RESEARCH PROTOCOL

Feasibility of Unattended Home Polysomnography and Comparison to In-laboratory Polysomnography in Pediatric Patients

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SYNOPSIS

Study Title	Feasibility of Unattended Home Polysomnography and Comparison to In-laboratory Polysomnography in Pediatric Patients
Objectives	1) To assess the feasibility of unmonitored polysomnography and 2) to compare apnea hypopnea index (AHI), average SPO_2, and SPO_2 nadir between unmonitored polysomnography and in-laboratory polysomnography in pediatric patients.
Study Period	2 years
Number of Subjects	100 children, ages 5 to 12 years of age
Study Design	Single-center, un-blinded, feasibility, methods comparison, and non-inferiority study
Inclusion and Exclusion Criteria	Inclusion Criteria a) 5- to 12-years-old b) Parental informed consent c) Suspected Sleep Disordered Breathing Exclusion Criteria a) Developmental delay b) Use of home oxygen c) History of Parasomnia (e.g. narcolepsy, restless leg syndrome, somnambulism) d) History of tracheal surgery e) History of tracheal stenosis f) History of Nocturnal Hypoventilation g) History of Central Sleep Apnea h) Use of a Ventilatory Assist Device (e.g. Non-Invasive Positive Pressure Ventilation)
Measurements	An unattended at-home overnight sleep study using a Type III portable monitor (polysomnography) will be performed on all subjects. All subjects will also have an inpatient, Type I monitored polysomnography performed in the St. Louis Children's Hospital Sleep Laboratory. For both studies the Apnea-Hypopnea Index, Average SPO_2, and SPO_2 nadir will be determined.
Outcomes	Primary outcome will be the feasibility of obtaining greater than or equal to 6 hours of data adequate for polysomnography analysis and determination of an apnea hypopnea index (AHI), average SPO_2, and SPO_2 nadir using un-attended polysomnography. Secondary outcomes will be the comparison of AHI, average SPO_2, and SPO_2 nadir between unattended and inpatient polysomnography. An exploratory outcome will be a comparison of the McGill Oximetry Score between unattended and inpatient polysomnography.

1. Background and Rationale: Childhood obstructive sleep apnea (OSA), defined by periodic, partial or complete obstruction of the upper airway during sleep, is a common disorder in pediatric patients. The prevalence of OSA in children is as high as 5%, and if untreated, OSA can result in significant deleterious behavioral, cognitive, and cardiovascular consequences [1]. First line treatment for pediatric OSA is tonsillectomy and adenoidectomy. This surgery is estimated to be curative in approximately 60% of patients, and even in patients where a complete cure is not achieved there is a significant reduction in symptoms in most cases [2]. Given the high prevalence and excellent treatment options, it is important that if OSA is suspected a diagnosis is made accurately and efficiently.

The current gold standard for the diagnosis of OSA is in-laboratory polysomnography (PSG), otherwise known as a Type I sleep study. However, in-laboratory PSG is expensive and time consuming as tests are administered by individuals specially trained in sleep medicine in an outpatient setting, and include seven or more channels to monitor sleep, cardiovascular parameters, oximetry, patient position, respiratory effort, and breathing. Furthermore, due to regional variations in sleep center locations, patients do not uniformly have access to centers that perform in-laboratory PSGs. Thus, there has been considerable interest in developing and validating methods to perform home sleep apnea testing, also known as portable monitoring. Indeed, the American Academy of Sleep Medicine (AASM) has recommended the use of portable monitoring as an alternative to in-laboratory PSG for the diagnosis of OSA in selected adult patients [3].

Type II studies are similar to Type I studies except they are not attended by a specially trained individual and can be administered in a subject's home. Type III portable monitoring uses fewer channels (generally 4 to 7) to obtain data than does in-laboratory PSGs, and does not usually have a registered sleep technologist present during the study. In certain circumstances this may reduce the fidelity of the data collected. However, portable monitoring has several advantages over in-laboratory PSGs, including reduced cost, increased patient accessibility, and critically, the ability to assess a more typical night's sleep, since the subject is sleeping in their own home instead of an unfamiliar sleep laboratory. However, while approved for adults, the latest guidelines on childhood OSA published by the American Academy of Pediatrics in 2012 concluded that there is insufficient data in children to either support or refute the utility of portable monitoring in the diagnosis of pediatric OSA [4,5]. Several studies have demonstrated the feasibility of both Type II and Type III portable monitoring in children across multiple age ranges [1,4-6], however direct comparison between portable monitoring and in-laboratory attended PSG in children is limited [1,6], and to quote the 2012 guidelines, "… *additional studies of ambulatory PSG in children of varying ages are needed."* In addition, continued technological advances in sleep monitor design has decreased the size of commercially available sleep monitors to the point that some are now size-appropriate for pediatric patients.

The purpose of the study proposed below is twofold. First we will test the feasibility of conducting portable sleep monitoring in school aged children using the Clevemed Sleepview (www.clevelmed.com), one of the smallest portable sleep monitors commercially available at 57 grams. Second we will perform a direct comparison between the results obtained with this portable sleep monitor and those obtained from a standard-of-care in-laboratory attended sleep study performed at the St. Louis Children's Hospital Pediatric Sleep Center. These comparisons will be offered to the families of school age children suspected of having sleep disordered breathing who present to the Washington University Pediatric Otolaryngology Department. We hypothesize that in-laboratory attended polysomnography and portable monitoring will yield similar results in the diagnosis of sleep disordered breathing in school aged pediatric patients. These initial comparisons will be conducted in otherwise healthy children. Future studies will expand this comparison to children with underlying comorbidities, including younger children and those with developmental delay.

2. Enrollment: Patients and their families who present to the Washington University Department of Pediatric Otolaryngology with a suspected diagnosis of sleep disordered breathing will be given information regarding the study in the otolaryngologist's office. A member of the research team will approach the patient and their family once they are identified as needing an in-laboratory sleep study as part of their work up for sleep disordered breathing. Written informed consent will be obtained from the patient's family and assent will be obtained from the patient at that time. The study group will consist of one hundred patients who require diagnostic PSG for sleep disordered breathing. Inclusion and exclusion criteria are based on independent risk factors for respiratory complications following tonsillectomy and adenoidectomy [7]. The Washington University Pediatric Otolaryngology clinic sees approximately 100 patients a month with tonsillar hypertrophy, snoring, or other concerns for sleep disordered breathing that would warrant a sleep study; the St. Louis Children's Hospital Sleep Laboratory performs approximately 1300 Type I sleep studies a year. We plan to enroll 125 patients in this study, assuming a 20% drop out rate from the study, with an end goal of one hundred study patients. Given the frequency with which patients present with concern for sleep disordered breathing this should be accomplishable in the planned time frame.

3. Eligibility:

3.1. *Inclusion Criteria*

- 3.1.1. 5- to 12-years-old
- 3.1.2. Parental informed consent
- 3.1.3. Suspected Sleep Disordered Breathing

3.2. *Exclusion Criteria*

- 3.2.1. Developmental delay
- 3.2.2. Use of home oxygen
- 3.2.3. History of Parasomnia (e.g. narcolepsy, restless leg syndrome, somnambulism)
- 3.2.4. History of tracheal surgery
- 3.2.5. History of tracheal stenosis
- 3.2.6. History of Nocturnal Hypoventilation
- 3.2.7. History of Central Sleep Apnea
- 3.2.8. Use of a Ventilatory Assistant Device

4. Methods:

4.1. Study design: Single-center, un-blinded, feasibility, and methods comparison study

4.2. Otolaryngology Clinic Assessment: Subjects will be identified from patients presenting to the Washington University in St. Louis Pediatric Otolaryngology Clinic who are suspected of having sleep disordered breathing. Subjects who are identified by an attending otolaryngologist as requiring polysomnography as part of their work up will then be approached by a member of the research team who will explain the study to the subject and their family and obtain informed consent. During this visit, subjects will also be administered a short, validated sleep questionnaire, the Modified STOP-Bang Tool for Stratifying OSA Risk in Adolescent Children [9]. This questionnaire is 8 questions and routinely administered in the Washington University Pediatric Otolaryngology offices.

4.3.1. Unattended Polysomnography: All eligible subjects will be asked to conduct an unattended, overnight sleep study performed in their home prior to in-laboratory polysomnography, using a standard Type III portable monitor. This study will be performed with

an FDA approved sleep monitor (e.g CleveMed SleepView or similar). Per American Academy of Sleep Medicine (AASM) guidelines, portable sleep monitoring will include air flow, respiratory effort, heart rate and blood oxygenation. Airflow will be measured using a nasal cannula and pressure transducer which is located within the home sleep test (HST) recording device. Respiratory effort will be recorded using Respiratory Inductance Plethysmography (RIP) belts that will go around the chest at the nipple line and around the abdomen at the navel level. Blood oxygenation and heart rate will be recorded by pulse oximetry that will be placed on one finger. Each study participant and their family will be shown and educated on how to apply each of the sensors by a member of the study team. Unattended sleep studies will be interpreted by an individual trained in sleep medicine. The first assessment of the Unattended sleep study for each individual patient will be readability of the recordings.

Polysomnography testing will determine the apnea hypopnea index (AHI), blood saturation oxygen nadir (SPO_2 nadir), and average blood oxygen saturation [3]. The AHI is defined as the average number of hypopneas (episodes of decreased breathing) and apneas (episodes of cessation of breathing) per hour of sleep. Apneas and hypopneas will be defined per the American Academy of Sleep Medicine manual for scoring sleep and associated events [10]. The objective is to obtain greater than or equal to 6 hours of data adequate for polysomnography analysis and determination of an apnea hypopnea index (AHI), average SPO_2, and SPO_2 nadir using home un-attended polysomnography.

A McGill Oximetry Score [11], which only uses the frequency and depth of SPO_2 desaturations throughout a night's sleep to assign a score of 1 (normal/inconclusive), 2 (mildly abnormal), 3 (markedly abnormal), and 4 (severely abnormal) will be also be assigned to each home sleep test.

Fidelity of data collection using at home sleep studies is reliable, but not 100% reliable [3]. For example, subjects may unconsciously remove the nasal cannula or the finger pulse oximeter in their sleep, resulting in data drop outs. A subject's parent or guardian will be requested to periodically monitor the subject throughout the night and be instructed on how to reapply sensors to minimize data drop outs. Should data from an initial sleep study be uninterpretable based on sleep study expert opinion we will ask the subjects to attempt the unattended sleep study an additional time. A recent study on the feasibility of Type II comprehensive (i.e. greater than 7 channel) pediatric sleep studies, reported that 91% of home sleep studies are successful on initial attempt and a total of 98% are successful after one repeat testing [12]. A 2013 assessment of Type III sleep studies performed both in a hospital setting (26 patients) and at home (75 patients) found that technically acceptable and interpretable studies were obtained from 93% of subjects [13].

Should data from the second sleep study be uninterpretable we will not proceed with further testing of these subjects by home sleep study. Regardless of whether a subject successful completes home sleep testing, in-laboratory polysomnography will still be performed as part of their work up for sleep disordered breathing.

4.3.2. *Parental Monitoring Plan for Unattended Polysomnography*: Parents will be instructed that while the device is FDA approved for use in adults it is not FDA approved in children and therefore they will need to monitor their child more closely during the night than they would have to during a typical night's sleep. Parents should remain in close enough proximity to hear their child should their child call out for them during the night for assistance with any aspect of the device. Parents will be instructed that improper routing of leads may result in a choking hazard. Parents will be instructed to inspect for proper effort belt, nasal cannula, and pulse oximeter placement at least every two hours. Parents will be instructed that should they ever feel the device presents a significant choking hazard to their child they should entirely remove the device and stop the study.

4.4. In-laboratory Polysomnography: All eligible subjects will have in-laboratory polysomnography as is routinely performed in the diagnostic work up for suspected sleep disordered breathing. The in-laboratory sleep study will be done at the St. Louis Children's Hospital Pediatric Sleep Center, which is an American Academy of Sleep Medicine accredited sleep disorder center. The Center is sound-proof, and has been designed to provide as natural and home-like an atmosphere as possible. Infrared monitoring equipment allows for patient observation from outside of the patient's sleep room. At least one parent is required to stay in the room overnight with the patient. A second parent can stay as well, but not required. The Center is located inside of St. Louis Children's Hospital within an inpatient medical unit, which is staffed with physicians and nurses 24 hours per day.

Per American Academy of Sleep Medicine (AASM) guidelines, in-laboratory sleep monitoring is attended by a specially trained technologist who sets up the sleep study, observes the subject throughout the duration of the sleep study, and is available to troubleshoot in real time any monitoring issues that may arise. In-laboratory polysomnography consists of 21 leads that measure electroencephalogram, electrocardiogram, air flow, respiratory effort, heart rate, activity, and blood oxygenation monitoring. In-laboratory sleep studies are scored by a trained Registered Polysomnographic Technologist or Registered Sleep Technologist and interpreted by a physician. Polysomnography testing will determine the sleep stages, apnea hypopnea index (AHI), blood saturation oxygen nadir (SPO_2 nadir), and average blood oxygen saturation, as defined above [3]. A McGill Oximetry Score will also be calculated for the in-laboratory PSG.

4.6. Subject assessments: The unattended home polysomnogram will record blood oxygen concentration, pulse rate, respiratory effort, air flow and respiratory effort. The in-laboratory polysomnogram will record these parameters and will also measure electroencephelography, electrocardiogram, and heart rate.

4.7. Conclusion of study: The study ends with the completion of the in-laboratory polysomnogram. Additionally, the study ends at any time the patient or parent/caregiver requests it to end. Appropriate treatment for any diagnosis of sleep disordered breathing will proceed based on the attending otolaryngologist recommendations. Recommendations and treatment will not be affected by participation in the investigation. As home sleep testing in pediatric patients is exploratory; only the in-laboratory sleep study will be used in making any diagnosis of sleep disordered breathing and in determining treatment options.

5. Data Collection and Monitoring

5.1. Clinical Assessments: At the completion of both the unattended and in-laboratory polysomnography we will determine an Apnea-Hypopnea Index, Average SPO_2, and SPO_2 nadir for each subject. An assessment of the technical quality of each study will be made. The in-laboratory polysomnogram will be scored and interpreted via standard practice for the St. Louis Children's Hospital Pediatric Sleep Center and included in the patient's medical record. The unattended polysomnogram will not be included in the patient's medical record and will only be accessible to study team members.

6. Outcome Measures

7.1. Primary Outcome Measure: The feasibility of obtaining greater than or equal to 6 hours of data adequate for polysomnography analysis and determination of an apnea hypopnea index (AHI), average SPO_2, and SPO_2 nadir using home un-attended polysomnography.

6.2. Secondary Outcome Measures

6.2.1. Comparison of AHI between unattended and in-laboratory polysomnography

6.2.2. Comparison of average SPO_2 between unattended and in-laboratory polysomnography

6.2.3. Comparison of SPO_2 nadir between unattended and in-laboratory polysomnography
6.2.4. Comparison of sleep disordered breathing diagnosis between unattended and in-laboratory polysomnography

6.3. Exploratory Outcomes Measure: Comparison of McGill Oximetry Scores between unattended and in-laboratory polysomnography.

6.4. Analysis: The primary outcome is the feasibility of obtaining an adequate sleep study from unattended polysomnography in pediatric patients. Percentages of studies that have 6 hours of data sufficient for analysis will be reported. The study will be defined feasible if 85% or more of participants provide 6 or more hours of analyzable data. Descriptive statistics will be used to describe the AHI, SPO_2 nadir, SPO_2 average, and diagnosis obtained using each method. Continuous secondary outcome measures will be compared using paired-t tests or its non-parametric equivalent Wilcoxon signed rank test. The Friedman test will be used to compare ordinal outcome measures. Agreement between home sleep testing and in-laboratory PSGs will also be compared using Bland-Altman Analysis [14]. A General Linear Model Approach will be used to explore the role of potential confounders including age, sex, weight, and race differences when performing analyses. If our hypothesis is correct, home sleep studies will be feasible in our study population.

7. Potential Risks

7.1. Unattended Polysomnography: There is minimal risk associated with the sleep study. Per AASM guidelines [3] unattended portable monitoring may be used to facilitate the diagnosis of OSA in adults and as such this is standard of care in that population. While no such recommendation for the use of unattended portable monitoring exists for pediatric patients, we will use an FDA approved device to perform the unattended polysomnography and patients and their families will be instructed in its use by a trained member of the research team. Patients and their families will also be provided a pictoral instruction manual on the proper application and use of the device. Family members will be instructed that the improper use of the device may present a choking hazard to their child. Family members will be instructed to listen out for their child throughout the night (for example by keeping bedroom doors open), and to check on their child for proper nasal cannula, effort belt, and pulse ox placement at least every two hours.

Patients may experience mild discomfort from the ambulatory sleep monitoring devices. Patients' family members may experience mild inconvenience during the setup of the sleep monitor, while monitoring of their child during the home sleep study, and should any trouble shooting be required during the time their child is asleep. Patients and their families may experience mild inconvenience if they are asked to perform a second sleep study due to results from the first study being uninterpretable.

7.2. In-laboratory Polysomnography: This is standard of care in the diagnosis of pediatric sleep disordered breathing. The in-laboratory polysomnogram is being conducted in an AASM accredited sleep disorder center that conducts 1300 sleep studies per year and has been in continuous operation since 1993. There is minimal risk associated with in-patient polysomnography. Patients may experience mild anxiety and discomfort by sleeping in an unfamiliar place for one night.

7.3 Steps Taken to Mitigate Risk: Studies are conducted under the supervision of the investigating physicians and personnel with specialty training in sleep medicine. Research team members are trained and experienced in performing research in human subjects, and in monitoring for adverse effects.

Inclusion and exclusion criteria, monitoring, and the clinical protocol are designed to ensure that risks are absolutely minimal. Subjects and their families are informed that participation is voluntary and they may refuse to participate and may withdraw from the study at any time without penalty. Subjects will be told that in the unlikely event of a physical injury as the direct result of study procedures, they will be cared for by a member of the investigating team at no cost, within the limits of the Washington University compensation plan.

During the unattended sleep study, there is minimal risk. Subjects will be in their own home and should the unattended sleep study equipment prove too much of a discomfort or too challenging for parents to maintain they will be free to remove the device at any time. A specific monitoring plan to minimize the possibility that the device could present a choking hazard is described above. In-laboratory, attended polysomnography is standard of care and as such carries minimal risk.

Regarding confidentiality; 1) all subjects will be assigned a study ID number, and 2) unattended polysomnography reports will be kept confidentially. They will be coded, with information linking code numbers to names kept at a separate location, under lock and key. 3) The link to identifiers will be destroyed at the end of the study. 4) Data will be stored under lock and key (office, file cabinet) and only the investigators and research team will have access. If data are published, there will be no link to identifiers. Study data will not be revealed to any organization, individuals other than the subjects, or the subjects themselves. 5) Study data from the unattended polysomnography will not be entered in subjects' medical records.

8. Management of Intercurrent Events

8.1. Adverse Experiences

The investigator will closely monitor subjects for evidence of adverse events. All adverse events will be reported and followed until satisfactory resolution. The description of the adverse experience will include the time of onset, duration, intensity, etiology, relationship to the study drug (none, unlikely, possible, probable, highly probable), and any treatment required.

8.2. Premature Discontinuation

If a subject withdraws from the study, the subject will be replaced to provide the required number of subjects. Subjects will be withdrawn if the investigator decides that discontinuation is in the best interest of the subject, or the subject requests withdrawal from the study.

9. Data and Safety Monitoring Plan

Studies conducted in the Departments of Pediatrics, Otolaryngology, and Anesthesiology follow the Washington University Institutional Review Board Policies and Procedures (last revision April 20, 2015). All individuals working on the study are required to read and be familiar with and compliant with the IRB Policies and Procedures. The specific monitoring plan for this investigation is commensurate with the risks and the size and complexity of the investigations planned. The potential risks are attributable to performing unattended polysomnography. Based on the small size and relatively low risk nature of the protocol, the investigating physicians are involved in the monitoring plan. A full DSMB is not needed. These individuals will review the annual summary of adverse events. In addition, they will review all reports of a Serious Adverse Event, or an Unexpected Adverse Event. The investigators will follow the requirements for principle investigator reporting requirements as outlined in Section X of the IRB Policies and Procedures.

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Appendix A: Modified STOP-Bang Tool for Stratifying OSA in Children
Modified from Combs (2015)[8]

1) **S**NORING: How often does your child snore loudly? **Don't know, never, rarely, occasionally, frequently, or almost always.**

2) **T**IRED: Is your child sleepy during the daytime? **Don't know, never, rarely, occasionally, frequently, or almost always.**

3) **O**BSERVED APNEA: Does your child stop breathing during sleep? **Don't know, never, rarely, occasionally, frequently, or almost always.**

4) BLOOD **P**RESSURE: Systolic or diastolic blood pressure greater than or equal to 95th percentile for height and age? **Yes or No?**

5) **B**ODY MASS INDEX: Greater than 95th percentile for age? **Yes or No?**

6) **A**CADEMIC PROBLEMS: Does your child have learning problems? **Don't know, never, rarely, occasionally, frequently, or almost always.**

7) **N**ECK SIZE: Is your child's neck circumference greater than the 95th percentile for age? **Yes or No?**

8) **G**ENDER: Is your child's **Gender** Male? **Yes or No?**

Answers with choice that include don't know, never, rarely, occasionally, frequently, or almost always are collapsed into a positive or negative response in the following manner:

1) Frequently or almost always is considered a positive response.
2) Don't know, never, rarely, or occasionally are considered a negative response.

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