



# The Longitudinal Effects of Orthodontic Therapy on the Obstructive Apnea Hypopnea Index (AHI).

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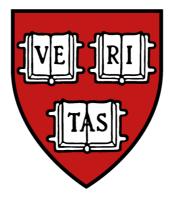
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## HARVARD UNIVERSITY Harvard School of Dental Medicine



The Longitudinal Effects of Orthodontic Therapy on the Obstructive Apnea Hypopnea Index (AHI). A Thesis Presented by Shaima Tabari

То

The Faculty of Medicine In partial fulfillment of the requirements For the degree of Doctor of Medical Sciences

Research Mentors: Dr. Mohamed I Masoud and Dr. Eliot S Katz

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#### The Use of Pretreatment Orthodontic Records as Predictors of Obstructive Sleep Apnea.

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**Abbreviations:** OSA, Obstructive Sleep Apnea; SDB, Sleep Disordered Breathing; PSQ, AHI; Apnea Hypopnea Index; Orthodontics; Tooth movement, Study models, Cephalometrics, Incisor retraction, Airway dimensions, Pediatric Sleep Questionnaire; ESS, Epworth Sleepiness Scale;

#### **ABSTRACT**

**Objectives:** To evaluate the cross-sectional relationship between sleep apnea and i) dental model measurements, ii) cephalometric measurements (skeletal, dental, airway) and iii) sleep-disordered breathing (SDB) questionnaires, in a convenience sample of orthodontic patients starting therapy.

**Materials and Methods:** Fifty-four orthodontic patients (male 46%, mean age 25.29±12.32) scheduled to start orthodontic treatment were prospectively evaluated with sleep studies, lateral cephalograms, intraoral dental scans and SDB questionnaires before orthodontic treatment. The primary outcome of interest was the obstructive Apnea Hypopnea Index (AHI) and whether or not the obstructive AHI score exceeded sleep apnea threshold. Predictors included dental model measurements, cephalometric (skeletal, dental, airway) measurements and SDB questionnaires: Epworth Sleepiness Scale and Pediatric Sleep Questionnaire.

**Results:** Results indicate statistically significant negative relationships between obstructive AHI and maxillary arch length (p=0.013), maxillary intercanine width (p=0.004), mandibular intercanine width (p=0.026), maxillary arch perimeter (p=0.010), SNB (angle between sella, nasion and supramentale) (p=0.043), upper incisor inclination (p=0.010) and position (p=0.001) (U1-NAdeg and U1-NAmm). Obstructive AHI had statistically significant positive relationship with upper airway length (p=0.007) (UAL) and pediatric sleep questionnaire (p=0.017).

**Conclusion:** Higher obstructive AHI scores were seen in an unselected population of orthodontic patients with posteriorly positioned and retroclined upper incisors, retrognathic mandible, increased length of the upper airway, decreased maxillary arch length, constricted maxillary and mandibular inter canine widths, decreased arch perimeter and higher pediatric sleep questionnaire. Orthodontists have an important opportunity to screen their patients with compatible findings for OSA.

#### **INTRODUCTION**

Obstructive sleep apnea (OSA) is a disorder resulting from partial or complete upper airway obstruction leading to frequent oxygen desaturation and disturbances in the sleep architecture.<sup>12</sup> Sleep disordered breathing (SDB) includes OSA and upper airway resistance syndrome (UARS) which affects 1-3% of children and about 20% of adults.<sup>24</sup> Even though increased upper airway resistance<sup>8-10</sup> is an essential feature of OSA, many patients showing signs of airway narrowing are able to sustain stable breathing through robust neuromuscular compensation, ventilatory control stability, and/or a high arousal threshold. <sup>2</sup> Untreated OSA has been associated with adverse clinical outcomes, including neurocognitive impairment ", cardiovascular morbidity " and mortality.<sup>1945</sup>

Majority of research in the field of OSA and dentistry references 2-dimension or 3-dimensional airway measures as extracted from a lateral cephalogram or a cone beam CT. Arens et al. undertook research measuring airway volumes using magnetic resonance imaging indicated poor correlation of the airway volume to the apnea-hypopnea index (r=0.07). <sup>16</sup> Patients with OSA have been reported to exhibit morphological features in their skeletal and soft tissue architecture, including a shorter intermaxillary space, <sup>17,8</sup> bimaxillary retrusion, <sup>19,9</sup> increased upper airway length especially in adult male ,<sup>42,12</sup> narrow nasopharyngeal airway, <sup>29</sup> increased tongue size,<sup>24</sup> inferiorly positioned hyoid bone, <sup>35,9</sup> smaller posterior airway space (PAS), <sup>27</sup> decreased pharyngeal diameter, <sup>27</sup> inferiorly positioned mandible, <sup>28</sup> elongated soft palate (children) <sup>29</sup> and anteriorly positioned maxilla in relation to cranial base. <sup>30</sup> Patients with OSA also have significantly increased overjet, reduced overbite, narrow maxilla, and shorter mandibular arches compared to age and gender-matched controls. <sup>31</sup> The association of dental arch morphologic features and OSA requires further investigation.

The orthodontic clinic provides an accessible medium for the possible detection of OSA. Approximately 15.1% of children (11 million) <sup>a</sup> and 1% of adults (2 million) <sup>a</sup> are orthodontic patients in the United States. More recent data would likely show an increase in the number of adult patients due to the increased use of esthetic orthodontic therapy. With such large numbers of children and adults seen by orthodontists each year, it is clear that orthodontist could play a pivotal role in the screening and referral of patients with OSA. Routine orthodontic records such as lateral cephalograms provide information on skeletal, dental, and airway measurements that may be informative relative to patients' OSA risk. Determination of OSA-related dental and cephalometric parameters, however, are necessary.

Several questionnaires have been developed to pre-screen patients for OSA. Both the pediatric sleep questionnaire (PSQ) and epworth sleep scale (ESS) questionnaires have been used to predict OSA.<sup>3435</sup>

The PSQ has been validated for OSA screening in children while the ESS has been validated in adults. One study of 450 children with OSA concluded that the PSQ sleep questionnaire and OSA-18 most significantly correlated with the polysomnography outcomes. \* The ESS has been shown to be a reliable, unidimensional scale that has been validated for use in both clinical and non-clinical patient samples. \*\*? ESS has been found to have only fair discriminatory ability in distinguishing patients with OSA, with a sensitivity of 66% at obstructive AHI cut-off of 5. \* No study to date has yet aimed to explore the relationship between the dental model measurements, cephalometric measurements (skeletal, dental, airway) and sleep disordered breathing questionnaire data with regards to the apnea hypopnea index (AHI) measured with a home portable sleep monitor in a presumably healthy orthodontic population.

The purpose of this study is to assess the predictive power between cephalometric measurements (skeletal, dental, airway), dental model measurements and sleep disordered breathing questionnaires to obstructive AHI and the presence of OSA in a sample of orthodontic patients who were not preselected prior to enrollment. The specific aims of this study are to identify the cross-sectional relationship between cephalometric measurements (skeletal, dental, airway), dental model measurements and sleep disordered breathing questionnaire measurements in a convenience sample of patients starting orthodontic therapy in order to identify the risk factors for OSA.

#### **MATERIALS AND METHODS**

#### Study design and participants

The study was designed as a prospective exploratory clinical study. The sample was derived from convenient sample of the population of patients seeking orthodontic therapy at The Harvard School of Dental Medicine between February 2017-December 2018. Sample size was calculated with 80% power and  $\alpha$  of 0.05. The subjects were not preselected based on presence or absence of obstructive sleep apnea (OSA) symptoms but were excluded if they had already begun orthodontic therapy or orthognathic surgery. Prior to participation, written consent was obtained from adult patients and from parents of children. Assent was obtained from the children. IRB approval was obtained.

For the purposes of the study, data was de-identified and each participant was assigned a study code number. Participants received gift certificates after completing key portions of the study. The de-identified sleep studies were scored by the same blinded investigator (ESK). Predictor variables analyzed in this study include cephalometric measurements (skeletal, dental, airway), dental model measurements and sleep disordered breathing questionnaires: pediatric sleep questionnaire and epworth sleepiness scale.

#### **MEASUREMENTS**

#### **Cephalometric measurements**

The lateral cephalograms were taken as part of the routine orthodontic records. The same Kodak 9000 machine was used to take all lateral cephalograms. The digital lateral cephalogram was uploaded onto Dolphin software system (version 11.9 Chatsworth, CA, USA) and traced by the same operator (ST). Measurements were re-analyzed one month apart in order to calculate the error of the method. Intrarater reliability was verified by performing repeat measurements on 20% of the measurements after a 1-month interval (r= 0.98; P<0.01). Dental cephalometric measurements made included: 1) measurements of the position and inclination of the upper and lower teeth: The degree and mm measures from the upper and lower incisors to the line from nasion (N) to subspinale (A point) and supramentale (B point) (U1-NAmm/deg, L1-NBmm/deg), angle between the lower incisors and the mandibular plane (IMPA), 2) overjet (OJ) and overbite (OB), 3) skeletal cephalometric measures of jaw relations: the angles formed between sella (S), nasion (N), subspinale (A point) and supramentale (B point) (SNA, SNB) and the angle formed from A point, nasion and B point (ANB), maxillary and mandibular unit lengths, upper and lower face heights and 4) airway cephalometric measures: Posterior, middle and superior airway spaces, retropalatal airway space, tongue length, hyoid to mandibular plane, upper airway length, uvula length and thickness (Fig 1).

#### **Dental model measurements**

These measurements were undertaken from an intraoral scan using the iTero Element scanner (Align Technology, California) as part of the orthodontic records. The STL file was uploaded into Ortho Insight  $3D^{\textcircled{\sc 0}}$  (MotionView, Tennessee) (Fig 2). Intra-rater reliability was verified by performing repeat measurements on 20% of the measurements after a 1-month interval (r= 0.91; P<0.01). The dental model measurements included: The maxillary and mandibular arch lengths defined as the perpendicular line from a point halfway between the central fossa of the first permanent molars to the contact point between the central incisor. The intercanine width which was measured between cusp tips of permanent canines. The intermolar widths measured from central fossae of the first permanent molars. The maxillary arch perimeter was measured from the mesial of the first permanent molar through the marginal ridges of the premolars and cingulum edges of the anterior dentition. The mandibular arch perimeter was measured from the mesial of the first permanent molar start arch perimeter was measured from the molar, through the buccal cusps of the premolars and incisal edge of the anterior dentition (Fig 2).<sup>344</sup>

#### **SDB** questionnaires

The pediatric sleep questionnaire is a validated quality of sleep symptom questionnaire consisting of 22 yes/no questions related to sleep related symptoms. <sup>42</sup> Each 'yes' answer was assigned a 1 and each 'no' a 0. An index between 0 and 22 was created, on which higher scores indicate higher probability of OSA. Epworth sleepiness scale is an 8 item questionnaire used to measure daytime sleepiness or sleep propensity in adults. A score of 1 indicates a slight chance of dozing, a score of 2 moderate and a score of 3 indicates a high chance of dozing. The final score is the sum. <sup>40</sup>

#### Portable sleep monitor scoring

The portable sleep monitor used in this study was the Braebon Medibyte sleep monitor (Ontario, Canada) consisting of nasal pressure cannula, snore microphone, respiratory effort belts, and oximetry. Subjects were provided with the monitor and a disposable patient kit and were instructed to wear it for one night before any orthodontic therapy had commenced. The de-identified data from the sleep monitor was then downloaded using the Braebon Medibyte software and blindly analyzed by the same sleep specialist using the American Academy of Sleep Medicine (AASM) guidelines (ESK). Hypopnea was defined as a 30% reduction in baseline nasal pressure resulting in either a 3% oxygen desaturation or an arousal. <sup>445</sup> A respiratory effort-related arousal was scored if there was flow limitation with a >30% reduction in the baseline nasal pressure tracing and crescendo snoring that was associated with a gasping breath and snorting. Obstructive AHII  $\geq$ 5 for adults and obstructive AHI  $\geq$ 2 for children was selected as cut-offs for having OSA.

#### STATISTICAL ANALYSIS

Descriptive statistics are presented, using means and standard deviations. Initial univariate analyses used t-tests for continuous variables and chi<sup>2</sup> tests was undertaken for the categorical variables to assess whether there were any significant differences between the main variables among patients with and without OSA.

All measurements and questionnaire scores were then subjected to further multivariate analyses, which adjusted for age, gender, and body mass index (BMI). These regression analyses estimated the extent to which each variable significantly predicted the continuous measure of obstructive AHI. To satisfy the assumptions of linear regression models, the natural log of obstructive AHI (ln[obstructive AHI]) was used in these analyses.

Analyses were carried out on the whole sample for measurements. For sleep questionnaires, separate analyses were also carried out for adults and children (epworth sleepiness scale for adults and pediatric sleep questionnaire for children). All statistical analyses were conducted using Stata/IC Version 15.1 (StataCorp, Tx, USA).

#### RESULTS

Demographic data for the population is presented in Table 1. Of the 54 patients, 5 (of the 16) children and 10 (of the 38) adults were found to have OSA. Mean BMI of the sample was  $22.7 \pm 3.67$  (min:16; max:30.8), suggesting a largely healthy, non-obese population. Mean age  $25.29\pm12.32$  (min:10; max:69). Table 1 depicts the univariate *t*-tests of the descriptive measurements.

#### **Cephalometric measurements**

Univariate t-tests of the cephalometric measurements are reported in Table 2. Statistically significant (p<0.05) differences between OSA and non-OSA was observed for distance from the upper central incisor to the NA line (U1-NAmm) (p=0.05), distance and angle of the lower incisor to the NB line (L1-NB deg, L1-NBmm) (p=0.02, 0.05) and upper airway length (p=0.03). Multivariate linear regression analyses were conducted separately for each of the measurements, adjusting for age, gender, and BMI. Only those measurements that showed a statistically significant association with obstructive AHI are reported (all others were non-significant predictors). Table 3 indicates that, at the time of evaluation for every 1 degree the maxillary incisors were retroclined relative to the NA line (U1-NAdeg), the mean obstructive AHI score increases by 3.15% adjusting for age, gender and BMI (p=0.010). Table 4 indicates that, at the time of evaluation for every 1mm the maxillary incisors were posteriorly positioned (U1-NAmm), the mean obstructive AHI score increases by 9.24% adjusting for age, gender and BMI (p=0.001). Table 5 indicates that, at the time of evaluation for every 1 degree the angle formed by sella-nasion to B point (SNB) decreases, the mean obstructive AHI score increases by 4.50% adjusting for age, gender and BMI (p=0.043). Table 6 indicates that, at the time of evaluation for every 1mm the upper airway length is increased, the mean obstructive AHI score increases by 4.0% adjusting for age, gender and BMI (p=0.007).

#### **Dental model measurements**

Univariate *t*-tests reported in Table 7 show the difference between OSA and non-OSA patients. Statistically significant (p<0.05) differences between OSA and non-OSA was observed for the maxillary arch length (p=0.02). Multivariate linear regression analyses were conducted separately for each of the measurements, adjusting for age, gender, and BMI. Only those measurements that showed a statistically significant association with obstructive AHI are reported (all others were non-significant predictors). Table 8 indicates that, at the time of evaluation for every 1 mm the maxillary arch length decreases, the mean obstructive AHI score increases by 6.76% adjusting for age, gender and BMI (p=0.013). Table 9 indicates that, at the time of evaluation for every 1 mm the maxillary intercanine

width decreases, the mean obstructive AHI score increases by 8.24% adjusting for age, gender and BMI (p=0.004). Table 10 indicates that, at the time of evaluation for every 1 mm the mandibular intercanine width decreases, the mean obstructive AHI score increases by 8.54% adjusting for age, gender and BMI (p=0.026). Table 11 indicates that, at the time of evaluation for every 1 mm the maxillary arch perimeter decreases, the mean obstructive AHI score increases by 3.74% adjusting for age, gender and BMI (p=0.010).

#### Sleep disordered breathing questionnaires

Univariate *t*-tests reported in Table 12 show a statistically significant (p<0.05) difference between OSA and non-OSA patients for pediatric sleep questionnaire (whole sample, p=0.02) and for children only (p=0.01), but not for epworth sleepiness scale. Multivariate linear regression analyses (Table 10) showed that at the time of evaluation, for every 1unit increase in the pediatric sleep questionnaire the mean of OSA increased by 6.93% adjusting for age, gender and BMI (p=0.017). No significant relationship was found in a multivariate analysis of obstructive AHI and epworth sleepiness scale.

#### Portable sleep monitor screening

Data analysis indicates that 5 out of the 16 children (31.25%) have OSA while 11 out of the 16 children (68.8%) do not have OSA. In the case of the adults, 10 out of the 38 adults (26.3%) have OSA while 28 out of the 38 adults (73.68%) do not have OSA.

#### DISCUSSION

The purpose of this study was to assess the predictive power between dental model measurements, cephalometric measurements (skeletal, dental, airway) and SDB questionnaires to sleep apnea in a sample of patients who were not preselected for sleep apnea prior to enrollment. Higher obstructive AHI scores were seen in an unselected population of orthodontic patients with posteriorly positioned and retroclined upper incisors, retrognathic mandible, increased length of the upper airway, decreased maxillary arch length, constricted maxillary and mandibular inter canine widths, decreased arch perimeter and higher pediatric sleep questionnaire. Dentists stand at the forefront of establishing the morphologic risk factors for OSA and therefore diagnosing and referring patients. Malocclusions are common in patients with OSA, but the optimal screening methodology has not yet been established. Previous work has utilized populations selected specifically for the presence or absence of OSA. 5/720 However, the present research differs from those studies in that our participants were not pre-selected by the presence of sleep-disordered breathing symptoms. Additionally, previous research utilized airway measurements as a measure of the likelihood of OSA. However, our study has used obstructive AHI since the correlation between airway dimension and AHI has been shown to be poor (r=0.07). • Our results indicate that a significant negative relationship between the distance and angle between the maxillary incisors to the line through nasion to subspinal A point (U1-NAmm, U1-NAdegree), maxillary arch length, maxillary and mandibular intercanine width, maxillary arch perimeter and the angle between sella, nasion and B point (SNB) with respect to OSA severity. A significant positive relationship between the upper airway length and PSQ with respect to OSA severity.

#### **Cephalometric findings**

We found that patients with an elevated obstructive AHI have more posteriorly inclined and positioned maxillary incisors as measured by U1-NAmm/deg compared with a low obstructive AHI. Previous research comparing patients with certain dentofacial morphology and OSA to non-obstructed controls has also found statistically significant difference with respect to incisors which were retroclined in patients with OSA. " It has also been found that retracting the upper incisors (in a 4 premolar extraction case with maximum anchorage) leads to a narrowing of the airway. "\* However, other studies have shown no changes after retracting the maxillary incisors in an orthodontic extraction case. These studies mentioned the airway changes as an adaption to airway morphology rather than a decrease in the airway size. \*\* The etiology behind associations between incisor inclination and OSA has not been well established. Whether or not orthodontically retracting or retroclining incisors has negative effect on obstructive AHI needs to be determined in a prospective longitudinal clinical trial. A retrognathic mandible is often related to Class II malocclusions and is

often related to OSA. \*\*\* Computed tomography (CT) tests have indicated larger airway length associated with the severity of OSA, they also indicate that the upper airway length to be greater in men compared to women (even when the data was normalized for body height). \*\*\*\* This may help explain the gender-related differences in OSA and male predisposition to pharyngeal collapse. \* These studies indicate an increase in the upper airway length is associated with OSA. According to Poiseuille's law: the resistance to flow is directly proportional to the length of the cylinder indicating the reason for patients with longer airways having a higher resistance to flow in effect increasing the collapsibility and resistance to flow within a longer airway. \*\*\* These studies also confirm in patients with OSA the hyoid bone was found to be more inferiorly positioned. \*\*\*\* The multivariate regression analysis controlling for age, gender and BMI undertaken for hyoid to mandibular plane (HMP) indicated a p value of 0.08. Perhaps future studies with a larger sample size could clarify this relationship.

#### **Dental model findings**

Our study on a healthy sample of patients showed significance in terms of a constricted maxillary and mandibular intercanine width, decreased maxillary arch length and decreased maxillary arch perimeter with respect to the obstructive AHI score adjusted for age, gender and BMI. Previous research comparing patients with OSA to non-OSA has found those patients with OSA to have a more constricted maxillary arch width. <sup>60</sup> They explained the cause of this to be from an altered position of the tongue, changing the balance between tongue and the cheeks or supine sleeping posture. <sup>61</sup> Extensive research has been undertaken in the field of sleep apnea and maxillary expansion which demonstrates that maxillary expansion leads to improvements in OSA. <sup>660</sup> In a meta-analysis of children with high arched or narrow palates who received rapid maxillary expansion less than 3 years prior to analysis, obstructive AHI improved from 8.9 to 2.7. For those who received treatment, the obstructive AHI improved from 7.1 to 1.5. <sup>660</sup> Furthermore, a 2018 study found that the presence of a narrow maxillary arch was more common in the high risk OSA group than the no risk group. <sup>60</sup>

#### Sleep disordered breathing questionnaires findings

The pediatric sleep questionnaire has been shown to be more effective at predicting OSA-related impairments such as quality of life, patient behavior, and daytime sleepiness than the use of polysomnography alone in children. \*\*\* The Epworth Sleepiness Scale has been shown to be predictive of daytime sleepiness in adults. <sup>a</sup> By utilizing the SRBD (sleep related behavior disorder) sub-scale, clinicians can improve the specificity of diagnosing OSA. <sup>a</sup> In the present study, the Pediatric Sleep Questionnaire (but not the epworth sleepiness scale) was found to be predictive of OSA in our orthodontic population.

#### Limitations

Limitations of this study include the following: The sample population which consisted of a heterogenous sample size of children and adults. The manner in which obstructive AHI was calculated: even though studies have shown the portable sleep monitor to have excellent results the overnight attended polysomnographic study is still the "gold standard" to diagnose OSA. <sup>76-9</sup> Another limitation is the small sample size, out of the 66 patients who initially participated 6 participants refused to wear the monitor and 6 participants did take initial records to commence orthodontic therapy. In terms of data collection, 4 out of the 54 patients lateral cephalograms were extracted from a limited field cone beam computed tomography which did not include the nasal bone. Every effort was made to identify the position of nasion accurately, but some inaccuracies may still remain. However, even with these limitations, we observed certain significant parameters related to OSA. Future prospective longitudinal research with the current sample will determine if orthodontically changing these variables significantly affects obstructive AHI over time.

#### CONCLUSION

In this cross-sectional study of patients starting orthodontic therapy, we found higher obstructive AHI scores in an unselected population of orthodontic patients to be associated wwith posteriorly positioned and retroclined upper incisors, retrognathic mandible, increased length of the upper airway, decreased maxillary arch length, constricted maxillary and mandibular inter canine widths, decreased arch perimeter and higher pediatric sleep questionnaire. We conclude that dentists could have an important role in screening patients for OSA by (1) measuring these dental and skeletal landmarks associated with OSA and (2) using PSQ to screen pediatric patients for OSA. Future research will follow this cohort longitudinally in order to identify changes in dental model measurements, cephalometric measurements and sleep questionnaire scores and their relationship to changes in obstructive AHI.

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Table 1: Descriptive population measurements.

	No O	SA	OS	SA		
	n= .	39	n=	15		
	Mean	SD	Mean	SD	Difference in Means	P-Value
Demographics:						
Age	23.56	8.35	29.80	18.86	-6.24	(0.10)
BMI	22.58	3.76	23.01	3.56	-0.43	(0.71)
Female	56.00%		47.00%			(0.53)
Male	44.00%		53.00%			(0.52)
Ethnicity						(0.60)
Caucasian (n=22)	35.90%		53.33%			
Hispanic/Latino (n=5)	10.26%		6.67%			
Asian (n=17)	35.90%		20.00%			
Other (n=10)	17.95%		20.00%			

Abbreviation: BMI: Body mass index, OSA: Obstructive sleep apnea.

T-test for the continuous variables reporting the mean, standard deviations, differences in means and p values.

Chi2 test for the categorical variables reporting the percentage and p values.

	No OSA		OSA		T-Tests	
	n= 39		n= 15			
	Mean	SD	Mean	SD	Difference in Means	P- Value
Cephalometric dental:						
U1-NA (degree)	24.31	7.96	20.69	6.52	3.62	(0.12)
U1-NA (mm)	5.61	3.34	3.74	2.22	1.87	(0.05)*
L1-NB (degree)	28.53	6.72	23.84	6.30	4.69*	(0.02)*
L1-NB (mm)	7.05	3.10	5.17	2.89	1.89*	(0.05)*
Overjet (mm)	4.05	1.42	3.46	1.82	0.59	(0.21)
Overbite (mm)	2.62	2.11	2.34	2.03	0.28	(0.66)
Cephalometric skeletal:						
SNA (degree)	83.50	4.20	82.30	3.95	1.20	(0.34)
SNB (degree)	79.70	4.48	78.92	3.78	0.78	(0.55)
ANB (degree)	3.79	2.36	3.38	2.68	0.41	(0.58)
Maxillary unit length (mm)	48.60	3.82	49.51	4.37	-0.91	(0.45)
Mandibular unit length (mm)	118.12	10.06	117.51	10.75	0.61	(0.85)
IMPA (degree)	94.21	6.25	91.41	7.38	2.80	(0.17)
Lower face height (mm)	58.10	2.29	56.97	2.46	1.14	(0.12)
Upper face height (mm)	41.90	2.29	43.03	2.46	-1.14	(0.12)
Cephalometric airway:						
Posterior airway space (mm)	10.32	3.61	9.99	2.24	0.33	(0.75)
Middle airway space (mm)	9.55	2.81	8.82	3.14	0.73	(0.41)
Superior airway space (mm)	9.61	2.71	9.86	3.00	-0.25	(0.77)
Hyoid to mandibular plane length (mm)	12.59	5.33	15.6	5.13	-3.01	(0.07)
Upper airway length (mm)	54.16	6.97	59.08	8.67	-4.92	$(0.03)^{3}$
Uvula length	33.84	4.80	34.69	3.59	-0.85	(0.54)
Tongue length	10.14	2.21	9.49	1.97	0.65	(0.32)
Retropalatal airway space (mm)	8.36	2.39	7.74	3.31	0.62	(0.45)

Table 2: Comparison of mean cephalometric measurements (t-test) for patients with and without OSA.

Abbreviations: U1-NA (degree): Upper incisors to the line formed by nasion to subspinale (A point) in degrees; U1-NA (mm): Upper incisors to the line formed by nasion to subspinale (A point) in mm; L1-NB (degree): Lower incisors to the line formed by nasion to supramentale (B point) in degrees; L1-NB (mm): Lower incisors to the line formed by nasion to supramentale (B point) in mm; SNA (degree): angle formed between sella, nasion and subspinale (A point); SNB (degree): angle formed between sella, nasion and subspinale (B point); SNB (degree): angle formed between the long axis of the lower incisor and mandibular plane angle.

Linear Model (Outcome: ln[Obstructive AHI])						
Coefficient p value						
U1-NA (degrees)	-0.032	0.010*				
Age	0.036	0.000*				
Gender	-0.373	0.051*				
BMI	0.014	0.622				

Table 3: Multivariate regression analysis for ln[Obstructive AHI] and U1-NA (degrees) adjusting for age, gender and BMI.

Abbreviations: U1-NA(deg): The angle in degrees formed by the upper incisors to the line joining nasion and subspinale (A point).

Obstructive AHI: Obstructive Apnea/Hypopnea Index

0,0						
Linear Model (Outcome: ln[Obstructive AHI])						
	Coefficient	p value				
U1-NA (mm)	-0.097	0.001*				
Age	0.038	0.000*				
Gender	-0.493	0.01*				
BMI	0.01	-0.7				

Table 4: Multivariate regression analysis for ln[Obstructive AHI] and U1-NA (mm) adjusting for age, gender and BMI.

Abbreviations: U1-NA(mm): The distance in mm formed by the upper incisors to the line joining nasion and subspinale (A point).

Obstructive AHI: Obstructive Apnea/Hypopnea Index

0						
Linear Model (Outcome: ln[Obstructive AHI])						
	Coefficient	p value				
SNB (degrees)	-0.046	0.043*				
Age	0.041	0.000*				
Gender	-0.387	0.053*				
BMI	0.003	0.927				

Table 5: Multivariate regression analysis for ln[Obstructive AHI] and SNB adjusting for age, gender and BMI.

Abbreviations: SNB(degrees): The angle formed between sella-nasion and B point (supramentale). This is an indication of the mandibular position with respect to the NB line.

aujusting for age, gender and BMI.				
Linear Model (Outcome: ln[Obstructive AHI])				
	Coefficient	p value		
Upper airway length (mm)	0.039	0.007*		
Age	0.032	0.000*		
Gender	-0.146	0.446		
BMI	-0.02	0.473		

 Table 6: Multivariate regression analysis for ln [Obstructive AHI] and upper airway length (mm) adjusting for age, gender and BMI.

1				I		
	No C	DSA	OS	A	T-Tests	
	n= 39		n= 39 n= 15			
	Mean	SD	Mean	SD	Difference in Means	P-
						Value
Maxillary arch length (mm)	32.06	3.74	29.38	3.15	2.68	(0.02)*
Maxillary intermolar width (mm)	47.47	3.26	48.19	4.43	-0.72	(0.52)
Maxillary intercanine width (mm)	35.23	3.38	34.02	2.30	1.21	(0.21)
Maxillary arch perimeter (mm)	76.22	6.70	72.93	6.11	3.29	(0.10)
Mandibular arch length (mm)	27.42	3.45	25.87	3.26	1.55	(0.14)
Mandibular intermolar width (mm)	41.99	3.54	43.10	3.67	-1.11	(0.31)
Mandibular intercanine width (mm)	27.02	2.70	25.91	1.50	1.12	(0.14)
Mandibular arch perimeter (mm)	66.37	6.44	64.27	5.77	2.10	(0.28)

Table 7: Comparison of mean dental model measurements (t-test) for patients with and without OSA.

Maxillary arch length measured: Perpendicular line joining the central fossa of the first permanent maxillary molars to a line drawn from the contact points of the central incisors.

Maxillary intermolar width: Line drawn from the central fossa of the first permanent maxillary molar to the contra-lateral central fossa of the first permanent maxillary molar. For those patients missing a first permanent molar the position of the central fossa was best estimated.

Maxillary intercanine width: Measured from the cusp tip of the maxillary permanent canine to the contra-lateral cusp tip of the maxillary permanent canine.

Maxillary arch perimeter: Measured from the mesial of the first permanent molar through the marginal ridges of the premolars and cingulum edge anterior dentition.

Mandibular arch length: Perpendicular line joining the central fossa of the first permanent mandibular molars to a line drawn from the contact points of the central incisors.

Mandibular intermolar width: Line drawn from the central fossa of the first permanent mandibular molar to the contra-lateral central fossa of the first permanent mandibular molar. For those patients missing a first permanent molar the position of the central fossa was best estimated.

Mandibular intercanine width: Measured from the cusp tip of the mandibular permanent canine to the contra-lateral cusp tip of the mandibular permanent canine.

Mandibular arch perimeter: Measured from the mesial of the first permanent molar through the marginal ridges of the premolars and cingulum edge anterior dentition.

Linear Model (Outcome: ln[Obstructive AHI])					
	Coefficient	p value			
Maxillary arch length (mm)	-0.070	0.013*			
Age	0.033	0.000*			
Gender	-0.466	0.022*			
BMI	0.011	0.685			

Table 8: Multivariate regression analysis for ln[Obstructive AHI] and maxillary arch length adjusting for age, gender and BMI.

Linear Model (Outcome: In [Obstructive AHI])				
	Coefficient	p value		
Maxillary intercanine width (mm)	-0.086	0.004*		
Age	0.039	0.000*		
Gender	-0.410	0.031*		
BMI	0.015	0.597		

Table 9: Multivariate regression analysis for ln [Obstructive AHI] and maxillary intercanine width adjusting for age, gender and BMI.

Linear Model (Outcome: ln[Obstructive AHI])					
	Coefficient	p value			
Mandibular intercanine width (mm)	-0.089	0.026*			
Age	0.037	0.000*			
Gender	-0.378	0.054*			
BMI	0.016	0.577			

Table 10: Multivariate regression analysis for ln[Obstructive AHI] and mandibular intercanine width adjusting for age, gender and BMI.

Linear Model (Outcome: ln[Obstructive AHI])						
Coefficient	p value					
-0.038	0.010*					
0.037	0.000*					
-0.477	0.019*					
0.010	0.719					
	Coefficient -0.038 0.037 -0.477					

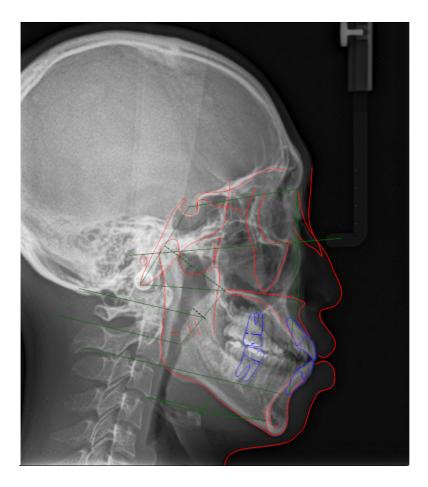
Table 11: Multivariate regression analysis for ln[Obstructive AHI] and maxillary arch perimeter adjusting for age, gender and BMI.

OSA.						
	No OSA n= 39		OSA n= 15		T-Tests	
	Mean	SD	Mean	SD	Difference in	P-
					Means	Value
Pediatric sleep questionnaire (whole sample)	2.92	2.89	5.41	3.69	-2.49	(0.02)*
Pediatric sleep questionnaire (children)	1.76	2.43	5.57	2.19	-3.81	(0.01)*
Epworth sleepiness scale (whole sample)	5.68	2.90	5.92	4.89	-0.23	(0.85)
Epworth sleepiness scale (adults)	5.52	2.58	6.38	5.24	-0.85	(0.56)

Table 12: Comparison of mean sleep disordered breathing questionnaires (t-test) for patients with and without OSA.

Linear Model (Outcome: ln[Obstructive AHI])					
Coefficient	p value				
0.067	0.017*				
0.045	0.000*				
-0.242	0.21				
-0.011	0.69				
	Coefficient 0.067 0.045 -0.242	Coefficient         p value           0.067         0.017*           0.045         0.000*           -0.242         0.21			

Table 13: Multivariate regression analysis for ln[Obstructive AHI] and pediatric sleep questionnaire adjusting for age, gender and BMI.



#### **Dental measurements:**

U1-NA (mm): Distance in mm from the upper incisor to the line joining nasion (N) to subspinale (A point) U1-NA (degrees): Angle in degrees from the upper incisor to the line joining (N) to subspinale (A point) L1-NB (mm): Distance in mm from the lower incisor to the line joining nasion (N) to supramentale (B point L1-NB (degrees): Angle in degrees from the lower incisor to the line joining (N) to supramentale (B point) Cverjet (mm): Horizontal distance between the incisal tip of the lower incisor to the incisal tip of the upper incisor.

Overbite (mm): Vertical overlap between the upper incisor and lower incisor

#### **Skeletal measurements:**

SNA (degrees): Angle in degrees between sella, nasion and subspinaleSNB (degrees): Angle in degrees between sella, nasion and supramentaleANB (degrees): Angle in degrees between SNB- SNAIMPA: Angle in degrees between the long axis of the lower incisor and mandibular plane angle

#### Airway:

Posterior airway space: Width of the airway space at the level of the tongue based, measured from the line from B point to gonion.

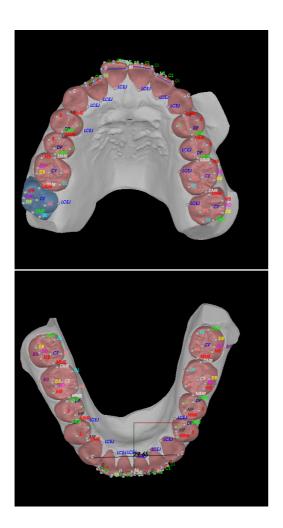
Middle airway space: Width of the airway space at the level of the tip of the uvula.

Retropalatal airway space: Narrowest part of the posterior airway space at the level of the soft palate.

Tongue length: Linear distance between the tongue tip to the epiglottis base.

Hyoid to mandibular plane: The perpendicular distance between the hyoid bone and the mandibular plane. Upper airway length: Vertical distance between the posterior hard palate and the hyoid bone.

Figure 2: Dental Model Measurements:



Maxillary arch length: The perpendicular line joining the central fossa of the first permanent molars to a line drawn from the contact points of the central incisors.

Maxillary intercanine width: The distance from cusp tip of permanent canines

Maxillary intermolar width: The distance from the central fossa of the first permanent molars

Maxillary arch perimeter: The measurements from the mesial of the first permanent molar through the marginal ridges of the premolars and cingulum edge anterior dentition

Mandibular arch length: The perpendicular line joining the central fossa of the first permanent molars to a line drawn from the contact points of the central incisors.

Mandibular intercanine width: The distance from cusp tip of permanent canines

Mandibular intermolar width: The measurements from the mesial of the first permanent molar through the marginal ridges of the premolars and cingulum edge anterior dentition

Mandibular arch perimeter: mandibular arch perimeter measured mesial of the first molar, through the buccal cusps of the premolars and incisal edge of the anterior dentition

#### Appendix 1:

#### Pediatric Sleep Questionnaire:

While sleeping, does your child... A2 . snore more than half the time? A3 . always snore? A4 . snore loudly? A5 . have ``heavy" or loud breathing? A6 . have trouble breathing, or struggle to breathe? A7 . seen your child stop breathing during the night? A24 . tend to breathe through the mouth during the day? A25 . have a dry mouth on waking up in the morning? A32 . occasionally wet the bed? B1. wake up feeling un refreshed in the morning? B2 . have a problem with sleepiness during the day? B4 Has a teacher or other supervisor commented that your child appears sleepy during the day? B6 Is it hard to wake your child up in the morning? B7 Does your child wake up with headaches in the morning? B9 Did your child stop growing at a normal rate at any time since birth? B22 Is your child overweight? C3. does not seem to listen when spoken to Directly C5 . has diffculty organizing task and Activities C8. is easily distracted by extraneous Stimuli C10 . fidgets with hands or feet or squirms in Seat C14. is `on the go' or often acts as if `driven by a motor' C18 . interrupts or intrudes on others (e.g. butts into conversations or games)

PSQ was scored = (number of questions answered yes)/(total number of questions answered yes or no excluding the questions answered don't know)<sup>35</sup>.

Appendix 2: Epworth Sleepiness Scale

0 = would never doze 1 = slight chance of dozing 2 = moderate chance of dozing 3 = high chance of dozing

Chance of Dozing (0-3)

Sitting and reading Watching TV Sitting, inactive in a public place (e.g. a theatre or a meeting)

As a passenger in a car for an hour without a break \_\_\_\_\_

Lying down to rest in the afternoon when circumstances permit \_\_\_\_\_

Sitting and talking to someone \_\_\_\_\_

Sitting quietly after a lunch without alcohol \_\_\_\_\_

In a car, while stopped for a few minutes in the traffic \_\_\_\_\_

ESS was scored= Sum of all numbers <sup>34</sup>.

# The Longitudinal Effects of Orthodontic Therapy on the Obstructive Apnea Hypopnea Index (AHI).

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**Abbreviations:** OSA, Obstructive Sleep Apnea; SDB, Sleep Disordered Breathing; PSQ, AHI; Apnea Hypopnea Index; Pediatric Sleep Questionnaire; ESS, Epworth Sleepiness Scale

# The Longitudinal Effects of Orthodontic Therapy on the Obstructive Apnea Hypopnea Index (AHI).

## ABSTRACT

**Objectives:** To investigate the longitudinal relationship between changes that occur during orthodontic treatment and the obstructive Apnea Hypopnea Index (AHI) in a convenience sample of orthodontic patients starting therapy.

**Materials and Methods:** Thirty-one subjects scheduled to start orthodontic treatment were prospectively evaluated with lateral cephalograms, intraoral dental scans, sleep disordered breathing questionnaires, and a home sleep study before the initiation of orthodontic therapy (T1) and after the majority of the desired tooth movement was completed (T2). The primary outcome variable was the change in obstructive Apnea Hypopnea Index ( $\Delta$ AHI) while the predictor variables were the changes in dental model measurements, changes in cephalometric measurements (skeletal, dental, airway) and changes in sleep disordered breathing questionnaire scores.

**Results:** Data from 31 subjects (male 48%, mean age  $25.52\pm12.23$ ) indicate that when controlling for age, gender and BMI, there were statistically significant (p<0.05) negative relationships between the change in the obstructive Apnea Hypopnea Index ( $\Delta$ AHI) and change in maxillary arch length (p=0.029) and mandibular intercanine width (p=0.045) between T1 and T2. No significant differences were found for changes in cephalometric (skeletal, dental, airway) measures or the sleep disordered breathing questionnaires. For every 1mm decrease in the maxillary arch length and mandibular intercanine width, there was a 10.24% and 20.47% increase in the mean obstructive AHI respectively.

**Conclusion:** Decreases in the maxillary arch length and mandibular intercanine width during orthodontic treatment were associated with an increase in obstructive Apnea Hypopnea Index. Further analysis with a larger more homogenous sample size utilizing lab-based polysomnography is required to confirm the link between orthodontic tooth movement and sleep quality.

### **INTRODUCTION**

Sleep disordered breathing is characterized by repeated episodes of complete or partial obstruction of the upper airway during sleep resulting in fragmented sleep patterns, oxygen desaturation, snoring and daytime somnolence. <sup>14</sup> Sleep disordered breathing commonly affects 10-20% of the adults population<sup>36</sup> and about 1-3% of the pediatric population <sup>164</sup>. It is a treatable condition which in children can affect growth, school performance and physical health<sup>9</sup>. In adults OSA has been linked to increase risk of motor vehicle accidents<sup>73011</sup>, hypertension<sup>12-4</sup>, cardiac disease<sup>61516</sup>, impaired concentration and neurocognitive changes<sup>17</sup>. Predisposing factors of OSA include obesity <sup>3</sup>, male gender <sup>3,18</sup>, African-American race <sup>3</sup>, neck circumference<sup>32</sup> and dental/craniofacial structure <sup>43920</sup>.

Orthodontic therapy includes a range of different treatment modalities to provide esthetics, function and stability. " A shift in treatment paradigm has been noticed in the field of orthodontics with an emphasis towards the soft-tissue relationship. <sup>22</sup> In recent years, concern has been raised regarding the effects of premolar extraction therapy, retraction of the incisors and resultant decrease of the airway space. Some have postulated that extraction of four premolars in patients with minimal crowding utilizing maximum <sup>23</sup> to absolute <sup>24</sup> anchorage leads to reduction of the airway predisposing patients to OSA. 2-3 It has been posited that this decrease in airway dimensions could, in turn, lead to breathing disorders such as OSA. Other studies have shown no change in airway dimension after retracting the incisors in an orthodontic extraction case. <sup>26–29</sup>. Imaging for these studies have been undertaken with patients in the upright position and awake, which may differ from sleeping patients. Additionally, none of these studies evaluated the relationship between upper airway dimension and sleep apnea severity. Magnetic resonance imaging studies indicates no correlation between the airway volume and Apnea Hypopnea Index (AHI) which is considered the standard of care for diagnosing obstructive sleep apnea (r=0.07). » A recent white paper report provided by the American Association of Orthodontics (AAO) indicates "conventional orthodontic treatment has never been proven to be an etiological factor in the development of sleep apnea" given the multifactorial nature of OSA.<sup>31</sup>

Previous research in orthodontics studying the effects of tooth movement has led to disparate results with respect to airway size. These results have been confounded given the heterogeneity in terms of anchorage used, population age and the fact that no measure of sleep propensity was established. The purpose of this study is to identify the relationship between changes in dental model measurements, cephalometric measurements (skeletal, dental, airway) and sleep disordered breathing questionnaires that occur during routine treatment to the changes in obstructive Apnea Hypopnea Index (AHI).

#### **MATERIALS AND METHODS**

## Study design and participants

The study was designed as a prospective exploratory clinical study. Participants were a convenience sample of patients seeking orthodontic therapy at the Harvard School of Dental Medicine between February 2017-December 2018. The sample size was calculated with a power of 80% and  $\alpha$  of 0.05. In an effort to determine the effects of orthodontic treatment on AHI in a typical orthodontic setting, the subjects were not preselected based on presence or absence of OSA symptoms but were excluded if they had already begun orthodontic therapy or had orthognathic surgery. Initial cephalometric radiographs, dental models, questionnaire data and sleep tests were taken at T1 before any orthodontic appliances were cemented and again at T2 when 1) the majority of the spaces had been closed in patients with extractions or spacing and 2) when 2mm or less of crowding was remaining in patients that started out with crowding. Prior to participation, written consent and assent was obtained from the adult patients, parents, and children. IRB approval was obtained. The de-identified sleep studies were scored by the same blinded investigator (ESK). Predictor variables were traced by the same operator (ST) blinded to the results of the sleep study. These variables include changes in cephalometric measurements (skeletal, dental, airway), changes in dental model measurements and changes in sleep disordered breathing questionnaires: pediatric sleep questionnaire and epworth sleepiness scale adjusted for age, gender and body mass index (BMI).

### **MEASUREMENTS**

### **Cephalometric measurements**

The lateral cephalograms were taken as part of the routine orthodontic records. The same Kodak 9000 machine was used to take all lateral cephalograms. The digital lateral cephalogram was uploaded onto the Dolphin software system (version 11.9 Chatsworth, CA, USA). Dental cephalometric measurements made included: 1) measurements of the position and inclination of the upper and lower teeth: The degree and mm measures from the upper and lower incisors to the line from nasion (N) to subspinale (A point) and supramentale (B point) (U1-NAmm/deg, L1-NBmm/deg), angle between the lower incisors and the mandibular plane (IMPA), 2) overjet (OJ) and overbite (OB), 3) skeletal cephalometric measures of jaw relations: the angles formed between sella (S), nasion (N), subspinale (A point) and supramentale (B point) (SNA, SNB) and the angle formed from A point, nasion and B point (ANB), maxillary and mandibular unit lengths, upper and lower face heights and 4) airway cephalometric measures: Posterior, middle and superior airway spaces, retropalatal airway space, tongue length, hyoid to mandibular plane, upper airway length, uvula length and thickness (Fig 1).

#### **Dental model measurements**

These measurements were undertaken from an intraoral scan using the iTero Element scanner (Align Technology, California) as part of the orthodontic records. The STL file was uploaded into Ortho Insight 3D (Ortho Insight 3D, MotionView, Tennessee) (Fig 2). The dental model measurements included: The maxillary and mandibular arch lengths defined as the perpendicular line from a point halfway between the central fossa of the first permanent molars to the contact point between the central incisor. The intercanine width which was measured between cusp tips of permanent canines. The intermolar widths measured from central fossae of the first permanent molars. The maxillary arch perimeter was measured from the mesial of the first permanent molar through the marginal ridges of the premolars and cingulum edges of the anterior dentition. The mandibular arch perimeter was measured from the mesial of the first molar, through the buccal cusps of the premolars and incisal edge of the anterior dentition (Fig 2).<sup>20,20,20</sup>

## **SDB** questionnaires

The pediatric sleep questionnaire (PSQ) is a validated quality of sleep symptom questionnaire consisting of 22 yes/no questions related to sleep related symptom. <sup>44</sup> Each 'yes' answer was assigned a 1 and each 'no' a 0. An index between 0 and 22 was created, on which higher scores indicate higher probability of OSA. Epworth sleepiness scale (ESS) is an 8-item questionnaire used to measure daytime sleepiness or sleep propensity in adults. A score of 1 indicates a slight chance of dozing, a score of 2 moderate and a score of 3 indicates a high chance of dozing. The final score is the sum. <sup>33,66</sup>

## Portable sleep monitor scoring

The portable sleep monitor used in this study was the Braebon Medibyte sleep monitor (Ontario, Canada) consisting of nasal pressure cannula, snore microphone, respiratory effort belts, and oximetry. Subjects were provided with the monitor and a disposable patient kit to be worn. The de-identified data from the sleep monitor was then downloaded using the Braebon Medibyte software and blindly analyzed by the same sleep specialist using the American Academy of Sleep Medicine guidelines (ESK). Hypopnea was defined as a 30% reduction in baseline nasal pressure resulting in either a 3% oxygen desaturation or an arousal. <sup>37,8</sup> A respiratory effort-related arousal was scored if there was flow limitation with a >30% reduction in the baseline nasal pressure tracing and crescendo snoring that was associated with a gasping breath and snorting. <sup>37</sup> Obstructive AHII  $\geq$ 5 for adults and obstructive AHI  $\geq$ 2 for children was selected as cut-offs for having OSA.

## **Statistical Analysis**

Descriptive statistics are presented, using means and standard deviations for movement of the upper and lower incisors. For each variable, the Pearson's correlation coefficient was estimated between the change in the variable and the change in a continuous measure of the natural log of obstructive AHI ( $\ln[\Delta \text{ obstructive AHI}]$ ) from T1 to T2.

All measurements and questionnaire scores were then subjected to further multivariate analyses, which adjusted for age, gender, and BMI. These regression analyses estimated the extent to which each variable significantly predicted the continuous measure of AHI. To satisfy the assumptions of linear regression models, the natural log of obstructive AHI ( $ln[\Delta obstructive AHI]$ ) was used in these analyses.

Analyses were carried out on the whole sample for measurements. For sleep questionnaires, separate analyses were also carried out for adults and children (ESS for adults and PSQ for children). All statistical analyses were conducted using Stata/IC Version 15.1 (StataCorp, Tx, USA).

## RESULTS

Demographic analysis before treatment indicate that of the 31 patients, 1 (of the 8) children and 5 (of the 23) adults were found to have OSA. Mean BMI of the sample was  $22.44 \pm 3.59$  (min:16; max:30.8), suggesting a healthy, non-obese population. Mean age was  $25.52 \pm 12.23$  (min:11; max:70) Table 1.

## **Cephalometric analysis**

Given the heterogeneity in terms of orthodontic treatment modalities, Table 2 describes the type of incisal movement that occurred in the sample. The upper incisors were proclined and advanced in 15 of the 31 subjects and were retracted and retroclined in 16 subjects. The lower incisors were proclined and advanced in 19 subjects and retroclined and retracted in 12 subjects. Pearson correlation coefficients between the obstructive AHI and cephalometric variables were undertaken and are shown in Table 3. All measurements were then subjected to further multivariate analyses, which adjusted for age, gender, and BMI. Multivariate regression analyses were conducted, adjusting for age, gender, and BMI. No significant relationships were found between changes in obstructive AHI and changes in the cephalometric measures.

## **Dental model measurements**

Pearson correlation for the dental model variable are presented in Table 4, which indicate a statistically significant difference (p<0.05) for the change in maxillary arch length (p=0.047) and for the change in mandibular intercanine width (p=0.033) with respect to changes in obstructive AHI. Multivariate regression analyses were conducted, adjusting for age, gender, and BMI. Table 5 indicates a negative relationship between the change in maxillary arch length and the change in obstructive AHI (p=0.029). For every 1mm decrease in the maxillary arch length there was a 10.24% increase in the mean obstructive AHI. Table 6 indicates a negative relationship between the  $\Delta$  mandibular intercanine width and  $\Delta$  obstructive AHI (p=0.045). For every 1mm decrease mandibular intercanine width there was a 20.47% increase in the mean obstructive AHI.

### Sleep disordered breathing questionnaires

Pearson correlation tests shown in Table 7 indicate no statistically significant difference in terms of  $\Delta$  questionnaire values to  $\Delta$  obstructive AHI.

#### DISCUSSION

The main finding of this study is that following orthodontic therapy the decrease in maxillary arch length and mandibular intercanine width is related to an increase in obstructive AHI. No measurements from the lateral cephalograms (of the awake patient standing upright) were predictive of changes in the AHI post-orthodontic therapy. Thus, orthodontic therapies decreasing the maxillary dental arch and mandibular intercanine width may place patients at risk for OSA. To our knowledge this is the first study indicating a relationship between orthodontic tooth movement and obstructive AHI.

The results of this study conform to the previous research<sup>30,40</sup> and the cross-sectional research of the same population which indicated that the decrease in maxillary arch length and decrease in mandibular intercanine width was related to an increase in the obstructive AHI. Previous research has been disparate with respect to the changes in airway dimension during orthodontic therapy. In adult studies with Class I bimaxillary protrusion (minimal crowding) treated with four premolar extractions utilizing absolute (skeletal bone anchors) to maximum anchorage (allowing minimal movement of the posterior dentition as anchors to bring the anterior teeth back) airway size was shown to decrease.<sup>213</sup> Whereas other studies have shown no change in airways diameter with respect to four premolar extractions. 26-2931.41-43 Germec-Cakan et al. 2011, showed space closure utilizing mesial movement of the posterior dentition may account for the increase in airway dimension. " In terms of the age demographics, growing adolescents with and without four premolar extractions have shown an increase in the airway dimension. **\*\*\*** This increase in the airway dimensions may be attributed to growth and development.<sup>45</sup> . Orthodontic movement of teeth following extractions and its effect on airway remains a controversial topic of discussion. According to the recent statement released by the American Association of Orthodontists (AAO) indicating conventional orthodontics has not been proven to be an etiological factors in the development of OSA. 31

Previous studies have used records (lateral cephalograms, CBCT) of the patient awake and standing upright which may not accurately reflect the airway configuration when supine. Supine positioning in adults can lead to prolapse of the mandible and base of the tongue causing upper airway obstruction. <sup>\*\*\*7</sup> In children (aged 1-10), obstructive sleep apnea syndrome (OSAS) is also caused by obstruction at the level of the adenoids and soft palate. <sup>\*\*</sup> Posture may also have an effect on lateral cephalograms which are used to assess a patient's airway status. In a non-apneic snoring population, there were significant decreases in the radiographic measurements for minimum post-palatal and post-lingual airway measurements in the supine position when compared to upright position, while mandibular protrusion even in the supine position resulted in significantly more functional space for the tongue. <sup>\*\*</sup> In apneic

populations and healthy controls, supine posture during the cephalogram measurements was associated with decreased posterior airway space and increased soft palate length, tongue length, and tongue thickness. <sup>so</sup>

Bodily retraction of the mandibular incisors and mandibular setback were associated with a reduction in middle pharyngeal airway space. <sup>a</sup> It has commonly been assumed that maxillary constriction causes nasal stenosis, which during the formative growth period of children may lead to mouth breathing and the development of "adenoid face". <sup>ass</sup> Rapid palatal expansion, used in combination with dentoalveolar appliances, has also been extensively studied and has been associated with a decrease in the nasal airway resistance <sup>sas</sup> expansion of the lower nasal cavity <sup>scs</sup>, upper nasopharyngeal spaces <sup>s</sup>, reduction in upper retropalatal space <sup>s</sup> as well as an increase in the oropharyngeal and laryngopharyngeal dimensions. <sup>set</sup> These changes in effect lead to an improvement in these patients Apnea Hypopnea Index (AHI). <sup>set</sup> Class III correction using limited maxillary widening and/or maxillary protraction was associated with increased nasopharyngeal, but not oropharyngeal, airway dimension. <sup>set</sup> The use of twin block therapy on children diagnosed with OSA and mandibular retrognathia has shown to have a decrease in the children's AHI scores. <sup>set</sup> Cistulli, et al. 1998 have shown that patients with maxillary constriction have an associated increase in the nasal resistance resulting in mouth breathing. <sup>en</sup> Pirila-Parkkinen et al. 2009 reported that children with diagnosed OSA to have narrower upper dental arches when compared with non-obstructed control children. <sup>set</sup>

The exact pathological mechanism underlying the development of OSA is still not fully established. Several structural and non-structural factors are believed to play a key role in the development of OSA. Structural factors include: obesity (central adiposity)<sup>3</sup>, soft tissue hypertrophy <sup>66</sup>, increased upper airway length<sup>67,70</sup>, enlarged tonsils and adenoid <sup>71</sup> and dental factors (such as retrognathia or maxillary constriction) <sup>96,165,72</sup>. Non-structural factors include: male gender, ethnicity (African-American) and family history. <sup>3</sup> This is the first study to establish a relationship between airway dimension and OSA status with orthodontic changes in tooth position. Further evaluation with a larger more homogenous sample size utilizing lab-based polysomnography is required to identify the link between orthodontic tooth movement and sleep quality.

## LIMITATIONS

Limitations of this study include the following: The heterogeneity in terms of population age, future studies would benefit from having more homogenous groups in terms of age since growth has been shown to affect airway size. Four patients had a limited cone beam computed tomograph (not fully displaying the nasal bone) at T1 and a lateral cephalogram at T2, all efforts were made to estimate the position of nasion at T1 but some error unrelated to the study's conclusion can be expected. In terms of AHI measurements, this study utilized a home sleep monitor. The gold standard for obstructive sleep apnea (OSA) diagnosis is overnight polysomnography in a sleep laboratory, access to this service is limited and may include long wait times<sup>10</sup>. Future research may benefit from having a labbased sleep study. AHI has a base value of zero, patients in whom the airway size increased would not have any identifiable changes in their AHI since there is no value below zero for AHI. Measure of airway collapsibility such as Pcrit would be required for future studies.<sup>10</sup> The orthodontic findings were very disparate with patients having different amounts of crowding/spacing ranging from moderate/severe to very mild. Future research would benefit from groups with more homogenous treatment modalities. However, even with these limitations, we did observe certain significant parameters.

#### CONCLUSION

In this longitudinal study of patients starting orthodontic therapy, we found that a decrease in the maxillary arch length and mandibular intercanine width is associated with an increase in obstructive Apnea Hypopnea Index. Further evaluation with a larger more homogenous sample size utilizing laboratory-based polysomnography is required to confirm the link between orthodontic tooth movement and sleep quality.

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	*			
	Mean	SD	Min	Max
Children (n=8)	13.5	2.07	11	17
Adults (n=23)	29.7	11.48	18	70
Age (n=31)	25.52	12.23	11	70
BMI (n=31)	22.44	3.59	16	30.8

Table 1: Population demographics at T2

Variable	n	Mean	SD	Min	Max
$\Delta$ Upper incisors					
Procline (degree)	15	4.987	4.76	0.1	17
Retrocline (degree)	16	-6.08	5.8	-16.8	-0.3
Δ Upper incisors					
Protract (mm)	15	1.13	1.04	0.1	3.4
Retract (mm)	16	-2.59	1.63	-5.4	0
Δ Lower incisors					
Procline (degree)	19	4.32	3.93	0.7	15.6
Retrocline (degree)	12	-5.48	4.51	-12.7	-0.8
Δ Lower incisors					
Protract (mm)	19	1.47	1.48	0.1	6.7
Retract (mm)	12	-2.37	1.65	-5.2	0

Table 2: Comparison of change of upper and lower incisor movements

This table indicates the movement of the upper and lower incisors relative to NA and NB lines, their mean, standard deviation and the minimum and maximum amount that the upper and lower incisors moved relative to NA and NB lines.

cephalometric variables		
Variable	R	p value
Cephalometric dental		
$\Delta$ U1-NA (deg)	206	.267
$\Delta$ U1-NA (mm)	306	.094
$\Delta$ L1-NB (deg)	238	.196
$\Delta L1$ -NB (mm)	291	.111
$\Delta OJ (mm)$	.124	.507
$\Delta OB (mm)$	.118	.527
Cephalometric skeletal		
$\Delta$ SNA (deg)	064	.731
$\Delta$ SNB (deg)	232	.210
$\Delta$ ANB (deg)	.242	.189
$\Delta$ IMPA (deg)	191	.303
$\Delta$ Maxillary length (mm)	.089	.634
$\Delta$ Mandibular length (mm)	.145	.437
Cephalometric airway		
$\Delta$ Posterior airway space (mm)	0.131	0.483
$\Delta$ Middle airway space (mm)	-0.04	0.814
$\Delta$ Superior airway space (mm)	0.042	0.823
$\Delta$ Retropalatal airway space (mm)	0.057	0.76
$\Delta$ Tongue length (mm)	-0.136	0.467
$\Delta$ Hyoid to mandibular plane (mm)	0.006	0.973
$\Delta$ Upper airways length (mm)	0.044	0.814
$\Delta$ Uvula length (mm)	-0.257	0.163
$\Delta$ Uvula thickness (mm)	0.141	0.448

Table 3: Pearson correlation between the changes in ln[Obstructive AHI] to change in cephalometric variables

Variable	R	p value
ΔMaxillary arch length	360	.047*
ΔMaxillary intermolar width	.003	.989
ΔMaxillary intercanine width	259	.160
ΔMaxillary arch perimeter	-0.287	0.118
$\Delta$ Mandibular arch length	133	.475
ΔMandibular intermolar width	239	.195
ΔMandibular intercanine width	383	.033*
ΔMandibular arch perimeter	174	.350

Table 4: Pearson correlation between the changes in ln[Obstructive AHI] to change in dental

\* Refers to significance at p<0.05

Table 5: Multivariate regression analysis for change in ln[Obstructive AHI] to change in maxillary
arch length adjusting for age, gender and BMI.

	Linear Model (Outcome: ln[Obstructive $\Delta$ AHI])		
	Coefficient	p value	
$\Delta$ Maxillary arch length (mm)	-0.108	0.029*	
Age	0.009	0.462	
Female	-0.413	0.151	
BMI	-0.006	0.88	

\* Refers to significance at p<0.05 N= 31, R= 0.221

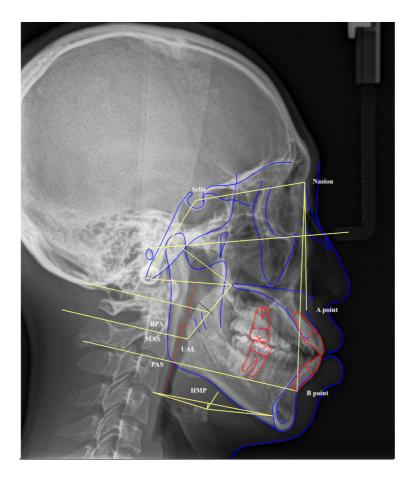
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	Linear Model (Outcome: $\ln[Obstructive \Delta AHI]$ )		
	Coefficient	p value	
$\Delta$ Mandibular intercanine width (mm)	-0.229	0.045*	
Age	0.002	0.854	
Gender	-0.320	0.257	
BMI	-0.017	0.681	

Table 6: Multivariate regression analysis for change in ln[Obstructive AHI] to change in mandibular intercanine width adjusting for age, gender and BMI.

\* Refers to significance at p<0.05 N= 31, R<sup>2</sup>= 0.187

Variable	R	R p value	
Pediatric sleep questionnaire (whole sample)	.194	.314	
Pediatric sleep questionnaire (children)	.358	.343	
Epworth sleepiness scale (whole sample)	.039	.866	
Epworth sleepiness scale (adults)	.164	.558	

Table 7: Pearson correlation between the change in ln[Obstructive AHI] to change in sleep disordered breathing questionnaires



## **Dental measurements:**

U1-NA (mm): Distance in mm from the upper incisor to the line joining nasion (N) to subspinale (A point) U1-NA (degrees): Angle in degrees from the upper incisor to the line joining (N) to subspinale (A point) L1-NB (mm): Distance in mm from the lower incisor to the line joining nasion (N) to supramentale (B point L1-NB (degrees): Angle in degrees from the lower incisor to the line joining (N) to supramentale (B point) Cverjet (mm): Horizontal distance between the incisal tip of the lower incisor to the incisal tip of the upper

incisor.

Overbite (mm): Vertical overlap between the upper incisor and lower incisor

## **Skeletal measurements:**

SNA (degrees): Angle in degrees between sella, nasion and subspinale

SNB (degrees): Angle in degrees between sella, nasion and supramentale

ANB (degrees): Angle in degrees between SNB- SNA

IMPA: Angle in degrees between the long axis of the lower incisor and mandibular plane angle

## Airway:

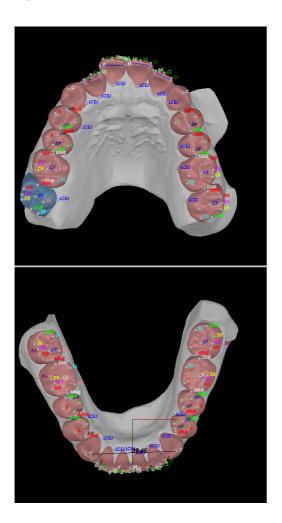
Posterior airway space: Width of the airway space at the level of the tongue based, measured from the line from B point to gonion (PAS).

Middle airway space: Width of the airway space at the level of the tip of the uvula (MAS).

Retropalatal airway space: Narrowest part of the posterior airway space at the level of the soft palate (RPA). Hyoid to mandibular plane: The perpendicular distance between the hyoid bone and the mandibular plane (HMP).

Upper airway length: Vertical distance between the posterior hard palate and the hyoid bone (UAL).

Figure 2: Dental Model Measurements:



Maxillary arch length: The perpendicular line joining the central fossa of the first permanent molars to a line drawn from the contact points of the central incisors.

Maxillary intercanine width: The distance from cusp tip of permanent canines

Maxillary intermolar width: The distance from the central fossa of the first permanent molars

Maxillary arch perimeter: The measurements from the mesial of the first permanent molar through the marginal ridges of the premolars and cingulum edge anterior dentition

Mandibular arch length: The perpendicular line joining the central fossa of the first permanent molars to a line drawn from the contact points of the central incisors.

Mandibular intercanine width: The distance from cusp tip of permanent canines

Mandibular intermolar width: The measurements from the mesial of the first permanent molar through the marginal ridges of the premolars and cingulum edge anterior dentition

Mandibular arch perimeter: mandibular arch perimeter measured mesial of the first molar, through the buccal cusps of the premolars and incisal edge of the anterior dentition

## Appendix 1:

## Pediatric Sleep Questionnaire:

While sleeping, does your child... A2 . snore more than half the time? A3 . always snore? A4 . snore loudly? A5 . have ``heavy" or loud breathing? A6 . have trouble breathing, or struggle to breathe? A7 . seen your child stop breathing during the night? A24 . tend to breathe through the mouth during the day? A25 . have a dry mouth on waking up in the morning? A32 . occasionally wet the bed? B1. wake up feeling un refreshed in the morning? B2 . have a problem with sleepiness during the day? B4 Has a teacher or other supervisor commented that your child appears sleepy during the day? B6 Is it hard to wake your child up in the morning? B7 Does your child wake up with headaches in the morning? B9 Did your child stop growing at a normal rate at any time since birth? B22 Is your child overweight? C3. does not seem to listen when spoken to Directly C5 . has diffculty organizing task and Activities C8. is easily distracted by extraneous Stimuli C10 . fidgets with hands or feet or squirms in Seat C14. is `on the go' or often acts as if `driven by a motor' C18 . interrupts or intrudes on others (e.g. butts into conversations or games)

PSQ was scored as the number of questions answered 'yes', creating an index between 0 and 22 . "Don't know" answers were discarded, and the overall score was pro-rated to account for the number of questions answered yes or no. Higher scores indicate higher probability of OSA. "

Appendix 2: Epworth Sleepiness Scale

0 = would never doze 1 = slight chance of dozing 2 = moderate chance of dozing 3 = high chance of dozing

Chance of Dozing (0-3)

Sitting and reading Watching TV Sitting, inactive in a public place (e.g. a theatre or a meeting)

As a passenger in a car for an hour without a break \_\_\_\_\_

Lying down to rest in the afternoon when circumstances permit \_\_\_\_\_

Sitting and talking to someone \_\_\_\_\_

Sitting quietly after a lunch without alcohol \_\_\_\_\_

In a car, while stopped for a few minutes in the traffic \_\_\_\_\_\_

ESS was scored= Sum of all numbers <sup>15</sup>.

## Appendix 3:

## **Treatment modality**

Crowding	12
4 premolar extractions	7
Distalization	3
Spacing	3
Distalization and expansion	1
Functional appliance- CII corrector	1
1 lower premolar extraction	1
2 lower premolar space created	1
2 upper premolar space created	1
1 lower incisor extraction	1

31

n