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AMERICAN COLLEGE OF CHEST PHYSICIANS

Description and Validation of the Apnea Risk Evaluation System*

A Novel Method To Diagnose Sleep Apnea-Hypopnea in the Home

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Study objectives: To evaluate the accuracy and practicality of the Apnea Risk Evaluation System (ARES; Advanced Brain Monitoring; Carlsbad, CA), a limited-channel system for diagnosing sleep apnea/hypopnea in the home.
Design: Prospective randomized study with blinded analysis.
Settings: Two independent, community-based, sleep-disorders centers and the participants' homes.
Participants: Two hundred ninety-nine subjects were recruited, including 210 consecutive willing patients referred by community physicians to the centers because of suspected sleep apnea; 36 "general medical" patients recruited from community physicians' offices; and 53 "presumably healthy" subjects recruited from community centers.
Measurements and results: Manual scoring of attended in-laboratory full-night or split-night polysomnography by trained technologists supervised by physicians board certified in sleep medicine, and automated scoring of the limited-channel system used attended in the laboratory and unattended at home. The definition of the polysomnography apnea-hypopnea index (AHI) and the ARES respiratory disturbance index was the total number of events divided by the study duration in hours. Two hundred eighty-four valid comparisons of in-laboratory simultaneous polysomnography and ARES and 187 valid comparisons of in-laboratory polysomnography with a separate 2 nights of unattended self-applied ARES Unicorder (Advanced Brain Monitoring) were obtained. A diagnostic AHI cutoff of > 10 was used to establish the accuracy and validity of the ARES. The concurrent in-laboratory comparison yielded a sensitivity of 97.4, a specificity of 85.6, a positive predictive value of 93.6, and a negative predictive value of 93.9; in-home comparison sensitivity, specificity, positive predictive value, and negative predictive value were 91.5, 85.7, 91.5, and 85.7, respectively.
Conclusions: The ARES demonstrated consistently high sensitivity and specificity for both in-laboratory and in-home recordings. In patients at risk for sleep apnea who do not *a priori* need an attended study, the ARES could provide a low-cost alternative to traditional polysomnography.
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Key words: apnea risk evaluation system; in-home monitoring; obstructive sleep apnea; polysomnography; pulse oximetry

Abbreviations: AC = alternating current; AHI = apnea-hypopnea index; ARES = Apnea Risk Evaluation System; CPAP = continuous positive airway pressure; DC = direct current; DE = desaturation event; IRB = institutional review board; OSA = obstructive sleep apnea; RDI = respiratory disturbance index; SpO$_2$ = oxygen saturation measured by pulse oximetry; TIB = time in bed

O bstructive sleep apnea (OSA) is a common human affliction that at some level of severity is both debilitating and potentially life threatening.[1,2] Its prevalence is high[3–5] and may be increasing along with the girth of persons in industrialized countries.[6,7] OSA causes daytime drowsiness and memory loss, and has been associated with hypertension, increased risk of congestive heart failure, coronary artery disease, cardiac arrhythmias, diabetes, and stroke.[8–13] OSA has been identified as a major public health concern.[2,14]

Despite the growing evidence that untreated OSA threatens public health, safety, and productivity, current estimates reveal that 93% of women and 82% of men with moderate-to-severe OSA remain undiagnosed.[15] In the United States, the diagnosis of

OSA is most often done by attended in-laboratory overnight polysomnography, frequently in combination with a titration of continuous positive airway pressure (CPAP) the same night if a significant number of apneas or hypopneas are detected in the initial portion of the study. Thus, the diagnostic portion of the study may last only 2 to 4 h. Laboratory polysomnography, which monitors sleep as well as breathing, is expensive and its availability has been judged insufficient to meet the need for case finding in North America and much of Europe.[16] A major justification for polysomnography vs more limited monitoring has been that it allows for the electrophysiologic recording of sleep. However, studies[17,18] specifically looking at the added benefit of the EEG for sleep staging have failed to show that it is necessary for the evaluation of sleep-disordered breathing.

The limited access to and expense of overnight polysomnography in combination with the lack of knowledge regarding OSA among physicians and the general public has resulted in the failure to diagnose and treat the majority of patients with OSA. It has been conservatively estimated[16] that "approximately 2,310 polysomnograms per 100,000 people per year would be required to adequately address the demand for diagnosis and treatment of patients with suspected OSA of at least moderate severity." This exceeds by a factor of 10 in most countries the actual capacity for polysomnography.[16] Polysomnography is technically complex, and simpler, less expensive methods for case finding for OSA (particularly in high-risk populations) are needed.

A number of limited-channel, in-home devices for the diagnosis of OSA have been described[19–23]; however, as a group they have not been recommended in the published practice parameters for in-home unattended studies.[24,25] The primary reason given is the lack of acceptable validation studies. But when a scheme classifying sleep apnea diagnostic systems into levels of complexity is used to simplify comparisons,[24] it has the effect of obscuring the validity of individual devices with acceptable validation studies. Based on the knowledge about sleep-related breathing disorders that has been gathered over the last 40 years, the application of basic pulmonary physiology, and the miniaturization of electronics that has occurred in the past few years, we postulated that an accurate and easy-to-use, low-cost system for diagnosing OSA could be developed. In this article, the apnea risk evaluation system is described, and the results from a large, multisite validation study of 284 subjects recorded concurrently with in-laboratory polysomnography and a subset of 187 subjects also recorded in their homes are presented.

Methods and Materials

The Apnea Risk Evaluation System (ARES; Advanced Brain Monitoring; Carlsbad, CA) employs a multivariate approach for the in-home assessment of OSA. The ARES Unicorder (Advanced Brain Monitoring) is easily affixed to the forehead by the user and acquires data on oxygen saturation, pulse rate, snoring level (microphone), and head position/movement (accelerometers). ARES Insight automated software (Advanced Brain Monitoring) uses oxygen saturation measured by pulse oximetry (SpO_2) as the primary signal, and analyzes changes in pulse rate, snoring sounds, head movement, and the slope of the resaturation curve to identify behavioral markers of arousal that follow desaturations events (DEs). The assumption is made that DEs that are terminated by arousal are due to obstructed breathing during sleep. The ARES questionnaire assesses preexisting risk factors for OSA, including age, gender, body mass index, neck circumference, daytime drowsiness, frequency of snoring, observed apneas, and history of hypertension. The ARES Insight software combines the automated analysis of the physiologic signals with the results from the analysis of the ARES questionnaire to provide an overall risk level for OSA. The system is also designed to identify unusual cases that require special review by a trained professional.

ARES Unicorder

The ARES Unicorder provides up to 14 h of a full-disclosure recording from a single-cell, 750 mA, nickel-metal hydride battery. The optical sensor for measurement of oxygenation levels in arterial blood and pulse rate contains infrared (880 nm) and red (660 nm) light-emitting diodes and a high-sensitivity photo diode cast in medical-grade silicone. Two digital potentiometers provide the dynamic offset and gain adjustment needed to accommodate the large dynamic range of the optical signals and allow the current driving the light-emitting diode and the resulting light intensity to be adjusted to accommodate differences in skin characteristics. Two dual-axis accelerometers are positioned orthogonal to each other to measure head position and head movement. A calibration device is used to adjust for systematic error resulting from the use of accelerometers to define static positions and the random error that results from manufacturing variability. Snoring sounds are obtained with a microphone with the input signal transformed via a hardware-derived integration envelope. A 32-megabyte flash card is used to record up to 2 nights of data.

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When the Unicorder device is turned on, it performs an initial hardware check and notifies the patient, via audio and visual alerts, of problems prior to the start of the recording (*ie*, low battery, missing patient information, hardware problems). When the initialization period is completed and the optical signals are optimized to the individual, the patient is notified that the study has successfully started. During the study, the firmware dynamically adjusts the gain and offset of the direct current (DC) range of the optical signals to maintain the alternating current (AC) component at approximately 10% of the dynamic range of the analog/digital converter. These adjustments accommodate differences in the amount of sensor pressure applied to the forehead sensor (Fig 1), the distribution of blood below the sensor, and the patterns of light reflectance through the skin. Unique audio and visual alerts are presented to notify the user that the Unicorder device has either fallen off or requires adjustment (*eg*, reposition on forehead, adjust the strap tension). The alert automatically turns off after 2 min of acceptable signal quality or when the user changes head position. At the end of 7 h of continuous recording, the Unicorder device discontinues data acquisition and switches to low-power mode to ensure there is sufficient battery capacity for a second night of recording.

The Unicorder devices are prepared for use by a sequence of operations provided for in the ARES Manager software when the device is connected via the universal serial bus port to a personal computer workstation. The ARES Manager provides notifications to avoid downloading session data from the ARES to a computer using a previously downloaded session number, or formatting the ARES for a new session before downloading existing session data (since formatting permanently erases existing session data). New patient information cannot be uploaded unless the battery is fully charged. The universal serial port interface used to transfer data is also used to recharge the battery. The ARES Manager conducts diagnostic checks and provides warning messages for technical problems requiring the ARES Unicorder to be repaired (*eg*,

damaged flash card, battery that will not hold a sufficient charge, or a forehead sensor that is disconnected).

To minimize artifact, maintain adequate systolic blood flow, and optimize comfort, the amount of pressure applied on the forehead sensor against the skin is controlled using a combination of disposable components. The elastic strap that maintains the Unicorder device in position connects at the back of the head with an eight-position strap tension adjustment to accommodate head circumferences ranging from 53 to 64 cm. The thickness and density of the foam placed behind the forehead sensor is optimized. A foam pad surrounding the forehead sensor is lined with fleece to wick away moisture. Stabilizing straps affixed to the elastic strap and the Unicorder device enclosure limit the pressure applied directly over the forehead sensor by the strap tension. The durometer of the medical grade silicone used in the forehead sensor was selected to provide an adhesive-like characteristic to help maintain the sensor firmly against the skin.

Insight Software

The ARES Insight software computes SpO_2 and pulse rate off-line from the recorded optical signals and applies automated algorithms to identify changes in SpO_2, pulse rate, head movement, and snoring level that result from abnormal breathing during sleep. Descriptions of the key algorithms are presented below.

SpO2: Extraction of the AC and DC components from the red and infrared optical signals (sampled at 100 Hz) is achieved using a number of filtering procedures. A 2.5-Hz finite impulse response filter suppresses high-frequency noise, a 0.05-Hz finite impulse response low-pass filter extracts the DC component, and an adaptive filter extracts the AC component from the red and infrared signal. The amplitude and mean DC level of each minimum-maximum pair is used to calculate the raw SpO_2 using the Lambert-Beers formula. Preliminary adjustment of the raw SpO_2 values are made based on the quality of the shape of each red and infrared pair, limited to a maximum of 100.5% and a minimum of 0%. Good, marginal, poor, or bad SpO_2 quality are determined based on the mean absolute change in the raw SpO_2 signal across overlapping 60-s windows, and then is used to adjust the smoothing filter and for quality-control purposes. Prior to submission of the raw SpO_2 signal to the smoothing filter, interpolation is performed across missing minimum-maximum pairs and separate slew limits (*ie*, the maximum allowable beat-to-beat change in SpO_2) are applied to desaturation, resaturation, and relatively flat regions.

The ARES introduces several improvements in the use of SpO_2 to identify abnormal respiratory events during sleep. First, the ARES reports SpO_2 in 0.1 increments in order to provide a smoother and more accurate indication of the desaturation level. Second, recognition of significant desaturations uses a stepped approach that is determined by the relationship between oxyhemoglobin saturation and the PO_2 (Table 1). Third, the shape and magnitude of the desaturation and resaturation are evaluated. The maximum allowable increase in SpO_2 that can occur between the point of maximum saturation and the nadir ("up-down" rule) is controlled. If the up-down threshold is exceeded during either the desaturation or resaturation, the dip requirements are reapplied after to the point of rule violation. If the dip requirements are not satisfied after the application of the up-down rule, the event is not called. If the nadir of the desaturation does not fall beyond the first 35% of the desaturation/resaturation region (*ie*, elapsed time between the points of maximum saturation and resaturation), the event is not called. The slope of the resaturation is evaluated in order to further characterize the desaturation/resaturation event. "Obstructive event" resaturations are characterized by a rapid increase in SpO_2 within a limited time range.

FIGURE 1. Patient wearing the ARES Unicorder.

DE Type/Baseline Spo$_2$, %	% Desaturation	% Resaturation
Major, DE 1 (red) or DE 2 (yellow)		
≥ 93 to 100	2.5	2.5
≥ 91.5 to 93	3.0	2.7
≥ 88 to 91.5	3.5	3.0
≥ 40 to 88	4.0	3.2
Minor, DE 4 (light blue)		
≥ 95 to 100	2.2	2.2
Arousal required		

For major DEs, a DE 1 is considered more likely to be an obstructive event than a DE 2, given it has a steeper resaturation slope. Minor desaturations (DE 4) must be accompanied by arousal indications to be considered significant events. For visual examples, see the red, yellow, and blues stripes, respectively, in the A-Spo$_2$ channel in Figure 2.

Pulse Rate: Pulse rate is obtained as a result of the Spo$_2$ computation described previously. A four-beat, weighted average is used to slightly smooth the pulse rate signal. Significant decreases and increases in the A-Hrate in Figure 2 are identified when the pulse rate increases (decreases) ≥ 8 beats per second compared to the previous 10 s. When pulse rate increases and decreases are contiguous, the yellow stripes that represent a heart rate decrease and the blue stripes that identify a heart rate increase are joined at the peak pulse rate.

Head Position: One of the two angle outputs from the accelerometer mounted parallel to the forehead is used to distinguish upright from supine head positions. The other angle output is combined with the angle output provided by the accelerometer perpendicular to the forehead to measure supine lateral and prone positions. The accelerometer outputs were combined based on the sensitivity of each accelerometer (which is influenced by its position relative to gravity vector). Transitions between angle inputs are smoothed in order to avoid misclassification as a sudden head movement. Two sets of ranges are used to define a given head position, primary and overlapping. If the head is within a primary range for at least 5 s, that position must be called. For example, if the head is not inclined (perpendicular head angle < 55° and ≥ − 5°) and the horizontal head angle is between 25° and − 25°, then the head must be in the supine position. To correctly assign head position in the overlapping region, dynamic changes in head position are monitored from the start of the study when the user is required to be supine. Starting from the supine position, if the horizontal head angle transitions past 80° or remains > 60° for > 5 s and then settles into the left overlapping region, the head position is assigned the left lateral position. Similar rules are implemented to define primary and overlapping regions between supine and right lateral, lateral, and left prone, and lateral and right prone positions.

Head Movement: The accelerometer signals are also used to identify gross movement that might result in poor-quality Spo$_2$ signals and subtle events used as arousal indicators. The power of the head movement in each second of data is normalized to the energy measures across the entire session to account for individual differences in movement during sleep. To avoid events being called solely as a result of a very quiet session, a minimum energy threshold is applied. Each of the five head movement levels are assigned and visually scaled (Hmov channel, Fig 2) for each second. In addition to using head movement as an arousal indicators, it is also used to identify periods with potentially compromised Spo$_2$ quality. When head movement levels, averaged across 60-s 75% overlapping windows, exceed the threshold, desaturation/resaturation events that occur in the region are excluded from the ARES respiratory disturbance index (RDI), and the region is excluded from the time-in-bed (TIB) calculation.

Snoring Level: The snoring sound signals (sampled at 10 Hz) are filtered and then integrated. The SD of the integrated signal is used to derive a snoring power measure that is analyzed to discriminate sound from silence, identify loud snoring, and detect crescendo snoring. Empirically derived scaling factors ensures that that the approach does not automatically cause some portion of the record to be classified as loud snoring due to the overall quietness throughout the night. Conversely, the scaling factor ensures that the loudest snoring is recognized in sessions with constant snoring. All contiguous periods of loud snoring that
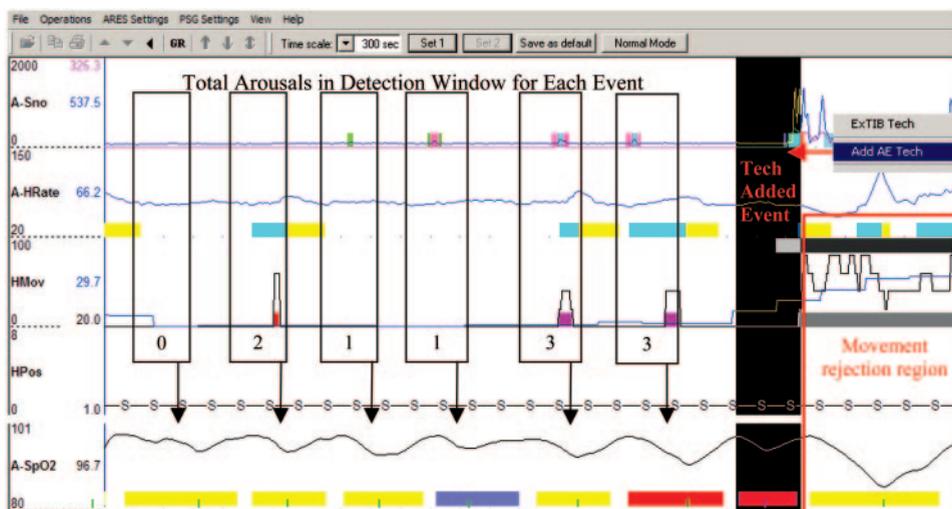

FIGURE 2. A-Sno = snoring; A-Hrate = heart rate; Hmov = head movement; HPos = head position (S = supine); A-Spo$_2$ = Spo$_2$; ExTIB = exclude from time in bed; AE Tech = technician inserted obstructive event.

exceed the threshold are marked. The blocks between the periods of loud snoring are analyzed independently in a second pass through the data. Crescendo and decrescendo snoring patterns are identified using peak detection techniques, whereby changes in sound over three sequential snores are assessed. Periods of no snoring followed by an abrupt snore are distinguished as indicative of an arousal. After all desaturation/resaturation events, pulse rate changes, snoring sound, and head movement arousal indicators are identified, the results are combined to associate desaturation/resaturation events with arousal indicators.

ARES RDI: Events automatically detected by the ARES Insight Software across signals are combined and the calculation of the ARES RDI is based on the TIB (total number of events/TIB). The start and stop TIB periods are automatically inserted but can be manually adjusted. Desaturation/resaturation and arousal events that occur during periods automatically excluded from the TIB calculation (*ie*, the patient is upright or during excessive head movement) are not included in the summary statistics. The ARES Insight software provides the option for manual editing of all events detected or missed by the ARES algorithms.

Clinical Study

Two hundred ninety-nine subjects underwent concurrent data acquisition with the ARES Unicorder device and standard in-laboratory polysomnography at the Murrieta Sleep Medical Clinic and Pomona Valley Hospital Sleep Disorders Center. Fifty-seven percent of all qualified, consecutive patients scheduled for sleep studies at the Murrieta Sleep Medical Clinic, Pomona Valley Hospital, or Long Beach Veteran's Administration consented to participate in the study. The patients from the sleep centers (n = 210) were referred for polysomnography by primary care physicians and specialist referrals (*eg*, ear, nose, and throat; cardiologists; pulmonologists). Of these, 70% underwent a split-night study. A subgroup of individuals with "general medical" conditions (*ie*, hypertension, cardiovascular disease or diabetes; n = 36) and "presumably healthy" subjects (n = 53) were recruited using advertisements placed in the North San Diego County community (*eg*, libraries, community centers), at Pomona Valley Hospital and in physician offices in Temecula and Murrieta. All individuals in this subgroup were provided with full overnight polysomnography. At the suggestion of the institutional review board (IRB), subjects were excluded from participation based on age (< 18 years or > 70 years) or being pregnant. Ethnic distribution included 75% white, 16% Latino/Hispanic, 4% African American, 4% Asian, and 1% Native American/Alaska native. This study protocol was approved by the IRB of Advanced Brain Monitoring, with deferring approval by the Pomona Valley Hospital and Long Beach Veteran's Administration IRBs. Informed consent was obtained from all subjects.

The Murrieta polysomnography studies were acquired using an Alice3 digital polysomnography system and Alice4 software (Respironics; Murrysville, PA). Signals included EEG (C4-A1, C3-A2), electro-oculogram, submental and bilateral tibial electromyogram, ECG, airflow (nasal cannula and nasal pressure [PTAF2; Pro-Tech Services; Woodinville, WA]), chest and abdominal motion (piezo bands), oxyhemoglobin saturation (Model 930 pulse oximeter; Respironics), body position, and snoring intensity. The Pomona studies were acquired using Sandman Elite V6.2 hardware and software (Nellcor Puritan Bennett; Kanata, ON, Canada). Signals included EEG (C4-A1, C3-A2, O2-A1, O1-A2), electro-oculogram, submental and bilateral tibial electromyogram, ECG, airflow (nasal thermistor and nasal pressure [PTAF2; Pro-Tech Services]), chest and abdominal motion (piezo bands), oxyhemoglobin saturation, and snoring intensity.

One hundred ninety-one patients were randomly assigned to wear the ARES Unicorder device in the home before (n = 57) or after (n = 134) polysomnography, as scheduling permitted. Of these, 144 patients were recruited from the population of patients scheduled for polysomnography, 43 patients were presumably healthy, and four patients were general medical patients.

Apneas and hypopneas were visually scored in the polysomnography records by trained technologists and reviewed by a physician board certified in sleep medicine who was blinded to the ARES signals. The definition for the polysomnography apnea-hypopnea index (AHI) and the ARES RDI was the total number of apneas and hypopneas divided by the study duration (in hours). The ARES RDIs were computed using primarily the desaturation/resaturation rules as presented in Table 1. Only ARES events resulting from the first step (*ie*, 2.2% dip) in the desaturation/resaturation rule required an accompanying arousal.

Data Analysis

The κ coefficient was used to assess the beyond-chance agreement between ARES RDI and polysomnography AHI, without using the assumption that the polysomnography was the "gold-standard" comparison. Assessment of the utility of the ARES, under the assumption that polysomnography with a clinical cutoff of AHI > 10 was the gold standard for identifying and quantifying OSA, included evaluation of correlations (using linear regression) agreement (using Bland-Altman plots), and pretest and posttest probabilities. Further analysis of diagnostic agreement between the polysomnography AHI and in-home ARES RDI to assess the influence of position was performed using a clinical cutoff of AHI/RDI > 20. Correlation analysis was applied to the differences between the polysomnography AHI and the in-home RDI in all positions vs only supine.

RESULTS

Of the 299 subjects undergoing polysomnography plus ARES in the laboratory, 15 patients were dropped from the study due to < 1.5 h of polysomnography recording time (n = 3), bad polysomnography oximetry (n = 9), or bad ARES oximetry (n = 3). Of the 191 subjects with polysomnography plus ARES in the home, 4 subjects were dropped due to insufficient in-home recording time. The number and age of the subjects whose records were used for the analysis of the polysomnography vs in-laboratory ARES (n = 284) and the polysomnography vs in-home ARES (n = 187) are stratified by gender in Table 2.

The κ coefficients for the polysomnography vs in-laboratory ARES (0.85) and in-home ARES (0.77) indicate an excellent agreement beyond chance (Table 3). There was significant correlation between the polysomnography AHI and the in-laboratory ARES RDI ($r = 0.96$) and in-home ARES RDI ($r = 0.88$); the corresponding Bland-Altman plots present a fairly tight distribution of the differences between polysomnography and ARES results (Figs 3–6). The sensitivity, specificity, and positive and negative predictive values for polysomnography vs in-laboratory

Table 2—Demographics of Participants in ARES Studies

| | Polysomnography vs In-Laboratory ARES (n = 284) | | | | Polysomnography vs In-Home ARES (n = 187) | | | |
| | Men | | Women | | Men | | Women | |
Diagnostic Group	No.	Age ± SD, yr	No.	Age ± SD, yr	No.	Age ± SD, yr	No,	Age ± SD, yr
Recruited from sleep laboratory referrals for polysomnography	131	48 ± 11.0	67	49 ± 9.6	97	48 ± 10.9	44	48 ± 9.6
Referred for polysomnography from general population	45	47 ± 14.0	41	47 ± 11.4	26	41 ± 12.7	20	39 ± 12.8

and in-home ARES RDIs are presented in Table 3. For AHI thresholds of 5, 10, 15, 20, and 30 events per hour, the in-home ARES sensitivity and specificity were 95.7/59.2, 91.5/85.7, 86.1/83.7, 86.9/85.4, and 79.4/100.0, respectively.

As expected, the results from comparison of polysomnography to in-home recordings were slightly less accurate as compared to simultaneous recordings in the laboratory. To assess positional influences on the 26 presumably false-positive or false-negative in-home ARES study results, the differences between the ARES RDI and polysomnography AHI were computed across all positions and only in the supine position. The correlation between these two measures, after excluding three subjects with no polysomnography time in the supine position, was 0.79. After accounting for positional influences and using a clinical cutoff > 20, the ARES provided a sensitivity of 97.6% and a specificity of 100.0% as compared to polysomnography. To investigate the influence of position on night-to-night variability, the Bland-Altman plot in Figure 7 compares time in the supine position as a percentage of the total TIB for in-home nights 1 vs 2. The Pearson correlation for the percentage of time supine between nights 1 and 2 was 0.77.

Table 3—Clinical Results From In-Laboratory and In-Home ARES vs Polysomnography

| | In-Laboratory ARES (n = 285) | | In-Home ARES (n = 187) | |
Results	± SD	95% Confidence Interval	± SD	95% Confidence Interval
κ score	0.85	0.77–0.89	0.77	0.66–0.85
Sensitivity	97.4	95.0–98.8	91.5	87.3–94.4
Specificity	85.6	80.4–88.5	85.7	78.8–90.6
Positive predictive value	93.6	91.3–94.9	91.5	87.3–94.4
Negative predictive value	93.9	88.3–97.1	85.7	78.8–90.6

DISCUSSION

The ARES was designed to detect OSA and to estimate its severity, and to do this accurately, simply, and inexpensively outside of the laboratory. The results of this study indicate that these design goals were met. In addition, the ARES was designed to identify arousal indicators, the "positionality" of sleep apnea, snoring frequency and loudness, and quiet (actigraphically estimated sleep) time, thus getting the most from a minimal set of transducers that could be packaged into a single-site data acquisition device. (The current version of the Unicorder device includes measurement of nasal pressure for airflow, but this signal was not used in the analysis of the data for this study.)

The arousal indicators include abrupt changes in pulse rate, head movement, and snoring sound that follow a desaturation. Pulse rate changes are a recognized indicator of autonomic arousal,[26–28] and of course are measured by the same optical signals that allow measurement of oxyhemoglobin saturation. Body movements frequently accompany arousals to breathe, and the same accelerometers that provide information about head (and thus pharyn-
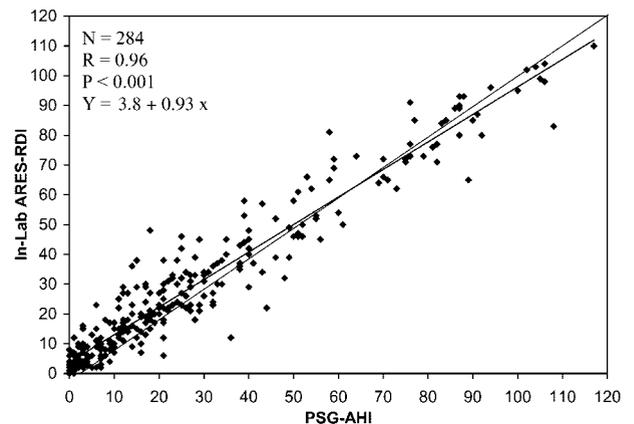

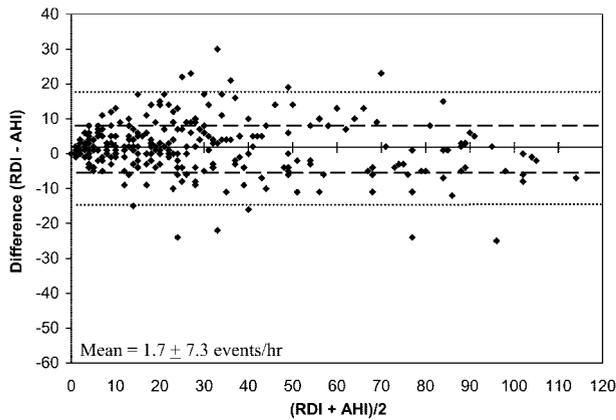FIGURE 3. Pearson's correlation between in-lab ARES-RDI and PSG-AHI.

Plot labels: N = 284; R = 0.96; P < 0.001; Y = 3.8 + 0.93 x. Y-axis: In-Lab ARES-RDI (0–120). X-axis: PSG-AHI (0–120).

FIGURE 4. Bland-Altman plot for PSG-AHI vs. in-lab ARES-RDI. References lines are ± 1 SD (dashed) and ± 2 SD (dotted).

FIGURE 6. Bland-Altman plot for PSG-AHI vs. in-home ARES-RDI. References lines are ± 1 SD (dashed) and ± 2 SD (dotted).

geal) position can be used to measure both gross and subtle head movements. Snoring, sound regularly accompanying obstructed breathing, usually indicates someone is asleep, and changes in snoring intensity, *eg*, crescendo snoring terminated by a sudden decrease or increase in noise, is an indicator of increasing effort ending in arousal. In this study, we did not directly compare these arousal markers to EEG-defined arousals. Such a comparison is planned as part of a separate clinical study using the latest version of the Unicorder device, in which changes in airflow can also be evaluated.

Gravity has a recognized influence on pharyngeal collapsibility and is the reason head position (usually inferred from body position) is an important measure when recording breathing during sleep. At least in this study differences in head position accounted for almost all of the discrepancy between the polysomnography in-laboratory and the ARES in-home results. Positional sleep apnea potentially can be treated with position restriction.[29] Also, there is
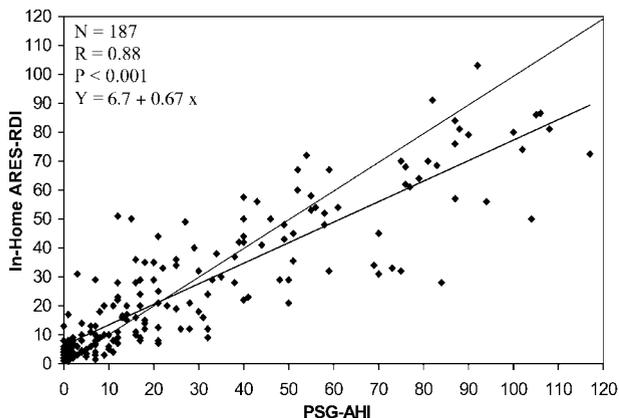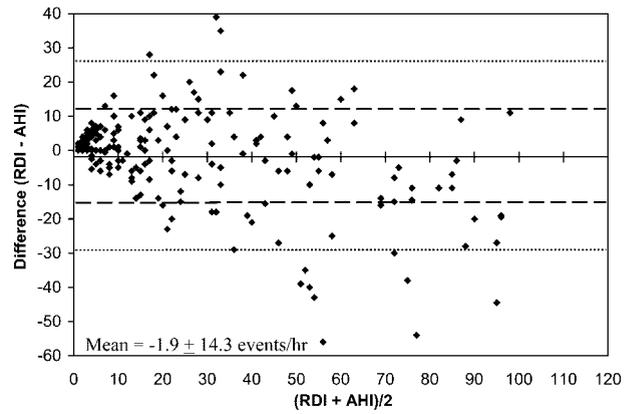
evidence that oral treatment devices such as mandibular advancement appliances are more likely to be effective in patients who have primarily supine OSA.[29–31]

The relationship between saturation and PaO_2 led to our inclusion of the starting saturation level in an algorithm to determine the significance of each DE (Table 1). We believe this stepped approach provides a more uniform measure of dip severity given the fact that a fall in saturation from 98 to 97% (from 112 to 92 mm Hg) reflects the same change in PaO_2 as a fall from 94 to 85% (from 70 to 50 mm Hg). At sea level, a 3% dip from approximately 97% reflects a change in PaO_2 that is equivalent to a 5% dip at an elevation of 500 m, or approximately an 8% drop at 1,000 m.

The RDI obtained by automated scoring of the limited-channel Unicorder recording was nearly identical to the AHI obtained by manually scoring the simultaneous polysomnography (Table 3). This is

FIGURE 5. Pearson's correlation coefficient between in-home ARES-RDI and PSG-AHI.
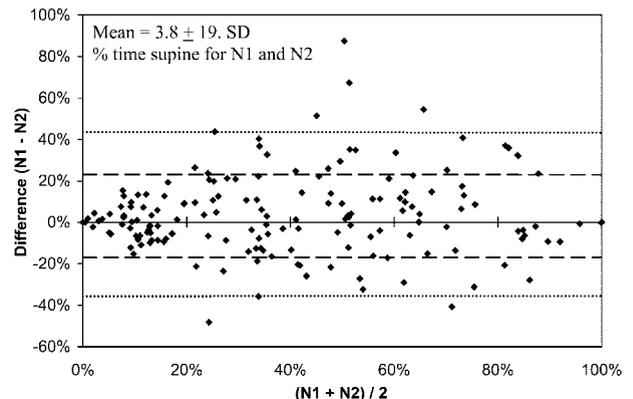

FIGURE 7. Bland-Altman plot for percent time supine in-home night 1 vs. night 2 excluding subjects with > 2.5 hours difference in time-in-bed between nights (n = 165). Reference lines are ± 1 SD (dashed) and ± 2 SD (dotted).

not surprising, as it simply reflects the fact that the ARES oximeter using analysis software and the oximeters used by the polysomnography systems using manual scoring were detecting the same events occurring over the same time period. Comparison of the polysomnography to in-home ARES, made at different times in different places, must allow for the true night-to-night variability in the frequency of abnormal breathing events. This is a factor independent of the types of recording devices, and has been shown to exist for patients studied on separate nights using the same equipment in the same laboratory.[32–34] The reasons for this variability are not completely understood, but certainly the known influence of sleep position and sleep stage on apnea frequency and severity of desaturations play a role. In the present study, we were able to quantify the night-to-night variability in sleeping position and demonstrate its influence on the differences between polysomnography and in-home recordings.

The concordance between the ARES vs polysomnography from laboratory and in-home recordings were similar to or slightly better than other reports of self-applied in-home OSA testing systems.[21,35] In addition to patients referred from sleep clinics, this study included a number of individuals recruited from the general community to assess the validity of the ARES. Of the 187 subjects who used the ARES in the home, 42 subjects (23%) were presumably healthy. Of the 36 general medical patients recruited from the community, 30 patients (83%) had a polysomnography AHI > 10 events per hour.

The reliability and ease of use of the ARES were supported by the fact that < 10% of the 206 participants studied in the home called for technical support. Half of these calls were to clarify directions, and the remainder were equipment inquiries with < 1% of the in-home studies delayed due to equipment malfunction. The majority of study participants reported that the ARES Unicorder device was comfortable and did not significantly disturb their sleep.

In our comparison of in-laboratory to in-home recordings, we were able to estimate the effect of gravity (*ie*, head position) on the in-home ARES RDI but could not account for the influence sleep state or stage. That is not to say that some idea of sleep state influence is unavailable in recordings that include position but not EEG and eye movements. If one can look at the timing of event clusters, and knows position, then an educated guess about the influence of rapid eye movement vs non-rapid eye movement sleep can be made.

The fact that the "gold standard" is nonstandard[17] became apparent in this study when two different polysomnography systems with oximeters from two different manufacturers were used in the comparison with the ARES. Eight of the nine records excluded as a result of the gross unresponsiveness of the polysomnography oximeter were related to one oximeter. These records were excluded because the established criteria for the event-by-event comparison required valid oximetry for both systems. It was subsequently discovered that the equipment was inadvertently set to a longer averaging window.

An additional problem in comparing two diagnostic strategies, noted by others, is the use of a single clinical cutoff to define sleep apnea.[36,37] This is, in a sense, only a statistical problem. In clinical practice, whether a polysomnography AHI or an ARES RDI is 8 or 12 or 16 events per hour should not influence the decision regarding treatment. The test does not define the OSA/hypopnea syndrome. It is simply one element in the entire clinical picture that the clinician should use when deciding what is going on and what to do about it.

An integral part of the ARES is a questionnaire that provides information about symptoms and anthropomorphic data.[38–41] This is used in two ways. First, it establishes prior probability of disease and can be used alone as a validated screening tool. It also serves as a flag to identify discrepancies between physiologic test results and questionnaire risk level, so that those studies can be manually reviewed and, if necessary, the patient referred for further evaluation. Very sleepy patients should not be told they do not have a problem because the test fails to show significant sleep apnea. If the automated scoring indicates the physiologic signals are normal but the ARES questionnaire identifies the patient as at risk for OSA, the report suggests the patient be referred to a sleep specialist for further evaluation.

One advantage of the in-home testing with the ARES is that 2 nights of recorded breathing are obtained, vs a typical 2 to 7 h in the laboratory, depending on whether a split-night or full-night study is done. A disadvantage of this system is that it is unattended and incapable of providing on-line information (other than the few indicators to the patient). Thus, it is an inappropriate choice in situations in which intervention might be required. Also, sleep is not recorded, so it is not a suitable replacement for polysomnography if sleep staging might be important, for instance if narcolepsy is suspected. However, for the vast majority of patients suspected of having sleep apnea, recording and staging sleep has not been demonstrated to be useful.[17]

Clearly, diagnosis is only one part, and the easier part, of the management of OSA. Treatment is the more difficult problem. The availability of automated, self-titrating CPAP machines, and evidence that patient self-titration often works, reduces the need for in-laboratory titration.[42,43] Treatment op-

tions other than CPAP exist and may be appropriate initial choices for certain patients.[30,44–47] Finally, the dilemma of selecting the appropriate treatment and of achieving patient compliance is independent of diagnostic test location or type. If less money is spent on diagnosis, then at least in a rational system of medical care more resources could be made available for patient treatment and follow-up.

The cost of the ARES was not directly addressed in this study. However, to the extent that automated analysis removes the requirement for manual scoring, then a major cost of traditional polysomnography is removed. Also, of course, there is no laboratory facility or nighttime technician cost with unattended home monitoring. If treatment with CPAP is indicated, then CPAP equipment cost may be increased by the difference in price between a CPAP unit that automatically determines the correct pressure and one that lacks this feature. However, the effort and thus costs required to optimize acceptance of and adherence to CPAP treatment is about the same whether or not the prescription is the result of a split-night study, automated titration, or patient self-titrated pressure. We estimate that the cost to the patient or payer of 2 nights with the ARES will range from one half to less than one third the cost of typical attended nocturnal polysomnography. The potential savings would be on the order of $300 to $700 per study.

Although only automated scoring of the ARES data were used for this study, the system does provide a full disclosure recording and the capability for review of all channels and manual scoring of events. The Insight software quality control function automatically identifies and presents regions in the record that should be visually scored as a result of gross head movement and suboptimal SpO_2 signal quality. Automated scoring, in addition to cost savings, offers advantages in consistency of event definition and recognition. A number of studies[37,48] have demonstrated that there can be wide discrepancies between different scorers scoring breathing events on the same recording.

In summary, this report of a large validation study of a limited-channel, in-home system for recording breathing and arousal indicators indicates that, using automated scoring, it can with a high degree of certainty diagnose and exclude important OSA. The fact that the recorder can be easily mailed and reliably self-applied suggests that it could be made available to almost any population at risk for OSA. It offers a relatively easy option for objectively following one facet of treatment outcome or disease progression. Combined with automated or self-titrated

CPAP and other treatments, it could be part of a low-cost option for the detection and management of OSA.

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