurements of the airway behind the soft palate, uvula, and the tongue [67]. Similarly, this study was based on patients with large incisor retraction and employed lateral cephalograms, which are not optimal for assessing the upper airway. Other studies found that premolar extraction

**Table 4.** Summary of findings table according to the GRADE approach for selected outcomes.

| | Anticipated absolute effects (95% CI) | | | |
|---|---|---|---|---|
| Outcome<br>Studies (patients) | Non-extraction group[a] | Difference with extractions | Quality of the evidence (GRADE)[b] | What happens with extractions |
| Palatopharynx volume<br>7 studies (536 patients) | +398.5 mm³ | 351.6 mm³ smaller (993.3 smaller to 290.2 greater) | ⨁⨁○○ moderate[c] | Little to no difference in palatopharynx volume |
| Oropharynx volume<br>6 studies (494 patients) | +1510.6 mm³ | 286.5 mm³ greater (1171.7 smaller to 1744.6 greater) | ⨁⨁○○ moderate[c] | Little to no difference in oropharynx volume |
| Glossopharynx volume<br>4 studies (341 patients) | +225.9 mm³ | 165.1 mm³ greater (1142.5 smaller to 1472.6 greater) | ⨁⨁○○ moderate[c] | Little to no difference in glossopharynx volume |
| Palatopharynx minCSA<br>4 studies (247 patients) | −5.7 mm² | 19.6 mm² smaller (43.7 smaller to 4.5 greater) | ⨁⨁○○ moderate[c] | Little to no difference in palatopharynx minCSA |
| Oropharynx minCSA<br>4 studies (381 patients) | +9.5 mm² | 23.0 mm² greater (10.7 to 35.3 greater) | ⨁⨁○○ moderate[c] | Little to no difference in oropharynx minCSA |
| Glossopharynx minCSA<br>2 studies (114 patients) | −11.7 mm² | 1.7 mm² smaller (33.8 smaller to 30.3 greater) | ⨁⨁○○ moderate[c] | Little to no difference in glossopharynx minCSA |

Intervention: comprehensive orthodontic treatment with fixed appliances or aligners with or without the extraction of premolars (either only 2 maxillary or 4 premolars)/Population: underage or adult patients (growing/non-growing) with different kinds of dental or skeletal malocclusions/Setting: university clinics and private practices (Australia, China, United States of America).
[a]Response in the non-extraction group is based on the response of included studies (random-effects meta-analysis of treatment changes).
[b]Starts from 'high'.
[c]Downgraded by one levels for imprecision due to the inclusion of non-randomized studies with serious/critical risk of bias.
CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; minCSA, minimum cross-sectional area.

with anterior retraction using maximum anchorage in adult bimaxillary protrusion patients had no considerable effect on the airway volume, cross-sectional area, or hyoid bone position [52, 53, 68, 69]. Among these studies, two studies that were included in the present review [52, 53] did not find any statistically significant difference in the effect of orthodontic treatment on either airway volume and or cross-sectional area or hyoid horizontal position between patients treated with 1st premolars' extraction and moderate or maximum anchorage [53]. In the present meta-analysis, no formal meta-regression of airway differences with average upper/lower incisor retraction could be performed, as limited data existed due to incomplete reporting and lack of open provision of the studies' datasets. Overall, even for such cases with very large incisor retraction, evidence on the association between incisor retraction and airway dimensions or breathing function remains inconclusive and no robust conclusions can be drawn.

The present study was based on CBCT measurements of the airways before and after comprehensive orthodontic treatment. It is though important to note that CBCT is not a standard imaging modality for the diagnosis of breathing disorders. First, the images acquired from CBCT can be influenced by many factors, including among others position of the head, inhalation or exhalation stage, and the instructions given to the patient (staying still, avoiding swallowing, holding breath, keeping lips relaxed, etc) during image acquisition and the various airway compartments show different reliability [70]. Furthermore, the acquired CBCT images are reconstructed in order to perform the needed measurements including delineation of areas of interest and manual/automatic thresholding of gray levels, while the operator's experience plays a crucial role in performing the processes [70]. Additionally, CBCT provides a static image of the upper airway and does not provide a functional assessment of the breathing capacity and, as such, it cannot replace polysomnography, which remains the gold standard for the diagnosis of sleep related breathing disorders including OSA.

## Strengths and limitations

This review has several strengths, including its pre-registration [71], a comprehensive and unrestricted literature search, critical appraisal of included studies' internal validity according to current guidelines [31], use of improved meta-analytical methods with improved performance [36], and transparent provision of the study's dataset [72]. Moreover, the present review was based on 3D imaging data from CBCT, which are more precise in evaluating the complex upper airway morphology compared to lateral cephalograms [18]. Additionally, contrary to previous systematic reviews, the present review was not based solely on aspects of statistical significance and p values but critically appraised the clinical relevance of any findings from included studies. As such, in most meta-analyses the results of included studies pertained to very minor effects that are of little clinical relevance (as their effects are contained in the white contour of the forest plots in Figs 1–2). Finally, the novel finding of the present review, which has not been reported from previous reviews, is the statistically significant difference in minCSA of the oropharynx that indicated that premolar extraction treatment is surprisingly associated with greater cross-sectional area compared to non-extraction patients.

There are, however, several limitations in this review. First, its recommendations can be only as strong as the quality of the primary material. As such, only retrospective non-randomized studies were included, and these have been shown to introduce bias [73]. Indeed, included studies did not compare borderline extraction/non-extraction cases that could be considered similar in all aspects (Supplementary Appendix 13) (i.e. that would have been randomized to either treatment protocol). Therefore, the provided meta-analyses might be prone to selection bias, which might influence this review's results. Furthermore, the present review was based on data on the size of the upper airways (that could be considered a surrogate endpoint) and not on breathing capacity or polysomnography, which can lead to the diagnosis of breathing disorders.

## Conclusions

Based on the results of existing retrospective before-and-after (cohort) studies on comprehensive orthodontic treatment, no statistically significant differences in upper airway volume or minCSA were found between extraction and non-extraction treatment protocols for the average patient. Patients treated with premolar extractions tended to show greater minimum cross-sectional area at the oropharynx than patients treated without extractions, but this is of little clinical relevance. Caution is warranted for the interpretation of these findings due to flaws of included retrospective studies with potential selection bias and confounding.

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## Author contributions

SNP, MZ, and AKP were responsible for study design; MZ and AKP were responsible for the literature search; SNP, MZ, and AKP extracted the data; SNP performed the statistical analysis; SNP, MZ, and AKP supervised the study; SNP, MZ, and AKP wrote the main manuscript text. All authors reviewed the manuscript.

## Conflict of interests

The authors declare no competing interests.

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## Data Availability

The dataset for this study is available (https://doi.org/10.5281/zenodo.14558018).

## Supplementary data

Supplementary data is available at *European Journal of Orthodontics* online.

## References

1. Flores-Mir C, Korayem M, Heo G, *et al*. Craniofacial morphological characteristics in children with obstructive sleep apnea syndrome: a systematic review and meta-analysis. *J Am Dent Assoc* 2013;**144**:269–77. https://doi.org/10.14219/jada.archive.2013.0113
2. Neelapu BC, Kharbanda OP, Sardana HK, *et al*. Craniofacial and upper airway morphology in adult obstructive sleep apnea patients: a systematic review and meta-analysis of cephalometric studies. *Sleep Med Rev* 2017;**31**:79–90. https://doi.org/10.1016/j.smrv.2016.01.007
3. Finke H, Drews A, Engel C, *et al*. Craniofacial risk factors for obstructive sleep apnea-systematic review and meta-analysis. *J Sleep Res* 2024;**33**:e14004. https://doi.org/10.1111/jsr.14004
4. Shreya S, Shetty V, Priya K, *et al*. Cephalometry as an aid in the diagnosis of pediatric obstructive sleep apnoea: a systematic review and meta-analysis. *J Oral Biol Craniofac Res* 2024;**14**:512–21. https://doi.org/10.1016/j.jobcr.2024.06.007
5. Kazmouz S, Calzadilla N, Choudhary A, *et al*. Radiographic findings predictive of obstructive sleep apnea in adults: a systematic review and meta-analysis. *J Craniofac Surg* 2024;**53**:162–80. https://doi.org/10.1016/j.jcms.2024.11.003
6. Altheer C, Papageorgiou SN, Antonarakis GS, *et al*. Do patients with different craniofacial patterns have differences in upper airway volume? A systematic review with network meta-analysis. *Eur J Orthod* 2024;**46**:cjae010. https://doi.org/10.1093/ejo/cjae010
7. Buck LM, Dalci O, Darendeliler MA, *et al*. Volumetric upper airway changes after rapid maxillary expansion: a systematic review and meta-analysis. *Eur J Orthod* 2017;**39**:463–73. https://doi.org/10.1093/ejo/cjw048
8. Julku J, Pirilä-Parkkinen K, Pirttiniemi P. Airway and hard tissue dimensions in children treated with early and later timed cervical headgear-a randomized controlled trial. *Eur J Orthod* 2018;**40**:285–95. https://doi.org/10.1093/ejo/cjx088
9. Bidjan D, Sallmann R, Eliades T, *et al*. Orthopedic treatment for class II malocclusion with functional appliances and its effect on upper airways: a systematic review with meta-analysis. *J Clin Med* 2020;**9**:3806. https://doi.org/10.3390/jcm9123806
10. Havakeshian G, Koretsi V, Eliades T, *et al*. Effect of orthopedic treatment for class III malocclusion on upper airways: a systematic review and meta-analysis. *J Clin Med* 2020;**9**:3015. https://doi.org/10.3390/jcm9093015
11. Cheung GC, Dalci O, Mustac S, *et al*. The upper airway volume effects produced by Hyrax, Hybrid-Hyrax, and Keles keyless expanders: a single-centre randomized controlled trial. *Eur J Orthod* 2021;**43**:254–64. https://doi.org/10.1093/ejo/cjaa031
12. Iwasaki T, Papageorgiou SN, Yamasaki Y, *et al*. Nasal ventilation and rapid maxillary expansion (RME): a randomized trial. *Eur J Orthod* 2021;**43**:283–92. https://doi.org/10.1093/ejo/cjab001
13. Momany SM, AlJamal G, Shugaa-Addin B, *et al*. Cone beam computed tomography analysis of upper airway measurements in patients with obstructive sleep apnea. *Am J Med Sci* 2016;**352**:376–84. https://doi.org/10.1016/j.amjms.2016.07.014
14. Galeotti A, Festa P, Viarani V, *et al*. Correlation between cephalometric variables and obstructive sleep apnoea severity in children. *Eur J Paediatr Dent* 2019;**20**:43–7. https://doi.org/10.23804/ejpd.2019.20.01.09
15. Ozbek MM, Memikoglu TU, Gögen H, *et al*. Oropharyngeal airway dimensions and functional-orthopedic treatment in skeletal class II cases. *Angle Orthod* 1998;**68**:327–36. https://doi.org/10.1043/0003-3219(1998)068<0327:OADAFO>2.3.CO;2. PMID: 9709833
16. Chen Y, Hong L, Wang CL, *et al*. Effect of large incisor retraction on upper airway morphology in adult bimaxillary protrusion patients. *Angle Orthod* 2012;**82**:964–70. https://doi.org/10.2319/110211-675.1
17. Guilleminault C, Abad VC, Chiu HY, *et al*. Missing teeth and pediatric obstructive sleep apnea. *Sleep Breath* 2016;**20**:561–8. https://doi.org/10.1007/s11325-015-1238-3
18. Behrents RG, Shelgikar AV, Conley RS, *et al*. Obstructive sleep apnea and orthodontics: an American Association of Orthodontists

White Paper. *Am J orthod Dentofacial orthop* 2019;**156**:13–28.e1. https://doi.org/10.1016/j.ajodo.2019.04.009

19. Larsen AJ, Rindal DB, Hatch JP, *et al*. Evidence supports no relationship between obstructive sleep apnea and premolar extraction: an electronic health records review. *J Clin Sleep Med* 2015;**11**:1443–8. https://doi.org/10.5664/jcsm.5284
20. Wiener RC, Hnat M, Ngan P. Sleep disruption and premolar absence, NHANES, 2017-2020: a cross-sectional study. *Community Dent Oral Epidemiol* 2024;**52**:809–16. https://doi.org/10.1111/cdoe.12983
21. Chen H, Aarab G, de Ruiter MH, *et al*. van der Stelt PF. Three-dimensional imaging of the upper airway anatomy in obstructive sleep apnea: a systematic review. *Sleep Med* 2016;**21**:19–27. https://doi.org/10.1016/j.sleep.2016.01.022
22. Mokhtar Q, Aziz TA, Lahcen O. Valuation of the effect of premolar extractions in the context of orthodontic treatment on vas: a systematic review of the literature. *Open Access Library J* 2024;**11**:1–2. https://doi.org/10.4236/oalib.1111783
23. Hu Z, Yin X, Liao J, *et al*. The effect of teeth extraction for orthodontic treatment on the upper airway: a systematic review. *Sleep Breath* 2015;**19**:441–51. https://doi.org/10.1007/s11325-015-1122-1
24. Orabi N, Flores-Mir C, Elshebiny T, *et al*. Pharyngeal airway dimensional changes after orthodontic treatment with premolar extractions: a systematic review with meta-analysis. *Am J Orthod Dentofacial Orthop* 2021;**160**:503–15.e3. https://doi.org/10.1016/j.ajodo.2021.03.013
25. Choi JY, Lee K. Effects of four first premolar extraction on the upper airway dimension in a non-growing class I skeletal patients: a systematic review. *J Oral Med Dental Res* 2022;**2**:1–16. https://doi.org/10.52793/jomdr.2020.3(1)-23
26. Higgins JPT, Thomas J, Chandler J, *et al*. *Cochrane Handbook for Systematic Reviews of Interventions Version 6.1 (Updated September 2020)*. Cochrane, 2020. Available at: http://www.training.cochrane.org/handbook
27. Page MJ, Moher D, Bossuyt PM, *et al*. explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. *BMJ* 2020;**2021**:n160. https://doi.org/10.1136/bmj.n160
28. Konstantonis D, Vasileiou D, Papageorgiou SN, *et al*. Soft tissue changes following extraction vs. nonextraction orthodontic fixed appliance treatment: a systematic review and meta-analysis. *Eur J Oral Sci* 2018;**126**:167–79. https://doi.org/10.1111/eos.12409
29. Jehan S, Zizi F, Pandi-Perumal SR, *et al*. Obstructive sleep apnea and obesity: implications for public health. *Sleep Med Disord* 2017;**1**:00019.
30. Sterne JAC, Savović J, Page MJ, *et al*. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;**366**:l4898. https://doi.org/10.1136/bmj.l4898
31. Sterne JA, Hernán MA, Reeves BC, *et al*. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 2016;**355**:i4919. https://doi.org/10.1136/bmj.i4919
32. Rama AN, Tekwani SH, Kushida CA. Sites of obstruction in obstructive sleep apnea. *Chest* 2002;**122**:1139–47. https://doi.org/10.1378/chest.122.4.1139
33. Stuck BA, Maurer JT. Airway evaluation in obstructive sleep apnea. *Sleep Med Rev* 2008;**12**:411–36. https://doi.org/10.1016/j.smrv.2007.08.009
34. Koretsi V, Eliades T, Papageorgiou SN. Oral interventions for obstructive sleep apnea. *Deutsch Arztebl Int* 2018;**115**:200–7. https://doi.org/10.3238/arztebl.2018.0200
35. Papageorgiou SN. Meta-analysis for orthodontists: part I–How to choose effect measure and statistical model. *J Orthod* 2014;**41**:317–26. https://doi.org/10.1179/1465313314Y.0000000111
36. Langan D, Higgins JPT, Jackson D, *et al*. A comparison of heterogeneity variance estimators in simulated random-effects meta-analyses. *Res Synth Methods* 2019;**10**:83–98. https://doi.org/10.1002/jrsm.1316
37. Knapp G, Hartung J. Improved tests for a random effects meta-regression with a single covariate. *Stat Med* 2003;**22**:2693–710. https://doi.org/10.1002/sim.1482
38. Papageorgiou SN. Meta-analysis for orthodontists: part II--Is all that glitters gold? *J Orthod* 2014;**41**:327–36. https://doi.org/10.1179/1465313314Y.0000000110
39. IntHout J, Ioannidis JP, Rovers MM, *et al*. Plea for routinely presenting prediction intervals in meta-analysis. *BMJ Open* 2016;**6**:e010247. https://doi.org/10.1136/bmjopen-2015-010247
40. Parrish LD, Roberts WE, Maupome G, *et al*. The relationship between the ABO discrepancy index and treatment duration in a graduate orthodontic clinic. *Angle Orthod* 2011;**81**:192–7. https://doi.org/10.2319/062210-341.1
41. Papageorgiou SN, Zyli M, Papadopoulou AK. Extraction of premolars in orthodontic treatment does not negatively affect upper airway volume and minimum cross-sectional area: a systematic review with meta-analysis. *Zenodo* https://doi.org/10.5281/zenodo.14558018
42. Guyatt GH, Oxman AD, Schünemann HJ, *et al*. GRADE guidelines: a new series of articles in the Journal of Clinical Epidemiology. *J Clin Epidemiol* 2011;**64**:380–2. https://doi.org/10.1016/j.jclinepi.2010.09.011
43. Carrasco-Labra A, Brignardello-Petersen R, Santesso N, *et al*. Improving GRADE evidence tables part 1: a randomized trial shows improved understanding of content in summary of findings tables with a new format. *J Clin Epidemiol* 2016;**74**:7–18. https://doi.org/10.1016/j.jclinepi.2015.12.007
44. Valiathan M, El H, Hans MG, *et al*. Effects of extraction versus non-extraction treatment on oropharyngeal airway volume. *Angle Orthod* 2010;**80**:1068–74. https://doi.org/10.2319/010810-19.1
45. Shannon TP. Oropharyngeal airway volume following orthodontic treatment: premolar extraction versus non-extraction [Dissertation/Thesis], 2012.
46. Stefanovic N, El H, Chenin DL, *et al*. Three-dimensional pharyngeal airway changes in orthodontic patients treated with and without extractions. *Orthod Craniofac Res* 2013;**16**:87–96. https://doi.org/10.1111/ocr.12009
47. Leslie CL, Harris EF. Oropharyngeal airway volume following orthodontic treatment: premolar extraction versus non-extraction [Thesis]. Ann Arbor (MI): The University of Tennessee Health Science Center, 2014.
48. Pliska BT, Tam IT, Lowe AA, *et al*. Effect of orthodontic treatment on the upper airway volume in adults. *Am J Orthod Dentofacial Orthop* 2016;**150**:937–44. https://doi.org/10.1016/j.ajodo.2016.05.013
49. Chen W, Liu YH, Xu Q. [Effect of maximum anchorage extraction on upper airway in adolescent patients with bimaxillary protrusion]. *Shanghai Kou Qiang Yi Xue* 2018;**27**:419–23.
50. Joy A, Park J, Chambers DW, *et al*. Airway and cephalometric changes in adult orthodontic patients after premolar extractions. *Angle Orthod* 2020;**90**:39–46. https://doi.org/10.2319/021019-92.1
51. Feizi AG. Evaluating oropharyngeal airway volume in patients with class II dental relationships with extraction vs non-extraction orthodontic treatment [Dissertation/Thesis], 2021.
52. Mostaghni E. The effect of orthodontic treatment with extraction on the upper airway dimensions and three-dimensional morphology: a retrospective study using cone-beam computed tomography technique, University of Nebraska Medical Center, 2021.
53. Guo R, Wang S, Zhang L, *et al*. Oropharynx and hyoid bone changes in female extraction patients with distinct sagittal and vertical skeletal patterns: a retrospective study. *Head Face Med* 2022;**18**:31. https://doi.org/10.1186/s13005-022-00334-1
54. Mladenovic M, Freezer S, Dreyer C, *et al*. Influence of second premolar extractions on the volume of the oral cavity proper: a control comparative cone-beam computed tomography volumetric analysis study. *Angle Orthod* 2024;**94**:31–8. https://doi.org/10.2319/031023-164.1
55. Mladenovic M, Freezer S, Dreyer C, *et al*. The orthodontic extraction of second premolars: the influence on airway volume. *Am J orthod Dentofacial Orthop* 2024;**166**:61–8. https://doi.org/10.1016/j.ajodo.2024.02.013

56. Chiang CC, Jeffres MN, Miller A, *et al*. Three-dimensional airway evaluation in 387 subjects from one university orthodontic clinic using cone beam computed tomography. *Angle Orthod* 2012;**82**:985–92. https://doi.org/10.2319/122811-801.1
57. Abramson Z, Susarla S, Troulis M, *et al*. Age-related changes of the upper airway assessed by 3-dimensional computed tomography. *J Craniofac Surg* 2009;**20**:657–63. https://doi.org/10.1097/SCS.0b013e318193d521
58. Fitch WT, Giedd J. Morphology and development of the human vocal tract: a study using magnetic resonance imaging. *J Acoust Soc Am* 1999;**106**:1511–22. https://doi.org/10.1121/1.427148
59. Zreaqat M, Hassan R, Samsudin R, *et al*. Three-dimensional analysis of upper airways in class II malocclusion children with obstructive sleep apnea. *J World Fed Orthod* 2022;**11**:156–63. https://doi.org/10.1016/j.ejwf.2022.08.001
60. Arens R, Marcus CL. Pathophysiology of upper airway obstruction: a developmental perspective. *Sleep* 2004;**27**:997–1019. https://doi.org/10.1093/sleep/27.5.997
61. Mitchell GS, Johnson SM. Neuroplasticity in respiratory motor control. *J Appl Physiol (Bethesda, Md. : 1985)* 2003;**94**:358–74. https://doi.org/10.1152/japplphysiol.00523.2002
62. Carroll JL. Developmental plasticity in respiratory control. *J Appl Physiol (Bethesda, Md. : 1985)* 2003;**94**:375–89. https://doi.org/10.1152/japplphysiol.00809.2002
63. Bavis RW, Mitchell GS. Long-term effects of the perinatal environment on respiratory control. *J Appl Physiol (Bethesda, Md. : 1985)* 2008;**104**:1220–9. https://doi.org/10.1152/japplphysiol.01086.2007
64. Kim DI. The effects of simulated arch constriction on upper airway function during sleep. *Doctoral dissertation*, University of British Columbia, 2024.
65. Vejwarakul W, Ko EW, Lin CH. Evaluation of pharyngeal airway space after orthodontic extraction treatment in class II malocclusion integrating with the subjective sleep quality assessment. *Sci Rep* 2023;**13**:9210. https://doi.org/10.1038/s41598-023-36467-9
66. Tabari S. The longitudinal effects of orthodontic therapy on the obstructive apnea hypopnea index (AHI). *Doctoral Dissertation*, Harvard School of Dental Medicine, 2019.
67. Wang Q, Jia P, Anderson NK, *et al*. Changes of pharyngeal airway size and hyoid bone position following orthodontic treatment of class I bimaxillary protrusion. *Angle Orthod* 2012;**82**:115–21. https://doi.org/10.2319/011011-13.1
68. Ning R, Guo J, Martin D. Effect of premolar extraction on upper airway volume and hyoid position in hyperdivergent adults with different mandibular length. *Am J Orthod Dentofacial Orthop* 2022;**161**:e390–9. https://doi.org/10.1016/j.ajodo.2021.01.027
69. Khalil RA, Salem WS. Three-dimensional evaluation of the airway morphology after miniscrew-supported en masse retraction in adult bimaxillary protrusion patients by using cone beam computed tomography: a single-arm clinical trial. *Int Orthod* 2024;**23**:100936. https://doi.org/10.1016/j.ortho.2024.100936
70. Zimmerman JN, Vora SR, Pliska BT. Reliability of upper airway assessment using CBCT. *Eur J Orthod* 2019;**41**:101–8. https://doi.org/10.1093/ejo/cjy058
71. Sideri S, Papageorgiou SN, Eliades T. Registration in the international prospective register of systematic reviews (PROSPERO) of systematic review protocols was associated with increased review quality. *J Clin Epidemiol* 2018;**100**:103–10. https://doi.org/10.1016/j.jclinepi.2018.01.003
72. Papageorgiou SN, Cobourne MT. Data sharing in orthodontic research. *J Orthod* 2018;**45**:1–3. https://doi.org/10.1080/14653125.2018.1440792
73. Papageorgiou SN, Xavier GM, Cobourne MT. Basic study design influences the results of orthodontic clinical investigations. *J Clin Epidemiol* 2015;**68**:1512–22. https://doi.org/10.1016/j.jclinepi.2015.03.008