DEPARTMENT OF THE AIR FORCE
59TH MEDICAL WING (AETC)
JOINT BASE SAN ANTONIO - LACKLAND TEXAS

19 APR 2016

MEMORANDUM FOR SGO20
ATTN: CAPT NICHOLAS SCALZITTI

FROM: 59 MDW/SGVU

SUBJECT: Professional Presentation Approval

1. Your paper, entitled **Pediatric Home Sleep Studies: A Prospective Study** presented at/published to **Combined Otolaryngology Spring Meeting, Chicago, IL 18-22 May 2016** with MDWI 41-108, and has been assigned local file #**16152.**

2. Pertinent biographic information (name of author(s), title, etc.) has been entered into our computer file. Please advise us (by phone or mail) that your presentation/publication was given. At that time, we will need the date (month, day and year) along with the location of your presentation. It is important to update this information so that we can provide quality support for you, your department, and the Medical Center commander. This information is used to document the scholarly activities of our professional staff and students, which is an essential component of Wilford Hall Ambulatory Surgical Center (WHASC) internship and residency programs.

3. Please know that if you are a Graduate Health Sciences Education student and your department has told you they cannot fund your publication, the 59th Clinical Research Division may pay for your basic journal publishing charges (to include costs for tables and black and white photos). We cannot pay for reprints. If you are 59 MDW staff member, we can forward your request for funds to the designated wing POC.

4. Congratulations, and thank you for your efforts and time. Your contributions are vital to the medical mission. We look forward to assisting you in your future publication/presentation efforts.

Linda Steel-Goodwin

LINDA STEEL-GOODWIN, Col, USAF, BSC
Director, Clinical Investigations & Research Support

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

1. TO: CLINICAL RESEARCH	2. FROM: (Author's Name, Rank, Grade, Office Symbol)	3. GME/GHSE STUDENT:	4. PROTOCOL NUMBER:
	Nicholas Scalzitti, Capt, O-3, SGO20	☒ YES ☐ NO	380563

5. PROTOCOL TITLE: **(NOTE:** For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.)

Comparison of Pediatric Home Monitoring versus Laboratory Polysomnography for Diagnosis of Obstructive Sleep Apnea

6. TITLE OF MATERIAL TO BE PUBLISHED OR PRESENTED:

Pediatric home sleep studies: a prospective study

7. FUNDING RECEIVED FOR THIS STUDY? ☐ YES ☒ NO FUNDING SOURCE:

8. DO YOU NEED FUNDING SUPPORT FOR PUBLICATION PURPOSES: ☐ YES ☒ NO

9. IS THIS MATERIAL CLASSIFIED? ☐ YES ☒ NO

10. IS THIS MATERIAL SUBJECT TO ANY LEGAL RESTRICTIONS FOR PUBLICATION OR PRESENTATION THROUGH A COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENT (CRADA), MATERIAL TRANSFER AGREEMENT (MTA), INTELLECTUAL PROPERTY RIGHTS AGREEMENT ETC.?
☐ YES ☒ NO **NOTE:** If the answer is YES then attach a copy of the Agreement to the Publications/Presentations Request Form.

11. MATERIAL IS FOR: ☒ DOMESTIC RELEASE ☐ FOREIGN RELEASE
CHECK APPROPRIATE BOX OR BOXES FOR APPROVAL WITH THIS REQUEST. ATTACH COPY OF MATERIAL TO BE PUBLISHED/PRESENTED.

☐ 11a. PUBLICATION/JOURNAL (List intended publication/journal.)

☐ 11b. PUBLISHED ABSTRACT (List intended journal.)

☐ 11c. POSTER (To be demonstrated at meeting: name of meeting, city, state, and date of meeting.)

☒ 11d. PLATFORM PRESENTATION (At civilian institutions: name of meeting, state, and date of meting.)
Combined Otolaryngology Spring Meeting, Chicago, IL; May 18-22, 2016

☐ 11e. OTHER (Describe: name of meeting, city, state, and date of meeting.)

12. EXPECTED DATE WHEN YOU WILL NEED THE CRD TO SUBMIT YOUR CLEARED PRESENTATION/PUBLICATION TO DTIC
NOTE: All publications/presentations are required to be placed in the Defense Technical Information Center (DTIC).

DATE	
4/1/2016	

13. 59 MDW PRIMARY POINT OF CONTACT (Last Name, First Name, M.I., email)	14. DUTY PHONE/PAGER NUMBER
Scalzitti, Nicholas, J; nicholas.j.scalzitti.mil@mail.mil	210-916-8040/ 210-594-4099

15. AUTHORSHIP AND CO-AUTHOR(S) List in the order they will appear in the manuscript.

LAST NAME, FIRST NAME AND M.I.	GRADE/RANK	SQUADRON/GROUP/OFFICE SYMBOL	INSTITUTION (If not 59 MDW)
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f.			

I CERTIFY ANY HUMAN OR ANIMAL RESEARCH RELATED STUDIES WERE APPROVED AND PERFORMED IN STRICT ACCORDANCE WITH 32 CFR 219, AFMAN 40-401_IP, AND 59 MDWI 41-108. I HAVE READ THE FINAL VERSION OF THE ATTACHED MATERIAL AND CERTIFY THAT IT IS AN ACCURATE MANUSCRIPT FOR PUBLICATION AND/OR PRESENTATION.

16. AUTHOR'S PRINTED NAME, RANK, GRADE	17. AUTHOR'S SIGNATURE	18. DATE
Nicholas Scalzitti, Capt, O-3	SCALZITTI.NICHOLAS.J.13007407 19	3/22/2016
19. APPROVING AUTHORITY'S PRINTED NAME, RANK, TITLE	**20. APPROVING AUTHORITY'S SIGNATURE**	**21. DATE**
Erik Weitzel, LtCol, Otolaryngology Residency program director	WEITZEL.ERIK.K.1018551485	3/23/2016

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

1st ENDORSEMENT (59 MDW/SGVU Use Only)

TO: Clinical Research Division 59 MDW/CRD Contact 292-7141 for email instructions.	22. DATE RECEIVED 3/24/2016	23. ASSIGNED PROCESSING REQUEST FILE NUMBER 16152
24. DATE REVIEWED 5 Apr 2016		25. DATE FORWARDED TO 502 ISG/JAC

26. AUTHOR CONTACTED FOR RECOMMENDED OR NECESSARY CHANGES: ☒ NO ☐ YES If yes, give date. _____ ☐ N/A

27. COMMENTS ☒ APPROVED ☐ DISAPPROVED

The article is approved.

28. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	29. REVIEWER SIGNATURE	30. DATE
Rocky Calcote, PhD, Clinical Research Administrator	CALCOTE.ROCKY.D.1178245844	

2nd ENDORSEMENT (502 ISG/JAC Use Only)

31. DATE RECEIVED	32. DATE FORWARDED TO 59 MDW/PA

33. COMMENTS ☒ APPROVED (In compliance with security and policy review directives.) ☐ DISAPPROVED

The article includes the required disclaimer. There do not appear to be any conflict of interest issues.

34. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	35. REVIEWER SIGNATURE	36. DATE
Heather Slawson, 1Lt, Assistant Staff Judge Advocate	SLAWSON.HEATHER.M.15169367 42	7 April 2016

3rd ENDORSEMENT (59 MDW/PA Use Only)

37. DATE RECEIVED	38. DATE FORWARDED TO 59 MDW/SGVU
13-Apr-16	18-Apr-16

39. COMMENTS ☒ APPROVED (In compliance with security and policy review directives.) ☐ DISAPPROVED

40. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	41. REVIEWER SIGNATURE	42. DATE
Kevin Iinuma, SSgt/E5, 59MDW Public Affairs	IINUMA.KEVIN.MITSUGU.1296227613 Digitally signed by IINUMA.KEVIN.MITSUGU.1296227613 DN: c=US, o=U.S. Government, ou=DoD, ou=PKI, ou=USAF, cn=IINUMA.KEVIN.MITSUGU.1296227613 Date: 2016.04.18 16:04:58 -05'00'	18-Apr-16

4th ENDORSEMENT (59 MDW/SGVU Use Only)

43. DATE RECEIVED	44. SENIOR AUTHOR NOTIFIED BY PHONE OF APPROVAL OR DISAPPROVAL ☐ YES ☐ NO ☐ COULD NOT BE REACHED ☐ LEFT MESSAGE

45. COMMENTS ☐ APPROVED ☐ DISAPPROVED

46. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	47. REVIEWER SIGNATURE	48. DATE

DEPARTMENT OF THE ARMY
BROOKE ARMY MEDICAL CENTER
3851 ROGER BROOKE DR.
FORT SAM HOUSTON, TX 78234

REPLY TO
ATTENTION OF:

MCHE-CI

May 13, 2013

MEMORANDUM FOR:	Nicholas Scalzitti, Capt, USAF, MC
FROM:	Brooke Army Medical Center (BAMC) Institutional Review Board
PROJECT TITLE:	[380563-1] Comparison of Pediatric Home Monitoring versus Laboratory Polysomnography for Diagnosis of Obstructive Sleep Apnea
REFERENCE #:	C.2013.061d
SUBMISSION TYPE:	New Project
ACTION:	APPROVED
APPROVAL DATE:	May 13, 2013
EXPIRATION DATE:	May 13, 2014
REVIEW TYPE:	Expedited Review

1. Congratulations! The Brooke Army Medical Center (BAMC) Institutional Review Board (IRB) reviewed and APPROVED your aforementioned protocol and supporting documents on May 13, 2013. The research is judged to constitute Minimal Risk. The protocol has been assigned control number C.2013.061d. Please refer to this designation in all correspondence.

Your protocol was reviewed for regulatory compliance under Expedited Review, in accordance with 32CFR§219.110(b) Federal Registry Category (1)(4)(5)&(6). Applicable OHRP (under 45CFR46), FDA (under 21CFR§50 and 56) and HIPAA (45CFR§160 and 164) regulations were also consulted, as appropriate.

2. This submission has received Expedited Review based on the applicable federal regulation.

a. The protocol is approved to enroll up to 40 subjects.

b. An assent process has been approved for all subjects in accordance with (IAW) 32 CFR§219.116 and 45 CFR§46.408. Use of a written, assent document is approved requiring the signature of all participants ages 13 - 17 years on the assent document in accordance with (IAW) 45CFR§46.408(e). The stamped, IRB-approved assent form must be used for enrolling subjects.

The requirement for permission by parents or guardians will be conducted in accordance with (IAW) 32CFR§219.116 and 45CFR§46.408. Use of a written, informed consent document is approved which encompasses all of the required elements of informed consent to provide documentation of permission by parents or guardians will be conducted in accordance with (IAW) 45CFR§46.408(d).The stamped, IRB-approved consent form must be used for enrolling subjects.

c. A HIPAA Authorization has been submitted and approved.

d. Funding is requested from the Department of Clinical Investigation.

3. The following documents were reviewed as part of the approval process:

- ***FINAL** - Child Assent - (Version 2, DATED: 04/14/2013)
- ***FINAL** - Consent Form - (Version 2, DATED: 04/13/2013)
- ***FINAL** - Data Collection - Data Collection Spreadsheet.xlsx (UPDATED: 01/23/2013)
- ***FINAL** - Data Collection - Data Collection Sheet.docx (UPDATED: 01/23/2013)
- ***FINAL** - DMRN Research Project Cover Sheet - DMRN Research Project Cover Sheet (UPDATED: 04/14/2013)
- ***FINAL** - HIPAA Consent/Authorization - (Version 2, DATED: 04/14/2013)
- ***FINAL** - Other - Device information brochure (UPDATED: 11/5/2012)
- ***FINAL** - Protocol - Part B_(Version 2, DATED: 04/13/2013)
- ***FINAL** - Protocol - Part A_(DATED: 01/01/2013)
- ***FINAL** - Questionnaire/Survey - Survey use of portable monitor.docx (UPDATED: 01/7/2013)

4. A Research Monitor is not required; protocol is no greater than minimal risk.

5. You are required to report all unanticipated problems involving risks to subjects or others (UPIRSOs) and Serious Adverse Events (SAEs) to the IRB. Any unanticipated adverse events must be reported to the Human Protection Administrator within 24 hours by phone at (210) 916-2598 or (210) 916-0606 or by email at BAMC_IRB_AE@amedd.army.mil.

6. Protocol C.2013.061d will automatically terminate on May 13, 2014. If you plan to continue beyond this date, the required continuing review progress report is due to the BAMC IRB no later than six weeks prior to the expiration date. The IRB will attempt to assist you by sending a reminder; however, submission of the continuing review report is your responsibility. Failure to submit the report on time will result in the expiration of your protocol and a requirement to cease all research activities until the entire protocol can be resubmitted.

7. Please be sure to maintain all records in accordance with the terms set forth in your protocol. You are required to have all records, including informed consent and HIPAA documents, available for review by the IRB or other federal agencies.

8. Any changes to your protocol, including any changes in personnel, may not be made without prior IRB approval. Please forward a request for any changes, along with their rationale, to the BAMC IRB for review and approval.

9. Please inform the IRB when the protocol is completed or changes status and forward any significant findings.

10. Please ensure that you remain in compliance with BAMC Memo 70-1. Review and approval of abstract and/or manuscript submissions should be made through the Department of Clinical Investigation prior to any release. Contact Ms. Natalie Klein at (210) 916-8227 for additional details.

11. If at any time you have questions regarding your responsibilities as a Principal Investigator, please contact LTC Jay Bucci at (210) 916-4405 or jay.bucci@us.army.mil. On behalf of the entire IRB, we wish you much success with your research protocol. We look forward to reviewing the progress of your study in the coming months.

This document has been electronically signed in accordance with all applicable regulations, and a copy is retained within our records.

Title: Pediatric home sleep studies: a prospective study.

Authors:

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Funding: None

Conflict of Interest: None

ABSTRACT

Introduction: Obstructive sleep apnea (OSA) affects 1-5% of pediatric patients. Untreated pediatric OSA is associated with neurocognitive impairment, behavioral problems, and cardiopulmonary dysfunction. Clinical diagnosis lacks sensitivity and specificity. Laboratory polysomnography is expensive, not always available, and is inconvenient for patients. Therefore, 90% of children undergo adenotonsillectomy without confirmatory diagnostic testing. Home sleep testing for OSA may alleviate these issues.

Objectives: Our study investigates a commercially available ambulatory monitor for the diagnosis of pediatric OSA. Feasibility and validity of the device in the pediatric population was compared to laboratory polysomnography.

Methods: A prospective, case-controlled study was conducted in children, ages 2-17. Subjects meeting inclusion criteria completed in-lab polysomnography simultaneously with ambulatory monitoring. Caregivers attempted home studies on two subsequent nights to compare the diagnostic capability between the home monitor and the in-lab study.

Results: Forty-five patients were enrolled. Thirty-three subjects completed simultaneous laboratory polysomnogram with portable monitoring. Twenty patients completed the home studies, with 16 completing 2 nights of monitoring. The measurement of AHI by the portable monitor was different than that obtained by the PSG with statistical significance for the comparisons of PSG vs. In-Lab ($p=0.0026$), PSG vs. Home 1 ($p=0.033$), and PSG vs. Home 2 ($p=0.033$). The sensitivity of the portable monitor for diagnosing OSA was best for the In-lab use at 81%, but only 69% and 70% for the uses at home on the 2 nights respectively. Interestingly, the comparison of AHI and LSAT measurements from the home sleep test in children age 6 and older did not differ significantly from the PSG.

Conclusion: This pilot study demonstrated differences between home sleep testing and in-lab polysomnography for the diagnosis of pediatric sleep apnea. These differences were predominantly found

to exist in the younger children. Larger prospective studies are needed prior to wider adoption, yet home studies have the potential to provide wider access with lower costs for the evaluation of pediatric sleep apnea.

Introduction

Pediatric obstructive sleep apnea (OSA) is estimated to affect between 1.2% and 5.7% of all children.[1] Common symptoms of pediatric OSA include snoring with associated gasps or pauses, poor sleep, fatigue, and daytime behavioral problems. Untreated OSA is increasingly being recognized as a risk factor for significant morbidity such as neurocognitive issues and metabolic, behavioral problems, learning and growth delays, and long-term heart and lung disease related to the sleep disturbance and repetitive hypoxemia.[2] In children, hypertrophy of the tonsils and adenoids is most often the source of airway obstruction, making OSA the most common indication for adenotonsillectomy in the pediatric population.[3]

The diagnosis of pediatric obstructive sleep apnea is based on a thorough history and physical exam, however, tonsil size does not necessarily correlate with diagnosis or severity of OSA.[4] Guidelines exist regarding the appropriate use of laboratory polysomnography (PSG) in cases where the diagnosis is uncertain.[1,3,5] However, in-lab PSG carries with it the inconvenience of a child and caregiver spending a night in the lab, as well as significant monetary expense. Also, pediatric sleep centers are often not readily available, leading to the inconsistent use of PSG in this population. Since less than 10% of children have a sleep study prior to tonsillectomy, it is possible that a significant number of children undergo the risk of surgery without an accurate diagnosis of OSA.[3]

Home sleep apnea testing (HSAT) is a well-accepted method for evaluating adult patients for sleep disordered breathing as part of an overall sleep evaluation.[6] In fact, HSAT has become the primary modality to evaluate OSA in adults as it has been shown to not be inferior to in-lab polysomnography in the adult population.[7] However, there is a considerable knowledge gap in the use of home sleep monitoring technology for the evaluation of pediatric sleep disordered breathing. In fact, clinical practice guidelines from the American Academy of Pediatrics, the American Academy of Otolaryngology, and the American Academy of Sleep Medicine each acknowledge the paucity of information on pediatric home monitoring systems for obstructive sleep apnea.[1,3,5] These guidelines cite a single article, by Jacob et al, as

the only significant evidence investigating the topic.[8] There is other research to suggest that home pulse oximetry monitoring alone does not correlate with laboratory sleep study data in the diagnosis of pediatric obstructive sleep apnea.[9] For these reasons, laboratory PSG is currently recommended for pediatric sleep apnea evaluation as there is a scarcity of validating information for current commercially available home monitoring systems.

Our study seeks to investigate if the use of a commercially available HSAT can aid in the diagnosis of pediatric obstructive sleep apnea. The goals of this pilot study were: 1. help determine if an unattended HSAT can provide usable and consistent data in the pediatric population when compared to an in-lab polysomnogram; 2. explore the feasibility and reproducibility of obtaining this data with such a monitor. The use of the home monitor could eliminate the inconveniences of lab PSG, and alleviate the issues of access, thereby reducing the number of children proceeding to tonsillectomy without a confirmed diagnosis of OSA.

Methods

This was a prospective, case-controlled study designed to investigate the use of unattended, home portable monitoring in children. Subjects were identified both in the ENT clinic and the Sleep Disorder Center clinic of the San Antonio Military Health System. Patients were required to be less than 18 years of age and exhibit the signs and symptoms of pediatric obstructive sleep apnea. Exclusion criteria included obesity, Down syndrome, craniofacial abnormalities, neuromuscular disorders, sickle cell disease, and mucopolysaccharidoses. These patients were excluded because they are most appropriately assessed by overnight polysomnography, as stated in the Clinical Practice Guidelines by the American Academy of Otolaryngology-Head and Neck Surgery.[3] The complexity of these patients precludes them from home sleep testing. Other exclusion criteria were previous tonsillectomy or adenoidectomy, or other airway surgery.

The study received Institutional Review Board approval at the San Antonio Military Medical Center. Subjects who met inclusion criteria were recruited and offered participation. Appropriate informed consent and assent were obtained. Data collection began with obtaining clinical information including demographics,

history, and physical exam data at an initial clinic visit. Subjects were then scheduled to have an overnight sleep study (PSG), which at this time is the standard test for these patients. In addition to the standard PSG, a portable monitor (Embletta Gold by Embla) was administered to the subject at the same time as the in-lab PSG. After the in-lab testing, the subject wore the portable monitor at home for up to two more nights. Respiratory data from the results of the in-lab sleep study and the three portable monitor uses were collected and recorded. Afterwards, the parent or guardian was asked to complete a survey entitled "Pediatric Portable Sleep Study Survey." This survey attempted to quantify the subjective complaints of snoring and restless sleep and inquire about the ease of use of the portable monitor. This completed the data collection portion of the study. There were no therapeutic interventions involved in this study.

Standard Overnight Polysomnography

All PSG studies were analyzed and reported by a fellowship-trained, board certified sleep physician (S.H. or P.O.) who was blinded to the results of the portable studies. Patients underwent standard overnight PSG using a data acquisition and analysis system (Sandman, Natus Medical Inc, USA). Respiratory measurements included chest wall and abdominal movements using chest wall and abdominal belts, nasal airflow measurements using air pressure transducer and nasal thermal sensor; oxygen saturation using oximeter, transcutaneous carbon dioxide (rcCO2) and end tidal carbon dioxide (etCO2). The PSG system used ProTech ZRIP respiratory inductive plethysmography effort sensors, ProTech PTAF Lite transducer, and Salter Labs Thermisense nasal pressure monitoring and gas sampling cannula and thermistor. The tcCO2 was recorded using SenTec Digital monitoring system (Therwil, Switzerland), and etCO2 was recorded using a capnography (Capnocheck Sleep, BCI, USA). PSG measurements also included electroencephalogram, electro-oculogram, and submental and bilateral anterior tibialis electromyograms. Video recordings were also obtained for each study. Sleep architecture was assessed using standard techniques (American Academy of Sleep Medicine – AASM). Snoring and limb movements were also scored. Recorded respiratory data included counts and indexes of the following: obstructive apneas, hypopneas, central apneas, and mixed apneas. All events were scored according to the AASM scoring guidelines for children by a registered PSG

technician. A respiratory event was scored as an obstructive apnea if it was associated with > 90% fall in signal amplitude for > 90% of the entire event compared to the baseline amplitude, the event lasted > 2 breaths, and there was continued or increased respiratory effort throughout the period of the event. A central apnea was scored if there was absent respiratory effort throughout the duration of the event, the even lasted 20 seconds or > 2 missed breaths, and was associated with an arousal/awakening or > 3% desaturation. A hypopnea was scored if the event was associated with > 50% fall in amplitude of the nasal pressure transducer, lasted > 2 breaths, and was associated with an arousal/awakening or > 3% desaturation. A mixed apnea event was scored when airflow decreased by >90% from baseline for at least 90% of the entire respiratory event, the duration of which was a minimum of two baseline breaths, which is associated with absent inspiratory effort in the initial portion, followed by resumption of inspiratory effort before the end of the event. The apnea-hypopnea index (AHI) was calculated as the number of apneas and hypopneas per hour of total sleep time (TST).

Portable Sleep Monitor

The portable monitor used was the Embletta gold device, which is designed to be applied by a layperson after receiving instruction by a technician or medical provider. This monitor consists of a nasal pressure cannula and thermistor to measure pressure and airflow. Respiratory effort is measured by Xactrace chest and abdominal belts. Oximetry is recorded via a digital probe with an averaging time of 1 second. A 3-lead electrocardiogram is also included to monitor heartrate. Manual scoring of apneas and hypopneas (AASM pediatric criteria) was done by a single sleep physician (S.H.), who was blinded to in-lab PSG results. All respiratory events observed by the portable monitor were combined to derive an AHI, which was compared with the AHI obtained from the standard in-lab PSG. The AHI for the HSAT was calculated as total number of events divided by the total study time.

Statistical Analysis

The first inferential question we addressed is whether evidence supporting the hypothesis that the

mean of several laboratory polysomnogram measurements is different from those of portable monitoring. Box-and-whisker plots are used to show the nature of the distributions of these measurements. Using the R package lattice, we obtain figures that compare the laboratory and portable measurements intuitively.[10] Each box corresponds to the first through third quartiles of the distribution, with the contained line representing the median value. The whisker portions correspond to the maximum and minimum values within 1.5 times the inter-quartile range (i.e. the length of the box). Outliers are illustrated as points outside the whiskers. Where the box-and-whisker plots are not symmetrical, non-normality is suggested and would help to guide our choice of statistical tests. Additionally, the intuitive interpretations yielded from these plots will help to confirm the statistical results.

Next, we employed a paired Wilcoxon signed rank test to compare the measurements for laboratory and portable sleep polysomnograms. We chose this approach for two reasons: (a) the nature of the hypothesis test is nonparametric, and (b) the results of the box-and-whiskers plots suggest that normality assumptions may be tenuous. These paired signed rank tests evaluate evidence for the hypothesis that the two samples come from distributions with the same location (i.e. mean). As usual, smaller p-values correspond to greater statistical evidence that we may reject the hypothesis of the means being equal. We perform this test in two arrangements: (a) the laboratory measurement is compared with each corresponding measurement using the portable setup, and (b) the laboratory measurement is compared with all other measurements at once. This latter test is called the omnibus test, which allows us to evaluate the performance of all portable arrangements at once.

In an effort to assess the reproducibility of the data obtained from the portable device, we compared the means of AHI and LSAT values obtained in the 3 conditions that it was used (In lab, Home 1, and Home 2). These comparisons were made using the Kruskal-Wallis rank sum test and depicted graphically with box-and-whisker plots. Next, to evaluate the efficacy of the portable machines directly, we assess the specificity and sensitivity of the device directly with regards to the diagnosis of OSA compared to the gold standard. To help illuminate the tradeoff inherent between specificity and sensitivity, we estimate receiver operating

characteristic (ROC) curves. By overlaying the AHI values that correspond with points on the ROC curve, we can also understand whether the rule that AHI > 1 is most desirable when diagnosing OSA using the portable machines.

Finally, we employ linear regression to model the mean absolute difference between the portable machine's AHI and that from the laboratory polysomnogram. By evaluating the impact of patient-level characteristics on measurement error, we can help to illuminate some guidelines and theorize for when the use of the portable machines may be advisable, and when it is likely that the portable machine's measurements will have too much error in diagnosis.

Results

Forty-five patients were enrolled in the study, and 33 subjects completed simultaneous laboratory polysomnogram with portable monitoring. Twenty patients completed the home studies, with 16 completing 2 nights of monitoring. Using the paired Wilcoxon signed-rank tests, we determined that the population-mean measurement of AHI by the portable monitor and the PSG had a statistically significant difference. Figure 1 depicts the corresponding box-and-whisker plots, where it is clear that there are structural differences in the distributional forms, variances, and means for PSG and portable measurements. For example, the figure clearly demonstrates that the range (0-17.5) of values obtained by the PSG is much greater than that obtained by the portable monitor. The pair-wise Wilcoxon comparisons for PSG vs. In-Lab ($p=0.0026$), PSG vs. Home 1 ($p=0.033$), and PSG vs. Home 2 ($p=0.033$) agree with the graphical interpretation.

In a similar way, LSAT comparisons between the portable monitor and the PSG did not match up well. In this case, the LSAT obtained for the In-Lab use and Home 1 use had statistically significant mean differences from the PSG ($p=0.0035$ and $p=0.029$ respectively), while the values from the Home 2 use did not indicate statistical evidence that the means were different ($p=0.64$). Again, this is depicted in a box-and-whisker plot (Figure 2), which demonstrates that the PSG captured a wider range of LSAT values, including more cases of a value less than 90%, than the portable monitor. The portable monitor in each circumstance

calculated total sleep time (TST) as higher than the PSG (In-Lab p=0.000022; Home 1 p=0.00036; Home 2 p=0.00048).

An analysis of the sensitivity and specificity of the portable monitor for the diagnosis of OSA (defined as AHI equal to or greater than 1) compared to the PSG was also performed (Table 1). The sensitivity (true positives/all patients with OSA per the PSG) of the home device was best when worn in the sleep lab, at 81.5%, while the sensitivity when wearing the monitor at home was lower (Home 1= 69.2%; Home 2= 70%). Evaluation of the specificity (true negatives/all patients that did not have OSA per the PSG) of the portable monitor revealed that the second night at home (Home 2) performed the best in this regard, with a specificity of 83.3%, while the use in lab had a specificity of 60% and Home 1 demonstrated a specificity of only 42.9%. Figures 3, 4, and 5 are graphical representations of the sensitivity and specificity of each use of the home monitor, showing when the home sleep test did and did not come to the same diagnosis (OSA or no OSA) compared to the polysomnogram. Circular points depict patients where the home sleep test and PSG agreed on the diagnosis (based on AHI cutoff of 1), and triangular points demonstrate instances of disagreement.

To test the reproducibility of the data obtained by the home sleep testing from night to night, the AHI and LSAT data from the 3 uses of the home sleep testing device were each compared with a Kruskal-Wallis rank sum test. In both instances, there was not sufficient evidence that these means were different from night to night as recorded by the device (p=0.41 for AHI measurements; p=0.31 for AHI measurements). Box-and-whisker plots of this data demonstrate the agreement of these values (Figures 6 and 7).

Receiver operating characteristic (ROC) curves were created to determine if different AHI cutoffs could be used to improve the sensitivity of the home test. For Home 2, the sensitivity could be increased to 90% by using an AHI value of 0.75 or greater to diagnose OSA (Figure 8). However, in this scenario, the specificity decreased to 65% (and therefore the likelihood of making a Type I error increased to 35%).

Linear modeling was performed to examine what factors were associated with greater error in the

portable machine compared to the gold standard. Interestingly, the 2 factors found to have statistical significance for degree of error were age and gender. Male patients had less error in AHI values from the home test compared to the PSG by an absolute margin of 3.24 (p=0.001). With respect to age, younger children (age 5 and under) showed much greater difference in AHI values than their older (age 6 and over) counterparts. The younger age group greater error by an absolute margin of 4.99 for their AHI than the older children (p=0.00003). These results are shown in Table 2.

To test how the HSAT did in older children, the Wilcoxon signed rank test was repeated to compare AHI and LSAT distributions between the portable monitor and the PSG for children age 6 and older. These comparisons did not show statistical significance between the populations for AHI (Home 1 p=0.55; Home 2 p=0.15) or LSAT (Home 1 p=0.24; Home 2 p=0.45) on either night at home. The HSAT performed well enough compared to the PSG in these older children to provide a sensitivity of 83% and specificity of 80% for diagnosis OSA. An ROC curve demonstrates that a sensitivity of 100% could be reached by lowering the AHI threshold to 0.75, but this would increase the likelihood of Type I error to 40% (Figure 9).

Discussion

Obstructive sleep apnea affects a significant proportion of the pediatric population (1-5%), and its long-term health effects have gained recognition.[3] The symptoms of OSA in the pediatric population are not always distinguishable from other disorders affecting sleep, attention, behavior, and cognition. The ability to predict the presence of OSA based on symptoms, caregiver concern, and tonsil size has not reliably replaced the gold standard of polysomnography.[11,12] However, average wait times for pediatric laboratory polysomnography have been reported to be greater than 6 weeks for 43% of providers, helping lead to a common practice pattern of proceeding to surgical treatment without objective evidence of OSA in > 90% of patients.[13] Thus, cost and access to care issues with respect to PSG have led to a need for other diagnostic options. In a time of limited healthcare resources, abbreviated screening tests such as

pulse oximetry monitoring may provide a cost-beneficial alternative to laboratory polysomnography but the limitations in sensitivity remain.[14]

Alternatives to testing with in-lab polysomnograpy have been explored with limited success in the pediatric population. Measuring the pattern of mandibular movements in pediatric patients has shown some positive correlation with changes in pulse transit time, another method proposed for detecting pediatric OSA.[15] Various biomarkers have also been explored as potential avenues to facilitate the identification of OSA in children, but with some limitations depending on the population being analyzed.[16,17] There is an increasing need to identify algorithms and technology which can identify pediatric patients who have OSA with high sensitivity and specificity.

Nocturnal pulse oximetry has been trialed as a simpler method of home monitoring to assess for sleep apnea in the pediatric population.[2,9,14,18] Brouillette et al found that a positive nocturnal oximetry trend graph (defined as 3 or more desaturation clusters of more than 4% from baseline as well as at least 3 desaturations to < 90%) had a high positive predictive value (97%) for pediatric obstructive sleep apnea.[2] However, this was in a population with a high (60%) pre-test probability of having OSA. They also found that a negative or inconclusive trend graph could not reliably rule out obstructive sleep apnea given a low sensitivity (43%).

In a related study, home pulse oximetry was found to be feasible and reproducible as usable data was obtained in 57 of 58 pediatric patients on consecutive nights of home monitoring.[9] However, when compared to in lab polysomnography, the home monitoring was found to have only 67% sensitivity and 60% specificity for identifying children with moderate OSA. Another limitation of this type of monitoring is that pulse oximetry alone can certainly not differentiate between obstructive and central apnea as a cause for hypoxemia, therefore limiting its diagnostic capability.

The feasibility of performing home monitoring in children presents different challenges than it does in adults. Recently, a publication from Canada found that the ApneaLink (ResMed, USA) portable

monitoring system had an excellent correlation to polysomnogram in detecting OSA, but this testing was done in an attended sleep laboratory.[19] This setup bypasses the added difficulties of a caregiver-administered home monitor, which is necessary to avoid the previously stated shortcomings of in-lab studies. While the device may possess the ability to detect and quantify OSA findings, finding it to be feasible and reproducible in the home setting is another task. Our study results suggest the increased problems that this poses. One of the only published studies to date showing the efficacy of home monitoring in children also evaded these challenges of caregiver setup.[8] In this study of 21 pediatric patients, there was found to be good correlation between laboratory PSG and home monitor results with respect to respiratory and arousal data, but the monitoring equipment was setup in the home by a sleep technician for each subject.

While it is generally accepted that many children with the signs and symptoms of OSA may proceed to adenotonsillectomy without a sleep study to confirm the diagnosis, it is important to realize that a consequence of this practice is that children are not stratified by severity of obstructive sleep apnea prior to treatment. It is known that the preoperative finding of moderate or severe OSA can help stratify the risk of post-operative respiratory complications in these children.[20,21] Wilson et al reported an increased risk of respiratory complications (odds ratio 7.2) for children with AHI > 5, while an oxygen nadir of 80% or less on pre-operative polysomnogram raised the rate of post-operative respiratory complications from 20 to 50%.[20] While the Clinical Practice Guideline from the American Academy of Otolaryngology recommends observing these children with severe OSA overnight in the hospital post-operatively, it readily admits that more than 90% of children proceed to adenotonsillectomy without polysomnography.[3] This is a noticeable knowledge gap in the care of these patients, and one that portable sleep monitoring could potentially narrow if found to be able to define the existence and severity of OSA in children.

Our study sought to test both the diagnostic capability of the portable monitor, as well as the reproducibility of the data obtained by the monitor. Regarding the diagnosis of OSA, the portable monitor

showed mixed results compared to the gold standard of laboratory polysomnography. The measurement of AHI by the portable monitor yielded a data set that was statistically different from that obtained by the PSG. This held true for each use of the portable device, both in the lab and at home. Using the device in both settings helps remove the difference that could be attributed to night-to-night variability in a patient's OSA. However, the differences found with device utilized in this study cannot be explained by this, as the monitor was used simultaneously with the PSG in the lab. Even in this concurrent setting, the AHI value did not compare favorably with the PSG, and the portable monitor had only 81% sensitivity and 60% specificity for the diagnosis of OSA. The portable monitor also failed to yield similar data to the PSG with respect to LSAT values, except when comparing the second night at home (Home 2).

Given these differences in the measurement of the respiratory parameters, the diagnostic ability of the portable monitor was less than would be desired in order for the home study to replace the PSG. The sensitivity of the monitor for diagnosing OSA for the 2 nights at home was near 70% for each use. However, the 30% Type-II error (false negative rate) associated with this would preclude the monitor to be used as an accurate screening test for OSA in the general pediatric population. Unfortunately, the specificity of the home monitor was also sub-optimal with respect to OSA diagnosis. The ROC curves created provide us with insight into how the portable monitor could be used as a screening tool to rule out OSA in children without the hassle of an overnight laboratory polysomnogram. By decreasing the AHI cutoff on the home sleep test to 0.75, the sensitivity for diagnosing OSA can be raised to 90% or greater, thereby offering a useful screening evaluation. The appropriate AHI value for diagnosing OSA on the portable monitor is an area for future investigation.

Interestingly, we were able to identify some factors that were predictive for obtaining poor results from the portable monitor. Of particular importance is the effect that age had on the ability of the device to compare favorably with the PSG. Children younger than age 5 had a significantly higher error with the portable device on comparison to the polysomnogram. The AHI and LSAT measurements did not statistically differ on the home sleep test from the PSG in children age 6 and older. The sensitivity and

specificity for OSA diagnosis in this age group were both > 80%. These figures would suggest that the device may be more appropriate for use in older children, where the diagnostic ability will be maximized. This result provides an area for further research, to better understand if this difference will hold in larger studies.

We do recognize a few weaknesses in our study. A common difference between in-laboratory polysomnograms and home sleep apnea testing is the period attributed to sleep. Sleep is measurable on gold standard test by assessing the EEG pattern and determining true sleep. In the HSAT, the recorded time is total study time and may not entirely include true sleep. The relative increase in time may artificially reduce the AHI compared to the PSG since the denominator in events/hour is greater. A second limitation is that a single HSAT device was used. Other devices may have produced different results, and these devices may require further study. Also, only 20 of our 33 subjects used the HSAT for a night at home, and just 16 of those used it for both nights. This discrepancy in the number of patients that completed each portion of the study limits the study by reducing the power of the comparisons. Also, this may introduce an unintended bias into the study, as caregivers of some subjects selected themselves out from the remaining portions of the study.

Conclusion

Our study sought to explore the diagnostic ability of a commercially available home sleep apnea test in the pediatric population, comparing it to the gold standard of in-lab polysomnography. As laboratory testing has challenges of cost and access to care, the need for alternative options for diagnosing OSA has come to the forefront. Our results in a small population found that the portable device did not perform well compared to the PSG in calculating the AHI and LSAT, or in diagnosing OSA. However, we did find that the results from the home sleep test were reproducible over multiple nights of use. Also, the results were significantly better in children age 6 and over, suggesting that older children may be

better suited for home sleep apnea testing. Additional studies on larger numbers of patients will be needed prior to widespread use of home sleep testing in children.

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Figure 1: Box-and-whisker plots of the AHI measurements for the PSG and each use of the home sleep monitor. Each box corresponds to the first through third quartiles of the distribution, with the contained line representing the median value. The whisker portions correspond to the maximum and minimum values within 1.5 times the inter-quartile range (i.e. the length of the box). Outliers are illustrated as points outside the whiskers. There are clear structural differences in the distributional forms, variances, and medians for PSG and portable measurements.

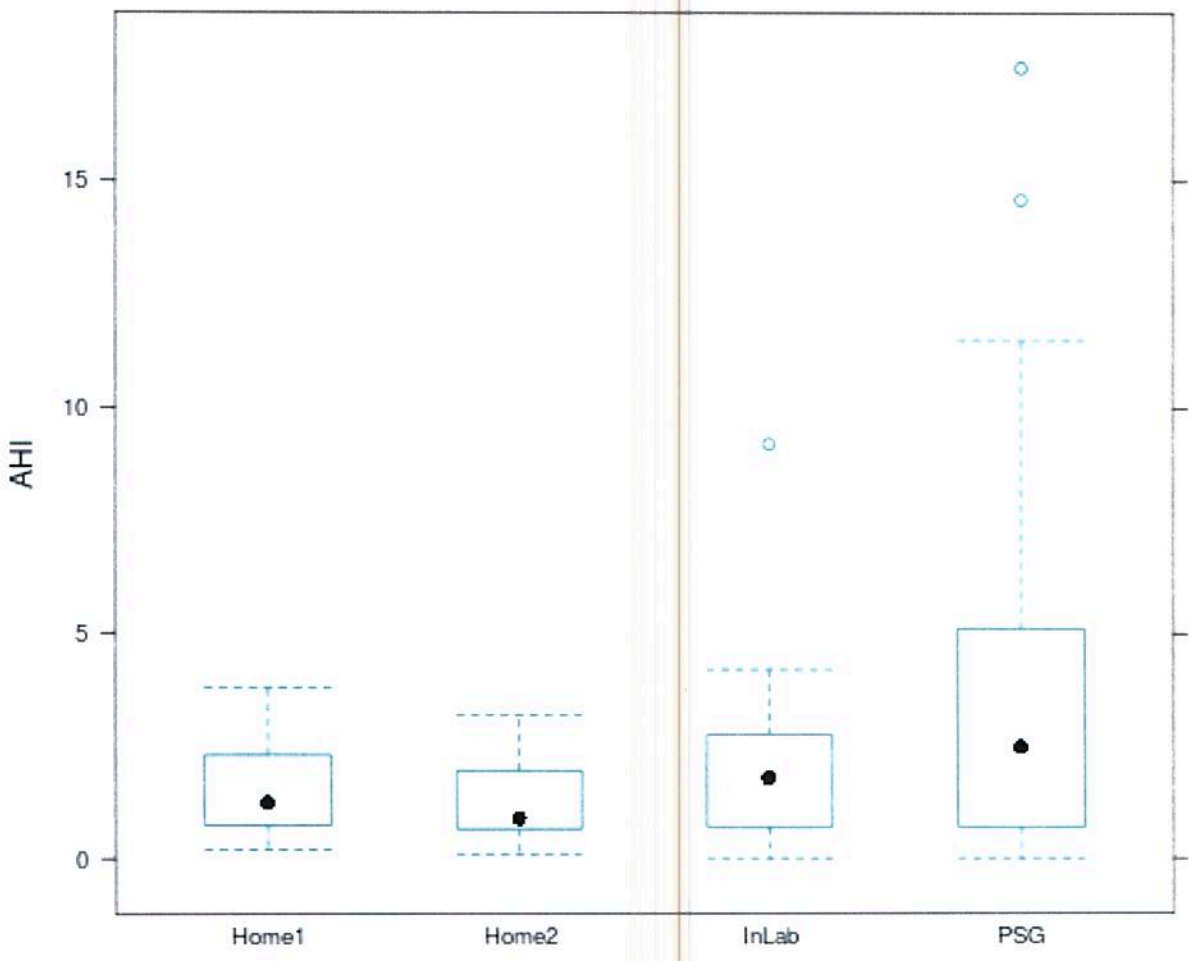

Figure 2: Box-and-whisker plots of the LSAT measurements for the PSG and each use of the home sleep monitor. Again, there are clear structural differences in the distributions obtained by the PSG and home sleep test.

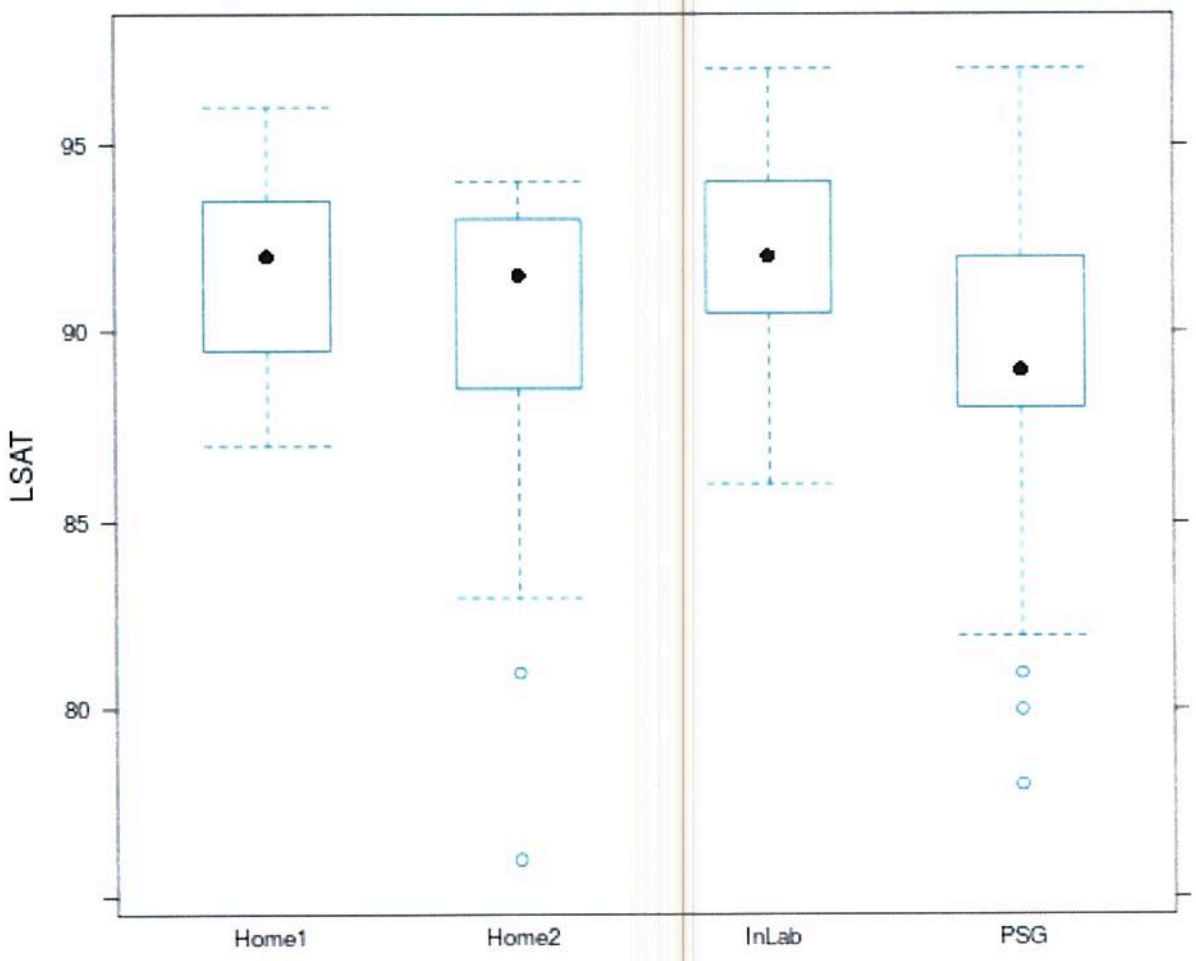

Figure 3: Comparison of the AHI values obtained by the PSG vs. those obtained by the portable monitor while worn in the lab. The dark solid lines represent an AHI value of 1. Circular points depict patients where the home sleep test and PSG agreed on the diagnosis (OSA or no OSA), and triangular points demonstrate instances of disagreement.

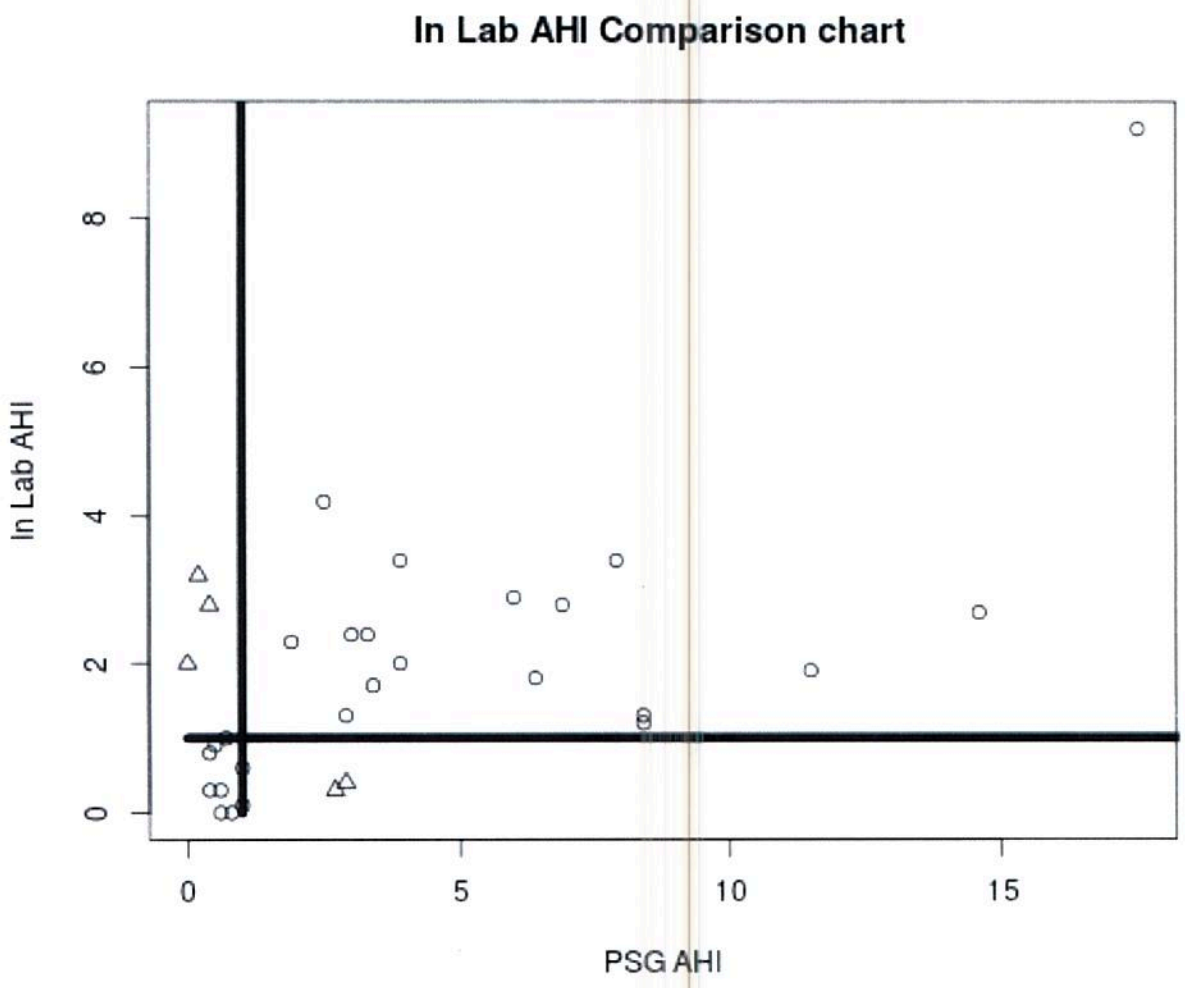

Figure 4: Comparison of the AHI values obtained by the PSG vs. those obtained by the portable monitor on the first night at home. The dark solid lines represent an AHI value of 1. Circular points depict patients where the home sleep test and PSG agreed on the diagnosis (OSA or no OSA), and triangular points demonstrate instances of disagreement.

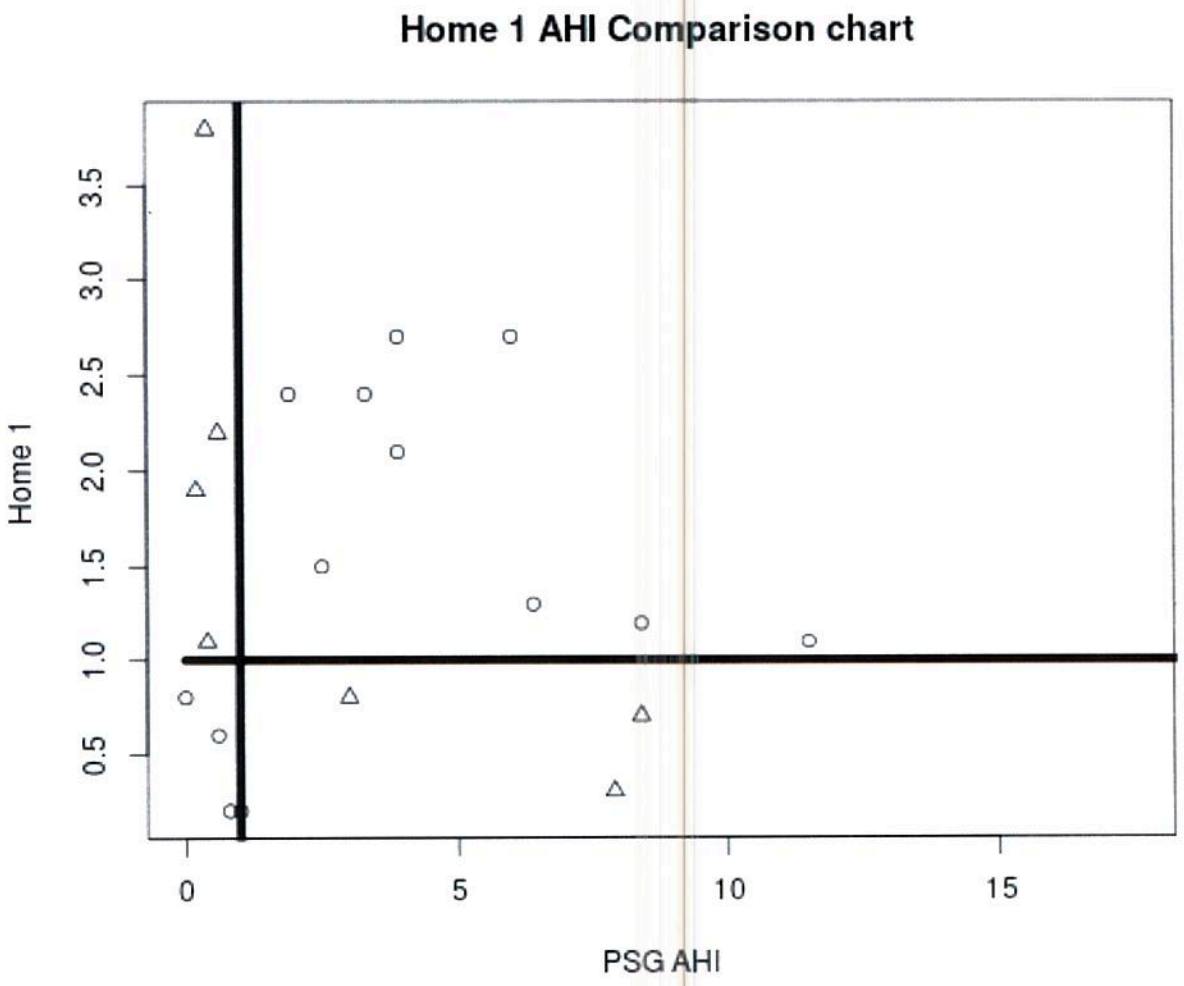

Figure 5: Comparison of the AHI values obtained by the PSG vs. those obtained by the portable monitor on the second night at home. The dark solid lines represent an AHI value of 1. Circular points depict patients where the home sleep test and PSG agreed on the diagnosis (OSA or no OSA), and triangular points demonstrate instances of disagreement.

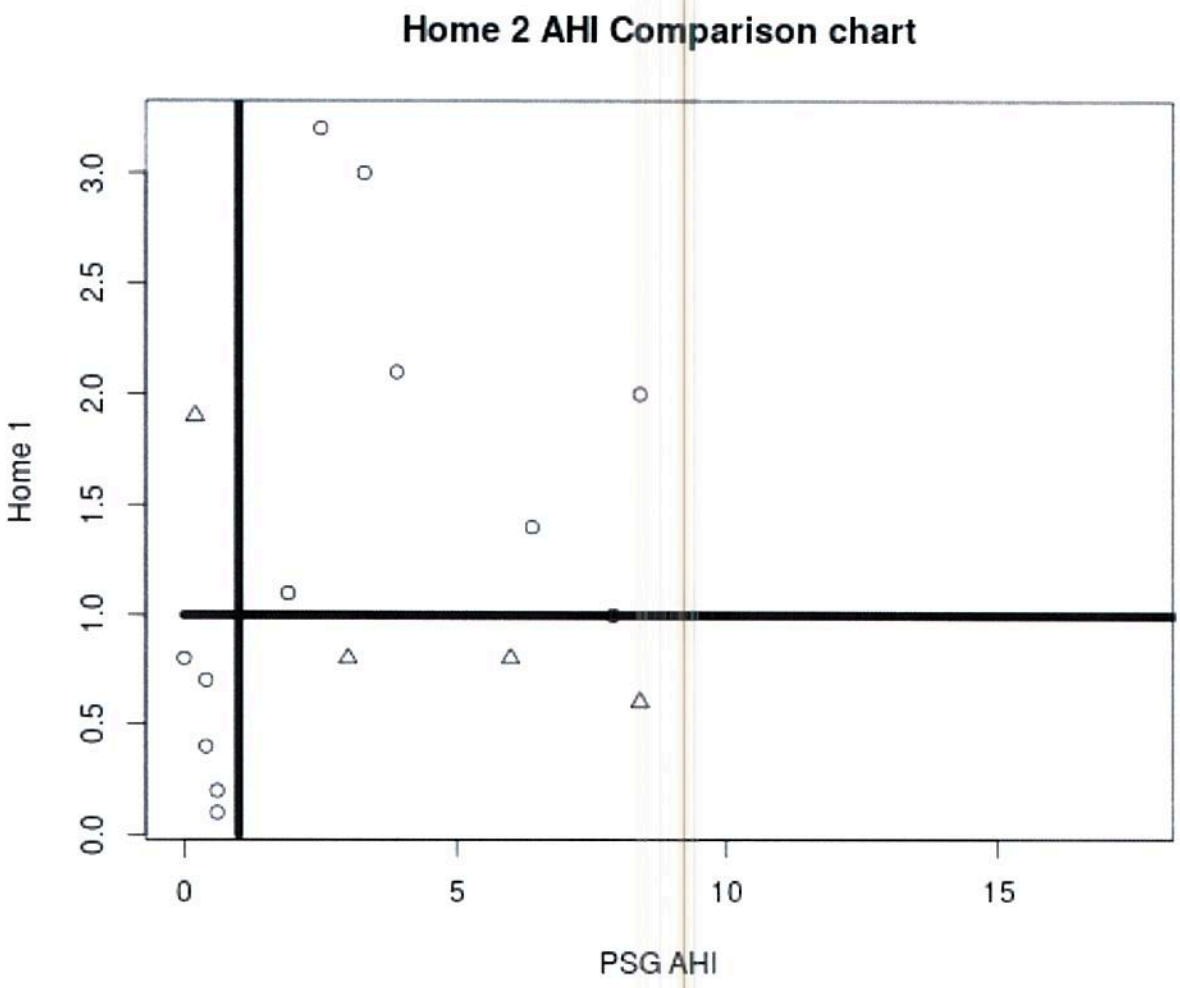

Figure 6: Box-and-whisker plots of the AHI measurements for each use of the home sleep monitor. These demonstrate the reproducibility of the data obtained by the device on different nights.

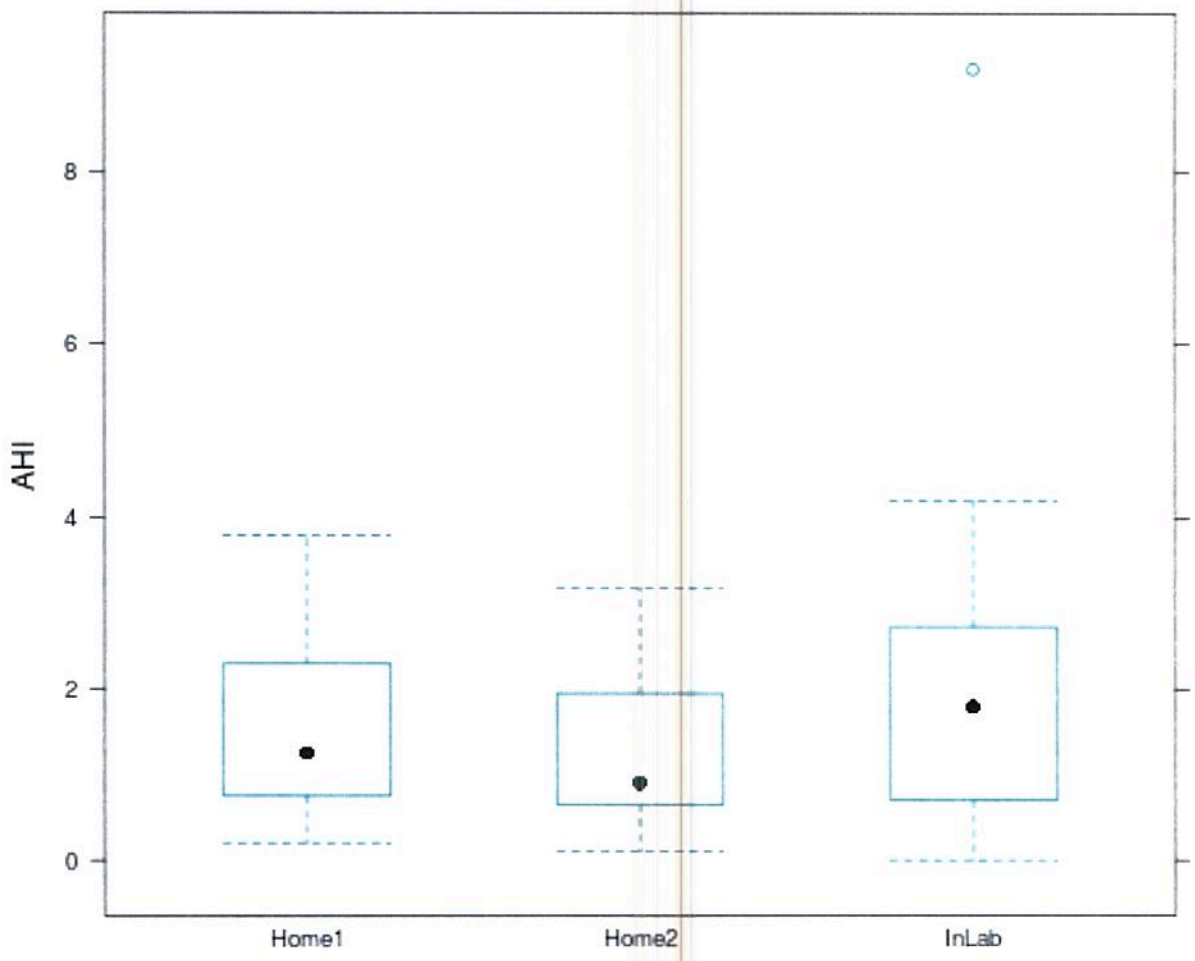

Figure 7: Box-and-whisker plots of the LSAT measurements for each use of the home sleep monitor. These demonstrate the reproducibility of the data obtained by the device on different nights.

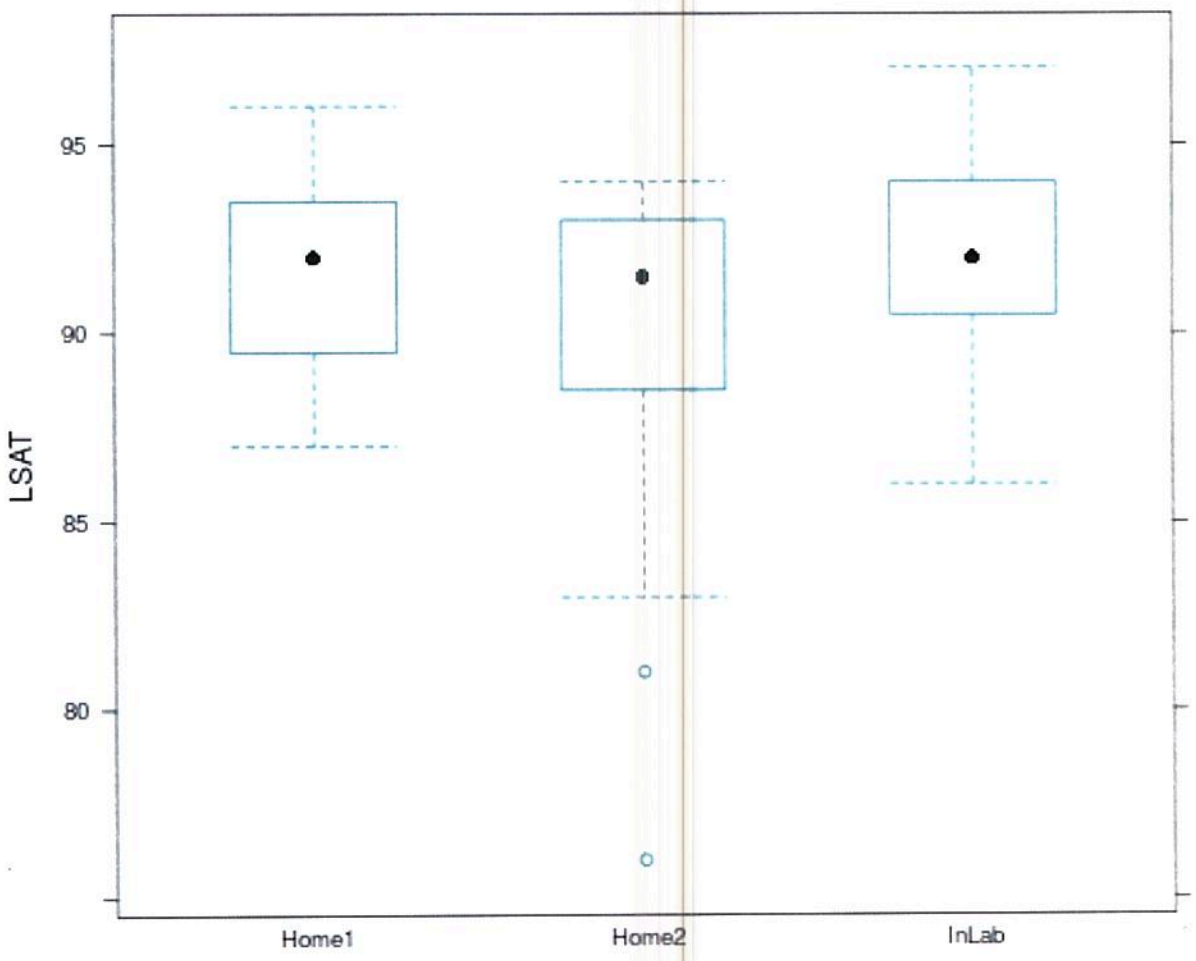

Figure 8: Receiver operating characteristic curve showing the tradeoff between power and probability of making a Type I error. If the cutoff for diagnosing OSA is changed to 0.75 for the home sleep test, the power increased to 90%, while the specificity decreased to 65%.

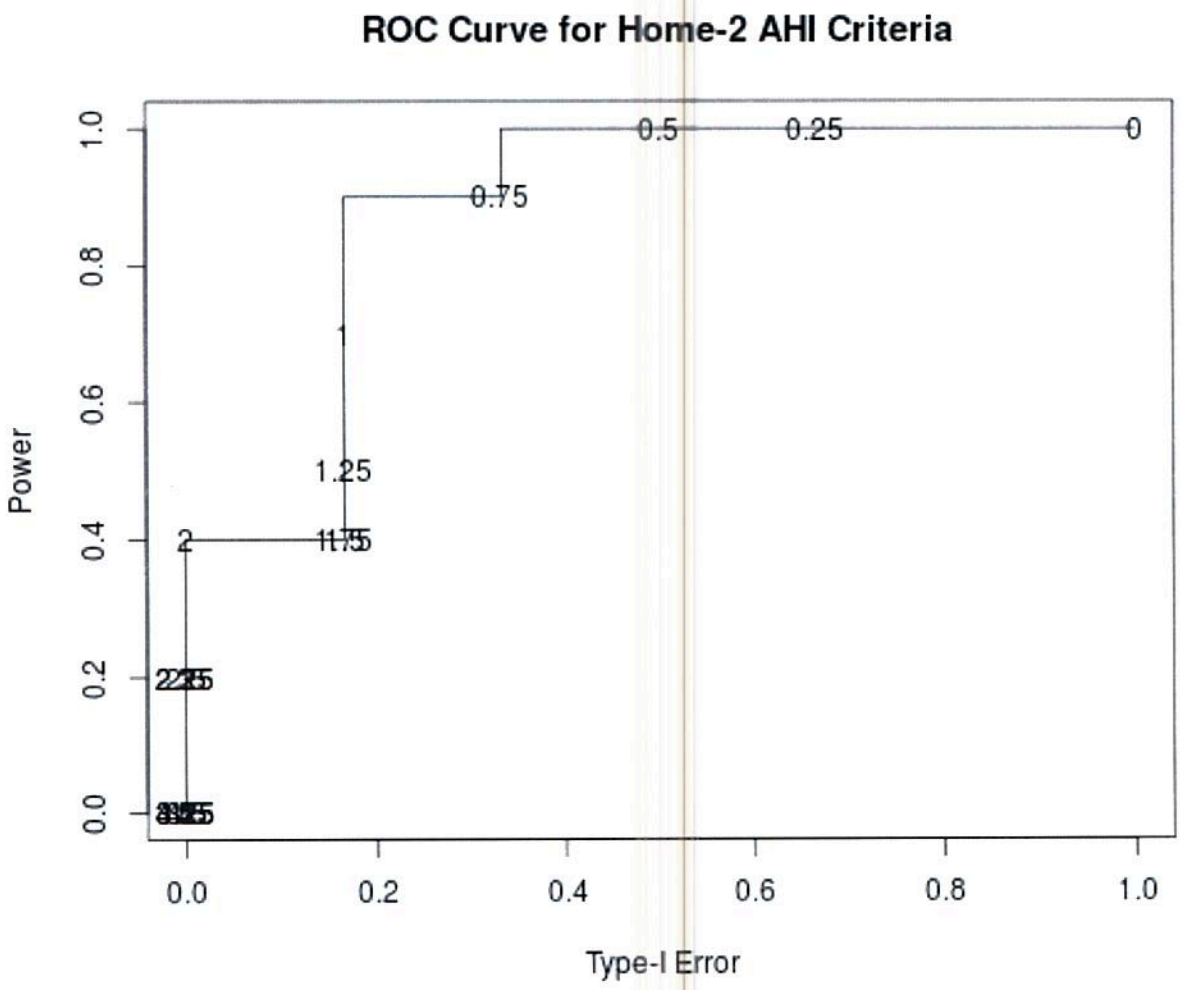

Figure 9: Receiver operating characteristic curve for the second night at home with the portable device. If the cutoff for diagnosing OSA is changed to 0.75 for the home sleep test, the power increased to 100%, while the specificity decreased to 60%.

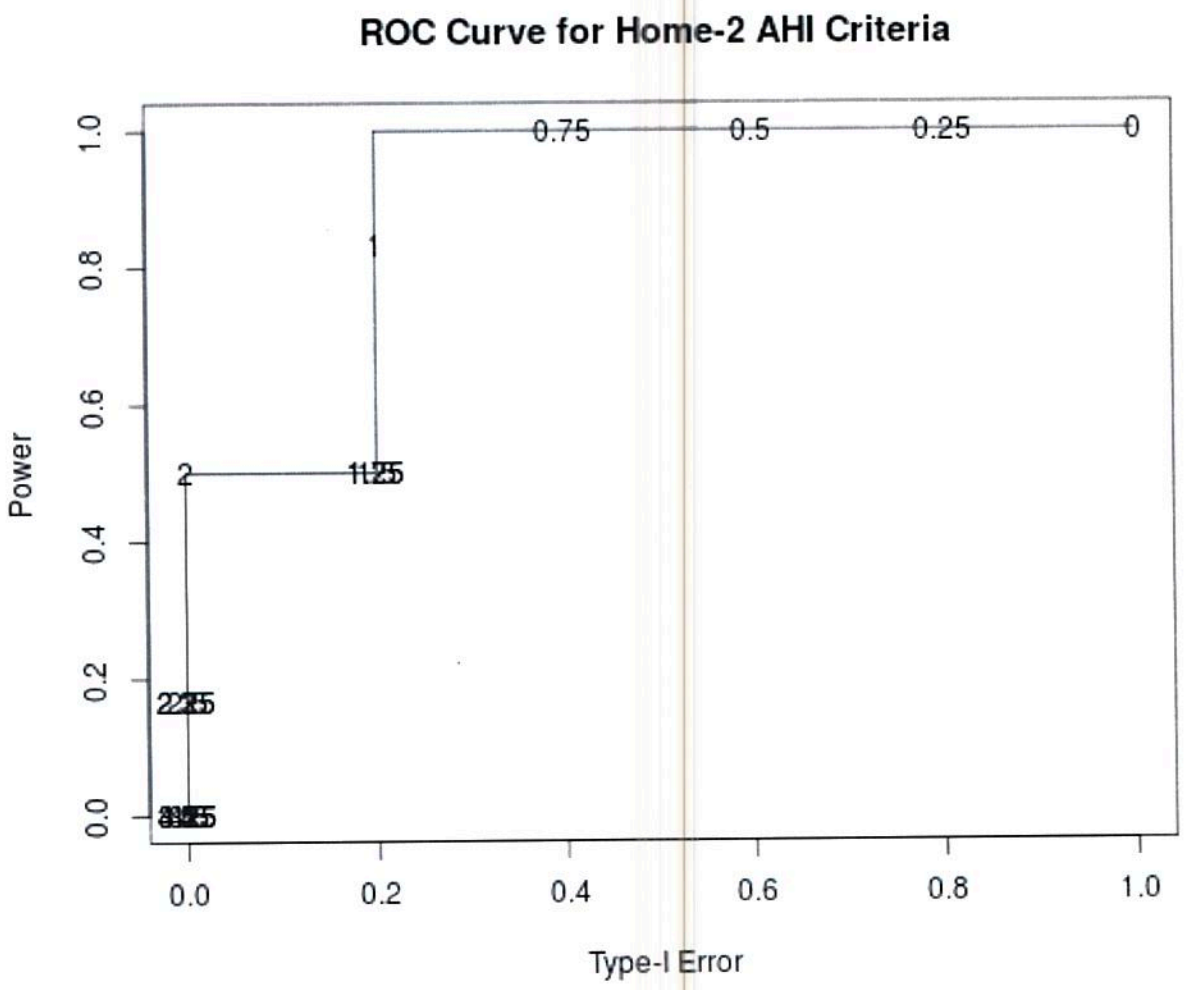

Table 1: Sensitivity and specificity of the home sleep test for use in each condition (In lab, Home 1, and Home 2) compared to the PSG for the diagnosis of OSA (defined as AHI greater than or equal to 1).

Use	Age	Sensitivity	Specificity
In Lab	All	.81	.60
Home 1	All	.70	.43
Home 2	All	.70	.83
In Lab	5 & under	1.00	.67
Home 1	5 & under	.75	.50
Home 2	5 & under	.50	1.00
In Lab	6 & over	.70	.63
Home 1	6 & over	.57	.33
Home 2	6 & over	.83	.80

Table 2: Linear regression analysis of gender and age. Males and older children had less error in AHI measurement by the portable monitor compared to the value obtained by the PSG. The absolute difference in AHI measurement for males was 3.24 less and for older children was 4.99 less.

Variable	Estimate	P-value
Male	-3.24	0.001
Age < 6	4.99	0.00003
Coefficient	4.47	5.4×10^{-8}