# ALTERED CRANIOFACIAL MORPHOLOGY IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA: A CLINICAL AND PHOTOGRAPHIC STUDY

by

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## Abstract

**Introduction**: With a reported prevalence of up to 5%, pediatric obstructive sleep apnea syndrome (OSAS) is a common childhood affliction. Consequences associated include growth delay, metabolic disturbance, impaired cognition, cardiovascular morbidity, and wake-time behaviour. Altered craniofacial morphology such as backwardly positioned jaws, small upper jaw/lower jaw ratios, and long narrow faces have been associated with pediatric OSAS. Standardized craniofacial digital photography is a readily available and safe imaging method that has been used in adult study populations; however, it has yet to be utilized in a pediatric population to assess its utility as a screening tool for OSAS.

**Objective**: Utilizing a systematic clinical examination, the prevalence of altered craniofacial morphology in children referred for overnight polysomnography at BC Children's Hospital will be assessed. Calibrated digital photographs will be analyzed to extrapolate any craniofacial findings associated with pediatric OSAS.

**Methods:** Patients aged 4-16 were recruited at BCCH to participate, undergoing an extra-oral and intra-oral orthodontic exam, the taking of one frontal and one lateral photograph, and completion of a standardized sleep questionnaire by the Parent/Guardian.

**Results**: 65 participants (29 female, 36 male, mean age 8.9 ± 3.1 years) were compared based on their AHI. 27 children had an AHI < 2/h (deemed not to have sleep apnea), 21 had mild OSAS (AHI 2 to 5/h), and 17 children were found to have severe OSAS (AHI >5/h). 19/65 participants (29.2%) were obese, and excluded from final analysis. Of the 44 remaining children, no

significant differences were found for any direct clinical measurements between children with and without OSAS. Analysis of the standardized craniofacial photographs revealed that children with OSAS had a more obtuse cervicomental angle (7° increase), and an increase in lateral facial height (6 mm increase). An increasing cervicomental angle, intercanthal distance and cricomental distance were all correlated with the severity of OSAS.

**Conclusion**: Aside from increases in cervicomental angle and lateral facial height, this study suggests altered craniofacial morphology may not be significantly associated with pediatric OSAS. Standardized craniofacial photography, in particular the measure of cervicomental angle, shows promise as a potential screening tool for OSAS, but requires further research.

## Lay Summary

Obstructive sleep apnea syndrome (OSAS) is a common childhood affliction that has a range of adverse health outcomes. While altered craniofacial morphology such as long faces and backwardly positioned jaws has long been associated with OSAS, sufficient evidence does not exist to support some of the causational claims made in the literature. An orthodontic exam and standardized digital photographs were recorded of children undergoing overnight sleep evaluation to assess which facial features may be associated with OSAS. The results showed that the angle formed between the neck, throat, and chin, was more obtuse in children with OSAS, and that children with shorter and wider faces may be more prone to OSAS than has been previously thought. Further research is required to validate standardized craniofacial photography as a screening tool in pediatric OSAS.

## Preface

The research topic of this project was suggested by Dr. Fernanda Almeida and the research question was identified and the project designed by Drs. Fernanda Almeida and Nelly Huynh. The data was collected by Evan Ayers and Mona Hamoda, with data analysis done by Evan Ayers with statistical assistance provided by Mary Wong and Dr. Fernanda Almeida. Evan Ayers prepared the Manuscript with content editing by Dr. Fernanda Almeida, Dr. Benjamin Pliska, Dr. Nelly Huynh and Dr. Kavita Mathu-Muju.

The study was approved by the University of British Columbia Office of Research Services, Humans Research Ethics Board (Certificate Number: HI 2-03285).

## Table of Contents

## List of Tables

## List of Figures

## List of Abbreviations

º: Degrees

%: Percentage

3-D: 3-Dimensional

AASM: American Academy of Sleep Medicine

AHI: Apnea Hypopnea Index

ANB: Angular difference between SNA and SNB angles.

AT: Adenotonsillectomy

BMI: Body Mass Index

CBCT: Cone Beam Computed Tomography

CCHS: Congenital Central Hypoventilation Syndrome

CPAP: Continued positive airway pressure

CRP: C-reactive protein

CT: Computed Tomography

IL: Interleukin

MPA: Mandibular plane angle

MRI: Magnetic Resonance Imaging

OSAS: Obstructive Sleep Apnea Syndrome

PSG: Polysomnography

SDB: Sleep Disordered Breathing

SNA: Sella-Nasion-A point angle

SNB: Sella-Nasion-B point angle

RME: Rapid Maxillary Expansion

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Finally, I would like to thank my fellow graduate students for their support and being part of my triumphs and struggles over the years.

## Dedication

This thesis is dedicated to Dr. Denny LDB Smith, professor emeritus, University of Manitoba, Faculty of Dentistry. Thank-you Denny for believing in me over the years. I would not have made it this far without your support, wisdom and guidance.

# Chapter 1: Introduction

## 1.1 Definition- What is Pediatric Obstructive Sleep Apnea Syndrome?

Sleep Disordered Breathing (SDB) represents a continuum of increasing upper airway resistance with snoring at one of the spectrum, and obstructive sleep apnea on the other, representing the most severe form.[1] Obstructive Sleep Apnea Syndrome (OSAS) is not a new syndrome, being first described over 40 years ago by Guilleminault and colleagues,[2] with the most recent classification system provided by the American Academy of Sleep Medicine (AASM), in the third edition of the International Classification of Sleep Disorders[3]

Sleep Disordered Breathing can by divided into central events or obstructive events. Central events are characterized by an absence or reduction in central respiratory motor output to respiratory muscles. Central OSA is rare and will not be discussed in this thesis. Obstructive events are characterized by breathing efforts against a closed, or partially closed, airway.[4] Obstructive Sleep Apnea Syndrome occurs when obstructive events repetitively occur during sleep, usually associated with a reduction in blood oxygen saturation or arousal.[5] The obstructions can be either partial or complete, and disrupt both sleep patterns and ventilation during sleep. They can be associated with a number of adverse health outcomes that will be described in section 1.4.

Obstructive Sleep Apnea Syndrome cannot be diagnosed solely by clinical signs nor symptoms, as these can overlap with less severe forms of SDB,[6] as well as other diseases such as chronic fatigue, periodic limb movements, and stress. The AASM recommends children undergo an overnight sleep study that utilizes polysomnography (PSG) in order to receive the most accurate

available diagnosis. Because pediatric OSAS can have significant negative health effect at both the population and individual level, it is essential that all health care providers who work with pediatric patient populations are familiar with this disease process, and understand when to refer, or how to treat, afflicted children appropriately.

### 1.2 Epidemiology

The prevalence of obstructive sleep apnea in children varies according to the population studied, and the methodology and criteria used for diagnosis. The generally accepted prevalence ranges from 1 to 5%,[7] with some authors indicating it may be seen in up to 10% of the pediatric (under age 18) population.[8] Despite the exact population prevalence not being universally agreed on, pediatric OSA is a relatively common disease, with a similar prevalence to asthma,[9] and will be encountered by most primary care physicians.

Variables that may be associated with pediatric OSA prevalence are ethnicity and gender. Bixler et al.[10] found that children of an ethnic minority (the majority of which, 58%, were African-American) had a significant increase in both SDB and mild OSA compared with the Caucasian children. Their finding agrees with previous studies[11,12] that have indicated ethnic minorities are at an increased risk for pediatric OSA. When gender is looked at, some research has indicated that males may be at an increased risk for pediatric OSAS,[13,14] however, not all studies are in agreement regarding this possible increased prevalence by gender.[15,16] Pediatric OSAS has been reported to have 2 peaks, the first occurring at age 2-6 years, associated with the presence of enlarging tonsils and adenoids, and the second occurring during adolescence, associated with weight gain.[17,18] The mixed results in the literature have led to the idea that the comparatively

larger weight gain that generally occurs in males relative to females during puberty may partially explain the increased prevalence of OSAS found in male adolescent children by certain studies.[19]

### 1.3 Pathophysiology

The pathophysiology of obstructive sleep apnea is complex and multi-factorial. Inadequate respiration (possibly along with episodes of hypoxemia) can lead to arousals from sleep and fragmentation of the sleep cycle.[4] As people afflicted with OSA do not have trouble breathing while awake, anatomy of the airway cannot be the sole contributor.[20] According to Dempsey et al.[4] the two critical sleep-induced changes that underlie OSA are changes in the passive mechanics of the upper airway, and reliance on chemosensitivity for control of respiratory motor output. In addition to anatomy and neuromuscular control, inflammation has been proposed as an additional etiological contributor to OSA.[21]

The physical size of the adenoids and tonsills are largest in children, typically peaking around 8 years of age, and gradually start to atrophy in adolescence.[17] For children with OSAS, large adenoids and tonsills have been shown to contribute to the anatomical obstruction that occurs during sleep.[7,22,23] Various grading have been developed to visually assess tonsillar size.[24,25] As objective assessment of tonsillar weight has been shown to correlate reasonably well ($r = 0.61$) with visual assessment,[26] visual grading scales can act as a useful screening tool. While adults with OSA tend to show a reduction in cross-sectional area of the upper airway[27], 3-Dimensional (3D) upper airway imaging has not been extensively utilized in a pediatric population, where both growth and radiosensitivity are concerns. Furthermore, 3D imaging cannot be done with the

subject asleep, calling into question the external validity of this approach in a syndrome that by definition, involves sleep.

### 1.3.1 Neuromuscular Control

The onset of sleep is characterized by a reduced muscle tone in the activation of the upper airway dilator muscles. People with OSA generally have longer and narrower airways,[27] relying on increased compensatory activation of airway dilator muscles to maintain airway patency when awake. However, when neuromuscular tone decreases as a result of sleep physiology, partial or complete airway obstruction can result leading to OSA. A cortical arousal can occur once increased blood carbon dioxide levels trigger a reset of respiratory rhythm to terminate the obstruction, which is typically followed by a brief period of hyperventilation.[20] Previous research has indicated that an interaction between the carotid and medullary chemoreceptors may be responsible for down-regulating this cortical stimulation, in an attempt to resume normal respiration.[28] When multiple obstructions occur, sleep becomes fragmented through the night, potentially leading to serious sequelae in children (section 1.4).

### 1.3.2 Inflammation

Inflammation has been cited as both a major contributor to, and a consequence of, pediatric OSAS.[7] It is thought that the intermittent hypoxemia seen in OSAS causes oxygen radicals to form in the vascular system.[7] Combined with the sympathetic activation caused from sleep arousals, systemic inflammation can potentially result. Supporting this reasoning, increased levels of C-reactive proteins (CRP) have been found in the blood plasma levels of children with OSA compared to controls.[29,30] However, other studies have not supported the relationship

between increased CRP levels and OSAS,[7] making the relationship uncertain. Both the severity of OSA and the co-morbidity of obesity are thought to be confounding factors in this relationship, as some sources regard obesity as a state of systemic inflammation,[7] and CRP levels have been shown to be higher in obese children when compared to non-obese children.[31] Additionally, obesity has been demonstrated to be a significant independent risk factor for pediatric OSAS, with as many as 55% of obese children being diagnosed with OSAS.[7]

A recent review looked at the role of various biomarkers (such as IL-2, IL-4, IL-6, IL-8, IL-10 and more), concluding that IL-6 shows promise as an inflammatory mediator in pediatric OSAS.[32] Recently, Gozel et al., found a reduced level of G protein-120 coupled receptors in pediatric OSA patients.[33] GPR 120 plays a role in modulating insulin resistance and lowering systemic inflammation,[33] therefore a reduction in its receptor would lead to an increase in systemic inflammation in children with a high sugar diet. Even if systemic inflammation levels are higher in children with OSAS, the literature supports a correlation, not causation. It is plausible that the inflammation exists due to the presence of the disease. As there is no evidence that inflammation is present prior to the onset of obstructive sleep apnea in children,[7] systemic inflammation is therefore correlated with OSA, and likely exacerbates the disease symptoms, but further research is needed before it can confidently be stated as a cause of pediatric OSAS.

### 1.3.3 Altered Craniofacial Morphology

In addition to adenotonsillar hypertrophy, altered craniofacial morphology is another anatomic factor associated with pediatric OSAS. Long-faced, mouth breathing children have been viewed as having an increased prevalence of OSAS despite empirical data for this association lacking in

the literature. Juliano et al.[34] evaluated 15 mouth-breathing children and 12 nose-breathing children via PSG and reported an increased prevalence of OSA the mouth breathing children. However, their definition of OSA used a cut-off point (AHI ≥1) that was more stringent than the generally agreed upon value (see section 1.5), making their results unclear. Pirilä-Parkkinen et al.[35] compared 41 children (22 males, 19 females, mean age 7.2 years) with PSG diagnosed OSAS both to 41 children with snoring, and to an asymptomatic control group of 41 matched children. The OSA and snoring groups had significantly more Cl II molar relationships (29% & 36% vs. 5% of sample), increased overjet (+1 mm), decreased maxillary intercanine width (-1.3 mm), and decreased lower arch length (-1 mm) when compared to the control group.[35] Additionally, the OSA group had statistically less overbite (by 0.8 mm), along with a higher number of children with an anterior open bite (7 vs. 0).[35] However, their data had major limitations, as the control group did not undergo PSG, and surgical treatment for sleep apnea was previously performed in nearly half (46%) of the OSA group and a quarter (24%) of the snoring group.[35] From this study, it is not possible to ascertain any causational relationship for altered craniofacial morphology in pediatric OSAS.

Katyal et al.[36] conducted a systematic review and meta-analysis that included all available randomized controlled trials, case-control trials or cohort studies with controls that evaluated the association between craniofacial dimensions and pediatric OSAS. From the 9 studies included in their review (with 6 being pooled for the meta-analysis), they found that children with OSAS had a decreased SNB angle (1.4º) when compared to children without symptoms of SDB.[36] However, the inclusion criteria used by Katayl et al.[36] for pediatric OSAS did not meet the gold standard of diagnosis, as participants included in their review were deemed to have OSAS diagnosed from a

variety of methods, including via questionnaire. Published in the same year, Flores-Mir et al.[37] conducted also conducted a systematic review and meta-analysis on the relationship between pediatric OSAS and craniofacial morphology. From the 9 studies included in their review (8 of which were included in the meta-analysis), they found children with OSAS had a decreased SNB angle (1.8º), an increased ANB angle (1.4º) and an increased mandibular plane to sella-nasion angle (4.2º) compared to the control group.[37] Unfortunately, the percentage of children with vertical mandibular growth and mandibular retrusion was unreported in the control group, making the precise relationship between altered craniofacial morphology and pediatric OSAS difficult to elicit.

Ngiam and Cistulli, recently reviewed the available literature regarding the association between dentofacial abnormalities and pediatric OSAS.[38] They found that in addition to mandibular retrusion and an increased mandibular plane angle, children with OSAS were more likely to have reduced mandibular length, increased anterior face height, a lower hyoid bone, an elongated soft palate and increased tongue size.[38] Dentally, maxillary constriction (with a high and narrow palate), anterior open bite, anterior and/or posterior-cross bite, decreased inter-molar width and dental crowding are all more likely to be seen in children with OSAS than in children without OSAS.[38] Obesity may also be a confounding factor in the relationship between craniofacial morphology and OSAS. Previous cephalometric research by Sadeghianrizi et al.[39] has indicated that obese adolescents have significantly larger facial dimensions than their non-obese counterparts, implying obesity may somehow alter craniofacial growth. This potential confounder has not been controlled for in previous studies. While it is clear from the literature that altered craniofacial morphology has some role in the etiology of pediatric OSAS, all current

studies have limitations in sample size and methodology, making the precise relationship difficult to elicit.

### 1.4 Sequelae

The most common sequelae of untreated pediatric OSAS are failure to thrive, cognitive deficits, and/or a decrease in neuropsychological function.[7] More specifically, children with OSAS demonstrate deficits in learning, memory, visuospatial skills, language and verbal skills, concept formation, mathematical abilities and executive function.[7] From a neurocognitive aspect, children with OSAS tend to exhibit periods of hyperactivity or even attention deficit disorder.[23] Daytime sleepiness is increased compared to control children, but is seen less commonly than in adults with OSA.[6] From a physiologic aspect, sequelae include reduced overall growth/failure to thrive,[7] nocturnal enuresis, metabolic morbidity (increased insulin resistance in children with concurrent obesity and/or dyslipidemia),[6] and in severe cases, cardiovascular morbidity[7] (including hypertension and/or endothelial damage).

### 1.5 Diagnosis

A variety of methods such as history, physical examination, nocturnal pulse oximetry, video recording, nap polysomnography and ambulatory polysomnography have been utilized in the diagnosis of pediatric OSAS. Perhaps of least utility are patient history and physical examination. In a review paper of 12 studies that compared patient history (typically along with clinical signs) to overnight PSG results, Brietze and Roberson reported that nearly every study (11/12) concluded these two measures were not reliable in diagnosing pediatric OSAS.0[40] More precisely, Marcus et al. [7] reported that patient history and physical examination have poor

positive predictive values of 65% and 46%, respectively. Nonetheless, American Academy of Pediatrics guidelines recommend that primary care physicians routinely screen for pediatric OSAS based on history of symptoms, referring the patient for further evaluation as indicated.

Overnight polysomnography is widely regarded as the gold standard in pediatric OSA diagnosis.[7,41] Supervised by accredited sleep technicians, polysomnography is a collection of simultaneously recorded physiologic measurements.[42] PSG measures cortical and sub-cortical arousals (through electroencephalogram, electooclulogram and submental-electromyogram), cardiovascular function (via electrocardiogram and pulse transit time), and respiratory function (via pulse oximetry, nasal thermal-pressure transducer, arterial oxyhemoglobin saturation, end tidal CO2, and/or esophageal manometry).[42] Additionally, thoracoabdominal effort is measured by respiratory inductive plethysmography, abdominal excrusion belts, and diaphragmatic/intercostal EMG.[21]

From these physiologic measurements, sleep architecture can be scored, and the presence or absence of sleep apnea can be determined based upon the apnea-hypopnea index (AHI), which is the number of apneas and hypopneas per hour. Apnea is defined as temporary cessation of breathing, and is recorded when the PSG peak signal excursions (airflow from an integrated nasal thermal-pressure transducer) drop $\leq$ 90% of baseline.[43] The AASM defines baseline as the mean amplitude of stable breathing and oxygenation in the 2 minutes preceding the event (in individuals with a stable breathing pattern during sleep), or the mean amplitude of the 3 largest breaths in the 2 minutes preceding onset of the event (in individuals without a stable breathing pattern during sleep).[44] Hypopnea is defined as abnormally slow or shallow breathing, and is

recorded on the PSG when peak signal excursions (nasal pressure in a diagnostic study) drop to 30% or less of pre-event baseline levels.[43] While there is no firm consensus in the literature on the exact AHI cut-off point between normal and disease for pediatric OSAS, an AHI of ≥1.5 events/hour is considered statistically abnormal in children[7], with most authors defining pediatric OSAS as occurring at an AHI ≥2.[45–47]

### 1.6 Screening Tools

While overnight polysomnography remains the gold standard for diagnosis pediatric OSAS, it is time consuming, costly, and not readily available. Therefore, adjunctive diagnostic tools are required to screen for the syndrome. These adjunctive diagnostic tools include questionnaires, along with clinical assessment data such as radiological imaging, and more recently, standardized craniofacial photography.[48]

#### 1.6.1 Questionnaires

In 2012, Spruyt & Gozal published data from their ordered questionnaire validated against overnight PSG data to serve as a screening tool for pediatric SDB.[49] From their 1,133 participant sample, they were able to find six hierarchically arranged questions, that when scored according to their formula, were able to screen for children at high risk of SDB when the overall cumulative score exceeded 2.72 out of 4.[49] Despite having a poor positive predictive value (35.4%), their questionnaire was shown to have excellent negative predictive value (92.7%),[49] making it a useful screening tool for physicians to assess which children do not have the disease, and further evaluate children whose score indicates they may have OSAS. While there are other validated questionnaires that can serve as screening tools for pediatric OSAS,[50,51] Spruyt &

Gozal's questionnaire [49] is preferred in this study due to its ease of completion for the parent/guardian.

### 1.6.2 Radiological Imaging

Various radiological techniques such as lateral cephalometrics, computerized tomography (CT) (both helical and cone-beam), and magnetic resonance imaging (MRI) have been used to investigate the relationship between hard and/or soft tissue morphology, and OSA. Shintani et al.[52] compared lateral cephalometric data from 140 children with OSA (mean age 4.5 ± 1.7 y) to a control group of 54 children (mean age of 4.7 ± 2.5 y), reporting that maxillary projection (given by a decreased SNA value) was significantly reduced in the OSA group. While multiple other smaller sample studies[34,53] have investigated the relationship between altered hard tissue craniofacial morphology in children and OSAS, results from the two recent systematic reviews[36,37] revealed the following "red-flags" can reliably be associated with pediatric OSAS: mandibular retrusion (via a decrease in SNB of under 2º), an increaed maxilla-mandibular discrepency (via an increase in ANB angle of under 2º), and an increased mandibular plane angle(3-4º). Despite these established associations, clear cut, cephalometic values that can reliably identify pediatic patients with or without OSAS have not been yet been found.

The largest limitations of 2D cephaolometrics are structural overlap and soft-tissue boundary identification. These limitations have largely been overcome by 3D imaging techniques such as MRI and CT. MRI has excllent soft tissue contrast and requires no ionizing radiation, however, it is expensive and has limited availability. Additionally, its long scanning time requires the patient to be still, which may necessiate partially sedating pediatric patients, which in turn, may decrease neuromuscular tone and alter their airway physiology[54]. Computerized tomography offers the

advantage of a short scan time, although requires exposure to ionizing radiation. Due to radiation concerns, limited CT studies have examined children with OSAS. However, Van Holsbeke et al.[55] utilized helical CT on 33 children (23 of which were assessed with OSAS via PSG). Using functional imaging (a computerized method that uses physical characteristics of the upper airway, including velocity, turbulence, pressure, wall sheer stress and resistances), to convert their CT data into a 3D model of the pharygneal airway, they found the OSAS sample had significantly less volume and cross sectional area in the region of the upper airway where the adenoids and tonsils overlap.[54] While numerous adult studies have examined airway morphology via CBCT, no studies have examined pediatric OSAS via this imaging modality.

### 1.6.3 Standardized Craniofacial Photography

Standardized photographs have a long history in dentistry, having been used in orthodontics since the early part of the 20$^{th}$ century,[56] with the technique being gradually improved over the decades.[57] As cephalometric radiography requires exposure to ionizing radiation as well as specialized equipment, Lee et al.,[58] utilized standardized craniofacial digital photography to assess adult participants for craniofacial phenotypic differences, comparing them on the basis of their PSG findings. Standardized frontal and profile photographs were taken of 114 adult subjects with OSA (defined as AHI $\geq$ 10/h) and 66 control subjects (AHI <10/h).[58] The photographs were digitally analyzed for linear, angular, area and volume measurements representing dimensions of various craniofacial regions. Once participants were matched for BMI, significantly smaller measurements in participants with OSA were found for mandibular length (4 mm), mandibular-nasion angle (2º), anterior neck space area (2 cm$^2$), and mandibular triangular area (2.5 cm$^2$). Additionally, adults with OSA had significantly larger (more obtuse)

cervicomental angles (13º),[58] as well as wider faces, given by inreases in both the face-width-midface depth angle (1.6º), and the mandibular width-length angle (2.7º)

To test whether craniofacial photography could accurately screen for sleep apnea, Lee et al., created a variety of statistical models to assess whether their photographic data could be used to predict which patients had OSA and which one did not.[48] They were able to find that a linear regression model consisting of 4 photographic measurements (increased face width, increased eye width, increased cervicomental angle, and decreased mandibular length) was able to correctly classify 76% of participants (sensitivity 86%, specificity 59%), according to whether they had OSA or not. Similarly, they created a classification and regression tree (CART) model that was able correctly predict which subjects had, or did not have, OSA 77% of the time.[48] From their study, Lee et al., were able to conclude that standardized craniofacial photography provides sufficient useful data to allow OSA risk stratification,[48] demonstrating its potential as a screening tool in adults.

In craniofacial photography, the relationship of the overlying superficial soft tissue shown in craniofacial photography must be considered with respect to the underlying hard tissue morphology. In a comparison of analogous lateral cephalometric to profile photographs on 123 children (aged 7-12), Gomes et al.,[59] reported that generally strong Pearson correlations coefficients were able to be found with the soft tissue to hard tissue counterparts. The ANB angle showed the strongest correlation between modalities ($r^2 = 0.74$ for males, $r^2=0.89$ for females) for anteroposterior measurements, while FMA ($r^2=0.81$) showed the strongest correlation for vertical measurements.[59] Additionally, strong intra-examiner reliability was found in the

photographic measurements, with ICC's generally exceeding 0.80.[59] Similarly, Staudt and Kiliaridis found relatively strong correlations between lateral photographs and lateral cephalograms in a mixture of Cl I and Cl III adult patients.[60] Interestingly, these strong correlations are higher than were previously reported in an earlier study.[61] While Zhang et al.[61] also demonstrated strong intra-examiner reliability of the photographic measurements, correlations to hard tissue analogues were only moderate (ranging from 0.4 to 0.6). Subjects of Caucasian descent had weaker correlations than those of African descent,[61] indicating possible variability by ethnicity. Finally, Sutherland et al.[62] compared facial bony dimensions via MRI to surface facial dimensions obtained by photographs. Statistically significant correlations were found for maxilla-mandibular relationship ($r^2$=0.8), lower face height ($r^2$=0.76), and mandibular length ($r^2$=0.67).

Given the above research,[48,58,59,62] standardized craniofacial photographs act as a reliable assessment of adults with OSA. Particularly appealing are its ease of use, wide safety margin, low cost, and wide spread availability compared to other imaging modalities. While there are few studies that have examined the utility of photographs in children as a screening tool, standardized craniofacial photography has been shown to be useful in screening children for congenital central hypoventilation syndrome (CCHS).[63] Todd et al.[63] found that certain anatomic measurements (such as upper lip height, and upper face height) were able to correctly predict children with CCHS 86% of the time. In terms of sleep medicine, only one published study has examined the utility of photographs as a screening tool for pediatric SDB.[64] Ikävalko et al.[64] screened 382 children via questionnaire for SDB and compared their screening results to lateral profile photographs. While their results suggested that certain measurements such as facial convexity

were important predictors in screening for pediatric SDB, a statistically significant difference was unable to be found.[64] However, their study was likely underpowered as only 8.6% of children were deemed to have SDB,[64] and diagnosis was done via questionarre, without the use of polysomnography. Furthermore, the photographs were analyzed by a variety of non-orthodontic practitioners, who lacked experience in identifying craniofacial landmarks, resulting in poor intra-examiner reliability.[64] The authors concluded that while craniofacial photography may be useful in identifying children at risk of SDB, clinicians need to be knowledgeable about facial growth and development in order to reliably utilize this method.[64] Most importantly, accurate diagnosis of the disease is essential to accurately evaluate the utility of craniofacial photography in pediatric OSAS, a critical factor that was missing from this study.

### 1.7 Treatment Options

A variety of treatment options exist for children with pediatric OSAS, ranging from no treatment, to surgical intervention. While over 40% of children with OSAS may show spontaneous resolution,[65] if left untreated, OSAS can have serious deleterious health outcomes, leading most experts to advocate for treatment.[7,66,67] One option that is supported by recent studies[68,69] is pharmacological management. Intranasal steroids can be an effective treatment option to manage mild-moderate pediatric OSAS (AHI $\geq$ 5). Unknown in the pharmacological approach is whether the steroids reduce OSAS by decreasing inflammatory markers, or whether they work by decreasing the size of the tonsils (for an unknown amount of time). As such, surgical removal of the tonsils and adenoids (adenotonsillectomy) remains regarded as the preferred treatment option in the management of pediatric OSAS.

### 1.7.1 Adenotonsillectomy

Adenotonsillectomy (AT) is typically recommended based upon clinical signs (tonsillar hypertrophy score ≥1) and symptoms (reported SDB).[7,23,70] As with any surgery, inherent risks are involved. While AT has a low complication rate, minor post-operative bleeding and pain can occur. Severe complications are rare, but can include infection, anaesthetic reactions, respiratory decompensation, velopharyngeal incompetence and even death.[7]

In a large, multi-centered randomized clinical trial of 464 children aged 5-9 that included pre-treatment and 7 month follow-up polysomnography, Marcus et al.[23] demonstrated both the effectiveness and limitations of early AT. Children who were assigned to the early AT were shown to have a significantly greater reduction in AHI when compared to the watchful waiting group (AHI decreased from 4.8 to 1.3 vs. 4.5 to 2.7, $p < 0.01$).[23] However, early AT was not universally successful. Despite excluding children with possible confounding conditions (severe OSAS, craniofacial syndromes, cardiac disease, behavioural disorders and obesity), early AT normalized PSG findings in just 79% of the children.[23] Therefore, while AT is an effective surgery in the majority of children with OSAS, removal of hypertrophic adenoids and tonsils may only be one of the treatment options required in some children.

### 1.7.2 Continued Positive Airway Pressure

Continued positive airway pressure (CPAP) has been used for treatment of sleep apnea in adults for over 35 years.[71] Nasal CPAP functions through continuously blowing air into the larynx, preventing the airway from collapsing.[72] CPAP is a proven treatment for mild to severe OSA in adults,[73] but relies solely on patient compliance to be effective. There has not been sufficient

research on this treatment modality in children to advocate CPAP as a definitive treatment option for pediatric OSAS.[7] However, one well designed study did find an improvement in AHI, reported sleepiness, and oxyhemoglobin levels in children using positive airway pressure at 6 month follow-up.[74] Despite the study's protocol that provided extra patient support, adherence was found to be poor.[74] 38% of the sample was lost to follow-up, while the remainder demonstrated a sub-optimal adherence of 5.3 ± 2.5 hours of nightly use.[74] Interestingly, this objectively measured data was lower than the subjective adherence reported by the parents (7.6 ± 2.6 hours per night),[74] highlighting the optimistic reports of compliance that patients can provide. Some clinicians have expressed concern over possible negative long term effects of CPAP on mid-face growth in children. While this has not been thoroughly examined, a recent small sample study did not show any difference in mid-face projection in children who used CPAP for at least 6 months compared to normative data.[75] Additional research regarding the use of CPAP in pediatric OSAS is needed, along with the development of specific pediatric devices and protocols. Therefore, at present, CPAP is not regarded as a primary treatment option in children, instead its use is advocated for in children who do not respond to AT, or for children with contraindications to surgery.[7]

### 1.7.3 Distraction Osteogenesis

Distraction osteogenesis is procedure used to lengthen bones. Following an osteotomy in the pertinent bone, a distraction device is placed between the two segments, slowly pulling them apart, allowing osteogenesis to occur in the gap and eventually lengthening the bone.[76] Children born with certain craniofacial abnormalities (such as Pierre-Robin sequence) typically have significant airway issues due to severe mandibular retrognathia, and may require mandibular

distraction osteogenesis. As expected, the increase in airway via distraction also improves the concurrent obstructive sleep apnea.[77] In a systematic review of 74 studies with a combined total of 711 pediatric patients with a variety of craniofacial syndromes that cause either unilateral or bilateral mandibular deficiency, Tahiri et al.[77] found mandibular distraction osteogenesis to be 95.6% successful in either resolving or improving OSAS as diagnosed by PSG. However, 24% of the children experienced complications (such as infection, parathesia, open bite, and scaring), indicating distraction osteogenesis is not without risks. Similar to mandibular distraction, patients with midface deficiency and OSAS, may benefit from midface distraction osteogensis, although there is a lack of research in this area.[38] While distraction osteogensis is typically reserved for children with craniofacial anomalies, one type of distraction that is often used in children without craniofacial syndromes or sequences is orthodontic maxillary expansion.

### 1.7.4 Orthodontic Treatment Options

#### 1.7.4.1 Maxillary Expansion

Maxillary expansion can be accomplished through the use of a tooth-borne device (typically from first molar to first molar), that runs across the palate and applies orthopedic force to separate the midpalatal suture. The maxillary and palatine bones disarticulate along the midpalatal suture with the expansion forces dispersing across the cranial and circum-maxillary sutures.[38] The procedure is indicated in patients with maxillary transverse constriction, who usually present with posterior cross-bites. Expansion can be defined as slow (SME; typically 0.25mm every 2-3 days) or rapid (RME; typically 0.25-0.50 mm per day)[78], with clinicians tailoring their protocol based upon the skeletal maturity of the patient.

Maxillary expansion has been thought to improve pediatric OSAS by increasing nasal width and volume, while decreasing maxillary sinus width and decreasing airway resistance.[79–81] Additionally, patients with mandibular retrusion have demonstrated an anterior repositioning of the tongue following rapid maxillary expansion,[38,82] possibly improving upper airway patency.

In 1998, Cistulli and colleagues[83] first demonstrated the efficacy of RME in adult OSA. Since then, numerous studies have examined the utility of RME in pediatric OSAS, although high level (level I) evidence is lacking. Pirelli et al.[84] evaluated a case series of 31 children with maxillary constriction, OSAS, and no adenotonsillar hypertrophy, with the children undergoing PSG evaluation before and after RME. Their AHI was found to normalize in all cases at 4 month follow-up[84]. Another study that followed their sample over a longer term found the improvement in AHI attributed to treatment with RME to be stable over a 36 month period.[85] Villa et al.[86] compared RME to AT in the treatment of pediatric OSAS. 25 children underwent AT, 22 children underwent RME and 5 underwent both. While both treatments were found to be effective, children in the AT group saw a greater improvement (AHI decreased from 17.25 ± 13.94 to 1.79 ±1, $p < 0.0001$) than the RME group (AHI decreased from 5.81± 6.05 decreasing to 2.64 ± 3.11, $p = 0.005$).[86] While initial interpretation of their results suggest RME may not be as effective as AT, it must be noted that the children who underwent AT initially had more severe OSAS than the children who underwent RME. Patient age, BMI, allergies, adenotonsillar hypertrophy, and the small sample size are all potential confounders, and further level I research is required. However, from the available literature, it is at least clear that when indicated by the presence of maxillary constriction, RME can help improve OSAS, and a multidisciplinary approach to treat the disease is may be required.

#### 1.7.4.2 Mandibular Advancement Appliances

Numerous studies have demonstrated that mandibular advancement appliances are effective in treating adult OSA.[87–89] They have been proposed to function by enlarging the pharyngeal airway predominantly at the velopharynx.[38] Surprisingly, there has been a lack of research in their utility in pediatric OSAS. Villa and et.[90] randomly assigned 19/32 children with OSAS to receive an oral advancement appliance. When compared to children who received no treatment, treated children all had a significantly lower AHI.[90] However, despite this improvement, only 50% of the treated children achieved a normal AHI after 6 months.[90] More recently, mandibular advancement appliances were demonstrated to significantly improve the AHI in a small sample where 8 children wore the device for 1 year. They were compared to 8 control children, who saw an increase in their AHI over the same period.[91] Further, large sample, clinical trials are needed to definitively evaluate the role of mandibular advancement appliances in pediatric OSAS, and more importantly to understand the characteristics of children who may benefit from this orthodontic treatment option.

### 1.8 Objectives

As described in this literature review, there is a lack of understanding regarding the amount altered craniofacial morphology contributes to the multi-factorial disease that is pediatric obstructive sleep apnea syndrome. While previous literature has established that an association does exist, the magnitude of this association remains to be clarified. Typically, a formal dental evaluation is not performed for children who are referred for overnight sleep evaluation via PSG. While some physicians may perform a basic assessment of maxillary constriction and

mandibular retrusion, altered craniofacial morphology is not universally screened for at Canadian sleep centres. Additionally, sleep physicians usually lack specialized education in dentofacial development, which is inherent in orthodontic specialty training.

Therefore, this research project has the following 2 objectives:

i) To utilize a systematic orthodontic clinical examination to assess the prevalence of altered craniofacial morphology (including dental morphology) in children undergoing overnight polysomnography.

ii) To assess whether standardized craniofacial photography can function as a valid screening tool for children at high risk of obstructive sleep apnea syndrome.

Considering the overlapping relationship between altered craniofacial morphology and obstructive sleep apnea syndrome, it is important that the extent of this relationship be further explored. Orthodontic treatments such as RME or functional appliances may improve OSAS, and treatments for OSAS may impact craniofacial morphology. While interventional studies look at the relative efficacy of different treatments, we have yet to establish the percentage of children with OSAS who have altered craniofacial morphology. Due to the limitations of cephalometric radiography (availability, exposure risk), craniofacial photography, if successfully validated, may serve as a practical screening tool, that primary care physicians may be able to eventually utilize.

## 1.9 Hypotheses

The null hypotheses for the study are as follows:

i) Children diagnosed via PSG with OSAS will not have a higher prevalence of altered craniofacial morphology than children without OSAS.

ii) Craniofacial photography will not be useful in predicting which children have OSAS and which children do not.

# Chapter 2: Material and Methods

## 2.1 Participants

Children referred to the Respirology department at British Columbia Children's Hospital for an overnight sleep study (via polysomnography) were recruited to participate in this study. Participants were recruited over a 1 year period, from December 2014 until December 2015. Inclusion criteria were age between 4-16, and successful completion of the polysomnography. Exclusion criteria were previous or current treatment for sleep apnea, previous or current orthodontic treatment, and a lack of proficiency in English. Ethical approval for the study was obtained from the University of British Columbia Research Ethics Board and BC Children's Hospital (ethical approval # H1 2-03285).

## 2.2 Methods

Parents/guardians and participants were approached and informed about the study prior to the sleep technician commencing PSG. Interested families were given REB approved consent forms (and assent forms, when needed) that explained the study's goals, procedures, and any possible risks or benefits. 2 different assent forms were used, one for children aged 7-13, and one for adolescents aged 14-16. After consent was obtained, the parents were given the Spruyt and Gozal 6-item sleep questionnaire[49] (Table 2-1) to complete while their child underwent a structured orthodontic clinical examination (Table 2-2 through Table 2-6). Following the orthodontic exam, standardized frontal and profile photographs were then taken for each patient. After completing the photographs, the sleep technicians then commenced the overnight sleep study set up, as well as recording the child's height and weight.

## 2.3 Spruyt and Gozal Sleep Questionnaire

The sleep questionnaire (Table2-1) was scored on a 5 point Likert scale (0-4), with the total score from the six questions being summed according to the following formula (where Q1 = raw score from question 1, Q2 = raw score from question 2, and so forth):[49]

$$A = (Q1 + Q2)/2$$

$$B = (A + Q3)/2$$

$$C = (B + Q4)/2$$

$$D = (C + Q5)/2$$

$$\text{Cumulative score} = (D + Q6)/2$$

As previously discussed, children who's cumulative score was under 2.72 were deemed to be at low risk for OSAS.[49]

**Table 2-1: Spruyt and Gozal sleep questionnaire**

| | | | |
|---|---|---|---|
| 1. Gender | ☐ Female ☐ Male | 2. Âge | _____ |
| 3. Date of Birth | ☐☐☐☐-☐☐-☐☐ (YYYY-MM-DD) | | |
| 4. Over the last 6 months | | | |
| *Do you ever shake your child to make him/her breathe again when asleep? (Shake child to breath) ?* | ☐ Never ☐ Rare (1 night per week) ☐ Occasional (2 nights per week) ☐ Frequent (3 to 4 nights per week) ☐ Almost always (more than 4 nights per week) | | |
| *Does your child stop breathing during sleep? (Apnea during sleep)?* | ☐ Never ☐ Rare (1 night per week) ☐ Occasional (2 nights per week) ☐ Frequent (3 to 4 nights per week) ☐ Almost always (more than 4 nights per week) | | |
| *Does your child struggle to breathe while asleep? (Struggle breathing when asleep)?* | ☐ Never ☐ Rare (1 night per week) ☐ Occasional (2 nights per week) ☐ Frequent (3 to 4 nights per week) ☐ Almost always (more than 4 nights per week) | | |
| *Are you ever concerned about your child's breathing during sleep? (Breathing concerns while asleep)?* | ☐ Never ☐ Rare (1 night per week) ☐ Occasional (2 nights per week) ☐ Frequent (3 to 4 nights per week) ☐ Almost always (more than 4 nights per week) | | |
| *How loud is the snore? (Loudness of snoring)?* | ☐ Hardly noticeable or low ☐ moderately strong ☐ Strong ☐ Very strong ☐ Extremely Strong | | |
| *How often does your child snore? (Snoring during sleep)?* | ☐ Never ☐ Rare (1 night per week) ☐ Occasional (2 nights per week) ☐ Frequent (3 to 4 nights per week) ☐ Almost always (more than 4 nights per week) | | |

| Comments: |
|---|
| |
| |

## 2.4 Clinical Orthodontic Examination

All participants underwent a structured orthodontic clinical exam by one of two calibrated orthodontists (EA or MH). The clinical exam form was divided into the following 5 components: overview, frontal-view, profile view, functional assessment and intra-oral exam.

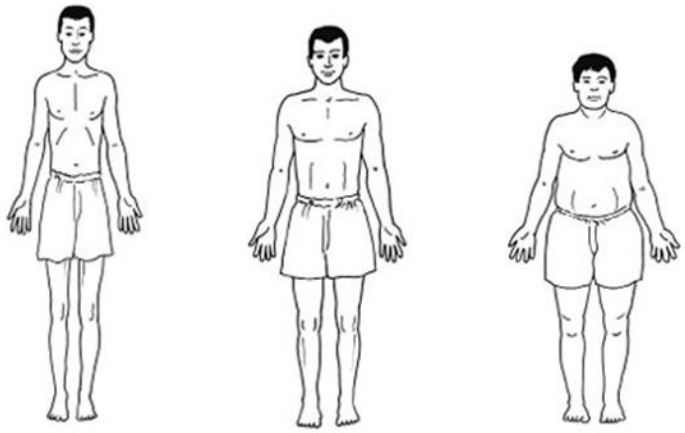
### 2.4.1 Overview

In this section (Table 2-2) any relevant notes from the patient's hospital chart, chief concern, country of origin of patient's family and body type (endomorph, mesomorph or ectomorph) were recorded. While body type could be considered subjective, the patient's weight and height were recorded by the hospital sleep technician's in order that BMI could be calculated according to the following formula [92]:

BMI = weight (kg)/height$^2$ ($m^2$).

As per CDC guidelines, children whose BMI met or exceeded the 95$^{th}$ percentile were deemed to be obese.[92]

**Table 2-2: Overview**

| | | |
|---|---|---|
| Chart Notes | | |
| Case Type – Chief Concern | | |
| Origins | Country of origin of mother : _____ | Country of origin of father : _____ |
| Body type<br>(if borderline, choose mesomorph) | ☐ Ectomorph ☐ Mesomorph ☐ Endomorph<br>  <br>Ectomorph Mesomorph Endomorph | |

### 2.4.2 Frontal View

Table 2-3 shows the data collected in the frontal-view examination. A brachycephalic facial type was recorded when the shape of the skull appeared shorter and more square than the typical mesocephalic human skull shape. A dolicocephalic facial type was recorded when the participant had a longer, more oval shaped head. Lower facial height was assessed based upon whether the lower anterior face height (measured from sub-nasale to soft-tissue menton) was less, equal to, or more than 1/3 of the overall face height (measured from trichion to soft-tissue menton). Mandibular symmetry was assessed based on the relation of the chin point to the facial midline. Similarly, the upper and lower dental midline were measured relative to the facial midline. Incisor and gingival display at both rest and at smile, were measured using a flexible plastic millimetre.

**Table 2-3: Frontal view**

| Front View | |
|---|---|
| 1. Type facial<br>(if borderline, choose mesocephalic) | ☐ Mesocephalic ☐ Brachycephalic ☐ Dolichocephalic |
| 2. Lower Face Height | ☐ Normal ☐ Increased ☐ Decreased |
| 3. Symmetry | ☐ Symmetric ☐ Mandible shift to the Right ☐ Mandible shift to the Left |
| 4. Dental Midlines<br>(midline – use cusp of upper lip) | Upper : ☐ on with facial midline ☐ shift to Right ☐ shift to Left; Amount : ____mm<br>Lower : ☐ on with facial midline ☐ shift to Right ☐ shift to Left; Amount : ____mm |
| 5. Incisor display at rest | ____mm |
| 6. Gingival display on smile | ____mm |
| 7. Incisor display on smile | ____mm |

### 2.4.3 Profile View

Table 2-4 shows the data collected from the profile view. Facial profile was assessed by measuring the angle formed between soft-tissue nasion to subnasale to soft-tissue pogonion. An acute angle indicates facial convexity, a straight line indicates a straight profile, and an obtuse angle indicates a concave profile. Skeletal position of the jaws was assessed clinically with respect to each jaw's position relative to the anterior cranial base. Lip position was determined relative to the plane formed between the tip of the nose to the anterior tip of the chin. Finally, the presence of lip strain on closing was determined by the presence of visible mentalis activity with the lips together.

**Table 2-4: Profile view**

| Profile View | |
|---|---|
| 8. Facial Profile | ☐ Straight  ☐ Concave  ☐ Convex  |
| 9. Skeletal position - Maxilla | ☐ Retrognathic ☐ Normal ☐ Prognathic |
| 10. Skeletal position - Mandible | ☐ Retrognathic ☐ Normal ☐ Prognathic |
| 11. Nasolabial Angle | ☐ Normal 90°-100 ° ☐ Acute (< 90 °) ☐ Obtuse (>100 °) |
| *Lip Position*<br>12. With respect to esthetic line : Upper lip | ☐ Normal ☐ Retrusive ☐ Protrusive |
| 13. With respect to esthetic line : Lower lip | ☐ Normal ☐ Retrusive ☐ Protrusive |
| 14. Lip strain to close<br>(mentalis strain only, slight opening without strain is "No") | ☐ Yes ☐ No |

### 2.4.4 Functional Assessment

Table 2-5 shows the data collected in the functional assessment portion of the orthodontic clinical examination. Tonsil size was evaluated according to the Standardized Tonsillar Hypertrophy Grading Scale[25] represented diagrammatically in Table 2-5.

**Table 2-5: Functional assessment**

| Functional | |
|---|---|
| 15. Tonsils | ☐ Removed  ☐ 1+  ☐ 2+  ☐ 3+  ☐ 4+ (kissing tonsils)  |
| 16. History of Mouth Breathing | ☐ Yes : ☐ During Day Time ☐ During Night Time<br>☐ No |

### 2.4.5 Intra-Oral Examination

Table 2-6 shows the data collected from the intra-oral examination, which included assessment of transverse, vertical and anterior-posterior discrepancies, as well as an arch length: tooth size perimeter analysis. Angle's molar classification was assessed for the right and left dentition, with class I being defined as the mesiobuccal cusp of the upper first permanent molar occluding with the buccal groove of the lower molar. Discrepancies from class I that were under ½ cusp (or 3 mm) were classified as class I. When the mesiobuccal cusp of the upper first molar occluded ½ cusp or more mesial to the buccal groove of the lower first molar, the participant was deemed to have a class II malocclusion. Conversely, participants were classified as class III when the mesiobuccal cusp of the permanent maxillary first molar occluded ½ cusp or more distal to the buccal groove of the permanent mandibular first molar. For participants without all permanent molars, their posterior occlusion was classified as flush terminal plane, mesial step or distal, as represented diagrammatically in Table 2-6.

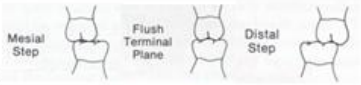
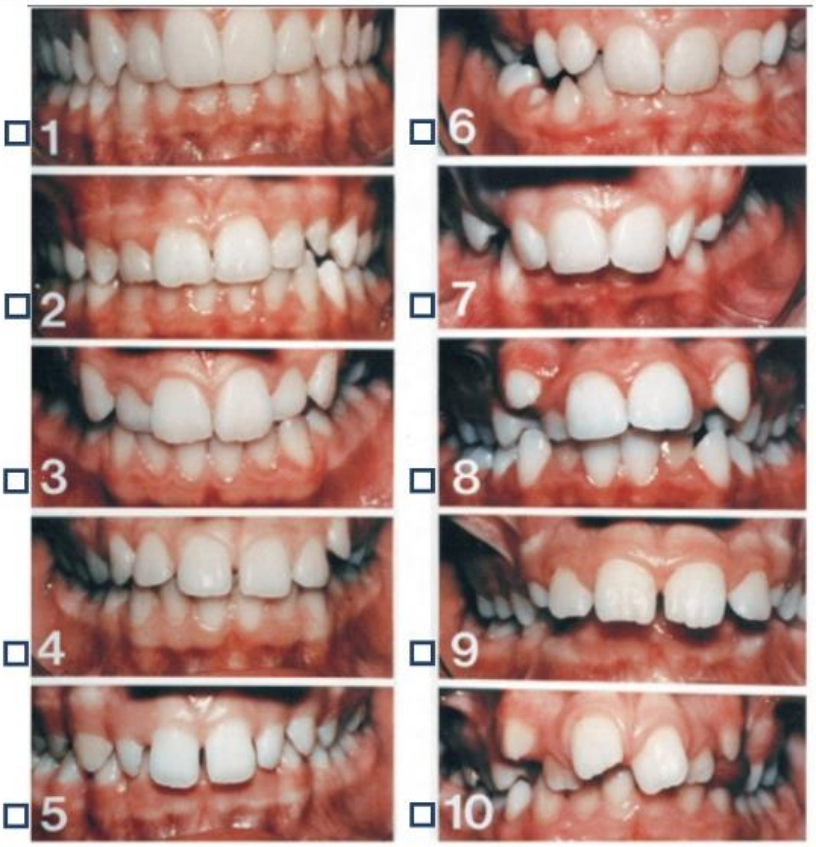
Using the methodology described by Björk [93], dental measurements were recorded according to the following descriptions: Overbite was measured as the averaged percentage of the vertical overlap of the upper centrals incisors over the lower central incisors. A lack of vertical overlap was deemed an anterior open bite, and was measured linearly. Similarly, overjet was recorded as the averaged horizontal overlap of the upper central incisors over the lower central incisors. If the lower central incisors were ahead of the upper central incisors, this was recorded as an anterior cross-bite, and measured in mm. Posterior crossbite was recorded when the buccal cusp of the upper tooth occluded lingual to the buccal cusp of the corresponding lower tooth. All posterior teeth present, whether primary or permanent, were assessed for crossbite. Crowding or

spacing was evaluated by calculating the amount of overlap or space between the interproximal contacts of erupted teeth. The overall crowding or spacing was divided into mild (1-3 mm), moderate (4-9 mm), or severe (>10 mm). Intercanine width and intermolar width were measured using a Boley gauge with 0.01mm accuracy. Intercanine width was measured from the cusp tip of the maxillary right to maxillary canines. Intermolar width was measured across the palate, from the junction of the mid-palatal groove at the gingival margin, from maxillary molar to maxillary molar.

The Index of Orthodontic Treatment Need (IOTN) [94] esthetic scale ranks malocclusion in terms of the perceived esthetic impairment in order to identify those who would most likely benefit from orthodontic treatment. Participants are ranked on a scale of 1-10 for overall occlusal attractiveness, with higher rankings indicating more severe malocclusions (Table 2-6).

## Table 2-6: Intra-oral examination

| Intra oral | |
|---|---|
| 17. Oral Habits | ☐ Yes ☐ No Since When :_____years |
| *Which?* | ☐ Nail Biting ☐ Biting lip/cheek ☐ Bruxism<br>☐ Sucking Thumb/finger ☐ Other :_____ |
| 18. Horizontal Excess<br>(taken at average of both central incisors, labial to labial) | *Overjet* : ☐☐☐ mm |
| 19. Vertical Excess<br>(taken at average of both central incisors, labial to labial) | *Overbite* : ☐☐☐ % |
| 20. Anterior OpenBite | *Open bite*: ☐☐☐ mm |
| 21. Posterior OpenBite Right | ☐☐☐ mm |
| 22. Posterior OpenBite Left | ☐☐☐ mm |
| 23. Odontogram | 8 7 6 5 4 3 2 1 \| 1 2 3 4 5 6 7 8<br>E D C B A \| A B C D E<br>E D C B A \| A B C D E<br>8 7 6 5 4 3 2 1 \| 1 2 3 4 5 6 7 8 |
| 24. Dental crossbite<br>(including edge-to-edge bite) | Anterior crossbite : ☐ Yes ; **IF YES** Number of maxillary teeth involved : ____<br>☐ No<br>Posterior crossbite : ☐ Yes<br>☐ Unilateral ; **IF YES** Number of maxillary teeth involved : ____<br>☐ Bilateral<br>☐ No |
| 25. Narrow Palate | ☐ Yes ☐ No |
| 26. CR/CO shift | ☐ Yes, Specify:<br>Posterior - anterior : _____<br>Vertically: _____<br>To the right : _____<br>To the left : _____<br>☐ No |
| 27. Intermolar distance<br>(measured from mid-palatal groove @ gingival margin) | ☐☐☐mm |
| 28. Intercanine distance<br>(measured from cusp tip) | ☐☐☐mm |
| 29. Tongue size | ☐ Normal ☐ Microglossia ☐ Macroglossia |
| 30. Arch Shape | Upper: ☐ U shape ☐ V shape<br>Lower : ☐ U shape ☐ V shape |
| 31. Palatal Depth | ☐☐☐mm |
| 32. Stage of dentition | ☐ Primary ☐ Mixed ☐ Permanent (No primary teeth present) |

| | | |
|---|---|---|
| 33. Molar Classification<br>(according to R and L sides) | Permanent : (<1/2 cusp = cl.1)<br>Right : ☐ I ☐ II ☐ III<br>Left : ☐ I ☐ II ☐ III |  <br><br>Primary/mixed :<br>Right : ☐ Mesial step ☐ Flush ☐ Distal Step<br>Left : ☐ Mesial step ☐ Flush ☐ Distal Step |
| 34. Canine Classification<br>(<1/2 cusp = cl.1) | Right : ☐ I ☐ II ☐ III<br>Left : ☐ I ☐ II ☐ III | |
| 35. Space Analysis | ☐ crowding<br>Upper : ☐ <3 mm ☐ 4-9 mm ☐ >10mm<br>Lower : ☐ <3 mm ☐ 4-9 mm ☐ >10mm<br>☐ spacing<br>Upper : ☐ <3 mm ☐ 4-9 mm ☐ >10mm<br>Lower : ☐ <3 mm ☐ 4-9 mm ☐ >10mm | |
| 36. IOTN esthetic scale<br>(match for overall occlusal attractiveness) |  <br> | |

## 2.5 Standardized Craniofacial Photographs

Frontal and profile digital photographs of the head and neck were obtained in a standardized fashion, in accordance with the University of Sydney's guidelines.[95] A single-lens digital camera (L830 Nikon Corp., Japan) was utilized to photograph the participants, with the beige wall at

BCCH serving as a consistent background. The children were photographed standing upright while assuming the natural head position. Prior to the photographs, the following anatomical landmarks were pre-identified on the subjects by palpation and marked using a small round sticker of various colours:

*Right gonion* –the most inferior, posterior and lateral point on the external angle of the mandible.

*Right infra-orbital ridge*- most inferior point on the margin of the bony orbit.

*Sternal notch*- most superior border of the sternum

*Soft tissue gnathion* –the most anterior, inferior point on the chin

*Soft tissue menton*- the most inferior point on the chin.

Standardized methods were used to align subjects for the photographs. For the frontal photograph, adequate exposure above the level of the sternal notch was required. Accessories such as glasses or necklaces were requested to be removed, and any children with long hair were asked to tie their hair back or place it behind their ear, ensuring adequate visibility of the right and left ear. Participants were asked to look straight ahead at the camera (located at least 1.5 m away) and to maintain a relaxed, neutral facial expression with their lips lightly touching. Participants were then asked to turn sideways, and look straight ahead at the doorway into their room. Calibrated, 3.0 cm washers were taped to the forehead and cheek of each child for the frontal and profile photographs, respectively, in order that linear distances could be digitally calibrated and measured.

Using image analysis software (Image J, *Bethesda, MD*), landmark digitization (Figure 2-1) was performed in accordance with the methodology from Lee et al.[58]. Table 2-1 and Table 2-7 list the

39 craniofacial landmarks that were captured as *x,y,* pixel coordinates on the image. The coordinates for each landmark were then transferred to a custom programmed spreadsheet (Microsoft Excel, *Redmond, WA*) that calculated a variety of linear, angular, area and volume craniofacial measurements (71 in total), described in Table 2-8.

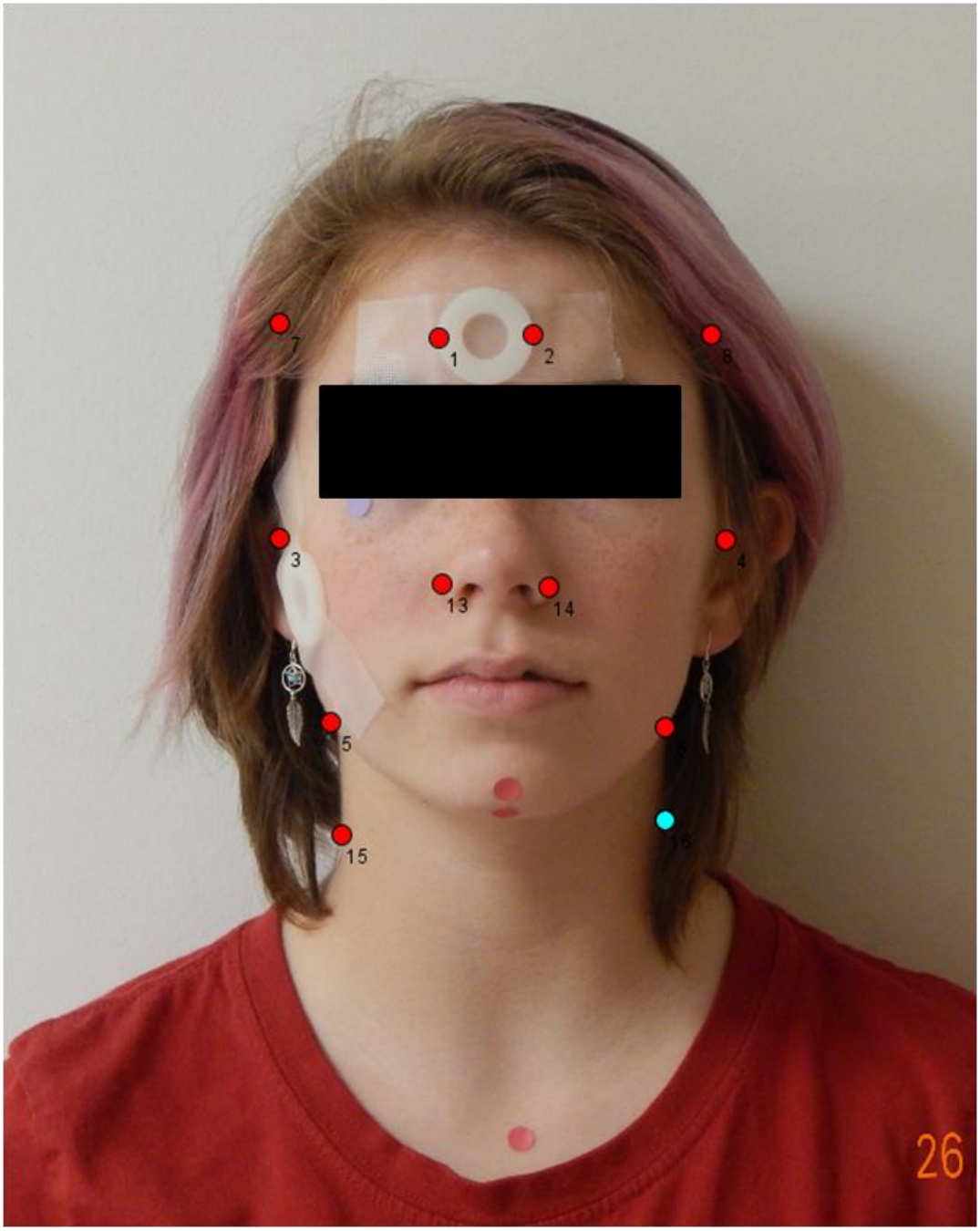



**Figure 2-1: An example standardized frontal photograph with landmarks digitally placed using image analysis software (Image J *v1.5, NIH, Bethesda, MD*).**

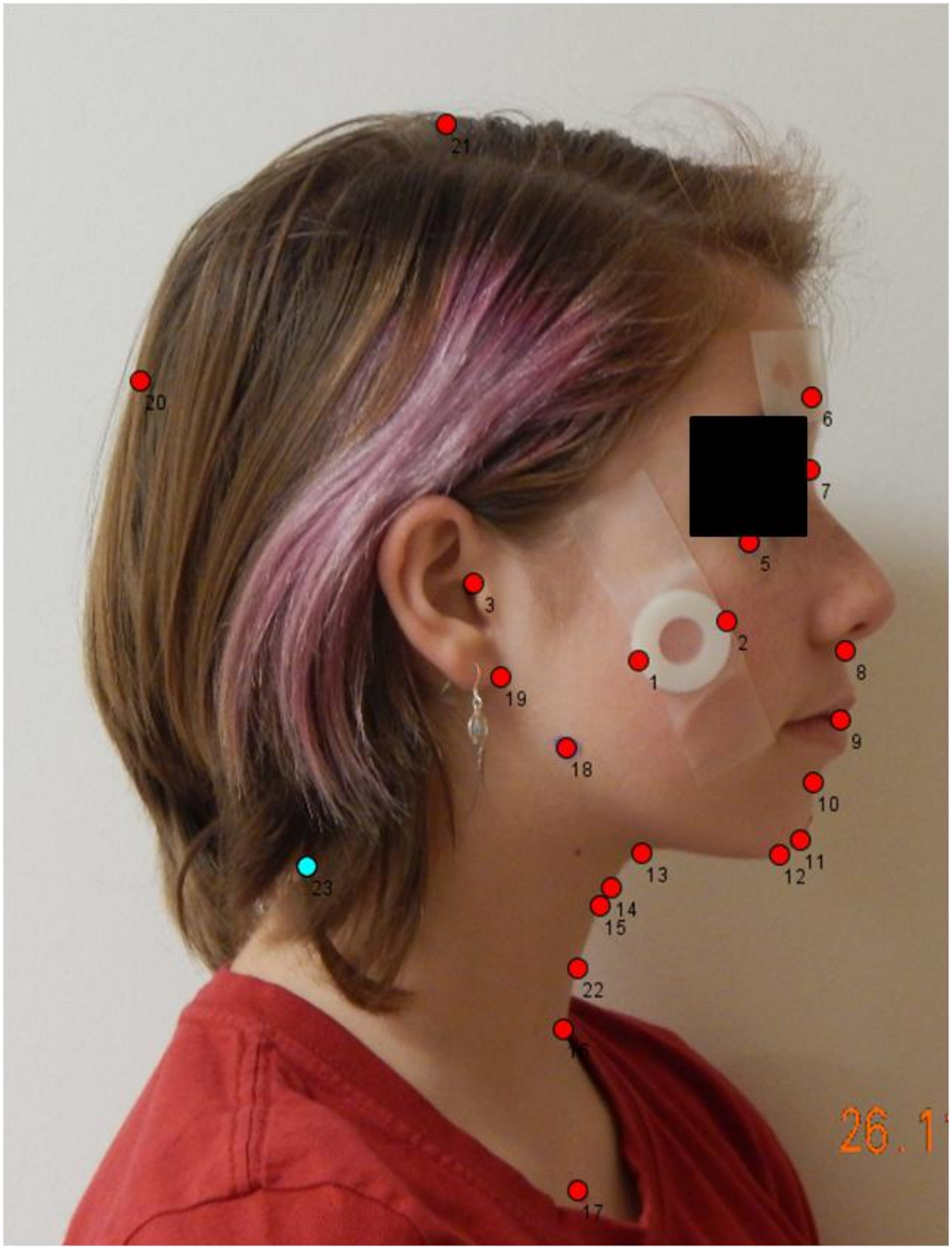



**Figure 2-2: An example standardized lateral photograph with landmarks digitally placed.**

**Table 2-7: Anatomical landmarks corresponding to frontal photograph from Figure 2-1.**
***Note R= right side of photograph, Left = left side of photograph.***

| Digital Point | Landmark | Abbreviation | Description |
|---|---|---|---|
| 1 | Washer Point 1 | *wp1* | 1st point on 3 cm washer that gives greatest diameter |
| 2 | Washer Point 2 | *wp2* | 2nd point on 3 cm washer that gives greatest diameter |
| 3 | Tragion Left | *tl* | Notch in external ear immediately superior to tragus |
| 4 | Tragion Right | *tr* | |
| 5 | Gonion Left | *gol* | Most inferior, posterior, and lateral point on angle of mandible |
| 6 | Gonion Right | *gor* | |
| 7 | Euryon Left | *eul* | Lateral point on skull marking the ends of the greatest transverse diameter |
| 8 | Euryon Right | *eur* | |
| 9 | Exocanthion Left | *exl* | Most lateral point on the outer commissure of the eye fissure |
| 10 | Exocanthion Right | *exr* | |
| 11 | Endocanthion Left | *enl* | Most medial point on the inner commmissure of the eye fissure |
| 12 | Endocanthion Right | *enr* | |
| 13 | Alare Left | *lal* | Most lateral point on the ala of the nose |
| 14 | Alare Right | *ral* | |
| 15 | Left neck | *lneck* | Most lateral point on the soft tissue neck |
| 16 | Right Left | *rneck* | |

**Table 2-8: Anatomical landmarks corresponding to profile photograph from Figure 2-2.**

| Digital Point | Landmark | Abbreviation | Description |
|---|---|---|---|
| 1 | Washer point 1 | *wp1* | 1st point on 3 cm washer that gives greatest diameter |
| 2 | Washer point 2 | *wp2* | 2nd point on 3 cm washer that gives greatest diameter |
| 3 | Tragion | *t* | Notch in external ear immediately superior to tragus |
| 4 | Exocanthion | *ex* | Most lateral point on the outer commissure of the eye fissure |
| 5 | Infraorbital rim | *sup* | The anterior edge of the bony orbit |
| 6 | Glabella | *g* | The most anterior portion of the forehead |
| 7 | Nasion | *n* | Junction of the forehead and nose |
| 8 | Sub-nasion | *sn* | The point of the angle between the nasal septum and upper lip |
| 9 | Stomion | *sto* | The median point of the oral slit when the lips are closed. |
| 10 | Sub-labiale | *sl* | The most posterior point in the labiomental fold |
| 11 | Gnathion | *gn* | The most anterior inferior point on the mandibular symphysis |
| 12 | Menton | *me* | The most inferior point on the mandibular symphysis |
| 13 | Cervical point | *cer* | Junction between the neck and the throat |
| 14 | Thyroid | *ty* | Most prominent portion of thyroid cartilage |
| 15 | Cricoid | *cr* | Most prominent portion of cricoid cartilage |
| 16 | Neck point | *np* | Most inferior posterior point on the anterior neck |
| 17 | Sternal notch | *ste* | Concavity between the neck and clavicles |
| 18 | Gonion | *go* | Most inferior, posterior, and lateral point on angle of mandible |
| 19 | Ramus | *ra* | The most posterior portion on the mandibular ramus inferior to the most inferior point of the lobulus auriculae |
| 20 | Opisthocranion | *op* | The most posterior point on the occipital portion of the skull |

| Digital Point | Landmark | Abbreviation | Description |
|---|---|---|---|
| 21 | Vertex | *V* | The most superior point on the parietal portion of the skull |
| 22 | Anterior neck | *aneck* | Most anterior point on the neck inferior to cricoid cartilage |
| 23 | Posterior neck | *pneck* | Most posterior point on the posterior neck |

**Table 2-9: List of linear, angular, area and volume measurements derived from standardized craniofacial photographs.** ***Measurements previously identified in the literature to be associated with OSAS are identified with an asterisk.***

| **Linear Measurements** | **Craniofacial Landmarks** |
|---|---|
| Upper face depth | *t-n* |
| Upper face depth – horizontal | *t-n (TH)* |
| Upper face depth – diagonal | *t-n (Diag)* |
| Mid face depth 1* | *t-sn* |
| Mid face depth 1 - horizontal | *t-sn (TH)* |
| Mid face depth 1 - diagonal | *t-sn (Diag)* |
| Mid face depth 2 | *t-pg* |
| Mid face depth 2 - horizontal | *t-pg (TH)* |
| Lower face depth 1 | *t-gn* |
| Lower face depth 1 - horizontal | *t-gn (TH)* |
| Lower face depth 1 - diagonal | *t-gn (Diag)* |
| Lower face depth 2 | *t-me* |
| Lower face depth 2 - horizontal | *t-me (TH)* |
| Lower face depth 2 - diagonal | *t-me (Diag)* |
| Total face height - vertical | *n-gn (TV)* |
| Total face height* | *n-gn* |
| Nose height - vertical | *n-sn (TV)* |
| Nose height | *n-sn* |
| Upper face height - vertical | *n-sto (TV)* |
| Upper face height | *n-sto* |
| Lower face height 1 - vertical | *sn-gn (TV)* |
| Lower face height 1* | *sn-gn* |

| **Linear Measurements** | **Craniofacial Landmarks** |
|---|---|
| Lower face height 2 - vertical | *sn-me (TV)* |
| Lower face height 2 | *sn-me* |
| Anterior mandibular height - vertical | *sto-gn (TV)* |
| Anterior mandibular height | *sto-gn* |
| Mandibular length 1* | *me-go* |
| Mandibular length 1 - diagonal | *me-go (Diag)* |
| Mandibular length 2* | *gn-go* |
| Mandibular length 2 - diagonal | *gn-go (Diag)* |
| Mandibular length 1 - horizontal | *me-t (TH)* |
| Posterior mandibular height - vertical | *t-go (TV)* |
| Posterior mandibular height | *t-go* |
| Lateral face height | *ex-go* |
| Maxillary mandibular depth 1 | *sn-me (TH)* |
| Maxillary mandibular depth 2 | *sn-gn (TH)* |
| Maxillary length - horizontal | *sn-t (TH)* |
| Tragion-cervical distance | *t-cer* |
| Tragion-cervical distance - diagonal | *t-cer (Diag)* |
| Tragion-thyroid distance | *t-thy* |
| Tragion-thyroid distance - diagonal | *t-thy (Diag)* |
| Tragion-cricoid distance | *t-cr* |
| Tragion-cricoid distance - diagonal | *t-cr (Diag)* |
| Thyromental distance - horizontal | *ty-me (TH)* |
| Thyromental distance | *ty-me* |
| Cricomental distance - horizontal | *cr-me (TH)* |
| Cricomental distance* | *cr-me* |

| **Linear Measurements** | **Craniofacial Landmarks** |
|---|---|
| Sternomental distance - horizontal | *ste-me (TH)* |
| Sternomental distance | *ste-me* |
| Sternomental distance - vertical | *ste-me (TV)* |
| Thyro-mandibular distance - vertical | *ty-go (TV)* |
| Thyro-mandibular distance | *ty-go* |
| Crico-mandibular distance - vertical | *cr-go (TV)* |
| Crico-mandibular distance | *cr-go* |
| Sterno-mandibular distance - vertical | *ste-go (TV)* |
| Sterno-mandibular distance* | *ste-go* |
| Sterno-tragion distance - vertical | *ste-t (TV)* |
| Cricomental space distance | *cer-cri-me* |
| Total craniofacial height | *v-gn* |
| Maximum cranial length | *g-op* |
| Neck depth* | *aneck-pneck* |
| Face width* | *tl-tr* |
| Mandible width | *gol-gor* |
| Maximum cranial width | *eul-eur* |
| Eye width | *exl-enl* |
| Intercanthal width | *enl-enr* |
| Biocular width | *exl-exr* |
| Nose width | *all-alr* |
| Neck width* | *nl-nr* |
| Neck Perimeter | *l-r-a-p-neck* |
| Lower facial height to total face height* | *n-gn/sn-gn* |
| **Angular Measurements** | |

| | |
|---|---|
| Maxillary depth angle | *t-n-sn* |
| Mandibular depth 1 angle | *t-n-pg* |
| Mandibular depth 2 angle | *t-n-gn* |
| Mandibular depth 3 angle | *t-n-me* |
| Maxillary-mandibular relationship angle* | *sn-n-pg* |
| Maxillary-mandibular relationship 2 angle | *sn-me-TH* |
| Maxillary-mandibular relationship 3 angle | *sn-me-FP* |
| Mandibular-nasion 1 angle* | *go-n-gn* |
| Mandibular-nasion 2 angle | *go-n-me* |
| Mandibular-subnasion 1 angle* | *go-sn-gn* |
| Mandibular-subnasion 2 angle | *go-sn-me* |
| Natural Head position angle | *t-sup-TH* |
| Head base Inclination angle | *t-n-TH* |
| Mandibular plane 1 angle* | *go-me-TH* |
| Mandibular plane 2 angle* | *go-gn-TH* |
| Mandibular angle* | *t-go-gn* |
| Facial axis angle | *n-t and go-gn* |
| Thyromental angle* | *pc-ty-me* |
| Cervicomental angle* | *np-cer-me* |
| Mandibular width-length angle* | *gor-me-gol* |
| Face width-mid face depth angle* | *tr-sn-tl* |
| Face width-lower face depth angle | *tr-me-tl* |
| **Area Measurements** | |
| Cricomental space area (sag) | *cer-cri-me* |
| Thyromental space area (sag) | *cer-thy-me* |
| Anterior neck space area (sag)* | *ste-cri-cer-me* |

| | |
|---|---|
| Submandibular soft tissue area (sag) | *cer-me-go* |
| Anterior neck soft tissue area (sag) | *cer-go-cri* |
| Total anterior neck soft tissue area (sag) | *go-me-cer-cr* |
| Posterior neck soft tissue area (sag) | *cri-go-pneck* |
| Total neck soft tissue area (sag) | *go-me-cer-cr-pneck* |
| Cranial base-maxillary triangle area (sag) | *t-n-sn* |
| Maxillary triangle area (sag) | *t-sn-me* |
| Mandibular triangle area (sag)* | *t-go-me* |
| Maxillary-mandibular box area (sag) | *t-sn-me-go* |
| Mandibular pharyngeal triangle area (sag) | *t-TV-TH-me* |
| Maxillary-mandibular pharyngeal box area (sag) | *t-TV-TH-me-sn* |
| Tragion-neck area 1 (sag) | *t-me-cr* |
| Tragion-neck area 2 (sag) | *t-gn-cr* |
| Mandibular cricoid area (ax) | *go-go-cri* |
| Cranial base triangle area (ax) | *tl-n-tr* |
| Cranial base area 1 (ax) | *tl-exl-exr-tr* |
| Cranial base area 2 (ax) | *tl-exl-n-exr-tr* |
| Maxillary triangle area (ax) | *tl-sn-tr* |
| Mandibular triangle area (ax) | *gol-me-gor* |

## 2.6 Overnight Polysomnography

An overnight, in-laboratory, level one PSG was conducted for every child by a trained and certified respiratory technologists. Each study lasted 8-10 hours, and included overnight monitoring of an electroencephalogram, electro-oculogram, electro-cardiogram, chin and anterior tibial electromyogram, nasal pressure transducer, oral thermistor, a snore sensor, respiratory inductive plethysmography, pulse oximetry, and end-tidal capnography, as well as

continuous video monitoring. The studies were scored by one of four sleep technicians at BCCH, using the XLTEC (*Oakville, Ontario*) data acquisition and analysis system, according to the American Academy of Sleep Medicine manual.[43]

Information obtained from each polysomnography included: sleep onset latency, REM onset latency, total sleep time, sleep efficiency, time spent in each sleep stage (percentage), and number and classification of arousals and snoring. Respiratory events included obstructive apneas and hypopneas, mixed apneas as well as central apneas and hypopneas.

The diagnosis and severity of OSA in children was based on the frequency of obstructive apneas, obstructive hypopneas, mixed apneas, central apneas and central hypopneas per hour during sleep as well as gas exchange characteristics. These were recorded as the obstructive apnea-hypopnea index (OAHI), central apnea-hypopnea index, baseline mean oxygen saturation and nocturnal hypoventilation. The severity of OSA was expressed using the obstructive apnea – hypopnea index (AHI), which was the sum of obstructive apneas and hypopneas per hour of sleep. An AHI of 2 events or more per hour was considered abnormal for this study.

The PSG reports were assessed and approved by a pediatric sleep physician (DW). The staff performing, scoring and approving the PSG study and report were blinded to the results from the questionnaires, orthodontic examinations, and photographs.

### 2.7 Statistical Analysis

The data contained a mixture of categorical and continuous variables. Categorical variables were analyzed using the Pearson chi-square test and Fisher's exact test. Continuous variables from the

clinical examinations and from the standardized photographs were analyzed using Student's *t*-test or the Mann-Whitney U-test as appropriate. Finally, Pearson correlation coefficients were used to assess the strength of any linear relationships between altered craniofacial morphology and pediatric OSAS. All statistical analysis was performed using SPSS (Chicago, IL).

### 2.8 Analysis of Error

For the clinical portion of the assessment, both examiners (EA and MH) were calibrated by using the above clinical examination forms to assess a series of intra and extra-oral photographs from 10 individuals who were not part of the study. Their findings were evaluated by an experienced orthodontist (BP) who provided feedback and correction as needed. Landmark identification from the calibrated photographs was performed by a single examiner (EA) with training provided by the University of Sydney. To assess intra-examiner reliability of landmark place, the photographs of 20 randomly selected participants were re-digitized 1 week apart.

# Chapter 3: Results

## 3.1 Error Analysis

Both co-efficient of variation (CV) and intraclass correlation coefficients (ICC's) were calculated for all of the measurements from the standardized craniofacial photographs by re-digitizing the frontal and lateral photograph of 20 randomly selected participants one week apart. Intra-examiner reliability was generally high, with an average ICC value of 0.93. However, the measurements of neck perimeter (ICC = 0.77), and cricomental space difference (ICC = 0.58) had the lowest reproducibility. The average CV for all measurements was 3.8, which was also affected by cricomental space having a low reproducibility (CV = 19.4), as well as the measure of natural head position angle (CV = 17.6). Due to logistical constraints at the hospital, and also due to the sleep study being a one-time evaluation, it was not possible to re-examine the same patient twice to assess the reproducibility of clinical measurements.

## 3.2 Sample

During the data collection period from December 11, 2014 to December 16, 2015, 102 children participated in the study. 5 children were excluded based on failing to meet the inclusion criteria (1 participant did not successfully complete the PSG, while 4 children had undergone previous treatment for OSAS). 32 participants were excluded from primary analysis due to having a syndrome or sequence with craniofacial morphological implications, and/or a syndrome that would pre-dispose them to be at an increased risk for OSAS. The final sample therefore consisted of 65 children, with a mean age of 8.9 years (± 3.1 y), with a range from 4-16 years. 36 participants (55.4%) were male, while 29 participants (44.6%) were female. The majority of the 65 participants, 51 (78.5%) were either of Caucasian descent, or were of another ethnicity with

craniofacial features that were deemed to be relatively similar to Caucasian derived normative values, while 8 children (12.3%) were of Asian descent, and 5 children (7.7%) were of African descent.

When divided on the basis of the presence and/or severity of obstructive sleep apnea (as diagnosed via overnight PSG), 38 children were diagnosed to have OSAS (AHI $\geq$ 2), with 27 children not having sleep apnea (AHI <2). When the 27 children without sleep apnea were further analyzed, 9 children were deemed to be truly asymptomatic as demonstrated by an AHI under 2 events/hour, along with a reported quiet or hardly noticeable snore that occurs infrequently (Spruyt & Gozal[49] Q5 score = 1; Q6 score $\leq$ 3). The other 18 children without OSAS were deemed to be snorers based on their Spruyt & Gozal[49] questionnaire results. When the 38 children with sleep apnea were examined on the severity of their disease, it was found that 21 children had mild-moderate OSAS (AHI 2-5), while 17 children had severe OSAS (AHI >5). Table 3-1 below summarizes the demographic distribution of participants based on their severity of sleep disordered breathing. No significant difference was found in the prevalence of OSAS by whether the total household income was above or below the regional median, however, only 33/65 participants completed the SES. There was a trend in the data for OSAS to vary by ethnicity, as 7/9 of the Asian children were deemed to have sleep apnea. However, due to the small number of children of Asian and African descent, testing for statistical difference by ethnicity was not performed.

**Table 3-1: Demographic distribution of the 65 children in the non-OSA and OSA groups**

| | Asymptomatic Controls *(n = 9)* | SDB without OSAS *(n=18)* | **Total Non-OSAS *(n=27)*** | Mild-moderate OSAS *(n=21)* | Severe OSAS *(n=17)* | **Total OSAS *(n=38)*** |
|---|---|---|---|---|---|---|
| Age (SD) | 8.5 (2.9) | 9.1 (3.1) | **8.9 (3.0)** | 8.7 (2.8) | 10.0 (3.4) | **8.9 (3.2)** |
| Male gender (%) | 5 (55.6) | 7 (39.8) | **12 (44.4)** | 12 (57.1) | 12 (70.6) | **24 (63.2)** |
| Caucasian or craniofacially similar *(n=51)* | 7 (77.8) | 15 (83.3) | **22 (81.5)** | 17 (81.0) | 12 (70.6) | **29 (76.3)** |
| Asian *(n= 9)* | 1 (11.1) | 1 (5.6) | **2 (7.4)** | 3 (14.3) | 4 (23.5) | **7 (18.4)** |
| African *(n= 5)* | 1 (11.1) | 2 (11.1) | **3(11.1)** | 1 (4.8) | 1 (5.9) | **2 (5.3)** |

### 3.3 Sample Analysis

Of the 27 children without sleep apnea, 12 were male, 15 were female. Of the 38 children with OSAS, 24 were male and 14 were female. As this difference was not statistically significant (chi-square, $p > 0.05$), the effect of gender on craniofacial morphology was also examined for key clinical and photographic variables. Clinical data were assessed using chi-square, while photographic data were assess using Student's t-test. Of the measurements (Table 3-2), only mandibular triangle area (*tragus-gonion-mentum*) showed a statistically significant difference with males having a larger area (17.0 $cm^2$ vs. 14.8 $cm^2$). As this was the only difference, it was determined that gender did not have an effect on craniofacial morphology in this sample, allowing for males and females to be grouped together for the remainder of the analysis.

**Table 3-2: Effect of gender on OSA, obesity and craniofacial morphology**

| | Males *(n=37)* | Females *(n=28)* | *p* |
|---|---|---|---|
| OSA | 24 | 14 | NS |
| Obese | 12 | 7 | NS |
| Tonsillar Size ≥ 3 | 9 | 11 | NS |
| Increased LFH | 4 | 4 | NS |
| Decreased LFH | 4 | 5 | NS |
| Convex profile | 8 | 6 | NS |
| Dolicocephalic | 6 | 6 | NS |
| Cl II molar | 6 | 9 | NS |
| Retrognathic Mandible | 8 | 8 | NS |
| Retrognathic Maxilla | 2 | 1 | NS |
| OB > 50% | 9 | 6 | NS |
| OJ > 5mm | 4 | 4 | NS |
| Anterior open bite | 3 | 1 | NS |
| Anterior x-bite | 4 | 4 | NS |
| Posterior x-bite | 5 | 4 | NS |
| Mouth breather | 27 | 19 | NS |
| V-shaped upper arch | 6 | 6 | NS |
| Crowding >3 mm | 23 | 17 | NS |
| Spruyt Gonzales score ≥ 2.72 | 17 | 12 | NS |
| Non-Caucasian ethnicity | 8 | 5 | NS |
| Mean intermolar width (mm) | 36.6 | 34.4 | NS |
| Mean intercanine width (mm) | 30.9 | 30.7 | NS |
| Mean mid-face depth (cm) | 11.6 | 11.1 | NS |
| Mean total face height (cm) | 11.4 | 11.2 | NS |
| Mean mandibular length 1 (cm*; me-go*) | 7.3 | 7.3 | NS |
| Mean mandibular length 2 (cm; *gn-go*) | 7.7 | 7.7 | NS |
| Mean cricomental distance (cm) | 5.9 | 6.2 | NS |

| | Males *(n=37)* | Females *(n=28)* | *p* |
|---|---|---|---|
| Mean sterno-mandibular distance (cm) | 9.3 | 9.4 | NS |
| Mean maxillary-mandibular angle (°) | 9.3 | 9.2 | NS |
| Mean mandibular-nasion angle (°) | 38.9 | 37.5 | NS |
| Mean mandibular subnasion angle (°) | 52.3 | 54.1 | NS |
| Mean mandibular plane angle 1 (°; *TH-go-gn*) | 22.3 | 24.1 | NS |
| Mean mandibular plane angle 2 (°;*TH-go-me*) | 16.6 | 19.3 | NS |
| Mean mandibular angle (°) | 119.6 | 123.9 | NS |
| Mean thyromental angle (°) | 126.2 | 127 | NS |
| Mean cervicomental angle (°) | 126.4 | 128.9 | NS |
| Mean mandibular width-length angle (°) | 73.1 | 71.2 | NS |
| Mean face width-mid face depth angle (°) | 62.1 | 62.9 | NS |
| Mean anterior neck space area ($cm^2$) | 13.9 | 15.0 | NS |
| Mean mandibular triangle area ($cm^2$) | 17.0 | 14.8 | 0.03 |

Because a 12 year age range separated the youngest of children in the study from the oldest of children, the effect of age was next evaluated in regard to OSAS. The sample was divided into a younger age group (age 4-11) and an older age group (age 12-16), in order to examine the effect of age on craniofacial morphology. Again, clinical data were assessed using chi-square, while photographic data were assessed using Student's t-test. No significant differences were found in the number of children in each age group with either OSAS or obesity (Figure 3-1). As expected due to growth, most linear and area craniofacial measurements for the older children were significantly larger (Table 3-3). For angular measurements, only the face width-mid face depth angle was significantly increased (2.6°) in younger children. As expected, older children had significantly less tonsillar hypertrophy than younger children (2 vs. 18; $p = 0.05$). Because these were the only significant difference between the two age groups, it was deemed appropriate to group the age groups together for all further analysis that involved angular measurements, and to separate the two age groups for linear or area measurements.

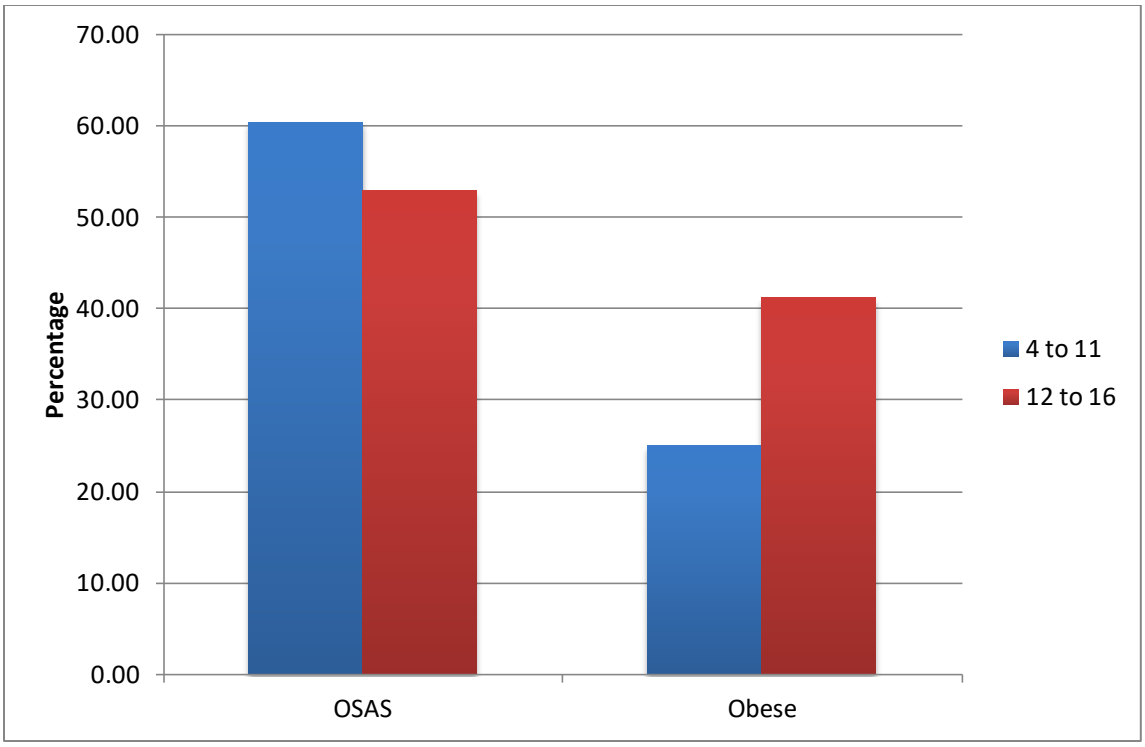



**Figure 3-1: Comparison of the percentage of children in the younger and older age groups with OSAS and obesity.** ***No differences were found to be statistically significant*****.**

**Table 3-3: Effect of age on OSA, obesity and craniofacial morphology**

| | Age 4-11 *(n=48)* | Age 12-16 *(n = 17)* | *p* |
|---|---|---|---|
| OSAS | 29 | 9 | NS |
| Obese | 12 | 7 | NS |
| Tonsillar size ≥ 3 | 18 | 2 | 0.05 |
| Increased LFH | 7 | 1 | NS |
| Decreased LFH | 5 | 4 | NS |
| Convex profile | 9 | 5 | NS |
| Dolicocephalic | 7 | 5 | NS |
| Cl II molar | 11 | 4 | NS |
| Retrognathic Mandible | 13 | 4 | NS |
| Retrognathic Maxilla | 2 | 1 | NS |
| OB > 50% | 13 | 2 | NS |
| OJ > 5mm | 5 | 3 | NS |
| Anterior open bite | 3 | 1 | NS |
| Anterior x-bite | 6 | 2 | NS |
| Posterior x-bite | 6 | 3 | NS |
| Mouth breather | 27 | 19 | NS |
| V-shaped upper arch | 10 | 2 | NS |
| Crowding >3 mm | 9 | 4 | NS |
| Spruyt Gonzales score ≥ 2.72 | 24 | 5 | NS |
| Non-Caucasian ethnicity | 8 | 5 | NS |
| Mean intermolar width (mm) | 34.7 | 38.2 | NS |
| Mean intercanine width (mm) | 29.0 | 35.9 | <0.001 |
| Mean mid-face depth (cm) | 11.1 | 12.4 | <0.001 |
| Mean total face height (cm) | 11.0 | 12.3 | <0.001 |
| Mean mandibular length 1 (cm; *me-go*) | 7.0 | 8.0 | 0.003 |
| Mean mandibular length 2 (cm; *gn-go*) | 7.4 | 8.4 | 0.004 |
| Mean cricomental distance (cm) | 5.7 | 6.8 | 0.001 |

| | Age 4-11 *(n=48)* | Age 12-16 *(n = 17)* | *p* |
|---|---|---|---|
| Mean sterno-mandibular distance (cm) | 8.9 | 10.6 | 0.002 |
| Mean maxillary-mandibular angle (°) | 9.1 | 9.8 | NS |
| Mean mandibular-nasion angle (°) | 37.8 | 39.0 | NS |
| Mean mandibular subnasion angle (°) | 52.7 | 54.4 | NS |
| Mean mandibular plane angle 1 (*TH-go-gn*) (°) | 21.3 | 23.8 | NS |
| Mean mandibular plane angle 2 (*TH-go-me*) (°) | 18.2 | 16.8 | NS |
| Mean mandibular angle (°) | 122.0 | 120.1 | NS |
| Mean thyromental angle (°) | 125.6 | 129.1 | NS |
| Mean cervicomental angle (°) | 126.4 | 130.4 | NS |
| Mean mandibular width-length angle (°) | 73.0 | 70.0 | NS |
| Mean face width-mid face depth angle (°) | 63.1 | 60.5 | 0.02 |
| Mean anterior neck space area ($cm^2$) | 13.2 | 17.9 | 0.006 |
| Mean mandibular triangle area ($cm^2$) | 14.7 | 19.9 | 0.001 |

The effect of obesity on OSAS and craniofacial morphology was evaluated next. Surprisingly, obese children were found to have a lower prevalence of OSAS (10/19, 52.6%) than non-obese children (28/44; 63.6%), however this difference was not significant. Obese children were found to have significantly different measurements for certain craniofacial measurements such as mid-face depth, face height, mandibular plane angle, and others (Table 3-4). Combining these differences with the findings from previous research,[39] obese children were subsequently excluded from further analysis. As 2 participants did not have their height and/or weight recorded, it was not possible to calculate their BMI, leaving 44 non-obese children for the remainder of the analysis.

**Table 3-4: Effect of obesity on OSAS and craniofacial morphology**

| | Obese *(n = 19)* | Non-obese *(n = 44)* | *p* |
|---|---|---|---|
| OSAS | 10 | 28 | NS |
| Tonsillar size ≥ 3 | 7 | 13 | NS |
| Increased LFH | 3 | 5 | NS |
| Decreased LFH | 2 | 7 | NS |
| Convex profile | 3 | 11 | NS |
| Dolicocephalic | 4 | 7 | NS |
| Cl II molar *(including subdivision)* | 5 | 11 | NS |
| Retrognathic Mandible | 6 | 10 | NS |
| Retrognathic Maxilla | 1 | 2 | NS |
| OB > 50% | 2 | 13 | NS |
| OJ > 5mm | 5 | 3 | NS |
| Anterior open bite | 3 | 1 | NS |
| Anterior x-bite | 2 | 5 | NS |
| Posterior x-bite | 6 | 3 | NS |
| Mouth breather | 14 | 32 | NS |
| V-shaped upper arch | 2 | 10 | NS |
| Crowding >3 mm | 2 | 11 | NS |
| Spruyt Gonzales score ≥ 2.72 | 10 | 19 | NS |
| Non-Caucasian ethnicity | 3 | 10 | NS |
| Mean intermolar width (mm) | 35.6 | 35.3 | NS |
| Mean intercanine width (mm) | 31.4 | 30.2 | NS |
| Mean mid-face depth (cm) | 12.0 | 11.1 | <0.01 |
| Mean total face height (cm) | 11.7 | 12.0 | 0.02 |
| Mean mandibular length 1 (cm; *me-go*) | 7.7 | 7.0 | NS |
| Mean mandibular length 2 (cm; *gn-go*) | 8.1 | 7.5 | 0.05 |
| Mean cricomental distance (cm) | 6.7 | 5.6 | <0.01 |
| Mean sterno-mandibular distance (cm) | 9.0 | 9.5 | NS |

| | Obese *(n = 19)* | Non-obese *(n = 44)* | *p* |
|---|---|---|---|
| Mean maxillary-mandibular angle (°) | 9.3 | 9.5 | NS |
| Mean mandibular-nasion angle (°) | 38.4 | 37.8 | NS |
| Mean mandibular subnasion angle (°) | 53.4 | 52.7 | NS |
| Mean mandibular plane angle 1 (*TH-go-gn*) (°) | 19.3 | 24.3 | 0.02 |
| Mean mandibular plane angle 2 (*TH-go-me*) (°) | 14.2 | 18.9 | 0.02 |
| Mean mandibular angle (°) | 120.8 | 121.5 | NS |
| Mean thyromental angle (°) | 123.5 | 127.9 | NS |
| Mean cervicomental angle (°) | 129.4 | 126.4 | NS |
| Mean mandibular width-length angle (°) | 71.5 | 72.6 | NS |
| Mean face width-mid face depth angle (°) | 61.7 | 62.7 | NS |
| Mean anterior neck space area ($cm^2$) | 13.6 | 14.6 | NS |
| Mean mandibular triangle area ($cm^2$) | 18.7 | 14.9 | 0.01 |

### 3.4 Clinical Comparison of OSAS vs. non-OSAS Children

Of the 44 non-obese participants, 6 (13.6%) were found to be asymptomatic controls, 10 (36.4%) had SDB without OSAS, 16 (36.4%) had mild-moderate OSAS, and 12 (27.3%) had severe OSAS. Demographic information on the final sample is shown in Table 3-5. In order to attain sufficient power, the children with SDB were grouped together with the asymptomatic control children. The measurements from the clinical examination were then compared (Table 3-6). In order to assess whether children with more severe disease were different from the children without OSAS, the 12 children with severe OSAS were also compared separately. While no statistically significant differences between the two groups were found, there was a trend in the data for children with OSAS to have an increased prevalence of mandibular arch crowding greater than 3 mm (18.7% vs. 35.7%). When the children with severe disease were compared to the children without OSAS, an increased prevalence of deep-bite malocclusions (defined as overbite > 50%) was found in the children with severe OSAS (41.6% vs. 25.0 %), although this difference was not statistically significant. Graphically, the differences between the groups are displayed in Figure 3-1.

**Table 3-5: Demographic distribution of children in control and OSA group**

| | Asymptomatic Controls *(n = 6)* | SDB without OSAS *(n=10)* | **Total Non-OSAS *(n=16)*** | Mild-moderate OSAS *(n=16)* | Severe OSAS *(n=12)* | **Total OSAS *(n=28)*** |
|---|---|---|---|---|---|---|
| Age (SD) | 8.7 (2.6) | 8.1 (3.2) | **8.3 (2.9)** | 8.1 (2.8) | 9.9 (3.7) | **8.9 (3.3)** |
| Male Gender (%) | 5 (83.3) | 3 (30.0) | **8 (50.0)** | 8 (50.0) | 8 (66.7) | **16 (57.1)** |
| Caucasian or craniofacially similar *(n=34)* | 5 (83.3) | 9 (90.0) | **14 (87.5)** | 12 (75.0) | 8 (75.0) | **20 (71.4)** |
| Asian *(n= 7)* | 0 | 1 | **1 (6.2)** | 3 (18.7) | 3 (25.0) | **6 (21.4)** |
| African *(n= 3)* | 1 | 0 | **1 (6.2)** | 1 (6.2) | 1 (8.3) | **2 (7.1)** |

**Table 3-6: Clinical variables of children without OSAS compared to children with OSAS**

| | | **Total non-OSAS *(n=16)*** | **Total OSAS *(n=28)*** | **Severe OSAS *(n=12)*** | ***p*** |
|---|---|---|---|---|---|
| **Anterior-Posterior Measurements** | Convex Profile | 6 (37.5%) | 5 (17.8%) | 3 (25.0%) | NS |
| | Retrognathic Mandible | 3 (18.7%) | 7 (25.0%) | 3 (25.0%) | NS |
| | Anterior Crossbite | 1 (6.3%) | 4 (14.3%) | 2 (16.6%) | NS |
| | Overjet ≥ 5mm | 2 (12.5%) | 3 (10.7%) | 2 (16.6%) | NS |
| | Class II Molar Relationship | 3 (18.7%) | 8 (28.6%) | 3 (25.0%) | NS |
| | Class II Canine Relationship | 4 (25.0%) | 9 (32.1%) | 3 (25.0%) | NS |
| **Vertical Measurements** | Dolicocephalic Facial Pattern | 3 (18.7%) | 4 (25.0%) | 1 (8.3%) | NS |
| | Increased Lower Face Height | 3 (18.7%) | 2 (7.1%) | 1 (8.3%) | NS |
| | Anterior open bite | 0 (0%) | 1 (3.6%) | 0 (0%) | NS |
| | Gingival display on smile ≥ 4mm | 1 (6.3%) | 3 (10.7%) | 1 (8.3%) | NS |
| | History of mouth breathing | 11 (68.8%) | 21 (75.0%) | 9 (75.0%) | NS |
| | Overbite ≥ 50% | 4 (25.0%) | 9 (32.1%) | 5 (41.6%) | NS |
| **Transverse Measurements** | Posterior Crossbite | 2 (12.5%) | 4 (14.3%) | 3 (25.0%) | NS |
| | Narrow Palate | 3 (18.8%) | 6 (21.4%) | 1 (8.3%) | NS |
| | V-shaped upper arch | 3 (18.8%) | 7 (25.0%) | 3 (25.0%) | NS |
| | Maxillary Intermolar width (mm) | 36.2 mm | 34.7 mm | 37.2 mm | NS |
| | CR/CO shift | 1 (6.3%) | 2 (7.1%) | 1 (8.3%) | NS |
| **Perimeter Measurements** | Upper arch crowding > 3mm | 3 (12.5%) | 7 (21.4%) | 3 (25.0%) | NS |
| | Lower arch crowding > 3mm | 3 (18.7%) | 10 (35.7%) | 2 (16.6%) | NS |

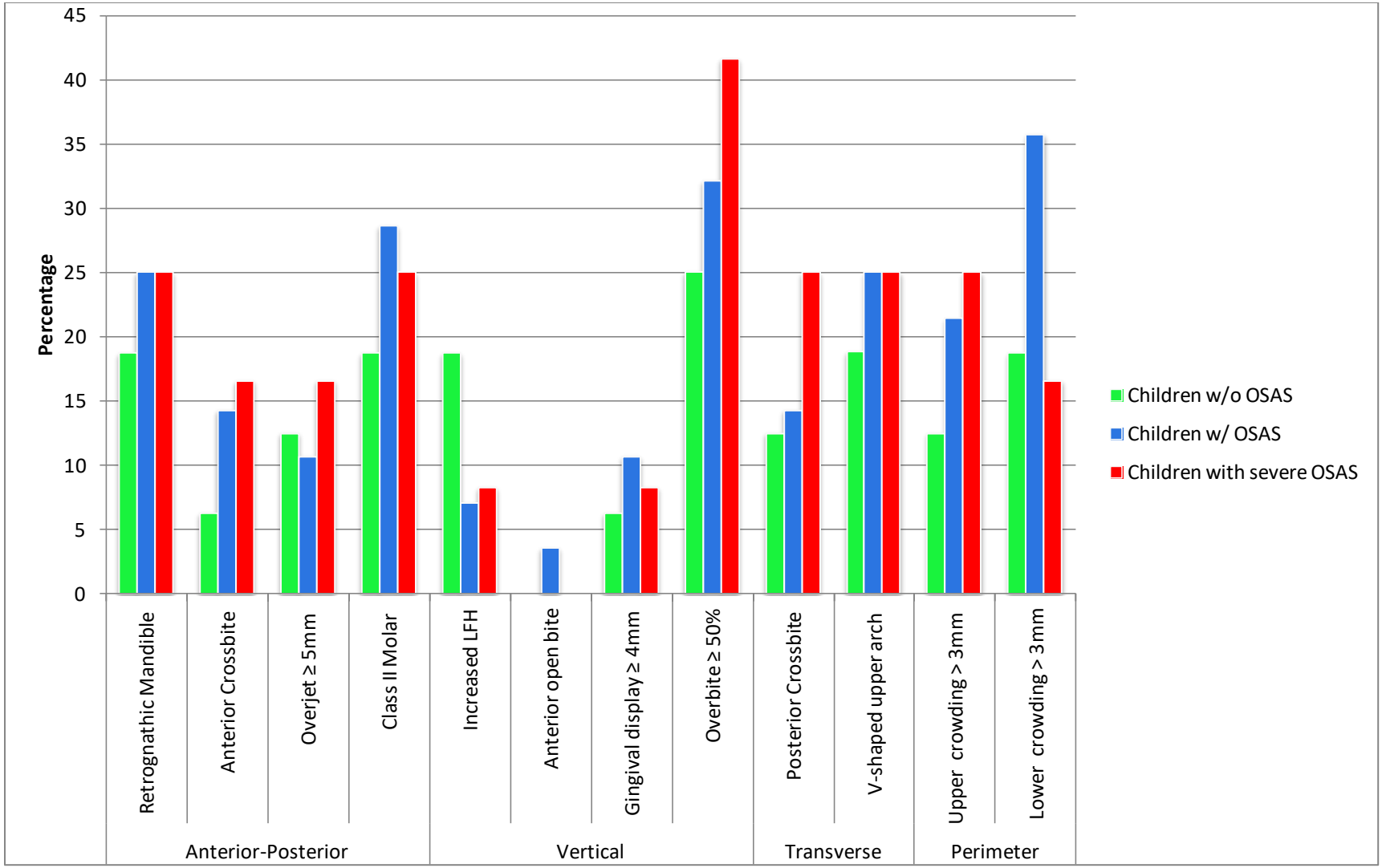



**Figure 3-2: Comparison of the percentage of children with and without OSAS on clinical measurements.** ***No differences were found to be statistically significant.***

### 3.5 Photographic Comparison of OSAS vs. non-OSAS

The 43 available standardized photographs (1 participant declined to participate in the photographic portion of the study) were then compared, it was found that of the 9 older children (aged 12-16), 6 children (66.7%) had OSAS, while 3 children did not. Of the 34 younger children (aged 4-11), 21 (61.8%) had OSAS, while 13 did not. To better understand which craniofacial measurements from the photographs may be associated with OSAS, photographic variables were then compared on the presence of OSAS, with the older children and younger children analyzed separately for all linear and area measurements. On average, children with OSAS tended to have a significantly more obtuse cervicomental angle (Figure 3-3) compared to the children without OSAS (129.2° vs. 121.5°, $p \leq 0.05$), showing an average increase of 7.7°. No other significant differences were found in angular measurements (Table 3-7). For the linear measurements, older children with OSAS showed significantly longer total facial heights, greater mandibular retrognathism relative to the true horizontal, and wider set eyes. For the younger children with OSAS, they were more likely to have an increase in lateral facial height (Figure 3-4) when compared to the children without OSAS (t-test, 9.6 cm vs. 9.0 cm, $p = 0.04$).

**Table 3-7: Angular craniofacial measurements from standardized photographs comparing non-obese children with and without OSAS**

| | **Non-OSAS** *(n=16)* | **OSAS** *(n=27)* | ***p*** |
|---|---|---|---|
| Mean maxillary-mandibular angle (°) | 9.7 | 9.3 | NS |
| Mean mandibular-nasion angle (°) | 37.8 | 37.9 | NS |
| Mean mandibular subnasion angle (°) | 52.5 | 52.8 | NS |
| Mean mandibular plane angle 1 (°; *TH-go-gn*) | 26.1 | 23.3 | NS |
| Mean mandibular plane angle 2 (°;*TH-go-me*) | 20.5 | 18.0 | NS |
| Mean mandibular angle (°) | 122.8 | 120.8 | NS |
| Mean thyromental angle (°) | 125.4 | 129.4 | 0.09 |
| Mean cervicomental angle (°) | 121.5 | 129.2 | 0.05 |
| Mean mandibular width-length angle (°) | 74.3 | 71.6 | NS |
| Mean face width-mid face depth angle (°) | 62.7 | 62.7 | NS |

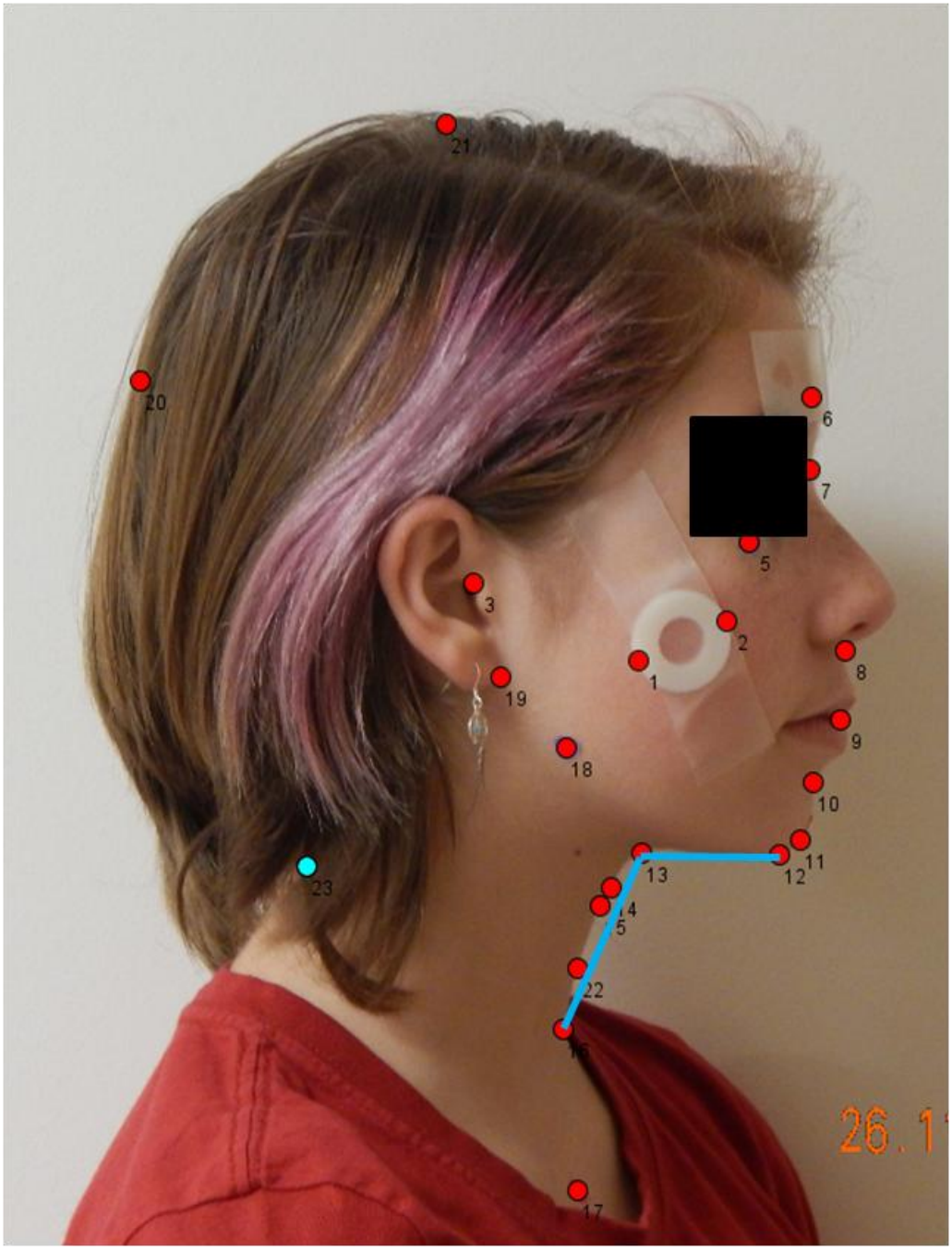



**Figure 3-3: Visual representation of the cervicomental angle, which was found to be increased in children with OSAS.**

**Table 3-8: Linear and area craniofacial measurements from standardized photographs comparing non-obese children with and without OSAS aged 12-16**

| | **Non-OSAS** *(n=3)* | **OSAS** *(n=6)* | ***p*** |
|---|---|---|---|
| Mean mid-face depth (cm) | 12.1 | 11.9 | NS |
| Mean total face height (cm) | 11.2 | 12.2 | 0.02 |
| Maxillary-mandibular depth 2 (cm) | 2.1 | 1.1 | 0.04 |
| Mean mandibular length 1 (cm*; me-go*) | 8.0 | 7.7 | NS |
| Mean mandibular length 2 (cm; *gn-go*) | 8.3 | 8.1 | NS |
| Mean cricomental distance (cm) | 6.1 | 6.2 | NS |
| Mean sterno-mandibular distance (cm) | 10.6 | 10.0 | NS |
| Intercanthal width (cm) | 3.2 | 3.7 | 0.04 |
| Lateral face height (cm) | 10.3 | 10.5 | NS |
| Mean anterior neck space area ($cm^2$) | 16.8 | 14.3 | NS |
| Mean mandibular triangle area ($cm^2$) | 20.3 | 20.3 | NS |

**Table 3-9: Linear and area craniofacial measurements from standardized photographs comparing non-obese children with and without OSAS aged 4-11**

| | **Non-OSAS** *(n=13)* | **OSAS** *(n=21)* | ***p*** |
|---|---|---|---|
| Mean mid-face depth (cm) | 10.7 | 11.0 | NS |
| Mean total face height (cm) | 10.7 | 10.9 | NS |
| Maxillary-mandibular depth 2 (cm) | 1.5 | 1.5 | NS |
| Mean mandibular length 1 (cm*; me-go*) | 6.6 | 7.0 | NS |
| Mean mandibular length 2 (cm; *gn-go*) | 7.0 | 7.4 | NS |
| Mean cricomental distance (cm) | 5.3 | 5.6 | NS |
| Mean sterno-mandibular distance (cm) | 7.9 | 8.7 | NS |
| Intercanthal width (cm) | 3.2 | 3.3 | NS |
| Lateral face height (cm) | 9.0 | 9.6 | 0.04 |
| Mean anterior neck space area ($cm^2$) | 13.8 | 14.5 | NS |
| Mean mandibular triangle area ($cm^2$) | 11.9 | 14.6 | NS |

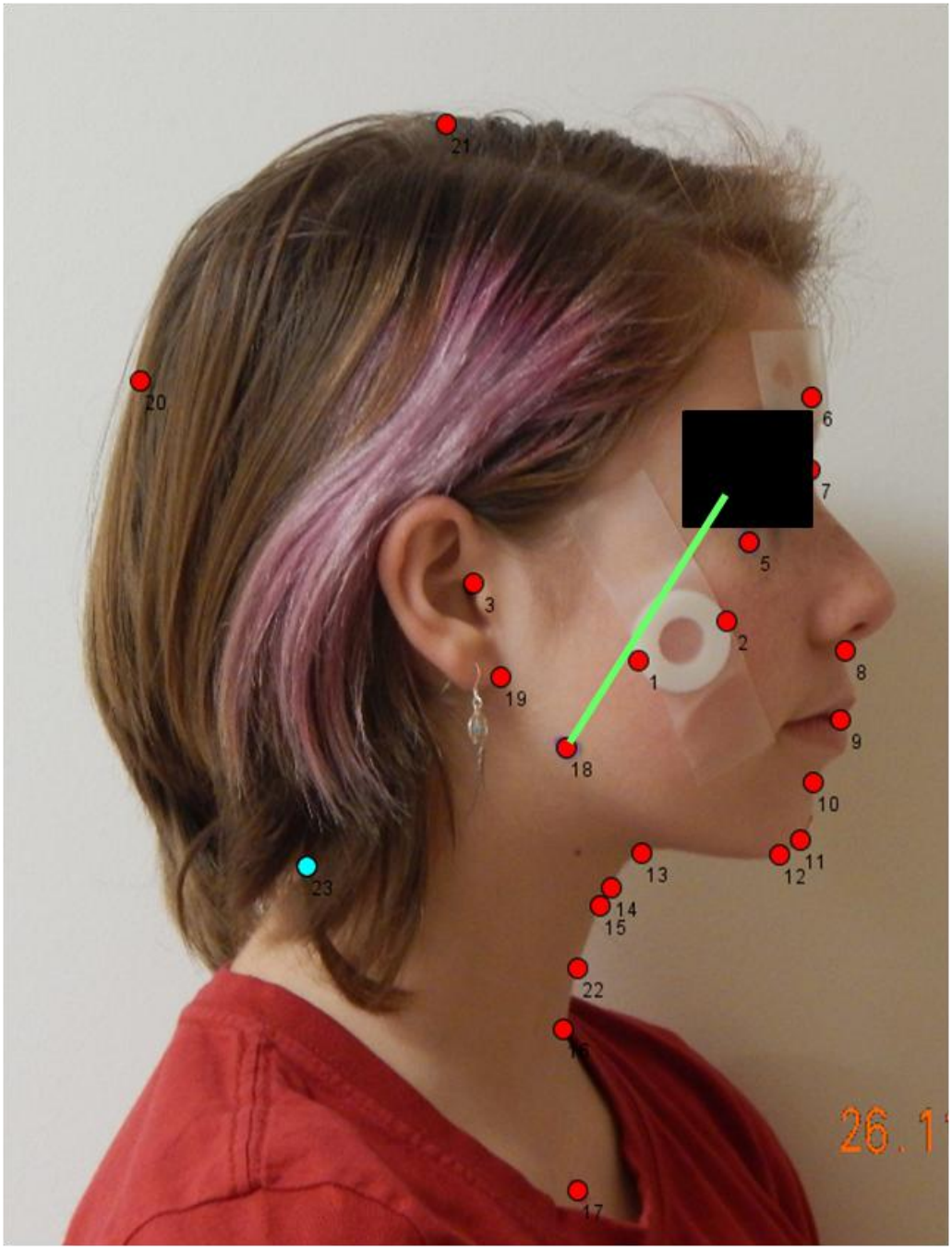



**Figure 3-4: Visual representation of the linear measure of lateral face height, which was found to be increased in children with OSAS.**

Linear relationships were then examined to see which craniofacial measurements were correlated with PSG data. As shown below in Table 3-9, when AHI, mean heart rate (HR), and mean oxygen saturation ($O_2$ sat) were correlated with variables previously associated with OSAS, several variables achieved statistical significance. Of the angular measurements, the cervicomental angle was significantly correlated with AHI ($r = 0.41$, $p < 0.01$). For the younger children, mandibular width, eye width, cricomental distance and total anterior neck space were all positively correlated with AHI. Due to the small number of older children, linear relationships were not assessed for this group. No significant correlations were found for either HR and $O_2$ saturation with the craniofacial measurements. Finally, the linear relationship between BMI and cervicomental angle was examined, with a significant positive correlation found ($r = 0.41$, $p < 0.01$).

**Table 3-10: Linear relationships between craniofacial measurements and PSG data. Older children (12-16 years) were removed for correlations involving linear measurements**

| | Correlation (r) | | |
|---|---|---|---|
| **Measurement** | **AHI (r)** | **Mean HR** | **Mean $O_2$ Saturation** |
| Maxillary-mandibular relationship angle (°) | -0.27 | -0.21 | -0.12 |
| Mandibular-nasion angle (°) | 0.18 | 0.08 | -0.12 |
| Mandibular width-length angle (°) | -0.13 | -0.01 | 0.29 |
| Face width-midface depth angle (°) | 0.12 | 0.22 | 0.07 |
| Cervicomental angle (°) | 0.41** | 0.20 | -0.28 |
| Face width (cm) | 0.32 | -0.07 | -0.22 |
| Eye width (cm) | 0.40* | -0.04 | 0 |
| Lateral facial height (cm) | 0.19 | 0.28 | 0.15 |
| Mid-face depth (cm) | 0.07 | -0.15 | -0.25 |
| Total face height (cm) | 0.10 | -0.10 | -0.10 |
| Lower anterior face height (cm) | 0.06 | -0.14 | -0.04 |
| Mandibular length (cm) | 0.23 | 0.11 | -0.14 |
| Mandibular width (cm) | 0.36* | 0.02 | -0.01 |
| Cricomental distance (cm) | 0.48** | 0.20 | -0.33 |
| Cricomandibular distance (cm) | 0.26 | -0.01 | -0.05 |

* $p < 0.05$
** $p < 0.01$

# Chapter 4: Discussion

## 4.1 General Discussion

The association between pediatric Obstructive Sleep Apnea Syndrome and altered craniofacial morphology has been made without sufficient evidence to support some of the claims existing in the literature. By applying the previously adult-derived method of standardized craniofacial photography[58] to a pediatric population, this study sought to assess the strength of these associations. Overnight polysomnography allowed accurate diagnosis of OSAS, while craniofacial photography allowed for digital facial measurements to be made without exposing children to ionizing radiation, and without the need for specialized equipment.

When craniofacial syndromes, obesity and other confounders were controlled for, no statistically significant differences were found in any of the direct clinical measurements. According to Mellion et al.[96] females encounter peak pubertal growth from 10-12, while males experience it at age12-14. Because only one measurement was found to be statistically different between males and females, the decision was made to separate the children into a younger or older group (based on their chronologic age) as an approximation of peak skeletal growth. People of African and Asian descent have demonstrated cephalometric differences when compared to people of Caucasian descent,[97–99] while other population groups have been found to be more cephalometrically similar to Caucasian derived normative data.[100–102] While Vancouver, British Columbia is a multi-cultural city, over 75% of participants were either of Caucasian descent, or were of another ethnicity with craniofacial features that were relatively similar to established Caucasian normative data, allowing for comparison of 3 main groups by ethnicity. Due to the

small number of participants of African or Asian descent, statistical testing by ethnicity was not valid.

An increased tendency toward lower arch crowding greater than 3 mm in children with OSAS was seen in the data but did not reach statistical significance. Only 3 children (18.7%) who did not have OSAS, had crowding over 3 mm, compared to 10 children (35.7 %) who had both significant crowding and OSAS. Janson et al.[103] found that increased mandibular arch crowding was associated with a decrease in mandibular length in their cephalometric and clinical study. As mandibular retrognathia is one of the "red-flags"[37] associated with pediatric OSAS, it logically follows that an increase in crowding would be seen in children with OSAS. While this was not found in our study, it is possible that a larger sample size may have resulted in this trend becoming a statistical difference. Similarly, this tendency toward an increase in crowding was also found by Pirilä-Parkkinen et al.[35] 2.4% of the children in their control group had 4 mm or more of lower crowding, compared to 17.1% of the children with OSA. As in our study, this difference approached, but did not reach statistical significance. Interestingly, Huynh et al.[22] found that mandibular crowding and reported mouth breathing had a statistically significant relationship when 604 children were assessed by clinical examination along with a sleep questionnaire. As oral respiration is another "red flag" linked to pediatric OSAS, our data indicates that mandibular arch crowding is a variable of interest that should be further examined in future research.

Comparison of the dental variables from this study to the similar variables from Pirilä-Parkkinen et al.[35] revealed a few interesting differences. Their study[35] showed the children with OSA had

significantly more overjet, shallower overbite and narrower dental arches compared to their control children. Comparatively, the children in this study had no significant differences in maxillary transverse measurements (Table 3-5) regardless of whether they had OSAS or not. Additionally, as only one child (2.3%) had an anterior open-bite, there was no difference found between groups. The low prevalence of anterior open bite found in this study population is in line with the reported prevalence in the overall population (4 %).[104] Surprisingly, the children without OSAS even had a trend towards a reduced intermolar width when compared to the children with OSAS by a difference of nearly 2 mm (5.2 mm vs. 7.1 mm). As this difference was not significant, the most logical explanation was that it occurred by chance. While their study may have had superior power with a sample size of 97 children, they also had a wide age range of children (3.8-11.4 years) that were analyzed all together.[35] Variation in growth and skeletal maturity between groups may have accounted for the differences they found in dental arch morphology, resulting in another potential confounder.

From the angular measures of the standardized craniofacial photographs, children with OSAS had a significantly more obtuse cervicomental angle (*np-ce-me*) by nearly 8° (121.5° vs. 129.2°, $p = 0.05$). A more obtuse cervicomental angle can occur due to inferior displacement of the soft tissue cervical point, typically due to an increase in submental tissue, which is correlated with obesity.[105] The increased cervicomental angle in patients with OSAS was not unexpected, as previous research in craniofacial photography in adult populations has found that an increased cervicomental angle can be predictive of OSA.[48,106] Lee et al.[58] also found that the adult patients with OSA in their study had a significantly more obtuse cervicomental angle, reporting an average difference of 13° between groups. Although, once matched for BMI and gender, this

difference was no longer statistically significant. [58] As all photographs were recorded in natural head position (NHP), one possibility is that individual variation in NHP could alter the recorded cervicomental angle. Children who either permanently or temporarily have greater head extension could have a more obtuse cervicomental angle. While temporary nasal obstruction has been demonstrated to cause a temporary extension in head position,[107] the conditions of this obstruction were not physiologically induced, the sample size was small, and the results showed wide variation in the degree of change depending on the time point of the measurements. Natural head position has been demonstrated by other studies to be a reliable and reproducible measure over a long term period.[108,109] As more recent research has indicated that children with a primary oral mode of respiration may have a permanent head extension,[110] it follows that that these children would have an increased cervicomental angle, strengthening the relationship between oral respiration and OSAS. As AHI and cervicomental angle showed a positive significant correlation, this measure will perhaps become regarded as future "red-flag" of pediatric OSA.

Another possible explanation of the increase in cervicomental angle seen in the children with OSAS is that an increase in sub-mental fat deposits and glossus enlargement may occur early on in the life of people who may become obese in the future. This would increase their cervicomental angle, possibly pre-disposing afflicted children to be at a higher risk of OSAS, while not yet deeming them to be obese based on their BMI. Kim et al.[111] have demonstrated than even when matched for BMI, an increase in tongue fat (diagnosed via MRI) is correlated with OSA in adults. It is possible that the increased cervicomental angle seen in this pediatric sample is due to soft tissue enlargement. Supporting this explanation is that even when the 19 obese children were removed from analysis, BMI and the cervicomental angle were still

positively and significantly correlated. Other plausible explanations could explain this increase in the cervicomental angle found in children with OSAS, and further research is needed beyond our study's data.

Lee et al.[58] found significant differences for angular measurements that were not found in our data. Their participants without OSAS had a larger mandibular-nasion angle (a measure of relative mandibular position; *go-n-gn*), while participants with OSA had wider faces, given by a larger mandibular width-length angle (*gor-me-gol*) and a larger face width-midface depth angle (*tr-sn-tl*). These angular differences between groups were not found to be significant in this study. The face width-midface depth angle and mandibular-nasion angles were identical between groups, while the children without OSAS had a nearly 3º larger mandibular width-length angle (Table 3-5). The future growth potential of the participants in this study is a possible explanation for the differences when the results of the two studies are compared.

Two commonly cited "red-flags" of altered craniofacial morphology are an increased mandibular plane angle and an increase in the ANB angle[36,37]. In contrast, this study found an average difference of only 0.6° in the maxillary-mandibular angle (a soft tissue approximation of the cephalometric ANB angle) between the children without and without OSAS, while children without OSAS actually had a 2.8° degree steeper mandibular plane angle than the children with OSAS. Neither difference between groups for maxillary-mandibular relationship nor mandibular plane angle was statistically significant. It should be noted that on average, the reported difference in these measures between children with and without OSAS has been small, typically 2° or less, for each measure. It is expected that a larger sample would be required to detect a

small difference. Additionally, younger children should have a larger ANB difference than older children, yet this has not been well controlled for in the literature, with a recent systematic review comparing children with an age range from 0-18 years[36].

While the older children did show statistically significant differences for 3 linear measurements, these differences can likely be attributed to chance, due to the small sample size. Of the linear differences for the younger age group, children with OSAS were found to have a 6 mm increase in lateral face height when compared to the children without OSAS (9.6 cm vs. 9.0 cm, $p< 0.05$). The measurement of lateral face height (*exo-go*) serves as an oblique measure of facial height. An increase in this measure may suggest a more posterior positioning of the mandibular ramus in the children with obstructive sleep apnea syndrome. Lee et al.[58] had also found a significant increase in lateral face height (4 mm) in their adult participants with OSA prior to controlling for BMI. Once their participants were matched for BMI, their adult participants with OSA had a significantly shorter mandibular length (by nearly 4 mm), as well as a decreased anterior neck space area (by 2 $cm^2$), and a decreased mandibular triangle area (by 2.5 $cm^2$).[58] These differences were not found in the sample of children with OSAS in this study, as no significant differences were found for mandibular length, anterior neck space area, or mandibular triangle area when the two groups were compared (Table 3-8).

Cricomental distance demonstrated the strongest correlation with AHI ($r = 0.48$, $p <0.01$). An increased distance from the cricoid cartilage to the most inferior point on the chin is an indicator of more inferiorly displaced cricoid, and in turn, a more inferiorly displaced hyoid bone. As previous research has found that OSAS in children is associated with an inferiorly displaced

hyoid,[112] the positive correlation between increasing cricomental distance and increasing AHI logically follows. Additionally, both eye width and mandibular width had significant positive correlations with AHI, indicating that children with wider faces may be at an increased risk of OSAS. It is speculated that the increased activity of hypertrophic facial muscles associated with brachycephalic facial types may contribute to restricting nocturnal airflow. However, as these correlations were only of moderate strength, caution must be exercised before any broad conclusions between these relationships can be made. Interestingly, after controlling for BMI, Lee et al.[58] found that these two measurements were the only ones significantly correlated with the severity of OSA in adults. Therefore, wide-face phenotypes may have a higher risk of OSA than has been previously thought.

### 4.2 Limitations of the Study

No prior study has attempted applying standardized craniofacial photography to a pediatric population to assess whether craniofacial is associated with OSAS. While 102 children participated in the study, the final sample size was rapidly reduced during data analysis to 44 children. As craniofacial syndromes and decreased neuromuscular control are commonly seen with OSAS,[7] it was expected some of the children referred for evaluation would also have one (or possibly both) of these associated conditions. However, more children with one or both of these conditions were present in the sample than were anticipated, underscoring the complex multi-factorial disease that pediatric obstructive sleep apnea syndrome is. A larger sample of children would improve statistical power, and this will be a goal of subsequent research. Using the study's data, post-hoc power calculations indicated that a sample size of 280 participants would have been required to find a statistical difference between children with OSAS and

children without OSAS in this study for the measure of mandibular plane angle, while 1380 participants would have been required to find a significant difference between groups for the soft tissue ANB angle.

Of the remaining 65 children that participated, almost 1/3 (29.2%) were obese, while 2 children did not have their height or weight recorded. Considering Vancouver's reputation as being one of the healthier cities in Canada, it was surprising that this number was essentially in-line with the national average (31.5%[113]). With a final remaining sample of 44 non-obese, non-syndromic children, statistical power may have been reduced. In retrospect, it is easy to think that a longer data collection period may have been indicated. Conversely, not every family was willing or able to participate in the project, and the period of time required to get an ideal sample size would have exceeded the time constraints of this project, and possibly exceeded the time allotted to the university by the hospital.

An additional study limitation was the utilization of a potentially biased sample of children to compare craniofacial morphology between. The children without OSAS were still referred for overnight PSG evaluation by their primary care physician on the suspicion that they may have had the disease. Only 9 children were deemed to be truly asymptomatic, as demonstrated by their low AHI and low questionnaire scores. Ideally, a larger true control group would be available to compare the craniofacial morphology of children with and without any sign of sleep disordered breathing. However, as overnight PSG is time consuming, costly, and has a lengthy wait list; it is not easily feasible to garner a large control group from the general population.

A final study limitation was the comparison of children based on their age. A special consideration when working with a pediatric population is the effect of growth. While an attempt was made to control for the linear differences in size between younger and older children, it did further dilute statistical power as the already small sample size was further divided. Growth follows a normal distribution, and as such, one 11 year old girl may be significantly more skeletally mature than another girl of the same age. This issue may be further compounded when comparing an 11 year old girl vs. an 11 year old boy, as the earlier onset of puberty in females may make the girl more comparable to a 14 year old boy. As over half of participants with OSAS (57%) were male, it is possible that when compared on the basis of disease presence, growth differences between genders may be a potential confounder. Orthodontists have long attempted to discover or develop the ideal assessment of skeletal maturity with only partial success.[114] While dividing participants on the basis of chronological age based on average skeletal maturation does pose inherent possible inaccuracies, it is superior to assessing young children up to mature teenagers together in a single group, as unfortunately occurs in the literatue[35–37]. Additionally, it does not necessitate exposing children to ionizing radiation, as is required by other radiological methods[115] used to assess skeletal maturity. Ultimately, when dealing with a growing population, there is no perfect way to control for the effects of growth.

### 4.3 Future Directions

It is anticipated that the data gathered from this study will be able to be combined with the data not only from subsequent researchers at the same study centre, but also with the data gathered nationally from other Canadian sleep centres with academic affiliations. Doing so, should yield a larger sample size and greater statistical power. While limited hospital resources should not

routinely allow for healthy children to undergo a sleep study, it is conceivable that some of the children that are periodically referred for overnight PSG are without the disease. Therefore, a larger sample would also likely yield a larger true asymptomatic control group. A true and adequately sized control group would strengthen the study's validity, and subsequent research in this area should strive to achieve this.

3-D photography with stereoscopic cameras is a technology that is becoming increasingly available at a lower price point. It is expected that if standardized craniofacial photography does become a useful screening tool for pediatric OSAS, the photographs will eventually be taken in this manner. One caveat is the rapid pace of technology. 3-D face scanners are now beginning to be incorporated into orthodontic practice. While they are currently integrated with CBCT scans, it is possible that a portable version of this technology that is separate from the 3-D radiography unit will find its way into future soft tissue analyses for OSAS. As orthodontics and sleep medicine move into a fully digital world, it is unknown what new technologies will next be applied to assist in diagnosing our patients. The only thing that is for certain is that digital approach is the way of the future.

## Chapter 5: Conclusion

1. When the 44 non-obese, non-syndromic children were compared on the basis of whether they had OSAS or not, no significant differences in craniofacial morphology were able to be found between groups on the basis of clinical measurements.
2. Standardized craniofacial photography allowed for an easy to use, readily accessible, and low-risk method of objectively evaluating craniofacial morphology. Children with pediatric OSAS were shown to have a more obtuse cervicomental angle, and increased lateral face height compared to children without OSAS. Additionally, a greater linear cricomental distance was positively correlated with the severity of disease. While standardized craniofacial photography, and the measure of the cervicomental angle, demonstrated promise, further validation is required before it can reliably be used as a potential screening tool for pediatric OSAS.
3. Two measures of facial width were significantly correlated with increasing severity of OSAS, indicating that children with short, wide faces may be more at risk of OSAS than has been previously thought.

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