Validation of ApneaLink Air home sleep testing in the diagnosis of obstructive sleep apnea in adolescent children

NCT03748771

October 16, 2017

UCSD Human Research Protections Program
RCHSD Only--New Biomedical Application
RESEARCH PLAN INSTRUCTIONS

Instructions for completing the Research Plan are available on the HRPP website.
The headings on this set of instructions correspond to the headings of the Research Plan.
General Instructions: Enter a response for all topic headings.
Enter "Not Applicable" rather than leaving an item blank if the item does not apply to this project.

1. PROJECT TITLE

Validation of ApneaLink Air home sleep testing in the diagnosis of Obstructive Sleep Apnea in Adolescent Children

2. PRINCIPAL INVESTIGATOR

Rakesh Bhattacharjee, MD - Pediatrics

3. FACILITIES

Rady Children's Hospital – Sleep Laboratory

4. ESTIMATED DURATION OF THE STUDY

1 year

5. LAY LANGUAGE SUMMARY OR SYNOPSIS (no more than one paragraph)

Obstructive sleep apnea (OSA) is highly prevalent in children affecting 2-3% of children and up to 10% of obese children. The reported prevalence is likely underestimated due to the lack of available laboratory polysomnography (PSG) testing for children. The high prevalence of OSA coupled with an increase in obesity, a major risk factor of OSA in children, has resulted in a significant strain for in laboratory PSG including children in the greater San Diego county. Currently, home sleep testing (HST) in children is restricted based on the limited availability of HST devices on children that have attained clearance by the US Food and Drug Administration (FDA). In this study, we will assess the feasibility and the validity of the ApneaLink Air HST device in children over the age of 12. The ApneaLink Air HST device is cleared for the diagnosis of OSA in adults and is frequently used amongst adult sleep medicine physicians. We will recruit twenty children over the age of 12 who will have their clinically indicated in laboratory PSG performed at Rady Children's Hospital. We will concurrent to their in-laboratory PSG have their sleep assessed using the ApneaLink Air device. Ten children will repeat the ApneaLink Air HST at home following their sleep study within one week, and the remaining ten children will in fact have their ApneaLink Air HST performed within one week prior to their in laboratory clinically indicated PSG.

6. SPECIFIC AIMS

1. To determine validity, feasibility, and accuracy of HST as a diagnostic tool for assessing children over the age of 12 for diagnosing OSA in children with symptoms compatible with OSA
2. To assess patient satisfaction with HST compared to in laboratory PSG in the diagnostic work up for pediatric OSA.

7. BACKGROUND AND SIGNIFICANCE

Obstructive sleep apnea (OSA) is a serious, common, and under diagnosed disorder that challenges healthcare resources. The typical presenting feature of OSA in children is snoring. The prevalence of snoring in children ranges from 3-12%[1] but the exact prevalence of OSA in children using an overnight in laboratory PSG is about 2-3%. OSA is associated with numerous adverse health outcome issues such as behavioral, neurocognitive, and cardiovascular, metabolic complications as well as overall decreased quality of life. Behavioral issues include depression,[2] behavior problems, aggression,[3] excessive daytime sleepiness,[4] and anxiety.[5] Neurocognitive issues include decreased IQ,[6] poor school performance,[7] decreased executive function,[8] learning difficulties, decreased information processing, decreased memory, poor visuo-spatial skills,[9] language, verbal skills, and attention deficits.[6] Cardiovascular complications range from endothelial dysfunction[10] systemic hypertension[11] to pulmonary hypertension secondary to recurrent hypoxia and hypercapnia leading to cor-pulmonale.[12] Asymptomatic degrees of pulmonary hypertension have been reported in up to 40% of pediatric patients with OSA.[13]

Comparing to the gold standard of in-laboratory PSG, other methods of diagnosing OSA including by history, physical examination, radiological studies, assessment of snoring and ambulatory PSG including home oximetry have reasonable specificity but limited sensitivity (high false negative rate)[1]. When in laboratory PSG is not available, clinicians are recommended to utilize these alternative approaches.

Notwithstanding, given the increased awareness of the complications related to Pediatric OSA more children are screened for OSA and undergo some form of diagnostic evaluation. While in-laboratory PSG remains the gold standard for diagnosing OSA in children, the dearth of Pediatric sleep labs and Pediatric sleep specialists has rendered it challenging to adequately diagnose children referred for symptoms suggestive of OSA. In addition to limited availability of in laboratory pediatric PSG which is also observed in the greater San Diego county, there is a high resource burden associated with obtaining an in laboratory PSG[1] as it requires specialized personnel, equipment, laboratory space, and the need for a child and at least one caretaker to spend the night outside the comfort of their homes.

HST is considered as a valid alternative to adults with OSA symptoms as it is more cost effective, convenient, and accessible. As a result HST has become the standard of care in adult sleep medicine[14] HST devices vary in the number of parameters that are typically recorded and hence there is variation in the sensitivity and specificity of HST devices when compared to the gold standard in diagnosing adult OSA.

Applicability of HST in children is rather limited as many children are intolerant to specific devices including the nasal cannula resulting in data collection that is lower quality or unacceptable altogether. Certainly, this limited tolerance is anticipated more often in younger children. Despite this preliminary studies have been encouraging. Brockman et al demonstrated a 93% success rate of HST conducted in children with an average age of 2.8 years of age and found no difference in success rates between in laboratory PSG and HST.[15] A recent systematic review corroborated the above conclusions and revealed a sensitivity of 76%, a specificity of 77%, and an area under the curve of 0.88 which attested to the fact that unattended HST perform well for predicting pediatric OSA.[16] However, further studies enabling head-to-head comparisons and validation of specific clinical algorithms are needed. The inability to determine total sleep time absence of EEG testing and subsequent inability to score respiratory events that culminate in arousal as opposed to desaturation and finally inability to identify sleep architecture[17] can culminate the utility of HST particularly in young children. While these issues may be more problematic in young children, HST may be more useful in adolescents with OSA as OSA during adolescence parallels what is observed in adults[17]

8. PROGRESS REPORT

N/A

9. RESEARCH DESIGN AND METHODS

Target Population:

Twenty nonsyndromic children over the age of 12 who will be undergoing a clinically indicated in laboratory PSG to rule out OSA will be approached for recruitment. In laboratory PSG testing is performed at Rady Children's hospital. In addition to children with syndromes or congenital disease, children with craniofacial abnormalities, congenital heart disease, and pulmonary hypertension will be excluded. Demographic data including age, race, sex, and obesity status will be collected.

Experimental procedure:

Of the twenty children recruited, ten will undergo home sleep testing (HST) no greater than one week prior to their in-laboratory PSG, while the other ten children will undergo HST no greater than one week following their in laboratory PSG. Participants who are randomized to receive the HST prior to their in-laboratory PSG will have the Resmed ApneaLink Air mailed to their home address. This will avoid the additional need for a study visit. All twenty children will also undergo their HST concurrent to their in-laboratory PSG. The rational for splitting children in these two groups is to equally distribute the effects of the first night evenly, in which

the sleep architecture including reduced total REM sleep time can vary in some children during their first ever sleep study. As the HST will be compared to the in-lab PSG, we would like to evenly distribute this effect by having two groups of ten children.

Upon obtaining consent by the PI, Dr. Rakesh Bhattacharjee, or the research coordinator, Janelle Celso, the subject will be provided with a verbal explanation and instructions on how to use the device These instructions (both Spanish and English version) will also be included with the device they will take home at the time of their sleep lab appointment. Information about how to apply the ApneaLink Air device at home will be demonstrated by sleep technologists who are members of the research team. A hotline number will be provided to the patients and parents in order answer questions or problem solve.

For home sleep testing (HST), the participants will use the Resmed ApneaLink Air™ device (Resmed, San Diego, USA). The ApneaLink Air is a device used to assess for sleep-disordered breathing. ApneaLink Air records five channels of information: respiratory effort, pulse and pulse oxygen saturation, nasal flow, body position and snoring. It includes a chest belt, nasal cannula, oximeter and recording device. This device is approved by the FDA for use in diagnosing OSA in adults. This device is not yet approved for use in the proposed subject population (12-17 years old) and the data obtained from this study may be used for the application of an FDA approval for children over 12. No clinical interventions will be implemented based on the results of the home sleep test.

This device is a non-significant risk device as it poses minimal risk or clinical harm to the pediatric population. The following criteria for a device to be deemed non-significant risk are met:

1. The device is NOT intended as an implant that presents a potential for serious risk to health, safety, or welfare of a subject
2. The device is NOT purported or represented to be for a use in supporting or sustaining human life that presents a potential for serious risk to the health, safety, or welfare of a subject
3. The device is NOT for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health that presents a potential for serious risk to the health, safety, or welfare of a subject
4. The device does NO otherwise present a potential for serious risk to the health, safety, welfare of a subject.

Furthermore, adolescents with suspected OSA (the study population) tend to parallel the OSA presentation of adults. Thus, no additional risk, other than those for adults, will incur to the patient if the device is used by the study population.

As stated, all subjects will have ApneaLink Air performed twice, once at home, and once during the sleep study. All of the components of the ApneaLink Air device will be placed in addition to the equipment used in the sleep lab. With exception to the nasal cannula, this should not interfere or result in additional discomfort to the in-lab sleep study. With regards to the nasal cannula, a 'splitter' will be used in which one nasal cannula will provide information on flow to both the ApneaLink Air device as well as the in-laboratory lab equipment (Nihon Koden, Irvine CA)

For ApneaLink Air testing performed at home, these subjects will receive a shipping box and return label to return the device following completion.

All children undergoing sleep study testing will have routine clinical surveys be performed. Some of this information will be gathered for research purposes to assess the pre-test probability of OSA. Following the home sleep test and in lab sleep test, all children will be interviewed by the research coordinator and asked questions concerning the child's experiences and comparing the two environments for their sleep test via a

telephone follow-up.

Data Analysis:
Descriptive statistics will be used to summarize the children's demographic and polysomnographic characteristics. Comparisons between in laboratory sleep study and HST will be conducted using Mann Whitney U-Test for not-normal data, and Student's t-test for normally distributed variables. Factors that may have influenced the interpretability of the recordings will be investigated using logistic regression. Age, gender, AHI, and BMI z- scores will be analyzed as independent variables in the logistic regression equation. Odds ratios and their 95% confidence intervals (95% CI) will be calculated. A p-value <0.05 will be considered statistically significant. Any information that will be sent to the sponsor will be de-identified.

The criteria for an unfeasible HST or HST failure will be defined as:

1. Loss of the nasal flow channel, or thoracic or abdominal sensor
2. Recordings with less than 4h of artifact-free recording time
3. Less than 4h of $Sp0_2$ signal

All studies will be scored by a trained sleep technician, and interpreted by Dr. Rakesh Bhattacharjee, in order to avoid variability. Both sleep scoring and sleep interpretations will be blinded from the findings of HST performed at home and in the sleep lab.

In the event that the HST is deemed not valid or inadequate when compared to the in laboratory PSG, the subject will remain in the study and will use this data to evaluate validity and feasibility of HST. Information

10. HUMAN SUBJECTS

Human subjects will be pediatric patients between the ages of 12-17, receiving a sleep study at Rady Children's Hospital as ordered by Dr. Rakesh Bhattacharjee to rule out OSA.

Inclusion criteria:

- Patients presenting with symptoms of OSA needing a sleep study
- Patients between the ages of 12 and less than 18 years

Exclusion criteria:

- Patients less than 12 years old and greater than 18 years old
- Children with syndromes or congenital disease including Down Syndrome, Prader-Willi syndrome, children with craniofacial disorders, and finally children with congenital heart disease or pulmonary hypertension

Pregnant women are not eligible to participate in the study as they have clinical parameters that would be different from the current study population. Children with cognitive impairment will also be excluded.

The research is not greater than minimal risk and thus falls under section 404 of 45 CFP 46 Subpart D.

11. RECRUITMENT AND PROCEDURES PREPARATORY TO RESEARCH

The research coordinator and PI will screen the PI's schedule and sleep lab schedule for potential subjects and approach them during their clinic visit or in the case for upcoming sleep studies will be approached over the phone. For cases that meet eligibility, the PHI that will be reviewed would be: patient name, parent name, phone number, medical record number, patient demographics (age, sex), clinical characteristics (diagnosis), and those undergoing sleep study for possible OSA. Once identified, data will be coded with a unique study

number. We are seeking a partial HIPAA waiver as the study poses minimal risk and subject recruitment cannot be feasibly complete without a HIPAA waiver. Documentation of waiver has been uploaded along with the research plan.

We will apply for a waiver of consent and HIPAA authorization to review PHI for subject eligibility. Loss of confidentiality is the only risk and we will take measures to minimize this. The study will not adversely affect the rights and welfare of the subjects, and could not feasibly be done without a waiver of consent or a HIPAA authorization.

a. *The research is minimal risk: the study poses minimal risk*: The only risk with the retrospective portion of this study is a breach of confidentiality. Section 16 discusses the steps we will take to ensure their privacy
b. *The waiver will not adversely affect the rights and welfare of the subjects:* We do not believe that granting the waiver will adversely affect the privacy rights and welfare of the individuals whose records will be used. No experimental procedures will be performed during this review. All possible methods to ensure confidentiality will be employed with the collection of chart data including (de-identification). Thus, any increase to the risk of confidentiality violation is very minimal and not at all anticipated.
c. *The research could not practicably be carried out without the waiver:* The HIPPA opt-out waiver will only be used to collect information from the medical records in order to identify eligible patients. It would be impractical to obtain permission and authorization from these patients because they may or may not be eligible for inclusion. Once these potential participants are identified and meet inclusion criteria, they will be consented to be included in the study.
d. As soon as the patient characteristics are identified, the PHI originally used to extract the data will be destroyed from the hard drive.
e. *Whenever appropriate, the subjects will be provided with additional pertinent information after participations.* Because all PHI will be destroyed at the completion of this study, it will not be possible to provide information after participation.
f. The study investigators will not re-use or disclose the PHI for any other purposes except for the research study outlined here.
g. The study investigator will provide any additional pertinent information as required by the IRB committee.

Potential participates in the clinic will then be approached for study recruitment after the decision for a sleep study has been made. Dr. Bhattacharjee will approach the subjects to present research opportunities at the end of a clinical appointment. Only patients undergoing a sleep study for OSA who agree to participate in this research study will be offered to complete HST using ResMed's ApneaLink™.

Children who are already scheduled for a sleep study to rule out obstructive sleep apnea in the sleep lab will also be approached over the phone if they meet inclusion criteria. Briefly, parents will be informed about study procedures and study risks over the phone (see phone script). For subjects ages 12 to less than 18, we will simply read the approved appropriate assent forms. There will be no phone script sent to the IRB for this matter. If parents and subjects are agreeable over the phone we will obtain verbal consent over the phone and either mail or email them copies of the consent form to sign or have the families sign the consent form in the sleep lab.

12. INFORMED CONSENT

Consent will be obtained in sleep clinic or sleep lab, in a private room, using a standard consent/assent form for adolescent participants and additional consent/assent forms for parental consent. In the clinic, consent will be obtained by clinical study staff or research coordinator. In the sleep lab, consent will be obtained by research

coordinators. All members of the research team have the necessary training to obtain consent. A code is assigned to each participant (random/alphanumeric). This code will be associated with the subject for the duration of the study.

We will identify minors from age obtained through clinical data. We will not accept subjects into the study who do not supply their age.

13. ALTERNATIVES TO STUDY PARTICIPATION

The study is entirely voluntary and the only alternative is not to participate. Not participating will confer no disadvantage to the participant.

14. POTENTIAL RISKS

With regards to HST, there are some minor discomforts associated with the set up and monitoring which include: developing redness, irritation, or a rash that might signal and allergic reaction. Furthermore, if the cannula is worn incorrectly, there appears to be a risk related to strangulation. The risks of home sleep studies are minimal and similar to risk encountered with an in-lab sleep study as mentioned in section 12. Further, steps will be taken to provide adequate education to subjects and parents prior to using HST at home.
There is a small potential risk of loss of confidentiality. Efforts described in section 15 will be taken in order to prevent this loss.

15. RISK MANAGEMENT PROCEDURES AND ADEQUACY OF RESOURCES

Patient confidentiality will be protected by assignment of a unique study number to all samples. No publication or written reports will link patient data with a name. Entry into the computer data files will require a password. The patient's full name will not be entered into the file but a log sheet with the study number and name will be kept in the PI's office in a locked file cabinet. The patient's full name is also logged into the RCHSD data base as required for all research subjects at RCHSD. Access to this database is password protected.

16. PRIVACY AND CONFIDENTIALITY CONSIDERATIONS INCLUDING DATA ACCESS AND MANAGEMENT

There is always the risk of subject information being released accidentally. We will make every effort to maintain patient privacy and confidentiality both during and following the study. Electronic study data will be de-identified by substitution of codes for names and hospital identifiers and will be stored on a secure disk for access by Investigator and study staff only and any hard copies will be stored in a locked cabinet. In all correspondence and in internal study reports that require identification of individual subjects, subjects will be referred to and known by their ID number and character name code. All subject data forms (CRF's) will only list the ID number. All research staff are CITI certified and have had impressed upon them the importance of confidentiality. This study does not involve the collection of sensitive personal information from subjects. Data will be stored only at UCSD sites and its use will be confined to that specified in this protocol and its approved amendments.

Data generated as a result of this study will only be made available for inspection upon request of the UCSD Human Research Protection Program.

17. POTENTIAL BENEFITS

There are no direct benefits to patients included in the study however there is great benefit to clinicians, patients and the scientific community. Children with symptoms of OSA endure long wait times to undergo diagnostic testing and sleep apnea. Researchers and clinicians could also use this study to determine the feasibility of HST in the context of diagnosing OSA which could reduce wait times but also improve the comfort for older children by having testing conducted in their own home.

18. RISK/BENEFIT RATIO

This project is categorized as a "minimal risk/no direct benefit" study: 45 CFR 46.404. The potential benefit to children with OSA is to validate the use of HST in diagnosing OSA in older children to be able to be used more

broadly in the clinical arena.

19. EXPENSE TO PARTICIPANT

None

20. COMPENSATION FOR PARTICIPATION

For participation in our study, the patients will be incentivized with a 100-dollar gift card to Amazon.com. The subject will receive $50.00 for each HST completed for a total of $100.00 after 2 HST studies.

21. PRIVILEGES/CERTIFICATIONS/LICENSES AND RESEARCH TEAM RESPONSIBILITIES

Rady Children's Sleep Lab

- Rakesh Bhattacharjee, MD (PI) has privileges at Rady Children's Hospital. He will be responsible for recruitment, consenting and answering questions with the study subjects, data analysis, interpretation of study results, and will be involved in subject recruitment in the sleep clinic. He has experience in all aspects of the proposed research.
- Janelle Celso B.S. is the Research Coordinator – She will be responsible for IRB modifications, recruitment, consenting, data collection and data analysis. She has all the training needed for her role.
- Gretchen Dever B.S., RRT-SDS – She will be responsible for IRB modifications, recruitment, consenting, data analysis, education of parents/subjects to applying the ApneaLink Air device for a sleep recording and assigning devices for each subject. She has all the training needed for her role.
- Alicia Poncy RPSGT - She will be responsible for recruitment, consenting, education of parents/subjects to applying the ApneaLink Air device for a sleep recording data collection and interpretation of study results. She has all the training needed for her role.
- Angela Rizzuto-RRT-SDS- She will be responsible for recruitment, consenting, data collection, education of parents/subjects to applying the ApneaLink Air device for a sleep recording and interpretation of study results. She has all the training needed for her role.

22. BIBLIOGRAPHY

References Cited:

1. Marcus CL, Brooks LJ, Draper KA, Gozal D, Halbower AC, Jones J, Schecheter MS, Sheldon SH, Spruyt K, Ward SD, Lehmann C, Shiffman RN: American Academy of Pediatrics. Diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics. 2012 Sep;130(3):576-84.
2. Galland BC, Dawes PJ, Tripp EG, Taylor BJ. Changes in behavior and attentional capacity after adenotonsillectomy. Pediatric research 2006; 59:711-716.
3. Chervin RD, Dillon JE, Archbold KH, Ruzicka DL. Conduct problems and symptoms of sleep disorders in children. Journal of the American Academy of Child and Adolescent Psychiatry 2003; 42:201-208.
4. Goodwin JL, Babar SI, Kaemingk KLet al. Symptoms related to sleep-disordered breathing in white and Hispanic children: the Tucson Children's Assessment of Sleep Apnea Study. Chest 2003; 124:196-203.
5. O'Brien LM, Mervis CB, Holbrook CRet al. Neurobehavioral implications of habitual snoring in children. Pediatrics 2004; 114:44-49.
6. Chervin RD, Ruzicka DL, Giordani BJet al. Sleep-disordered breathing, behavior, and cognition in children before and after adenotonsillectomy. Pediatrics 2006; 117:e769-778.
7. Chervin RD, Clarke DF, Huffman JLet al. School performance, race, and other correlates of sleep-disordered breathing in children. Sleep medicine 2003; 4:21-27.
8. Kohler MJ, Lushington K, van den Heuvel CJ, Martin J, Pamula Y, Kennedy D. Adenotonsillectomy and neurocognitive deficits in children with Sleep Disordered Breathing. PloS one 2009; 4:e7343.
9. Spruyt K, Capdevila OS, Kheirandish-Gozal L, Gozal D. Inefficient or insufficient encoding as potential primary deficit in neurodevelopmental performance among children with OSA. Developmental neuropsychology 2009; 34:601-614.
10. Bhattacharjee R, Kim J, Alotaibi WH, Kheirandish-Gozal L, Capdevila OS, Gozal D. Edothelial dysfunction in children without hypertension: potential contributions of obesity and obstructive sleep apnea. Chest. 2012 Mar; 141 (3): 682-691.
11. Kwok KL, Ng DK, Cheung YF. BP and arterial distensibility in children with primary snoring. Chest 2003; 123:1561-1566.
12. Duman D, Naiboglu B, Esen HS, Toros SZ, Demirtunc R. Impaired right ventricular function in adenotonsillar hypertrophy. The international journal of cardiovascular imaging 2008; 24:261-267.
13. Tal A, Leiberman A, Margulis G, Sofer S. Ventricular dysfunction in children with obstructive sleep apnea: radionuclide assessment. Pediatric pulmonology 1988; 4:139-143.

14. Trikalinos TA, Ip S, Raman Get al. AHRQ Technology Assessments *Home Diagnosis of Obstructive Sleep Apnea-Hypopnea Syndrome*. Rockville (MD): Agency for Healthcare Research and Quality (US), 2007.
15. Brockmann PE, Perez JL, Moya A. Feasibility of unattended home polysomnography in children with sleep-disordered breathing. International journal of pediatric otorhinolaryngology 2013; 77:1960-1964.
16. Certal V, Camacho M, Winck JC, Capasso R, Azevedo I, Costa-Pereira A. Unattended sleep studies in pediatric OSA: a systematic review and meta-analysis. The Laryngoscope 2015; 125:255-262.
17. Tan HL, Kheirandish-Gozal L, Gozal D. Pediatric Home Sleep Apnea Testing: Slowly Getting There! Chest. 2015 Dec; 148 (6): 1382-95
18. Tapia IE, Karamessinis L, Bandla P, Huang J, Kelly A, Pepe M, Schultz B. Gallagher P, Brooks LJ, Marcus CL. Polysomnographic values in children undergoing puberty: Pediatrics vs. adult respiratory rules in adolescents. Sleep. 2008 Dec; 31(12): 1737-44

23. FUNDING SUPPORT FOR THIS STUDY

Pending industry sponsored funding from ResMed Inc.

24. BIOLOGICAL MATERIALS TRANSFER AGREEMENT

N/A

25. INVESTIGATIONAL DRUG FACT SHEET AND IND/IDE HOLDER

N/A

26. IMPACT ON NURSING STAFF

There is no anticipated impact on nursing or ancillary staff.

There is no anticipated impact on nursing or ancillary staff.

The investigators and study staff have no relevant conflicts of interest for this study.

28. OTHER APPROVALS/REGULATED MATERIALS

N/A

29. PROCEDURES FOR SURROGATE CONSENT AND/OR DECISIONAL CAPACITY ASSESSMENT

N/A

Version date: 3/17/14