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SCIENTIFIC INVESTIGATIONS

A single-arm, open-label, multicenter, and comparative study of the ANNE sleep system vs polysomnography to diagnose obstructive sleep apnea

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Study Objectives: Evaluate per-patient diagnostic performance of a wireless dual-sensor system (ANNE sleep) compared with reference standard polysomnography (PSG) for the diagnosis of moderate and severe obstructive sleep apnea (OSA) with a minimum prespecified threshold of 80% for both sensitivity and specificity.

Methods: A multicenter clinical trial was conducted to evaluate ANNE sleep vs PSG to diagnose moderate and severe OSA in individuals 22 years or older. For each testing approach, apnea-hypopnea index (AHI) was manually scored and averaged by 3 registered sleep technologists blinded to the other system. Average variations > 15% were adjudicated by a sleep medicine physician.

Results: In a total of n = 225 participants (mean age 53 years, range 22–88 years), PSG diagnosed 30% (n = 68) of participants with moderate or severe OSA (AHI ≥ 15 events/h) compared to 29% (n = 65) diagnosed by ANNE sleep (P = .55). The sensitivity and specificity for ANNE sleep were 90% (95% confidence interval: 80–96%) and 98% (95% confidence interval: 94–99%), respectively. Strong correlation was shown in terms of final AHI (r = .93), with an average AHI bias of 0.5 (95% limits of agreement: –12.8 to 11.8). The majority of users noted comfort with using the ANNE sleep in the home setting. No adverse events were noted.

Conclusions: Using PSG as the gold standard, ANNE sleep demonstrated high sensitivity and specificity for the diagnosis of moderate or severe OSA.

Clinical Trial Registration: Registry: ClinicalTrials.gov; Name: Comparative Study of the ANNE™ One System to Diagnose Obstructive Sleep Apnea; URL: https://clinicaltrials.gov/ct2/show/NCT04643782; Identifier: NCT04643782.

Keywords: obstructive sleep apnea, polysomnography, home sleep apnea testing, diagnostic testing, wireless sensors, flexible electronics, patient preferences

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Obstructive sleep apnea (OSA) is widely underdiagnosed and access to gold-standard diagnostic testing (polysomnography) is limited, expensive, and uncomfortable.

Study Impact: We performed a multicenter clinical trial to compare the diagnostic performance of a flexible wireless dual-sensor system to diagnose moderate and severe OSA compared with in-laboratory polysomnography in adults aged 22 years or older. Compared with polysomnography, ANNE sleep demonstrated 90% sensitivity, 98% specificity, and 95% accuracy for moderate and severe OSA determined by the apnea-hypopnea index.

INTRODUCTION

Of the estimated 24.4 million Americans who have obstructive sleep apnea (OSA), approximately 90% of cases remain undiagnosed.[1–3] Untreated OSA contributes to a 2-fold increase in health care expenditures given its associated risks for hypertension, myocardial infarction, stroke, metabolic disorders, and motor vehicle accidents.[4–7] Efforts to increase the accessibility and efficiency of diagnosis are fundamental to improved identification of patients with OSA.

Currently, polysomnography (PSG) performed at an accredited sleep center is the gold standard for OSA diagnosis. Although the number of these facilities is rising, geographic availability varies considerably, resulting in unequal access.[8] The ongoing coronavirus disease 2019 (COVID-19) pandemic has also changed the landscape of sleep diagnostics.[9] In an effort to mitigate risk of exposure for both patients and staff, sleep laboratories have reduced their capacity. Furthermore, a single night of PSG may be subject to a "first night effect" in which the unfamiliar environment and equipment reduce the

quantity and quality of sleep, thereby contributing to the night-to-night variability in sleep-disordered breathing.[10,11] Thus, there is a growing need for home-based options to minimize COVID-19 exposure, reduce cost and time to diagnosis, while accommodating patient preferences.

As an alternative to PSG, a home sleep apnea test (HSAT) is used for patients with a high pretest probability of OSA. While HSATs do not include electroencephalography, electrooculography, or electromyography sensors, all of which are required to define wake and sleep stages, the American Academy of Sleep Medicine (AASM) endorses HSAT use in selected, medically uncomplicated patients.[12] Studies comparing the diagnosis of OSA in the home compared with an accredited sleep laboratory demonstrated minimal differences in subsequent outcomes or treatment adherence when used in the appropriate patient population.[13,14] Although HSATs offer a home-based alternative to PSG, there are still limitations of these systems. Type 3 and type 4 HSATs are often associated with underestimation of disease, given the use of total recording time, rather than total sleep time, of a study to determine the apnea-hypopnea index (AHI), leading to an estimated false-negative rate of 13–20%, with particularly poor discrimination of mild to moderate disease.[15,16] Additionally, home studies have higher failure rates compared with PSG, lack real-time feedback of test adequacy, and have their own "first night" effect.[17–19] A wrist-mounted device (WatchPAT; Itamar Medical Ltd, Caesarea, Israel) worn overnight at home has increasingly been studied as another technology to perform a sleep test in the home.[20] The WatchPAT system is intended for single use and subsequent disposal. Some studies have demonstrated that WatchPAT may overestimate respiratory disturbances, given potential difficulties in distinguishing respiratory arousals from spontaneous arousals or periodic limb movements.[21] Additional concerns include high cost and dependency on automated scoring algorithms that make the raw signal difficult to interpret by physicians.[21]

Given these limitations, there is a need for well-validated, home-based diagnostic systems for OSA with greater usability, comfort, affordability, and comparable accuracy to PSG. Furthermore, a system capable of real-time assessment of study adequacy paired with the capacity to reuse and recharge for multiple nights of testing would be valuable. Recent advances in soft, flexible electronics have enabled a wide range of biomedical applications including intensive care unit–grade monitoring in the home.[22–24] The primary objective of this study was to validate a new flexible wireless dual sensor system (ANNE Sleep; Sibel Health, Niles Illinois) mounted on the chest and finger for the diagnosis of moderate and severe OSA compared with the reference standard, PSG, in the laboratory setting.

METHODS

Pivotal trial: ANNE sleep vs PSG

We performed a multicenter clinical trial to evaluate the accuracy, sensitivity, and specificity of the ANNE sleep system as a diagnostic tool for moderate and severe OSA in adults compared with PSG. Individuals at least 22 years old with either suspected OSA (based on history or physical examination), or prescribed either PSG or HSAT study by a health care provider, were eligible. Consenting individuals provided demographics and medical history and completed a sleep survey to ensure eligibility. Individuals were excluded if they had a medical condition posing a health risk related to trial participation or interfering with trial completion, such as oxygen dependence, respiratory muscle weakness secondary to neuromuscular disease, awake or sleep-related hypoventilation, chronic opioid use, dementia, severe insomnia, inability to follow instructions, severe skin abnormalities, implanted pacemakers or defibrillators, stroke, or pregnancy.

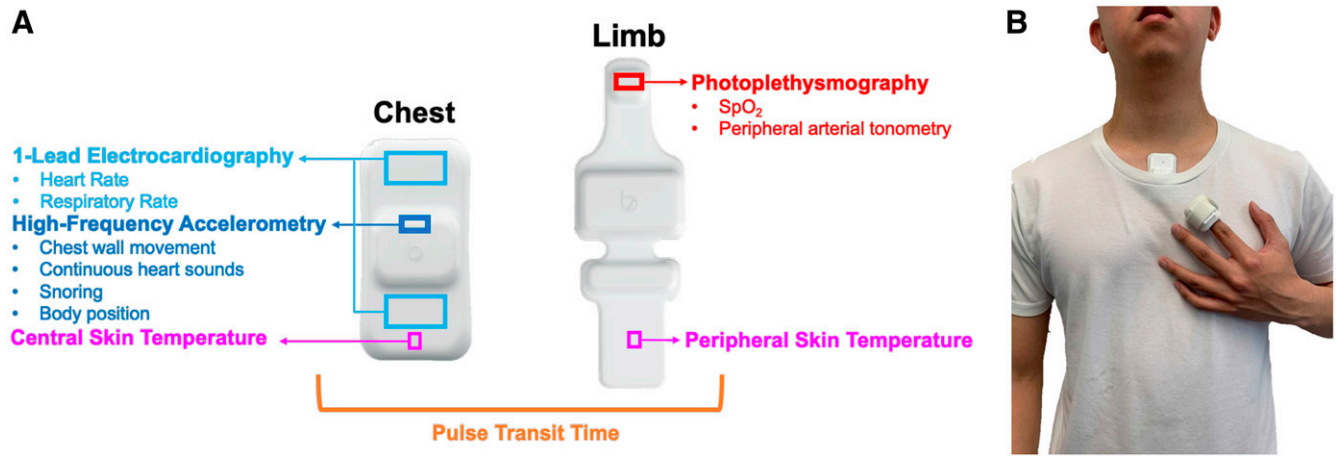
Enrolled eligible participants completed PSG supervised by a respiratory sleep technologist for 1 night at an AASM-certified sleep center. Concurrent with PSG, ANNE sleep sensors were applied by a study coordinator. Data were collected by both systems simultaneously. Participants completed a sleep diary and a usability survey postprocedure. The study was approved by Northwestern University and the Carle Foundation Hospital Institutional Review Boards (IRB ID: STU00213322 and IRB ID: 20NCI3196) and registered at ClinicalTrials.gov (NCT04643782). All participants provided written consent prior to participation.

Both PSG and ANNE sleep outputs were manually scored by 3 blinded registered sleep technologists. Scoring of PSG data followed the guidelines in *The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications* (version 2.6) using a 4% oxygen desaturation criteria for hypopneas.[25] The respiratory sleep technologists were provided the ANNE sleep scoring manual for guidelines to score the ANNE sleep data. Sleep-disordered breathing events were identified through collective evaluation of the multiple channel outputs for chest wall movement, peripheral arterial tonometry (PAT) for an attenuated signal, arterial oxygen saturation (SpO_2), heart rate, and snoring. ANNE sleep's sleep-wake classifier is based on an artificial intelligence–enabled classifier that combines recurrent and convolutional neural networks. If the inter–respiratory sleep technologist mean variation for either PSG or ANNE-determined AHI exceeded 15%, a board-certified sleep medicine physician blinded to the experimental condition provided the final determination of AHI after review of the raw data per AASM and ANNE sleep scoring manual guidelines.

Equipment

The novel system used in both the pivotal and pilot studies (ANNE One; Sibel Health) is pictured in **Figure 1**; it consists of 2 flexible wireless sensors, 1 placed at the suprasternal notch (ANNE chest) and the second wrapped around the index finger (ANNE limb). Both sensors are Food and Drug Administration–cleared as part of a continuous physiological monitoring system for patients 18 years or above to aid in clinical decision making. The ANNE chest unit contains a single-lead electrocardiogram sensor, high-frequency 3-axis accelerometer, and temperature sensor, and is capable of continuous measurement of heart rate, respiratory rate, chest wall movement, body position, and skin temperature. Direct mechanical coupling of the 3-axis accelerometer to the skin at the suprasternal notch with a bio-compatible, single-use adhesive accesses this anatomical location of high

Figure 1—Experimental system.



The components applied to the body for the experimental system (ANNE sleep) are shown (**A**). They consist of 2 soft, flexible, wireless sensors that couple to the suprasternal notch and the index finger. The onboard sensors include 1-lead ECG, 3-axis high-frequency accelerometry, thermography, and transmissive mode photoplethysmography. Collectively, these onboard sensors generate measurements for heart rate, respiratory rate, chest wall movement, continuous heart sounds, snoring, body position, SpO_2, skin temperature at both a central and peripheral location, and peripheral arterial tonometry. The sensors are software-linked, enabling time synchronization to derive pulse arrival time and pulse transit time. The sensors are mounted (**B**) on the suprasternal notch and finger with single-use consumables. ECG = electrocardiography, SpO_2 = arterial oxygen saturation.

information density. This enables continuous stethoscope-like detection of snoring, respiration, and seismocardiography.[22] The ANNE limb unit, coupled to the index finger with a latex-free, biocompatible adhesive, has a photo-plethysmograph to measure SpO_2, PAT, and temperature. The accuracy and performance of the system have been published previously for core vital signs.[24] ANNE sleep's accuracy in quantifying total sleep time was validated against PSG records via 30-second epochs. The mean absolute percentage error for total sleep time was 17% with a mean difference of 12.9 minutes.

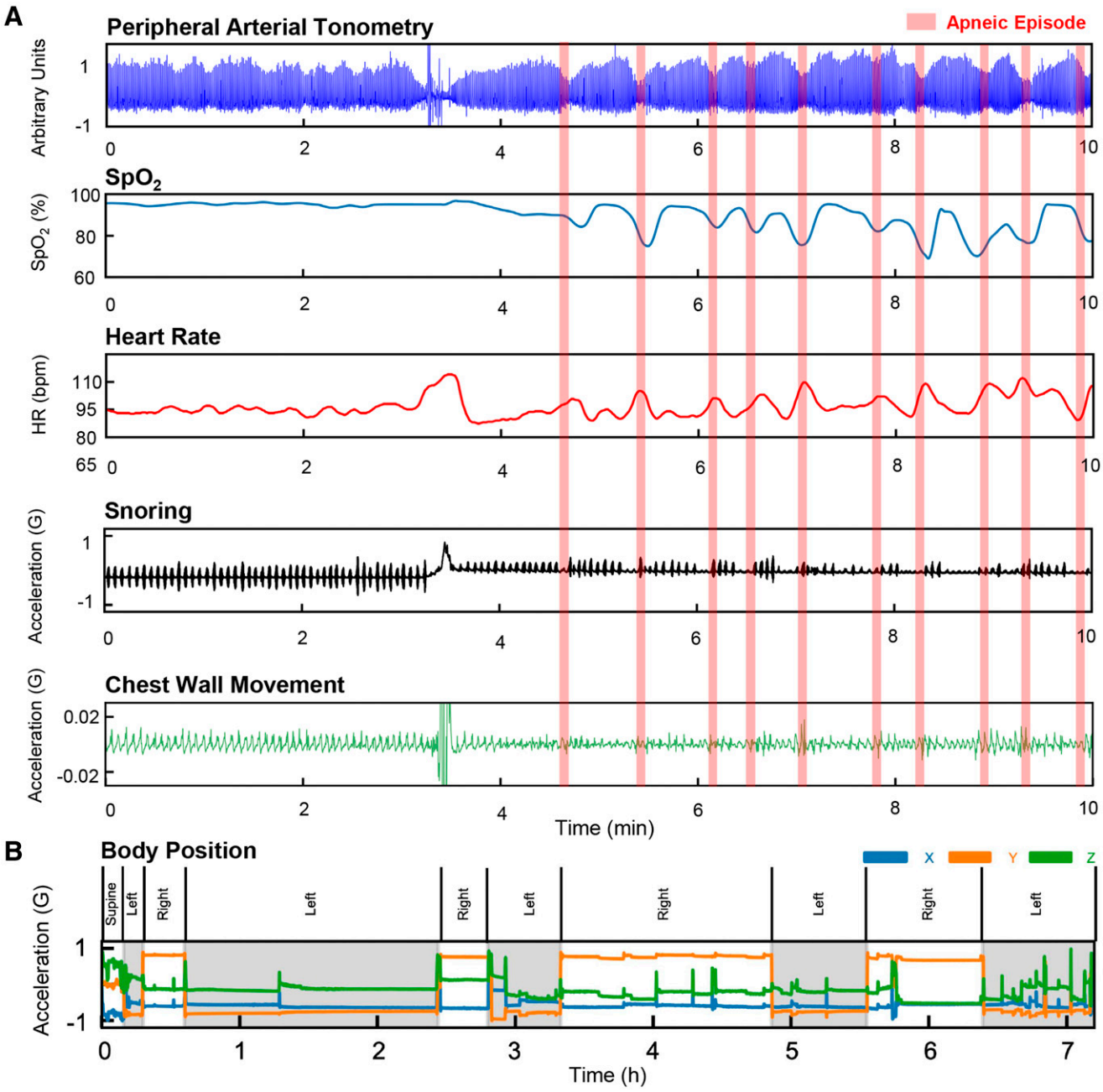
Figure 2 demonstrates data outputs from the system. Both sensors record data on board and can stream and store all output channels of physiological data to a mobile device via encrypted Bluetooth. Data are then automatically transmitted to a secure cloud for analysis. Furthermore, the sensors are software-linked and time-synchronized to produce continuous measurements of pulse transit time (PTT) as a novel index. PTT represents a time interval that corresponds to a pulse wave traveling from the aortic valve to the finger, providing a reliable measurement of continuous blood pressure.[26] Previously, PTT has been further established as a reliable method to differentiate obstructive and central sleep respiratory events, and respiratory effort.[27,28] Systematic reviews have concluded the utility of PTT as an important digital biomarker of OSA in both children and adults without the need for a nasal cannula or thermistor—PTT has been described previously with a sensitivity of 93% and specificity of 96% for differentiating obstructive and central respiratory events against standard techniques.[27,29–31] We illustrate the utility of PTT derived from the ANNE sleep system to identify both central sleep apnea and OSA events compared with flow and respiratory inductance plethysmography outputs from gold-standard systems. In cases where obstructive events occur, the PTT signal is more variable with a sloped appearance. In cases where central apnea events occur, the PTT signal is flat (**Figure 3**).

Statistical methods

The primary endpoints of the pivotal study were sensitivity and specificity of ANNE sleep to diagnose moderate and severe OSA compared with PSG with a prespecified goal of at least 80% for both sensitivity and specificity. An AHI between 15 to 30 events/h was defined as moderate OSA and an AHI greater or equal to 30 events/h was designated as severe disease. Sensitivity was defined as the proportion of participants with moderate or severe OSA by PSG correctly identified by ANNE sleep. Specificity was defined as the proportion of participants without moderate or severe OSA by PSG with similarly negative testing by ANNE sleep. Secondary endpoints included ANNE sleep accuracy and positive predictive values (PPVs) and negative predictive values (NPVs) for moderate and severe OSA. Accuracy was defined as the proportion of true results. PPV was defined as the proportion of participants accurately identified as having moderate or severe OSA of the total number of positive screening tests. NPV was defined as the proportion of participants correctly screening negative among the total number of negative tests.

We determined point estimates and 95% confidence intervals (CIs) for sensitivity, specificity, accuracy, area under the curve (AUC) of the receiver operating characteristic (ROC) curve, PPV, and NPV of ANNE sleep to diagnose moderate and severe sleep apnea compared with PSG. We also calculated the diagnostic characteristics for AHI cutoffs of 5, 15, and 30 events/h. Bland-Altman plots and linear regressions for AHI were generated to evaluate bias between mean differences and to estimate a 95% interval of differences between ANNE sleep and PSG.[32] It was determined, a priori, that a minimum sample size of 181

Figure 2—Outputs of the experimental system.



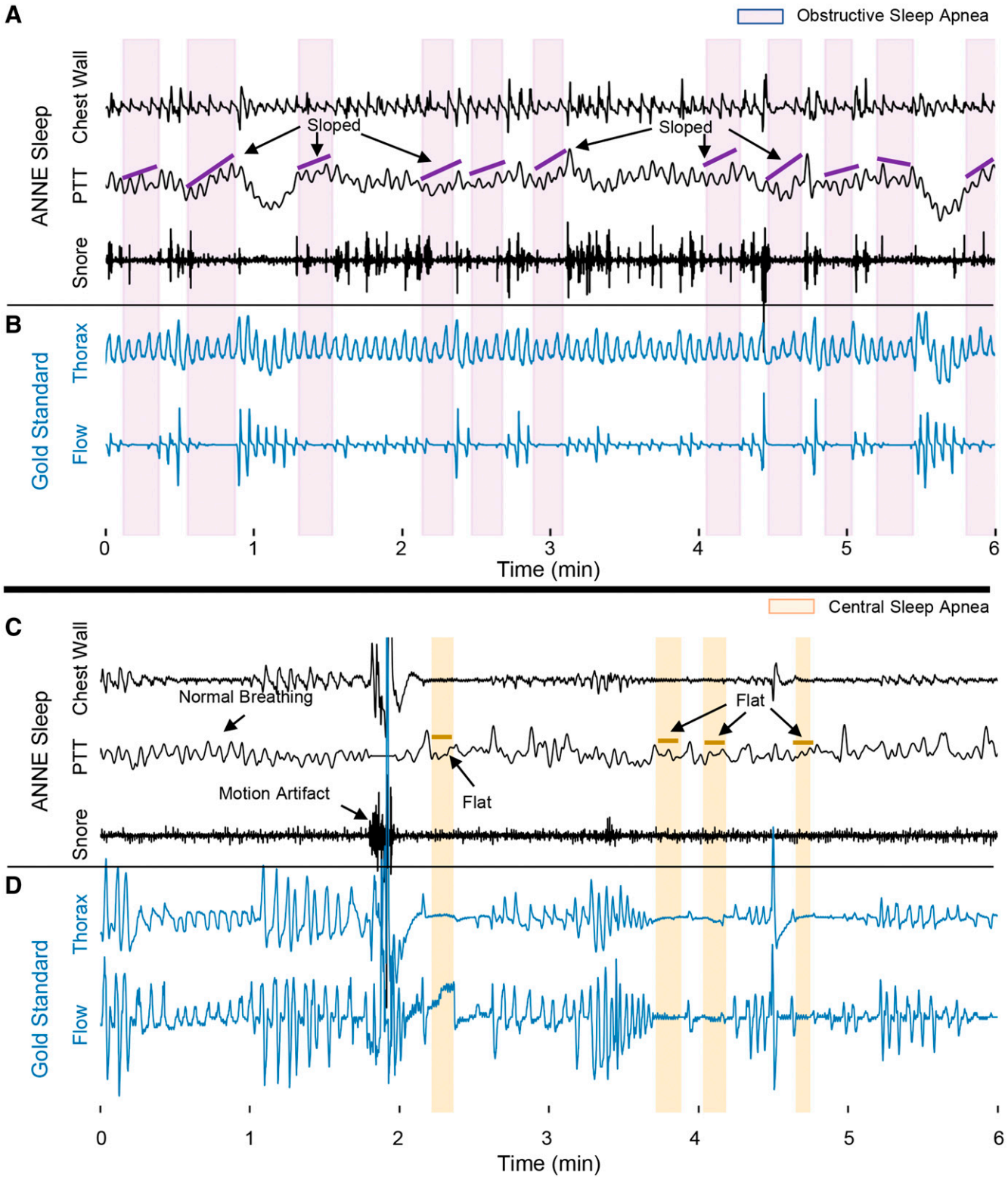
The outputs of the ANNE sleep system are shown derived from a suite of onboard sensors. (**A**) The outputs derived from the ANNE limb sensor for PAT and SpO_2 and ANNE chest sensor for heart rate, snoring, and chest wall movement. During apneic events, there is clear illustration of PAT attenuation, heart rate increases, SpO_2 drops, snoring changes, and chest wall movement changes. (**B**) The system accurately determines body position changes based on the ANNE chest sensor. bpm = beats per minute, HR = heart rate, PAT = peripheral arterial tonometry, SpO_2 = arterial oxygen saturation.

participants would be required to achieve 80% power to detect (1) sensitivity at least as large as 0.80, based on a target significance level of .05 with a 1-sided binomial test, and (2) specificity at least as large as 0.80, based on a target significance level of .05 with a 1-sided binomial test after accounting for an estimated 10% missingness. Statistical programming and analyses were performed independently by HealthCore, using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

A total of 287 individuals were recruited from 4 clinical sites in Illinois between May 11, 2021, and November 17, 2021. A total of n = 225 individuals were included in the final analysis after accounting for patient cancellations and withdrawals (**Figure S1** in the supplemental material). The mean age of participants was 53 years (standard deviation [SD] 14 years) and 56% were women.

Figure 3—PTT derived from experimental system.



(**A**–**D**) PTT represents a time interval that corresponds to a pulse wave traveling from the aortic valve to the finger, which can be used to distinguish central and obstructive sleep apnea events. In the case of obstructive events, PTT varies with a sloped appearance given the movement of the chest. In the case of central events, PTT remains relatively flat given the lack of movement of the chest. PTT = pulse transit time.

The mean body mass index (BMI) of participants was 31.2 kg/m^2, and 83% were considered overweight or obese by BMI. Nearly one-third of patients (n = 73) reported a history of hypertension and 12.5% (n = 28) had a history of diabetes (**Table 1**).

Overall, the mean PSG-derived AHI was 13.4 (SD 16.7) events/h and mean ANNE sleep–derived AHI was 12.9 (SD 15.1) events/h. Forty percent of the cohort had a normal AHI based on PSG (n = 91), compared to 37% (n = 83) by ANNE sleep; 30% of the cohort had mild OSA by PSG-derived AHI (n = 66), compared to 34% (n = 77) by ANNE sleep; 16% of the cohort had moderate OSA by PSG (n = 37), compared to 19% by ANNE sleep (n = 43). Last, 14% of the cohort had severe OSA by PSG (n = 31) compared to 10% (n = 22) by ANNE sleep (**Table 2**). PSG diagnosed 30% of the cohort (n = 68) with moderate or severe OSA based on an AHI ≥ 15 events/h compared to 29% (n = 65) identified by ANNE sleep (P = .55). Variation in scoring exceeding 15% by respiratory sleep technologists required adjudication by a sleep medicine physician in 42% of PSG studies (n = 94) and in 8% of ANNE sleep studies (n = 19).

The sensitivity and specificity for ANNE sleep in the diagnosis of moderate to severe OSA were 89.7% (95% CI: 79.9–95.8%) and 97.5% (95% CI: 93.6–99.3%), respectively (**Figure 4**). The overall accuracy between ANNE sleep and PSG was 95.1% (95% CI: 91.4–97.5%). The PPV and NPV were 93.8% (95% CI: 85.0–98.3%) and 95.6% (95% CI: 91.2–98.2%), respectively. The overall bias was –0.5 events/h (95% limits of agreement: –12.8 to 11.8). AHI determined by PSG and ANNE sleep showed a correlation of r = .93 (95% CI: 0.91 to 0.94). Furthermore, in post hoc analyses we determined the diagnostic performance of ANNE sleep vs PSG at cutoffs of 5, 10, and 15 events/h for AHI (**Table 3**).

Overall, 93% of participants agreed or strongly agreed that ANNE sleep sensors would be easy to use at home and reported they could see themselves using the ANNE sensors at home for monitoring sleep. A subanalysis of user preferences for older adults in this study (≥65 years; n = 43) reported similarly high comfort levels using the ANNE sensors and expressed potential interest in future home use. There were no serious adverse events during the study.

DISCUSSION

This validation study demonstrated a high level of per-patient diagnostic agreement between ANNE sleep and PSG for moderate and severe OSA. The ANNE sleep system achieved a sensitivity of 89.7% and specificity of 97.5% with gold-standard in-laboratory PSG, meeting our prespecified threshold of at least 80% for sensitivity and specificity. The cohort used in this validation study was appropriately representative of a high-risk cohort of patients undergoing diagnostic testing for OSA; overall, 60% of the cohort had some level of dysfunctional breathing, while approximately 30% had moderate to severe disease.[25] Additionally, comorbidities of obesity, hypertension, and diabetes were highly prevalent.

Although the study was primarily designed to characterize performance of ANNE sleep to diagnose moderate to severe

Table 1—Participant demographics (n = 225).

	Values
Age, mean (SD), y	52.7 (14)
Sex, n (%)	
Male	98 (43.6)
Female	127 (56.4)
Race, n (%)	
American Indian or Alaska Native	1 (0.4)
Asian	20 (8.9)
Native Hawaiian or other Pacific Islander	1 (0.4)
Black or African American	26 (11.6)
White	164 (72.9)
More than 1 race	10 (4.4)
Ethnicity, n (%)	
Hispanic or Latino	19 (8.4)
Highest education level completed, n (%)	
Some high school	1 (0.4)
High school graduate (or equivalent)	21 (9.3)
Some college or technical school	50 (22.2)
College graduate	152 (67.6)
Current employment status, n (%)	
Employed	146 (64.9)
Unemployed	26 (11.6)
Retired	48 (21.3)
Retired due to disability	4 (1.8)
BMI, mean (SD), kg/m^2	31.2 (7.1)
BMI categories,* n (%)	
Underweight	4 (1.8)
Normal	34 (15.1)
Overweight	73 (32.4)
Obese	113 (50.2)
Medical history, n (%)	
Diabetes	28 (12.4)
Hypertension	73 (32.4)
Atrial fibrillation	5 (1.7)
Other cardiopulmonary disease	6 (2.1)
Cardiopulmonary disease requiring hospitalization	6 (2.1)
OSA disease severity,† n (%)	
Normal	91 (40.4)
Mild	66 (29.3)
Moderate	37 (16.4)
Severe	31 (13.8)

*BMI categories: underweight = BMI < 18.5 kg/m^2, normal weight = BMI 18.5 to < 25 kg/m^2, overweight = BMI 25 to < 30 kg/m^2, and obese = BMI ≥ 30 kg/m^2. †OSA disease severity: normal = AHI < 5 events/h, mild = AHI 5 to < 15 events/h, moderate = AHI 15 to < 30 events/h, and severe = AHI ≥ 30 events/h. AHI = apnea-hypopnea index, BMI = body mass index, OSA = obstructive sleep apnea, SD = standard deviation.

Table 2—Subjects categorized by OSA severity by PSG and ANNE sleep.

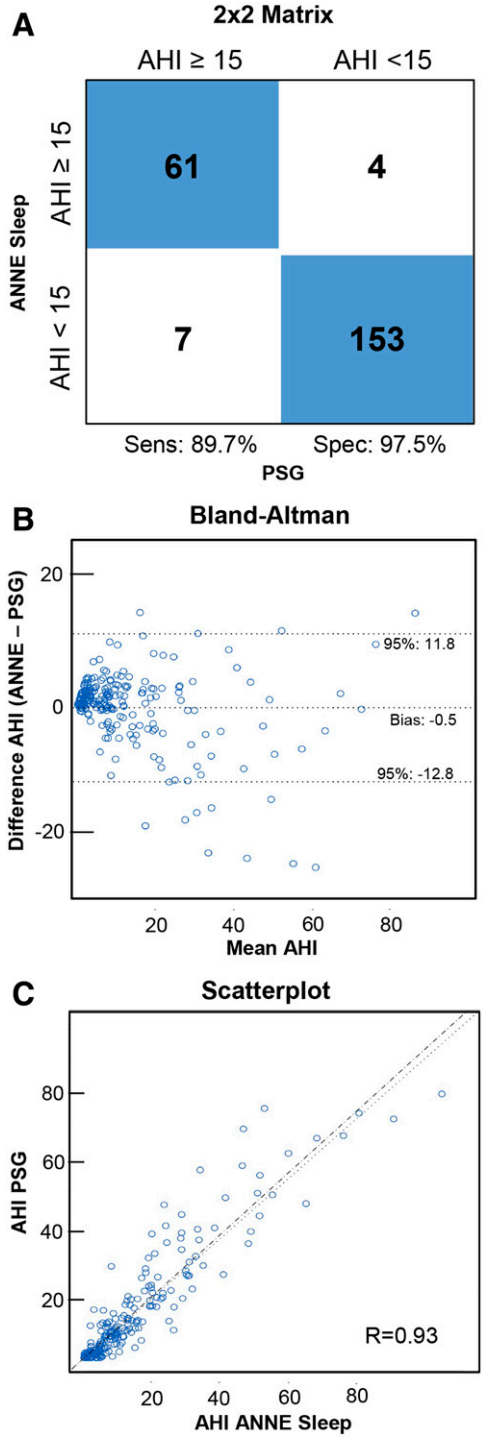
OSA Severity*	PSG-Derived AHI	ANNE Sleep–Derived AHI
Normal	91 (40.0)	83 (37.0)
Mild	66 (30.0)	77 (34.0)
Moderate	37 (16.0)	43 (19.0)
Severe	31 (14.0)	22 (10.0)

Values are presented as n (%). *OSA disease severity: normal = AHI < 5 events/h, mild = AHI 5 to < 15 events/h, moderate = AHI 15 to < 30 events/h, and severe = AHI ≥ 30 events/h. AHI = apnea-hypopnea index, OSA = obstructive sleep apnea, PSG = polysomnography.

OSA, we demonstrated strong discriminatory agreement of ANNE sleep at all clinically relevant thresholds of disease severity with an AUC of at least 0.8 at each AHI cutpoint of 5, 15, and 30 events/h.[33] ANNE sleep underestimated the PSG AHI minimally by a mean of 0.5 events/h and, although it performed well for the a priori diagnostic designation of moderate and severe apnea, it was less accurate at the higher end of apneic events, differentiating moderate from severe disease. Arguably, differentiation of moderate from severe disease has fewer clinical implications, given the AASM recommendation to treat all patients with moderate disease (AHI ≥ 15 events/h) even in the absence of symptoms according to the AASM guidelines.[25] Furthermore, maintaining a high PPV is fundamental to preventing overdiagnosis and therefore increasing accessibility and reducing cost. A post hoc analysis of variable AHI cutoffs demonstrated that a threshold of 15 or more events/h maximized both the sensitivity and specificity of ANNE sleep and the AUC of 0.94. Furthermore, we demonstrated less interrater variability of ANNE sleep when compared with the interrater variability of PSG. Exploration of the clinical applicability of fully automated ANNE sleep scoring is under way.

In light of the global disease burden of OSA, affecting an estimated 24% of men and 9% of women, most of whom are undiagnosed, innovation to improve access to efficient, accurate, high-quality diagnostic testing is of utmost importance.[34] The COVID-19 pandemic has accelerated the interest in wearable devices and home-based diagnostic tools. While PSG does offer high accuracy and low failure rates as a supervised study, it remains prohibitively labor-intensive, inconvenient, costly, and uncomfortable, potentially leading to decreased total sleep time, lower sleep efficiency, and reduction in rapid eye movement sleep that may compromise its diagnostic value.[35] HSAT systems address some of the limitations of PSG, given their home-based use and lower costs. However, a negative HSAT in the setting of high clinical suspicion still requires confirmatory PSG evaluation.[36] Randomized clinical trial–based cost-effectiveness analyses comparing HSAT and PSG generally favor home-based screening, although the margin of benefit narrows when considering the lower accuracy of HSAT, higher

Figure 4—AHI scored by experimental system compared with PSG.



(**A**) A 2 × 2 matrix for the diagnosis of moderate to severe OSA for ANNE sleep and PSG. (**B**) Bland-Altman plot for AHI between ANNE sleep and PSG. (**C**) The scatterplot illustrates high linear agreement between AHI derived from ANNE sleep compared with AHI derived from PSG. AHI = apnea-hypopnea index, OSA = obstructive sleep apnea, PSG = polysomnography, Sens = sensitivity, Spec = specificity.

Table 3—Diagnostic performance of ANNE sleep vs PSG at AHI thresholds.

AHI Cutoff (events/h)	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)	Accuracy	PPV (95% CI)	NPV (95% CI)	LR+	LR−
5	0.96 (0.92–0.99)	0.86 (0.77–0.92)	0.91 (0.87– 0.95)	0.92	0.91 (0.85–0.95)	0.94 (0.87–0.98)	6.7	0.04
15	0.90 (0.8–0.96)	0.97 (0.94–0.99)	0.94 (0.90–0.97)	0.95	0.94 (0.85–0.98)	0.96 (0.91–0.98)	35.2	0.11
30	0.65 (0.45–0.81)	0.99 (0.96–0.99)	0.82 (0.73–0.90)	0.94	0.91 (0.71–0.99)	0.95 (0.91–0.97)	62.6	0.36

AHI = apnea-hypopnea index, AUC = area under the curve, CI = confidence interval, LR = likelihood ratio, NPV = negative predictive value, PPV = positive predictive value, PSG = polysomnography.

technical failures, and requirements for confirmatory testing.[18,37,38]

It is important to note that there are multiple HSAT systems commercially available. Traditional type 3 HSAT systems (eg, Philip's Alice NightOne, Murrysville, PA) include a large base unit strapped to the chest with multiple cable connections that allow for a single night use before being returned for refurbishment. Alternatively, WatchPAT (Itamar Medical Ltd, Caesarea, Israel) is a single-use disposable wrist-bound system that first used PAT to assess apnea events.[17,20] In addition, SomnaPatch (Somnarus Inc, Mountain View, CA) was recently Food and Drug Administration–cleared as a single-use system with a nasal cannula and a forehead mounted pulse oximeter.[37] The ANNE Sleep system, also FDA-cleared as a diagnostic platform for sleep-related breathing disorders in 2022, offers several potential advantages over these existing solutions. The unique soft mechanics and low-profile nature of the ANNE sleep system allow for mechanical deformation with natural body movement and lower skin contact stress, enabling high-fidelity monitoring and comfort.[24] Thus, the ANNE sleep system allows for more natural sleeping positions and automatically determines body position over a sleep night via the chest sensor (**Figure 2A**). This may offer a more realistic assessment of AHI and reduce the first-night effects observed with both PSG and traditional type 3 HSAT systems.[39] Furthermore, the ANNE sensors are fully rechargeable and reusable by the users themselves, allowing for multiple testing nights without the need to dispose of the system or reset it. Currently, the WatchPAT system is a single-use disposable device. This is a relevant advantage as multiple nights of home testing may be beneficial to increase diagnostic performance and reduce the impact of night-to-night variability of AHI; in a previous study of 47,423 adults, the average nightly variation of HSAT-derived AHI was 5.5 events/h, leading to a change in classification of severity of disease (mild, moderate, or severe) in one-third of the sample.[39] Furthermore, ANNE sleep's ability to link to ubiquitous mobile devices offers near-immediate data transfer to a secure cloud for analysis after each night, which may further reduce the need for confirmatory PSGs. Finally, the ANNE sleep system offers continuous electrocardiogram measurements unlike other HSAT systems and WatchPAT, and derives total sleep time and core body position from the chest sensor, mitigating limb movement artifacts.

There are several important limitations to acknowledge. First, our scoring criteria do not differentiate between apnea and hypopnea events. Although apneas and hypopneas are delineated clearly in AASM scoring guidelines, there is little empirical evidence of the clinical significance of differentiating these events.[40] Several studies have shown that differentiating apneas and hypopneas results in limited clinical differences in treatment outcomes, or imaging findings.[41–44] In addition, 1 study showed no differences in clinical comorbidities for patients with higher apnea indices compared with hypopnea indices—in fact, scoring apneas and hypopneas together, as done here with the experimental system, may increase interrater reliability and save resources in technician and physician time.[40] While the system has the potential to distinguish central vs obstructive apnea events via PTT, the population addressed in this study was selected for a high pretest probability for obstructive apnea. Finally, the ANNE sleep sensor system was deployed under optimal conditions in this study—applied by a trained study coordinator in a sleep laboratory. Future efforts are ongoing to further validate the ANNE sleep system's performance in the home setting by users themselves and the system's ability to distinguish central from obstructive events.

CONCLUSIONS

Given the large burden of undiagnosed OSA and the ongoing COVID-19 pandemic, which has further driven the demand for virtual care, there remains a continued clinical need for more diagnostic platforms suitable for the home setting. Herein, we show high accuracy and strong positive user feedback for ANNE sleep compared with PSG for OSA. The advantages of the ANNE sleep system include reusability of both sensors with a simple sanitization wipe, enabling a potential lower cost per night. In addition, future opportunities include assessment of improved diagnostic performance with multiple sleep nights with minimal patient discomfort.

ABBREVIATIONS

AASM, American Academy of Sleep Medicine
AHI, apnea-hypopnea index
BMI, body mass index
CI, confidence interval
HSAT, home sleep apnea test
NPV, negative predictive value
OSA, obstructive sleep apnea
PAT, peripheral arterial tonometry
PPV, positive predictive value

PSG, polysomnography
PTT, pulse transit time
SD, standard deviation

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