PEDIATRIC SLEEP QUESTIONNAIRE USED TO ASSESS SLEEP-RELATED BREATHING DISORDERS IN A WESTERN PENNSYLVANIA PRIVATE ORTHODONTIC PRACTICE

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Sleep related breathing disorders (SRBD) in children have a reported prevalence of 4-11% and manifest as behavioral, physical, and/or academic deficiencies. SRBD in children include snoring, obstructive sleep apnea (OSA), and hypopnea. Unlike adults, OSA incidence in pediatric patients occurs equally in males and females, with the greatest incidence from ages 2-8 years old. The greater incidence during this age range is primarily due to larger pharyngeal lymphatic tissues, which regress as the patient progresses into adolescence. After puberty, the prevalence of OSA increases more in boys than girls, which could be due to testosterone-induced changes. The gold standard for measuring SRBD is an overnight polysomnograph, which is burdensome to both the patient and the parent. For this reason, numerous questionnaires have been created to help identify patients at risk for SRBD. The Pediatric Sleep Questionnaire (PSQ) is a 22-point questionnaire which can be scored quickly and easily. When more than one third of the answers are answered positively, there is an increased likelihood that the patient would have positive signs of SRBD on a polysomnograph. With a specificity of 81% and a sensitivity of 85%, the questionnaire is a powerful tool for identifying patients who may be at a higher risk for SRBD. By looking at 1500 consecutive PSQ given to all patients under the age of 18 as part of the routine medical history, the prevalence of SRDB in pediatric orthodontic patients in a private practice in Western Pennsylvania will be estimated in an effort to describe how common this disorder may be in a common orthodontic environment.

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PREFACE

I would like to express sincere gratitude to GKG Orthodontics for the amount of dedication that the staff members and doctors put in for data collection for this project. With their efforts, I was able to collect a large amount of data from outside of the dental school population and use patients from their private practice. Thank you all very much.

1.0 BACKGROUND

1.1 SLEEP-RELATED BREATHING DISORDERS

Sleep-related breathing disorders (SRBD) are a spectrum of disorders that range from mild snoring to severe obstructive sleep apnea (OSA). At the mild end of this spectrum is primary snoring. Primary snoring is classified as being more than 3 nights per week of snoring (Dehlink & Tan, 2016; Kaditis, et al., 2016). Snoring does not cause arousal from sleep, nor are there any effects on gas exchange or blood oxygen desaturation.

Upper airway resistance syndrome (UARS) is the next level of SRBD and is considered to be borderline OSA (Downey III, Perkin, & MacQuarrie, 1999). UARS presents as sleep arousals and sleep fragmentation but is not associated with apneas, hypopneas, or oxygen desaturations (Chervin, Hedger, Dillon, & Pituch, 2000; Lumeng & Chervin, 2008; Kaditis, et al., 2016). The sleep arousals and fragmentation cause daytime morbidities that are similar to that in patients with OSA.

At the most severe end of the SRBD spectrum is OSA. This disorder is characterized by apneas and hypopneas that cause abnormal ventilation and is associated with a decrease in blood oxygen saturation as well as sleep arousals and fragmentation (Lumeng & Chervin, 2008). Apneas are defined as a cessation in airflow for at least two respiratory cycles and are associated with a decrease in blood oxygen saturation (Alsubie & BaHammam, 2017). Hypopneas are defined as a

decrease in airflow to the lungs, either due to shallow breathing or a decrease in ventilation and can also be associated with a decrease in blood oxygen saturation (Kaditis, et al., 2016).

1.2 ETIOLOGY OF SLEEP-RELATED BREATHING DISORDERS

Sleep related apneas have three generalized etiologies: central, obstructive, or combination. Central apneas occur when the phrenic nerve is not functioning properly, and therefore there is no chest wall movement or effort to breathe (Hans, 2016). This is not something that can easily be changed and is therefore not a main focus of this paper. The main focus of this paper is obstructive sleep apnea which occurs when there is a chest wall movement with a decrease in airflow.

In children, these obstructive sleep apneas can be caused by a variety of morphologic differences occurring in the upper airway. An increase in upper airway collapsibility or a narrowing in the upper airway are main etiologies of sleep-related breathing disorders (Dehlink & Tan, 2016). Collapsibility of the upper airway can be caused by a decrease in muscle tonicity or secondarily from inflammation due to asthma or allergies. Upper airway narrowing can be caused by tonsil and/or adenoid hypertrophy, macroglossia, micrognathia, midfacial hypoplasia, or a variety of syndromes (Dehlink & Tan, 2016). A study performed by Graf et al. (2016) showed that within a group of snoring children, the posterior airway space, as depicted on a lateral cephalogram, was reduced.

However, these morphologic differences are not the only etiology for sleep-related breathing disorders; there are many other contributory risk factors.

1.3 RISK FACTORS

One of the major risk factors in adults with OSA is obesity, yet there has been some debate on the effect of obesity in pediatric OSA patients. Bonuck et al. (2015) found a direct link between obesity and sleep-disordered breathing in children. Dehlink and Tan (2016) suggest that obesity alone is not a major determinate of obstructive sleep apnea, but when combined with hypertrophy of adenotonsillar tissue there is an increase in OSA prevalence to 46.6%. Alsubie and BaHammam (2017) indicate that in obese pediatric patients, neither neck circumference nor adipose thickness are predictors of upper airway collapsibility and therefore are not predictors of OSA. They attributed this observation to children being better able to maintain airway patency with an increase in muscular activity as an adaptive means during sleep.

In a study by Yu et al. (2003) obese and non-obese children with OSA were studied. They found that patients with OSA, compared to those with snoring alone, had a more inferiorly-placed hyoid, enlarged soft palate and reduced width of the upper airway at the soft palate. In obese patients, the tongue was longer, and the soft palate was more enlarged. In non-obese patients, there was a reduced anteriorposterior width of the nasophaynx. The previously mentioned studies that pertain to OSA and obesity indicate that there is a complex relationship between these two factors.

An additional risk factor for pediatric OSA is found in those children who have been previously diagnosed with asthma (Ehsan, Kercsmar, Collins, & Simakajornboon, 2017). Patients with severe asthma have a higher prevalence of SRBD, and those who have been previously diagnosed with OSA have a 3.62 times greater risk of having unresolved severe asthma after 12-months. The prevalence of severe asthma, or asthma that is poorly controlled is 5-10%. Oftentimes, these patients have nocturnal symptoms that are similar to those related to OSA, which can lead to false positive answers on diagnostic tests such as the Pediatric Sleep Questionnaire (PSQ). With

both asthma and SRBD, various inflammatory mediators have been identified, possibly linking these two diseases together through the presence of inflammation. However, when properly diagnosed, OSA can be treated in these patients with adenotonsillectomy to help improve asthma control (Ehsan, Kercsmar, Collins, & Simakajornboon, 2017).

It has been suggested that prevalence of SRBD could be different based on demographic characteristics. It has been reported that Malaysian patients were more likely than Chinese or Indian patients to experience SRBD (Chng, Goh, Wang, Tan, & Ong, 2004), and African American patients were three to four times more likely than Caucasian patients to experience SRBD (Rosen, et al., 2003). It was also reported that males have a 50-100% higher prevalence of SRBD than females (Lumeng & Chervin, 2008). Testosterone-induced changes, such as muscle mass enlargement could be a contributing factor to males having a greater prevalence of OSA after puberty, but it is most likely not the only cause (Alsubie & BaHammam, 2017).

Whether or not age has an effect on the prevalence of SRBD is currently a matter of debate. According to Lumeng and Chervin (2008) there are no obvious patterns of change in SRBD, depending on age. A study performed by Owens et al. (2000) that utilized three different sleep habit questionnaires showed that there was a higher prevalence of sleep disturbances in children of kindergartner age through those in second grade, when compared to children in third and fourth grade. Other studies have shown a connection between an increase in SRBD and oropharyngeal lymphatic tissue hypertrophy, which is most apparent in children of preschool to early grade school age (Biggs, et al., 2015; Alsubie & BaHammam, 2017).

1.4 SYMPTOMS IN PEDIATRIC PATIENTS

Children afflicted with sleep-related breathing disorders (SRBD) exhibit a wide range of symptoms which may significantly impact the daily life of the patient as well as their parents and teachers. Because their symptoms differ, pediatric patients do not have the same diagnostic criteria for SRBD as adults. The most apparent symptom in adult OSA patients is excessive day time sleepiness. However, only 15% of children with diagnosed obstructive sleep apnea meet adult pathology criteria (Downey III, Perkin, & MacQuarrie, 1999). The daytime symptoms of pediatric patients can include ADHD, daytime sleepiness, school difficulties, failure to thrive and emotional difficulties. Daytime symptoms often need to be combined with those that occur at night to aid in the diagnosis of SRBD. The nighttime symptoms found in children include snoring, restlessness, difficulty breathing, and enuresis. Nighttime bed-wetting is attributed to these children experiencing an inhibition of the normal arousal commonly resulting from changes in bladder pressure (Dehlink & Tan, 2016).

Sleep disturbances, possibly caused by apneas or hypopneas, present as daytime hyperactivity and difficulty concentrating (Miano, et al., 2016; Dehlink & Tan, 2016; Alsubie & BaHammam, 2017). For this reason, sleep disturbances are now included as part of the ADHD diagnostic criteria. As many as 20-25% of pediatric patients with ADHD have been reported as having sleep problems (Miano, et al., 2016). Many pediatric patients with OSA exhibit poor school performance, falling to the bottom 10% of their class, which may be attributable to their ADHD-like symptoms (Dehlink & Tan, 2016).

Cardiovascular disorders are also apparent in pediatric OSA patients, presenting a severe comorbidity. Frequently, there is a decrease in cardiac remodeling (Dehlink & Tan, 2016) as well as an increased risk for hypertension and right ventricular hypertrophy (Alsubie & BaHammam,

2017). During exercise, there is also a decrease in cardiac output and oxygen consumption. In addition, there can be an increase in levels of LDL and a reduced level of HDL (Dehlink & Tan, 2016). If OSA goes undiagnosed in children, these cardiovascular abnormalities can lead to possible death in adulthood.

1.5 DIAGNOSIS OF SLEEP-RELATED BREATHING DISORDERS

1.5.1 Polysomnography

Currently, the gold-standard test for the diagnosis for both adult and pediatric sleep-related breathing disorders, including obstructive sleep apnea, is the overnight polysomnograph at a sleep center. These tests are time-consuming, costly and are burdensome to the patient. However, they are highly diagnostic and there are specific cut-off values for describing the severity of obstructive sleep apnea. Classifications for OSA severity is based on the number of apneas and hypopneas that occur each hour, which make up the apnea-hypopnea index (AHI). In a healthy child, the number of obstructive apnea-hypopnea events per hour should be less than or equal to one. Mild OSA in pediatric patients is classified as 2-5 apnea-hypopnea events in an hour. Moderate OSA is between 6-10 events per hour, and severe is more than 10 apnea-hypopneas in an hour (Dehlink & Tan, 2016). These values are much lower than the adult OSA severity guidelines, as diagnosed with AHI and polysomnography. Only 15% of children diagnosed with OSA will meet the guidelines set for adult OSA (Downey III, Perkin, & MacQuarrie, 1999).

The gold standard, polysomnography, is best at identifying gross abnormalities, such as those apneas and hypopneas present in patients with OSA (Downey III, Perkin, & MacQuarrie,

1999). However, primary snoring and UARS do not always present with oxygen desaturation, and can be a more subtle abnormality and therefore, would not be identified as an abnormality during polysomnography. This could lead to a possible underrepresentation of those patients with a SRBD.

1.5.2 Alternatives for Diagnosis

To circumvent the use of burdensome overnight polysomnographs, a variety of alternative tests have been proposed for the diagnosis of sleep disorders (Dehlink & Tan, 2016). Clinical sleep records are useful for primary screening of potential OSA cases. These records include a clinical history, physical exam and subjective symptoms. The physical exam should involve checking for tonsillar hypertrophy, macroglossia, high palatal vault, obesity, failure to thrive at any point in life, retrognathia, micrognathia and any potential underlying syndromes (Alsubie & BaHammam, 2017).

According to Dehlink and Tan (2016), respiratory polygraphs can be used, which comprise of polysomnography without the EEG, EMG, and EOG. These types of tests will often underestimate the AHI because not all hypopneas will immediately affect the oxygen saturation, but often such unrecorded hypopneas may result in immediate arousal.

Another option is the take-home nocturnal pulse oximetry, which is a more convenient option for patients. However, they may often yield high false negatives or inconclusive results. Finally, there are also ambulatory respiratory polygraphs or polysomnographs that can be utilized. These tests are not given in a lab setting but are utilized at home. These tests yield results that may be closer to a typical night's sleep, since the patient is not in a sleep center. However, when compared to a laboratory administered test, the data may be limited in use (Dehlink & Tan, 2016).

In adult patients, two potential biomarkers have been identified that could be linked to OSA: interleukin-6 and interleukin-10. For pediatric patients, though, there are few, if any biomarkers indicative of OSA. De Luca et al. (2015) found that a combination of a number of biomarkers may have potential to identify pediatric OSA. The biomarkers are kallikrein-1, uromodulin, urocortin-3 and oroscomucoid-1. It is possible that with accurate biomarkers, patients at risk for OSA may be more easily identified in the future.

1.5.3 Questionnaires

The least burdensome of all of the screening techniques for pediatric OSA is the administration of a questionnaire to the patient's parents or guardians. To date, numerous sleep-related questionnaires have been created. These questionnaires are similar in that they rely on questions pertaining to perceived breathing abnormalities during sleep as well as day-time symptoms. It is critical that questionnaires probe symptoms and not just the presence of snoring as a positive finding, because some children diagnosed with OSA had no history of snoring (Lumeng & Chervin, 2008).

An 8-question pediatric OSA questionnaire, entitled *I'M SLEEPY*, was created as a quick screening tool for sleep clinic patients (Kadmon, Chung, & Shapiro, 2014). The eight questions pertain to abnormal breathing at night, BMI, tonsil and adenoid size as well as day time symptoms such as irritability and difficulty focusing. The questionnaire, with an 82% sensitivity and 50% specificity, is only ideal in patients at high risk for having OSA. This questionnaire is ideal for patients at sleep centers, who have already been suspected to have a high risk for OSA based on prior symptoms but is not ideal for the typical orthodontic patient in private practice.

The Pediatric Sleep Questionnaire (PSQ) is a 22-point questionnaire that is designed for pediatric patients between 2 and 18 years of age. This questionnaire was found to be both valid and reliable, with a sensitivity of at least 85% and a specificity of at least 81%, when more than 7 positive answers were considered to be an abnormal test result (Chervin, Hedger, Dillon, & Pituch, 2000). On abnormal test results with this cutoff value, there was approximately a 3 times greater risk of OSA on polysomnograph when compared to those with less than 8 positive answers (Chervin, et al., 2007).

Though other questionnaires have been proposed, only the PSQ has the diagnostic accuracy to be used as a screening tool for SRBD (De Luca Canto, et al., 2014). Despite this, the PSQ and all other questionnaires to date, are not considered to be truly diagnostic, and therefore cannot replace polysomnography for diagnosis of pediatric SRBD. Rather, these questionnaires can be used as a screening tool and promote discussion with parents about the potential for SRBD, thus facilitating proper referral as needed.

1.6 TREATMENT

Treatment for pediatric SRBD is typically done in a step-wise manner, using the least invasive interventional therapies before resorting to more invasive treatments. In patients with mild OSA or those patients with adenotonsillar hypertrophy, there is a possibility of spontaneous remission (Dehlink & Tan, 2016; Lumeng & Chervin, 2008). According to Chervin et al. (2015), habitual snoring will resolve without treatment in one-third to one-half of the patients within 1-3 years. Of those patients from 5 to 9 years of age, 46% showed resolution of OSA on polysomnograph with an AHI value of less than 2 after 7 months of monitoring (Chervin, et al., 2015). The resolution

was seen in non-obese and non-black patients with mild OSA, as defined as less than 5 apnea-hypopnea episodes per hour. These findings suggest that patients with mild OSA, low PSQ values, low amounts of snoring and low AHI values without obesity may benefit from further observation before beginning any treatment.

Due to the conflicting evidence in the literature pertaining to the link between obesity and pediatric SRBD, there is no general consensus on weight loss as a suitable treatment for pediatric patients. Typically, this is a first line of treatment for adult patients, but the same cannot be assumed for pediatric patients. Dehlink and Tan (2016) suggested that weight loss may be suitable for those pediatric patients who are obese or overweight and that did not have spontaneous resolution of their symptoms. In contrast, Bonuck et al. (2015) suggested that increasing a child's sleep could be the most effective method of reducing obesity.

In pediatric patients that are diagnosed with OSA due to enlarged tonsils and/or adenoids, there are two treatment options. For mild cases, a 6-12 week course of nasal corticosteroids can be administered in order to reduce the size of the adenoids (Dehlink & Tan, 2016). For more severe cases of enlarged pharyngeal lymphatic tissue, treatment with adenotonsillectomy provides nearly an 80% cure rate (Alsubie & BaHammam, 2017; Dehlink & Tan, 2016). Though the reported success rate is high, the presence of OSA may recur after the initial treatment improvement. In a study by Huang et al. (2014), 68% of children treated with adenotonsillectomy experienced a worsening of AHI 3 years post-surgery. This recurrence was associated with nocturnal bedwetting, age, change in BMI, and AHI 6 months post-surgery.

There are contradictory thoughts on the effects of maxillary expansion and its effect on breathing. A study by Guilleminault et al. (2008), showed that patients with a narrow maxilla and moderate OSA benefit from both tonsillectomy and expansion. However, this study was retracted

a year following its publication due to incomplete and inaccurate descriptions of the methodology involved. A systematic review (Camacho, et al., 2017), showed that AHI values can be reduced by 50-70% in pediatric OSA patients with a narrow maxillary transverse dimension that have received RME. The patients that benefit most from RME treatment are those with small or no tonsils, compared to those with large tonsils. This systematic review also demonstrated an improvement in oxygen saturation, but no clear predictive factors were found. Numerous other studies looked at anatomic changes and show that there is an increase in nasal cavity volume after expansion treatment (El & Palomo, 2014; Görgülü, Gokce, Olmez, Sagdic, & Ors, 2011; Oliveira, et al., 2008; Fastuca, Perinetti, Zecca, Nucera, & Caprioglio, 2015). Fastuca et al. (2015) demonstrated significant volumetric changes between the middle and upper airway following expansion, and an association with increased blood oxygen levels and decrease in AHI events. There have not been any studies on whether RME provides any improvement of cardiovascular function or behavior (Dehlink & Tan, 2016). Biggs et al. (2015) postulated that resolution of SRBD, as indicated by an AHI of less than 1 with no snoring on polysomnograph, has little long-term effects on cognition or behavioral outcomes. Despite all of these studies that have been performed, there is still a lack of controlled and long-term follow-up studies to follow the natural progression and possible spontaneous resolution of pediatric OSA and maxillary expansion (Camacho, et al., 2017)

If the previously mentioned conservative treatments do not yield results, a positive airway pressure (PAP) machine can be used during sleep (Alsubie & BaHammam, 2017; Dehlink & Tan, 2016). This treatment is typically burdensome to the patient but will help maintain a patent airway with reduced oxygen desaturations and sleep arousals. Regardless of the treatment that is used for patients with diagnosed OSA, they should have a polysomnograph before and after treatment to determine if the breathing disorder has improved (Dehlink & Tan, 2016).

1.7 PREVALENCE OF SLEEP-RELATED BREATHING DISORDERS

The prevalence of any amount snoring, regardless of nights per week, in pediatric patients is at least 34% (De Luca Canto, et al., 2014). The mildest form of SRBD, primary snoring, has a prevalence of 7.5% (Dehlink & Tan, 2016). A concern for many practitioners is that patients who exhibit primary snoring may be at risk for developing OSA with age or weight gain (American Academy of Sleep Medicine, 2005). Though snoring is frequently associated with OSA, 25-47% of children diagnosed with OSA have no history of loud snoring, which may lead to an underestimation of OSA prevalence (Rosen, et al., 2003)..

More severe forms of pediatric SRBD have a variable reported prevalence ranging from 0.7-15%. Graf & Neuschulz (2016) reported that the prevalence of OSA in children is between 0.7-2%. Similarly, Alsubie & BaHammam (2017), reported the prevalence to be around 1-2% of pediatric patients. Using the PSQ, Lumeng & Chervin (2008), found that the prevalence of SRBD was 11.1% when using more than one-third positive responses as the cutoff threshold value for determining if the test was positive. Biggs, et al. (2015), reported the prevalence of pediatric SRBD to be 12-15% of the population.

The reported prevalence has such a wide range due to the lack of a single definition for sleep related breathing disorders (Lumeng & Chervin, 2008). Many studies do not delineate between snoring, primary snoring, UARS, and OSA. Despite the lack of a single definition for sleep related breathing disorders, it is an important public health problem due to the comorbidities and symptoms that present in affected children.

Research on the prevalence of sleep disordered breathing in private orthodontic practice is important for clinicians to know in order for them to determine if implementation of SRBD screening techniques is merited in their own private practices. Currently, most prevalence studies

are conducted at sleep centers, where the patients have been referred due to a practitioner believing that they may have some type of sleep-disordered breathing, which is not indicative of the general orthodontic population that is seen in a private practice. Depending on the overall prevalence of SRBD in private orthodontic practice, it may or may not be beneficial to screen every new pediatric patient for these conditions.

2.0 PURPOSE OF THE PRESENT STUDY

The overall goal of this study was to determine the prevalence of sleep-related breathing disorders within the patient population of a private orthodontic practice in suburban Pittsburgh, Pennsylvania, using the Pediatric Sleep Questionnaire (PSQ). We hypothesized that the prevalence would be 11% when using the PSQ and more than one-third of questions answered positively to define an individual as having a sleep-related breathing disorder, similar to the results found by Lumeng and Chervin (2008). A secondary goal of the study was to determine the relative importance of each of the 22 items of the PSQ to identify individuals with sleep-related breathing disorders and examine if there are a few questions in particular that could be used to identify positive test responses. We hypothesized that all of the questions are of equal importance and none in particular are more indicative of a positive test result.

3.0 MATERIALS AND METHODS

This study was a secondary analysis of anonymized data from the clinical records of children under the age of 18 years old who were consecutively screened for orthodontic treatment at a private practice in Wexford, Pennsylvania, a northwestern suburb of Pittsburgh, Pennsylvania between August 23, 2016 and December 8, 2017. Before the consultation appointment, all parents or guardians of patients under the age of 18 years old were asked to complete the 22-question Pediatric Sleep Questionnaire (PSQ) as part of the routine medical history examination, seen in Figure 1. Pediatric Sleep Questionnaire (PSQ). The 22 questions were answered as "yes", "no", or "I don't know". Missing answers were given the same designation as the "I don't know" answer selection. The treatment coordinator recorded the patient's age, sex, treatment that was suggested by the orthodontist, and if the patient had ever received a tonsillectomy or adenoidectomy previously.

The answers to the PSQ were de-identified by the treatment coordinator, and the patients were assigned a unique identifier that consisted of two letters and three or four numbers. The answers to the questionnaires were recorded, regardless of the treatment rendered or suggested by the orthodontist. The prevalence of patients in a Pittsburgh suburb private orthodontic practice with an increased risk for sleep related breathing disorders (SRBD), as indicated by 8 or more positive responses on the PSQ, was calculated and compared to previous prevalence studies. Logistic regression was performed to determine if age and sex were confounding variables for obtaining a positive test result. Each of the 22-questions was also assessed using an exploratory factor analysis to determine if a positive answer to any specific question or questions indicated a

greater risk factor for SRBD. This study protocol was approved by the University of Pittsburgh IRB.

Airway History			
Patients Age:	**For internal use only:**	• Exp	• Non-exp
Sex:	Number:	• Initial	• Final
If this patient is under the age of 18 please answer the following questions:			
While sleeping, does your child…			
…snore more than half the time?		□Yes □No □Don't Know	
…always snore?		□Yes □No □Don't Know	
…snore loudly?		□Yes □No □Don't Know	
…have "heavy" or loud breathing?		• Yes □No □Don't Know	
…have trouble breathing, or struggle to breathe?		□Yes □No □Don't Know	
Have you ever seen your child stop breathing during the night?		□Yes □No □Don't Know	
Does your child…			
…tend to breathe through the mouth during the day?		• Yes □No □Don't Know	
…have a dry mouth on waking up in the morning?		□Yes □No □Don't Know	
…occasionally wet the bed?		□Yes □No □Don't Know	
Does your child…			
…wake up feeling *un*-refreshed in the morning?		□Yes □No □Don't Know	
…have problem with sleepiness during the day?		□Yes □No □Don't Know	
Has a teacher or other supervisor commented that your child appears sleepy during the day?		□Yes □No □Don't Know	
Is it hard to wake your child up in the morning?		□Yes □No □Don't Know	
Does your child wake up with headaches in the morning		□Yes □No □Don't Know	
Did your child stop growing at a normal rate at any time since birth?		□Yes □No □Don't Know	
Is your child overweight?		□Yes □No □Don't Know	
This child often does not seem to listen when spoken to directly.		□Yes □No □Don't Know	
This child often has difficulty organizing tasks and activities.		□Yes □No □Don't Know	
This child is often easily distracted by extraneous stimuli.		□Yes □No □Don't Know	
This child often fidgets with hands or feet or squirms in seat.		□Yes □No □Don't Know	
This child is often "on the go" or often acts as if "driven by a motor".		□Yes □No □Don't Know	
This child often interrupts or intrudes on others (e.g. butts into conversations or games)		□Yes □No □Don't Know	
Have your child's tonsils/adenoids been removed?		□Yes □No □Don't Know	
And if so, when?			

Figure 1. Pediatric Sleep Questionnaire (PSQ)

4.0 RESULTS

The sample consisted of 1,527 consecutively screened pediatric orthodontic patients. The sample consisted of 723 males (47.63%) and 795 females (52.37%) with an overall mean age of 9.59±2.73 years, the age distribution is shown in Figure 2.

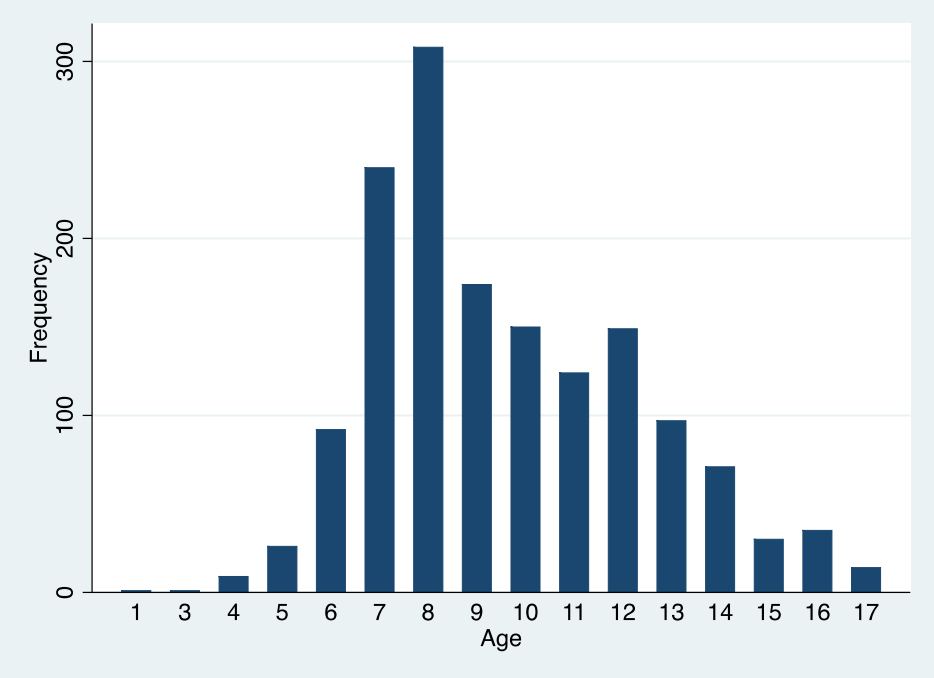

Figure 2. Age distribution of the consecutively screened pediatric patients.

Within this sample, 4.99% (76 patients) had 8 or more positive responses to the pediatric sleep questionnaire, indicating that their PSQ screening was positive for an increased risk of having a sleep-related breathing disorder. The distribution of the total number of positive responses for each individual PSQ is shown in Figure 3.

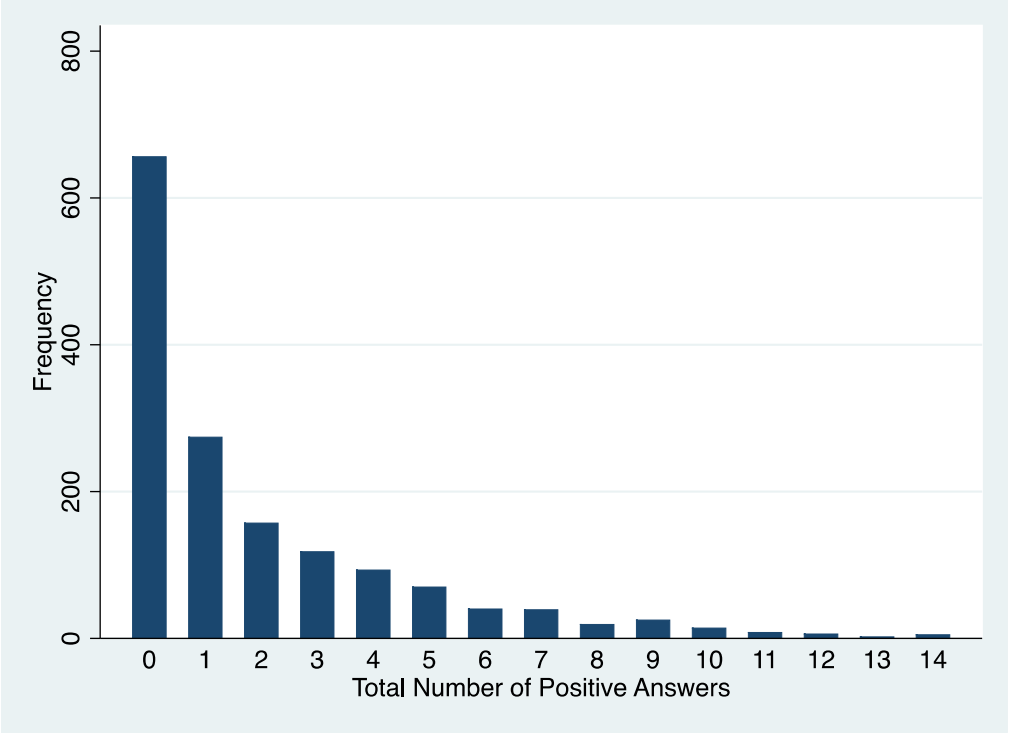

Figure 3. Frequency of the total number of positive answers for each Pediatric Sleep Questionnaire (PSQ).

Of those patients with a negative PSQ result, indicated by less than 8 total positive responses, a majority (656 patients, 42.99%) had 0 total positive question responses, shown in Table 1. The next most frequent PSQ result was those with one positive response, seen in 274 patients (17.96%). 33.88%, or 517, of the patients had PSQ results that ranged from 2 to 7 total positive responses. Of those patients with a positive PSQ result, most had either 8 total positive question responses (19 patients, 1.25%), or 9 total positive question responses (25 patients, 1.64%). 2.29% (35) of the patients had 10 to 14 total positive responses. No patients in this study had more than 14 total positive responses.

Table 1. Frequency of total number of positive answers for each PSQ.

Total "yes"	Frequency	Prevalence (%)	Cumulative Percent (%)
0	656	42.99	42.99
1	274	17.96	60.94
2	157	10.29	71.23
3	118	7.73	78.96
4	93	6.09	85.06
5	70	4.59	89.65
6	40	2.62	92.27
7	39	2.56	94.82
8	19	1.25	96.07
9	25	1.64	97.71
10	14	0.92	98.62
11	8	0.52	99.15
12	6	0.39	99.54
13	2	0.13	99.67
14	5	0.33	100.0
Total	1,526	100	

The frequency of having a positive response to each of the individual 22 questions of the Pediatric Sleep Questionnaire are shown in Table 2. The least frequent positively answered questions of the PSQ were questions 5, 6, and 12 with a total of 22, 19, and 45 positive responses, respectively. The most frequent positively answered questions of the PSQ were questions 13, 19, 20, 21, and 22 with a total of 205, 265, 254, 200, and 220 positive responses, respectively.

Table 2. Total number of positive responses to each individual question of the PSQ

Question	Total Positive Responses
1: Snores more than half of the time	127
2: Always snores	66
3: Snores loudly	107
4: Has "heavy" or loud breathing	161
5: Has trouble breathing, or struggles to breathe	22
6: Seen your child stop breathing during the night	19
7: Tends to breathe through the mouth during the day	173
8: Has a dry mouth on waking up in the morning	163
9: Occasionally wets the bed	140
10: Wakes up feeling *un*-refreshed in the morning	158
11: Has problems with sleepiness during the day	92
12: A teacher has commented that they appear sleepy during the day	45
13: It is hard to wake them up in the morning	205
14: Wakes up with headaches in the morning	59
15: Has stopped growing at a normal rate at any time since birth	75
16: Is overweight	87
17: Does not seem to listen when spoken to directly	123
18: Has difficulty organizing tasks and activities	189
19: Easily distracted by extraneous stimuli	265
20: Fidgets with hands or feet or squirms in seat	254
21: "On the go" or acts as if "driven by a motor"	200
22: Interrupts or intrudes on others	220

Patients with a positive result for the PSQ, those with a total of 8 or more positive responses, were broken down by age (Figure 4). Using a two-sample t-test, there was no significant difference ($p=0.50$) between the ages of the patients with a positive PSQ test result, and those patients who had a negative PSQ test result. For the patients with a negative test result, their mean age was 9.6±2.7 years. The patients with a positive test result had a mean age of 9.6±2.5 years.

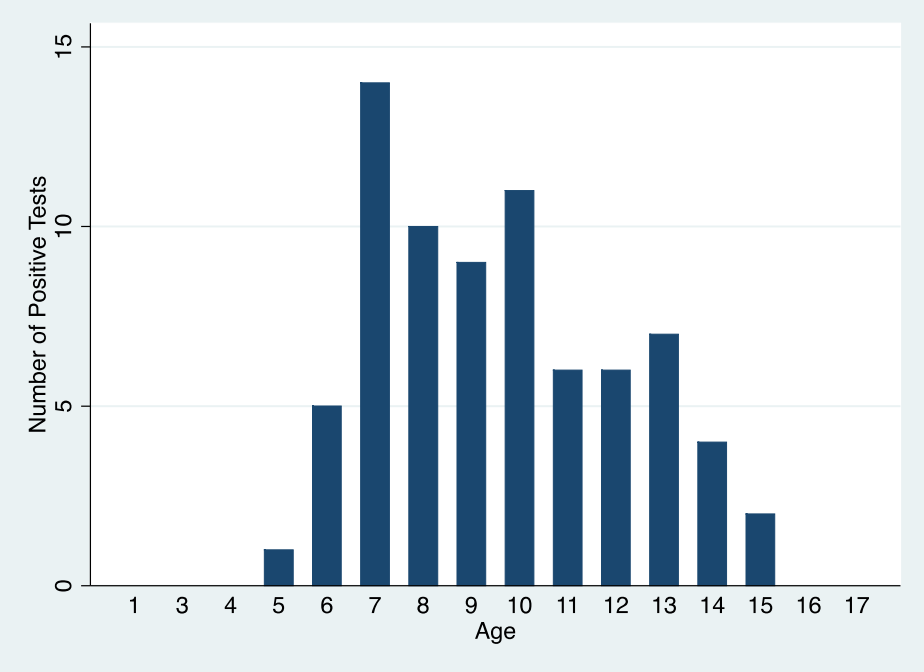

Figure 4. Total number of positive PSQ results based on patient age.

The percentage of patients of each age that had a positive test result as shown in Table 3. Patients that 10 years old and 13 years old had the highest prevalence, with 7.3% and 7.2%, respectively. The patients that had no presence of a positive test were 4, 16, and 17 years old. 8 year old children had the next lowest prevalence at 3.2% having a positive result.

Table 3. Percentage of patients from each age, ranging 4-17 years old, with a positive PSQ result.

Age of Patient	Percent with Positive PSQ Result (%)
4	0
5	3.8
6	5.4
7	5.8
8	3.2
9	5.2
10	7.3
11	4.8
12	4.0
13	7.2
14	5.6
15	6.7
16	0
17	0

On logistic regression, age is not a confounding factor for having a positive PSQ result (odds ratio: 0.998, CI [0.915-1.088]), as shown in Table 4. However, sex of the patient influences having a positive PSQ result (odds ratio: 2.102, CI [1.289-3.428]). Males have a 2.1 increased odds, compared to females, for having a positive PSQ test result, when adjusting for age. Nine surveys were incomplete with unreported sex or age, which resulted in exclusion from the logistic regression.

Table 4. Logistic regression of positive PSQ test result

Logistic regression — Number of obs = 1,513
LR chi2(2) = 9.32
Prob > chi2 = 0.0094
Log likelihood = -290.81402 — Pseudo R2 = 0.0158

SleepApnea	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
Sex	2.102536	.5245837	2.98	0.003	1.289342	3.428614
Age	.9979265	.0439535	-0.05	0.962	.9153928	1.087902
_cons	.0346143	.0159532	-7.30	0.000	.0140265	.0854202

As seen in Table 5, within the population sampled that had an overall negative PSQ test result, 769 (53.29%) of the patients were females, and 674 (46.71%) were males. Of the 75 patients with a recorded sex and overall positive test result, 26 (34.67%) of the patients were female and 49 (65.33%) were male. The overall prevalence of positive test results in female patients was found to be 3.27%, while the prevalence of a positive test result for males was 6.78%.

Table 5. Frequency of PSQ test results and sex of patient

	Sex		
PSQ Test Result	Female	Male	**Total**
Negative	769	674	1, 443
Positive	26	49	75
Total	795	723	1,518

Using an exploratory factor analysis and Eigenvalues, we attempted to identify any factors, or groups of questions, that could be used to predict a positive PSQ test response. In determining the number of factors, a Scree plot of Eigenvalues was used (Figure 5). Three different factors were identified within the PSQ, shown in Table 6. Each of the three factors consisted of three or more questions with none of the questions loading on more than one factor. The greatest Eigenvalue identified was 4.36, which accounts for 19.8% of the variance found in positive PSQ results.

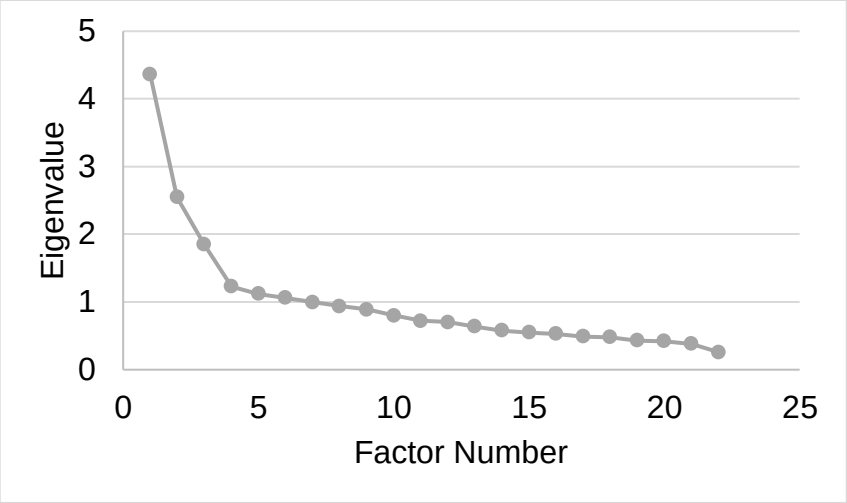

Figure 5. Scree plot of the exploratory factor analysis

Table 6. Three associated factors from exploratory factor analysis and their associated Eigenvalues

Factor Number	Eigenvalues	Variance (%)
1	4.36	19.8
2	2.55	11.6
3	1.85	8.5

The first factor that was identified had an Eigenvalue of 4.36 and consisted of six different questions, all with loading values greater than 0.5 (Table 7) which indicates a solid factor (Costello & Osborne, 2005). The questions all related to symptoms of ADHD and account for 19.8% of the positive PSQ test results.

Table 7. Loading values of each question for Factor 1.

PSQ Question Number	Question	Loading
17	This child often does not seem to listen when spoken to directly	0.57
18	This child often has difficulty organizing tasks and activities	0.65
19	This child is often easily distracted by extraneous stimuli	0.70
20	This child often fidgets with hands or feet or squirms in seat	0.68
21	This child is “on the go” or often acts as if “driven by a motor”	0.56
22	This child often interrupts or intrudes on others	0.64

The second factor identified had an Eigenvalue of 2.55 and consisted of three questions, all of which pertained to snoring characteristics (Table 8). This factor accounts for 11.6% of the PSQ test variance. The loading values for each of the questions were moderate and similar to each other.

Table 8. Loading values of each question for Factor 2

PSQ Question Number	Question	Loading
1	Snores more than half the time	0.51
2	Always snores	0.53
3	Snores loudly	0.51

Finally, the third factor identified had an Eigenvalue of 1.85 and consisted of three questions related to daytime sleepiness (Table 9). This factor accounts for 8.5% of the variance of the PSQ. The loading values for each question were moderate.

Table 9. Loading values of each question for Factor 3

PSQ Question Number	Question	Loading
10	Wakes up feeling unrefreshed in the morning	0.58
11	Has problems with sleepiness during the day	0.57
12	Teacher or other supervisor has commented that child appears sleepy during the day	0.59

5.0 DISCUSSION

The aim of this project was to describe the prevalence of pediatric sleep-related breathing disorders using the Pediatric Sleep Questionnaire (PSQ) in a private orthodontic practice in Western Pennsylvania. Data from previous research studies showed a wide prevalence range, primarily due to different definitions of sleep disordered breathing and the differing populations that were being measured. The prevalence of pediatric sleep-related breathing disorders in the present study was found to be 4.99%. The prevalence found in this study was lower than the reported prevalence of 11.1% (Lumeng & Chervin, 2008), and higher than the reported 0.7-2% (Graf & Neuschulz, 2016) and 1-2% (Alsubie & BaHammam, 2017).

With a relative low prevalence of 4.99% of patients, it is important to consider the overall utility of this questionnaire. Despite the PSQ having a high sensitivity and specificity, the low prevalence leads to a low positive predictive value (PPV). Predictive values are not fixed values that are inherent to the questionnaire, but rather, are dependent on the specificity, sensitivity, and the prevalence of the disorder. Positive predictive value indicates the proportion of the patients who actually have a SRBD that had a positive questionnaire outcome. Negative predictive value (NPV) indicates the proportion of patients who do not have a SRBD that had a negative questionnaire result.

$$PPV = \frac{Sensitivity\ x\ prevalence}{(Sensitivity\ x\ prevalence) + (1 - specificity)\ x\ (1 - prevalence)}$$

$$NPV = \frac{Specificity\ x\ (1 - prevalence)}{[Specificity\ x\ (1 - prevalence)] + [(1 - sensitivity)\ x\ prevalence]}$$

When the overall prevalence of disease is low, the positive predictive values become lower and the negative predictive value is higher. Given the 4.99% prevalence of identified SRBD in this

population, and the assumed PSQ sensitivity of 85% and specificity of 81%, the positive predictive value is only 19%. For any positive PSQ test, the probability that the test is a true positive is 19%, and the probability that the test is false is 81%. This means that almost one out of every 5 children that has a positive PSQ test result will actually have a SRBD. Meanwhile, the other 4 children will not actually have a SRBD, but actually had a false positive test result. The prevalence that we determined using the PSQ most likely overestimates the actual prevalence of SRBD in private orthodontic practice. The actual prevalence is probably closer to 1%, with 4% of the patients having a false positive result. This study should be considered as a higher estimate of prevalence for SRBD in pediatric patients.

With the same assumed sensitivity and specificity, the NPV is 99%. For any negative PSQ test, the probability that the test is a true negative is 99%, and the probability that the test is a false negative is 1%. This means that nearly all of the children identified by the PSQ as not having a SRBD, will not actually have a SRBD.

With such a low PPV and a high NPV, this indicates that the PSQ yields a very high number of false positive values and a negligible number of false negatives. For orthodontists in private practice, this indicates that routine use of the PSQ to screen all new children that may be at high risk for SRBD could potentially result in excess referrals to a sleep specialist, when the children, indeed, do not actually have a SRBD. To help decrease the number of false positive tests and specialist referrals, the PSQ could be used in combination with a thorough physical examination and discussion with the parents about the child's behavior, as well as sleep habits, and any other risk factors such as asthma, allergies, or obesity.

We found that sex of the patient has an effect on having a positive PSQ result, however, age does not have an effect. Males have a 2.1 times greater chance of having a positive PSQ result

that females. This agrees with prior studies indicating that males may be at an increased risk for having a SRBD (Alsubie & BaHammam, 2017; Lumeng & Chervin, 2008).

From the exploratory factor analysis, three seemingly related factor were identified as being possible indicators for a positive PSQ test result; ADHD, snoring, and daytime sleepiness. This data reduction strategy suggests that for clinicians, instead of using the entire 22-point PSQ, it may be just as useful to discuss these three topics with the parents on the initial examination. Simple questions can be utilized, such as: "Does your child have symptoms of ADHD or diagnosed ADHD? Explain your child's snoring. Is your child tired during the daytime?". In this study, the strongest factor identified was the one with questions pertaining to ADHD symptoms.

There are several limitations to this study. Our prevalence rate estimate is based on a private orthodontic practice in the suburbs of Pittsburgh, Pennsylvania. The prevalence estimate may not be generalized to other orthodontic practices in other parts of the country with a different demographic of pediatric patients. Most of our patients were between ages 7 and 12, so we may have underestimated the number of children younger than 7 years old that have larger lymphoid tissue and those older than 12 years old going through puberty, which may be risk factors for having a SRBD.

The PSQ was originally validated using patients found at a sleep center (Chervin, et al., 2007). This is not similar to this sample population, which consisted of children presenting for routine orthodontic treatment. Future research would be needed to determine if any of these children were referred to an otolaryngologist (ENT), and how many of them were diagnosed with a SRBD using the gold standard test, polysomnography. Using these diagnoses, a sensitivity and specificity of the PSQ could be validated for this orthodontic patient study population.

In using an exploratory factor analysis, there is no gold standard to confirm the findings. It can only be used to exploring the data and suggesting a reduction in the number of questions utilized to identify a positive test result (Costello & Osborne, 2005). The results of this analysis suggest that three questions about the patient's symptoms can be utilized, but this cannot identify causality of SRBD and should be used as adjunct means for identifying patients at risk for SRBD.

In summary, the prevalence of SRBD in this population was found to be 4.99%. In addition, this study found that males had a greater chance of having a SRBD than females, regardless of their age. When initially screening pediatric patients that may be at risk for SRBD, it may be just as beneficial as administering of the PSQ for the clinician to inquire the parents about the child's ADHD related symptoms, snoring, and daytime sleepiness.

6.0 CONCLUSIONS

The prevalence of sleep-related breathing disorders at a private orthodontic practice in Western Pennsylvania, as determined by routine administration of the PSQ, was found to be 4.99%. Age was not a confounding variable for a positive PSQ result. Sex was found to be a confounding variable, with males having a 2.1 times greater chance of having a positive test than female patients. Due to the low prevalence of SRBD in this private orthodontic practice, it is not suggested to incorporate the PSQ alone in routine pediatric medical histories to help identify patients who are at high risk of having a SRBD, but rather the PSQ can be used as an adjunct to a full clinical exam. In addition, discussing the patients ADHD related symptoms, snoring, and daytime sleepiness with the parents on initial exam may be beneficial at identifying patients at an increased risk for SRBD.

APPENDIX A

IRB EXEMPTION

Pitt Seal

University of Pittsburgh
Institutional Review Board

3500 Fifth Avenue
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)
http://www.irb.pitt.edu

Memorandum

To: Tina Poulson

From: IRB Office

Date: 10/30/2017

IRB#: PRO17020147

Subject: Pediatric Sleep Questionnaire used to assess sleep related breathing disorders in a Western Pennsylvania private orthodontic practice

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The above-referenced project has been reviewed by the Institutional Review Board. Based on the information provided, this project meets all the necessary criteria for an exemption, and is hereby designated as "exempt" under section

45 CFR 46.101(b)(4)

Please note the following information:

- Investigators should consult with the IRB whenever questions arise about whether planned changes to an exempt study might alter the exempt status. Use the "**Send Comments to IRB Staff**" link displayed on study workspace to request a review to ensure it continues to meet the exempt category.
- It is important to close your study when finished by using the "**Study Completed**" link displayed on the study workspace.
- Exempt studies will be archived after 3 years unless you choose to extend the study. If your study is archived, you can continue conducting research activities as the IRB has made the determination that your project met one of the required exempt categories. The only caveat is that no changes can be made to the application. If a change is needed, you will need to submit a NEW Exempt application.

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.

BIBLIOGRAPHY

Alsubie, H., & BaHammam, A. (2017). Obstructive Sleep Apnoae: Children are not little adults. *Paediatr Respir Rev.*(21), 72-79.

American Academy of Sleep Medicine. (2005). International classification of sleep disorders: diagnostic and coding manual. 2nd edition. Westchester, IL: American Academy of Sleep Medicine.

Biggs, S., Walter, L., Jackman, A., Nisbet, L., Weichard, A., Hollis, S., . . . Horne, R. (2015). Long-term cognitive and behavioral outcomes following resolution of sleep disordered breathing in preschool children. *PLoS ONE, 10*, 9.

Bonuck, K., Chervin, R., & Howe, L. (2015). Sleep-disordered breathing, sleep duration, and childhood overweight: a longitudinal cohort study. *Journal of Pediatrics, 166*(3), 632-639.

Camacho, M., Chang, E., Song, S., Abdullatif, J., Zaghi, S., Pirelli, P., . . . Guilleminault, C. (2017). Rapid Maxillary Expansion for Pediatric Obstructive Sleep Apnea: A Systematic Review and Meta-Analysis. *The Laryngoscope*, 1712-1719.

Chervin, R., Ellenberg, S., Hou, X., Marcus, C., Garetz, S., Katz, E., . . . Rosen, C. (2015). Prognosis for spontaneous resolution of OSA in children. *Chest, 148*(5), 1204-1213.

Chervin, R., Hedger, K., Dillon, J., & Pituch, K. (2000). Pediatric Sleep Questionnaire (PSQ): validity and reliability of scales for sleep-disordered breathing, snoring, sleepiness, and behavioral problems. *Sleep Medicine*, 21-32.

Chervin, R., Weatherly, R., Garetz, S., Ruzicka, D., Giordani, B., Hodges, B., . . . Guire, K. (2007). Pediatric Sleep Questionnaire: Prediction of Sleep Apnea and Outcomes. *Arch Otolaryngol Head Neck Surg*, 216-222.

Chng, C., Goh, D., Wang, X., Tan, T., & Ong, N. (2004). Snoring and atopic disease: a strong association. *Pediatric Pulmonology, 28*, 210-216.

Costello, A. B., & Osborne, J. W. (2005, July). Best Practices in Exploratory Factor Analysis: Four Recommendations for Getting the Most From Your Analysis. *Practical Assessment, Research & Evaluation, 10*(7), 2-9.

De Luca Canto, G., Pacheco-Pereira, C., Avdinoz, S., Major, P., Flores-Mir, C., & Gozal , D. (2015). Biomarkers associated with obstructive sleep apnea: a scoping review. *Sleep Med Rev, 23*, 28-45.

De Luca Canto, G., Singh, V., Major, M., Witmans, M., El-Hakim, H., Major, P., & Flores-Mir, C. (2014). Diagnostic capability of questionnaires and clinical examinations to assess sleep-disordered breathing in children. *JADA, 145*(2), 165-178.

Dehlink, E., & Tan, H. (2016). Update on paediatric obstructive sleep apnoea. *Journal of Thoracic Disease, 8*(2), 224-235.

Downey III, R., Perkin, R., & MacQuarrie, J. (1999). Upper airway resistance syndrome: sick, symptomatic but underrecognized. *Sleep, 16*, 620-623.

Ehsan, Z., Kercsmar, C., Collins, J., & Simakajornboon, N. (2017). Validation of the pediatric sleep questionnaire in children with asthma. *Pediatric Pulmonology, 52*, 382-389.

El, H., & Palomo, J. (2014). Three-dimension evaluation of upper airway following rapid maxillary expansion: a CBCT study. *Angle Orthodontist, 84*(2), 265-273.

Fastuca, R., Perinetti, G., Zecca, P., Nucera, R., & Caprioglio, A. (2015). Airway compartments volume and oxygen saturation changes after rapid maxillary expansion: a longitudinal correlation study. *Angle Orthodontist, 85*(6), 955-961.

Görgülü, S., Gokce, S., Olmez, H., Sagdic, D., & Ors, F. (2011). Nasal cavity volume changes after rapid maxillary expansion in adolescents evaluated with 3-dimensional simulation and modeling programs. *AJO-DO, 140*, 633-640.

Graf, I., & Neuschulz, J. (2016). Sleep-disordered breathing in orthodontic practice: Prevalence of snoring in children and morphological findings. *Journal of Orofacial Orthopedics, 77*, 129-137.

Guilleminault, C., Quo, S., Huynh, N., & Li, K. (2008). Orthodontic expansion treatment and adenotonsillectomy in the treatment of obstructive sleep apnea in prepubertal children. *Sleep, 31*(7), 953-957.

Hans, M. (2016). Sleepless in Orlando: teenagers and sleep disordered breathing. *AAO Annual Session.* Orlando, FL.

Huang, Y.-S., Guilleminault, C., Lee, L.-A., Lin, C.-H., & Hwang, F.-M. (2014). Treatment outcomes of adenotonsillectomy for children with obstructive sleep apnea: a prospective longitudinal study. *Sleep, 37*(1), 71-76.

Kaditis, A., Alvarez, M., Boudewynx, A., Alexopoulos, E., Ersu, R., Joosten, K., . . . Verhulst, S. (2016). Obstructive sleep disordered breathing in 2- to 18-year-old children: diagnosis and management. *European Respiratory Journal, 47*, 69-94.

Kadmon, G., Chung, S., & Shapiro, C. (2014). I'M SLEEPY: A short pediatric sleep apnea questionnaire. *International Journal of Pediatric Otorhinolaryngology, 78*, 2116-2120.

Lumeng, J., & Chervin, R. (2008). Epidemiology of pediatric obstructive sleep apnea. *Proceedings of the American Thoracic Society, 5*, 242-252.

Miano, S., Esposito, M., Foderaro, G., Ramelli, G., Pezzoli, V., & Manconi, M. (2016). Sleep-related disorders in children with attention-deficit hyperactivity disorder: preliminary results of a full sleep assessment study. *CNS Neuroscience & Therapeutics, 22*, 906-914.

Oliveira, N., Da Silveira, A., Viana, G., Kusnoto, B., Smith, B., & Evans, C. (2008). Relationship between rapid maxillary expansion and nasal cavity size and airway resistance: short- and long-term effects. *AJO-DO, 134*, 370-382.

Owens, J., Spirito, A., McGuinn, M., & Nobile, C. (2000). Sleep habits and sleep disturbance in elementary school-aged children. *Developmental and Behavioral Pediatrics, 21*, 27-36.

Rosen, C., Larkin, E., Kirchner, H., Emancipator, J., Bivins, S., Surovec, S., . . . Redline, S. (2003). Prevalence and risk factors for sleep-disordered breathing in 8- to 11-year-old children: association with race and prematurity. *Journal of Pediatrics, 142*(4), 383-389.

Yu, X., Fujimoto, K., Urushibata, K., Matsuzawa, Y., & Kubo, K. (2003). Cephalometric analysis in obese and nonobese patients with obstructive sleep apnea syndrome. *CHEST, 124*(1), 212-218.

Zhao, Y., Nguyen, M., Gohl, E., Mah, J., Sameshima, G., & Enciso, R. (2010). Oropharyngeal airway changes after rapid palatal expansion evaluated with cone-beam computed tomography. *AJO-DO, 137*, 71-78.