Portable-Monitor Testing: An Alternative Strategy for Managing Patients With Obstructive Sleep Apnea

Samuel T Kuna MD

Portable-monitor testing is being used increasingly in ambulatory management pathways for the diagnosis and treatment of patients with obstructive sleep apnea. Wide varieties of portable monitors are commercially available and they range from single-channel recorders to units that record a full polysomnogram. Recent comparative effectiveness research studies have shown that clinical outcomes of patients with a high pretest probability for obstructive sleep apnea who receive am-

Samuel T Kuna MD is affiliated with the Pulmonary, Critical Care, and Sleep Section, Philadelphia Veterans Affairs Medical Center, and with the Division of Pulmonary, Allergy and Critical Care, Department of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania.

Dr Kuna presented a version of this paper at the 45th RESPIRATORY CARE Journal Conference, "Sleep Disorders: Diagnosis and Treatment" held December 10-12, 2009, in San Antonio, Texas.

This research was partly supported by the Veterans Health Administration, Health Services Research and Development grant IIR04-021-2.

Dr Kuna has disclosed relationships with Philips Respironics and Embla.

Correspondence: Samuel T Kuna MD, Division of Pulmonary, Allergy, and Critical Care, University of Pennsylvania School of Medicine, 3624 Market Street, Suite 205, Philadelphia PA 19104. E-mail: skuna@mail.med.upenn.edu.

bulatory management using portable-monitor testing have similar functional outcomes and adherence to continuous positive airway pressure treatment, compared to patients managed with in-laboratory polysomnography. The cost-effectiveness of portable-monitor testing and its potential to improve patient access to diagnosis and treatment requires further investigation. *Key words: sleep; polysomnogram; continuous positive airway pressure; CPAP; comparative effectiveness research.* [Respir Care 2010;55(9):1196–1212. © 2010 Daedalus Enterprises]

Introduction

Home, unattended sleep studies using portable portable monitors are being used in ambulatory management pathways to diagnose patients with obstructive sleep apnea (OSA) and initiate them on positive-airway-pressure treatment.[1,2] Acceptance of this emerging new technology has been impeded by the lack of evidence-based medicine informing healthcare providers how to use these monitors in clinical practice. In addition, until recently, the Centers for Medicare and Medicaid Services (CMS) and private healthcare insurance carriers in the United States restricted coverage for continuous positive airway pressure (CPAP) treatment to beneficiaries diagnosed with OSA on in-laboratory attended polysomnography. As a result, the use of portable-monitor testing in the United States has largely been limited to sleep specialists in health maintenance organizations and the Veterans Health Administration. Recent and anticipated events, however, presage a far greater role for portable-monitor testing in the private sector. Comparative effectiveness research studies evaluating in-laboratory versus ambulatory management of patients with OSA are providing more evidence on how to use this technology.[3-5] In addition, CMS recently issued 2 National Coverage Decisions extending coverage of CPAP treatment to its beneficiaries diagnosed with OSA by use of portable-monitor testing.[6,7] Private carriers are already starting to follow this lead. Finally, the CMS reimbursement fee for polysomnography is in the process of being reevaluated and, given the changes in clinical practice of polysomnography since the last assessment, it is widely anticipated that the current fee will be reduced, narrowing the current large difference in reimbursement between in-laboratory polysomnography and home portable-monitor testing.

Sleep medicine is a relatively nascent specialty that has largely been structured both scientifically and financially around the in-laboratory polysomnogram. Confronted with the growing importance of portable-monitor testing in the management of patients with OSA, many questions arise. What portable monitor should be used? Which patients are best suited for portable-monitor testing? How should portable monitors be incorporated into the current clinical management of OSA? Should non-sleep specialists be able to perform sleep testing? How will the emergence of portable-monitor testing affect the future growth and development of the specialty of sleep medicine?

Current Practice Parameters to Diagnose OSA and Initiate CPAP Therapy

In-laboratory polysomnography, a recording of physiologic signals to assess sleep stages and respiration during sleep, remains the accepted standard to diagnose OSA and initiate CPAP treatment.[8] This testing requires patients to spend 1–2 nights in a sleep laboratory, uses expensive equipment, and must be attended by a technologist. To initiate CPAP treatment, the most widely used treatment for OSA, the current standard is for an attendant technician to manually titrate CPAP during polysomnography to identify the optimal pressure level required for treatment.[9,10] The optimal CPAP setting is defined as the lowest pressure that eliminates all or most apneas and hypopneas. The patient is then prescribed CPAP nightly at that pressure setting. Although full-night diagnostic and manual CPAP titration polysomnograms are recommended, split-night polysomnograms (one night of testing that includes both diagnostic testing and manual CPAP titration) are frequently performed when the apnea-hypopnea index (AHI) on the initial diagnostic portion of the study is greater than 20–40 events/hour.[8,11,12] The split-night polysomnogram imposes substantial time constraints on the ability to obtain the required information and has been reported to provide inadequate information regarding the prescription of the fixed pressure needed for treatment in about 15% of patients.[13-15] Despite the drawbacks of the split-night study, its wide use is driven by limited resources and reimbursement policies.[16]

In-Laboratory Polysomnography: the Accepted Standard, With Limitations

Whatever role portable-monitor testing eventually attains, in-laboratory attended polysomnography will remain the accepted standard test for the diagnosis and management of OSA. It is important, however, to recognize the limitations of polysomnography. Although polysomnography is a physiological recording, almost all of the recorded signals are uncalibrated, and the manual scoring is based largely on pattern recognition of qualitative signals. Com-

pounding this limitation, the sensors and equipment made by manufacturers to record the studies and process the data are not standardized.

Other limitations of polysomnography are the current criteria used for stage sleep and score abnormal respiratory events. The current scoring criteria for sleep staging were established a half century ago to characterize sleep in normal individuals.[17,18] Those criteria are not always applicable to patients with disrupted sleep patterns due to repetitive apneas and hypopneas. For example, with the requirement of more than 15 seconds of any sleep stage on a 30-second epoch to score sleep state, repetitive obstructive apneas of short duration occurring between relatively longer arousal periods can be associated with epochs scored as "wakefulness" and therefore be excluded from the AHI calculation, the primary measure of disease severity.

Differences in scoring criteria for respiratory events can result in large differences in the AHI.[19,20] In accordance with CMS requirements, the American Academy of Sleep Medicine (AASM) recommends that scoring of hypopneas on clinical sleep studies requires at least a 30% reduction in thoracoabdominal movement or air flow, compared to baseline, for at least 10 seconds, and a 4% or greater oxygen desaturation.[6,17] However, the AASM also endorses an alternative criteria for scoring hypopneas that requires at least a 50% reduction in chest wall movement or air flow, compared to baseline, for at least 10 seconds and either a 3% or greater oxygen desaturation and/or an arousal on electroencephalogram (EEG).[17] Finally, a third set of AASM criteria have been recommended for the scoring of clinical research studies that does not require an associated oxygen desaturation or arousal, provided that the reduction in air flow is greater than 50% of baseline.[21] Applying the latter 2 scoring criteria to a portable monitor recording that does not include an EEG signal will not detect hypopneas associated with arousals that would otherwise be scored on polysomnogram. Because of the different criteria for scoring hypopneas, it is critically important for studies to detail the criteria used to score respiratory events on both the polysomnogram and portable monitor recordings.

Probably the greatest weakness of polysomnography is the poor correlation that any of its variables have with patients' symptoms and treatment outcomes.[22-27] Patients with a mildly elevated AHI may present with severe daytime sleepiness, while patients with a high AHI may have minimal symptoms.[28,29] Compounding this problem is the poor correlation between polysomnographic measures of disease severity and measures of cardiovascular risk. Although growing evidence indicates that patients with OSA are at increased risk for systemic arterial hypertension and cardiovascular disease, it is still unknown whether these are indeed causal relationships and whether these risks apply just to patients with more severe OSA or even to patients without OSA (AHI $<$ 5 events/hour) who snore.[30-38] This lack of association of polysomnographic results with clinical symptoms and outcomes has prevented selection of an accepted treatment threshold based on AHI or any other polysomnographic measurement. Comparative studies attempting to validate portable-monitor testing require such a threshold for the statistical calculation of sensitivity, specificity, and likelihood ratios.

Limited In-Laboratory Resources Are Driving the Use of Portable-Monitor Testing

The Wisconsin Sleep Cohort Study in middle-age adults reported that moderate to severe OSA (AHI $\geq$ 15 events/hour) affects 4% of adult females and 9% of adult males, and large majorities of these individuals were undiagnosed.[39-41] These results were published in 1993 and very likely underestimate the current prevalence of OSA in the United States population, given the dramatic increase in obesity over that past 25 years.[42] The prevalence of OSA and its association as an independent risk factor for motor-vehicle accidents, hypertension, and cardiovascular disease have made it a major public health issue. Although many private sleep laboratories have an acceptable patient wait time for in-laboratory attended polysomnography, patient wait time in many capitated, federal, and public healthcare systems in developed countries can exceed 6 months.[43,44] The problem is compounded in less-developed regions, where facilities for laboratory-based management are generally very limited. In addition, in-laboratory polysomnography is expensive and therefore unavailable to most patients without health insurance. These considerations justify the move toward portable monitoring in at least a proportion of patients. In 2005, an editorial on international clinical practices for the diagnosis of patients with OSA apnea commented:

> Faced with the dilemma of how to treat the "flood" of patients presenting with symptoms suggestive of sleep-disordered breathing, physicians are using non-conventional approaches for diagnosis and treatment-approaches not based on solid evidence. Most surprising…is the widespread use of ambulatory approaches to diagnosis rather than full in-laboratory polysomnography. With the increased recognition of sleep apnea, systems for delivering diagnosis and treatment are overwhelmed. Physicians are trying to cope but, even with creative approaches, waiting lists for diagnosis and treatment are unacceptably long. There is a need to rethink current strategies.[45]

Types of Portable Monitors for the Diagnosis of OSA

The current lack of standardization of commercially available portable monitors for sleep testing is one of the acknowledged barriers preventing their acceptance in rou-

Table 1. Current Classification of the Different Types of Sleep Studies

Sleep Test	Description	Personnel	Minimum Signals Required
Level 1	Polysomnography performed in a sleep laboratory	Attended	Minimum of 7 signals, including EEG, EOG, chin EMG, ECG, air flow, respiratory effort, and oxygen saturation
Level 2	Portable polysomnography	Unattended	Same as Level 1
Level 3	Portable testing limited to sleep apnea	Attended and unattended	Minimum of 4 signals, including ECG or heart rate, oxygen saturation, and at least 2 channels of respiratory movement, or respiratory movement and air flow
Level 4	Continuous recording of one or two signals	Unattended	Usually pulse oximetry; a minimum of 3 signals required for CMS reimbursement

EEG = electroencephalogram
EOG = electrooculogram
EMG = electromyogram
CMS = Centers for Medicare and Medicaid Services
(Adapted from Reference 47.)

tine clinical management pathways. Although portable monitors are intended primarily for unattended home recordings, they can be used under either attended or unattended conditions and in a variety of locations, including the sleep laboratory and healthcare facilities (eg, to perform tests on hospitalized patients). Scoring of the recordings may be totally automated or manual with the assistance of computer software. The monitors differ widely in the number and types of signals recorded, the sensors used to record the signals, and the electronic processing of the signals. As stated in a recent practice parameters statement on portable-monitor testing, "There is no universally accepted platform for generating simplified studies in the diagnosis of OSA. This means that results obtained for a particular device are applicable to that device and cannot be extrapolated to other devices, even those of the same class."[46] This lack of uniformity limits the ability to perform meta-analyses and evidence-based reviews. Previous evidence-based reviews have evaluated the results of research studies performed using monitors within a particular category, without consideration of the technological differences that exist among these monitors. While further standardization of portable monitors is needed, important technological questions remain to be answered before we can determine the ideal portable monitor for diagnosis of OSA. We still need to determine which signals are essential and how the signals should be acquired in terms of sensors employed, sampling rate, and filtering.

A task force on portable-monitor testing created by the American Sleep Disorders Association (the current AASM) in 1994 classified 4 different levels of sleep testing (Table 1).[47] Standard in-laboratory polysomnography attended by a technologist is designated as a Type 1 test. Portable monitors are categorized based on the particular level of study they record (Types 2–4). While this classification is still in wide use, it is outdated. With the technological advances achieved since that classification was created, a current portable monitor can be configured to perform as a Type 2, 3, or 4 device and record any other combination of signals. In addition, advances in technology have resulted in new measurement techniques that are not considered by the current classification scheme.

Type 2 Portable Monitors

Type 2 portable monitors record the same montage of signals recorded on an in-laboratory diagnostic polysomnogram. Type 2 studies performed in individuals both at home and in-laboratory are of similar quality, with slightly less Stage 1 non-rapid-eye-movement sleep on the home studies.[48] Type 2 monitors are rarely used for clinical testing because of the inefficiency of technologists having to travel to the patients' homes to set up and retrieve the monitors. Type 2 monitors may have a role in testing hospitalized patients in their hospital rooms and out-patients coming to a centralized testing location. Type 2 monitors have proven useful in clinical research studies.[49-52] Compared to in-laboratory polysomnography, home-unattended polysomnography with a Type 2 monitor decreases an individual's burden of participating in research studies, allows greater flexibility in scheduling studies within fixed protocol timelines, and increases the feasibility of using the same recording equipment across clinical sites in multicenter studies. Standards for using Type 2 monitors in clinical research studies were established by the Sleep Heart Health Study and replicated in the Sleep AHEAD study (Action for Health in Diabetes).[50,53] Rigorous training, certification, and quality-control measures in those studies resulted in excellent quality of the recordings and low failure rates.

Table 2. Signals Recorded During Laboratory Polysomnograph Versus With a Typical Type 3 Portable Monitor*

Signal	Laboratory Polysomnograph	Portable Polysomnograph
Electroencephalogram	Yes	No
Electrooculogram	Yes	No
Chin electromyogram	Yes	No
Electrocardiogram	Yes	No
Nasal pressure	Yes	Yes
Snoring	Yes	Yes
Respiratory effort	Yes	Yes
Body position	Yes	Yes
Pulse oximetry	Yes	Yes

* Note that the type 3 portable monitor does not record signals that distinguish sleep from wakefulness and therefore does not allow determination of sleep stages.

Type 3 Portable Monitors

Type 3 portable monitors record a minimum of 4 signals, including electrocardiogram (ECG) or heart rate, oxygen saturation, and at least 2 channels of respiratory movement, or respiratory movement and air flow. As shown in Table 2, Type 3 portable monitors do not record EEG, electrooculogram, or chin-muscle activity and therefore cannot detect whether the patient is awake or asleep during the recording. Type 3 devices are increasingly being used clinically to diagnose patients with OSA, but are not able to diagnose other sleep disorders such as narcolepsy and periodic limb movement disorder. The major advantage of Type 3 monitors is that patients can be instructed to apply the sensors to themselves at home, eliminating the inefficiency of sending technologists to the home. In addition, Type 3 monitors can identify patients with central sleep apnea and Cheyne-Stokes respiration who should receive subsequent management with in-laboratory testing. Current Type 3 monitors use nasal pressure, with or without oro-nasal thermistor, as a surrogate marker for air flow. Most validation studies comparing Type 3 monitors to polysomnography were performed with Type 3 monitors using only the oro-nasal thermistor as the measure of air flow. Unlike the oro-nasal thermistor signal, nasal pressure has a linear relationship with air flow, except at extremes.[54-56]

Type 4 Portable Monitors

Almost all Type 4 portable monitors record oxygen saturation via pulse oximetry and one or more additional signals. To qualify for CMS reimbursement a Type 4 study must have at least 3 signals. Monitors detecting respiratory events primarily on the basis of an oxygen desaturation event should be particularly useful in patients who are obese and have a coexisting pulmonary disorder such as COPD, conditions that make it more likely that apneas and hypopneas will be associated with oxygen desaturation. In the obese adults (body mass index 36.3 $\pm$ 5.6 kg/m^2) with Type 2 diabetes participating in the Sleep AHEAD study, the mean AHI on the Type 2 recordings at baseline was 20.5 $\pm$ 16.8 events/hour and the mean oxygen desaturation index was 17.6 $\pm$ 14.7 events/hour.[50] The similarity of the 2 measures suggests that overnight pulse oximetry may be an adequate diagnostic test for OSA in obese, type 2 diabetics. A disadvantage of Type 4 testing is that it does not distinguish central from obstructive apneas and, unless an air flow channel is present, cannot detect the presence of Cheyne-Stokes respiration.

Innovative Signals and Approaches to Portable-Monitor Testing

Novel technologies have been developed for portable monitors that are not used in standard polysomnography.[57] For example, actigraphy has been evaluated as a surrogate marker of sleep and wakefulness to improve the calculation of AHI.[58] In one commercially available Type 3 monitor, the sensors that record nasal pressure, oximetry, head movement, snoring, and respiratory effort (venous pulsations) are contained in a head band placed around the forehead.[59] Some monitors incorporate other novel sensors that detect cardiac and autonomic responses to sleep-disordered breathing. One such device measures peripheral artery tone from a sensor on the finger that estimates changes in vascular flow, a measure that reflects variations in breathing and sleep-related arousals.[60,61] Unfortunately, the technological advances in portable monitors far outstrip our knowledge about their utility in clinical practice. The wide diversity in portable monitors complicates the ability to compare results across monitors and generalize results obtained with one particular monitor.

Establishing the Optimal Role of Portable Sleep Monitors

Debate continues as to whether portable-monitor testing should be used to include as well as to exclude the diagnosis of OSA in the general population, or play a more limited role (eg, diagnosing patients with a high pre-test likelihood of the disorder).[62] Currently, Type 3 portable monitors are most commonly being used to diagnose OSA, and it is recommended that symptomatic patients with a negative Type 3 recording have an in-laboratory polysomnogram to exclude the possibility of a false negative study.[63] Using the monitors to include and exclude the diagnosis of OSA in the general population would result in a larger percentage of negative studies, increasing the demand for in-laboratory polysomnography. If portable-monitor test-

ing is limited to patients with a high-likelihood of OSA, strategies will need to be developed that identify that cohort. Clinical prediction rules, including the Multivariable Apnea Prediction Index, Sleep Apnea Clinical Score, and Berlin Questionnaire, have been used to identify individuals with a high pre-test likelihood of OSA, but these instruments have largely been used in research studies and have not been adequately tested in clinical management pathways.[64-67]

Validation of Portable-Monitor Testing

Direct Comparison of Portable Monitor Recordings to Polysomnography

One approach to validating the portable monitors for sleep testing is to compare their performance to that of standard in-laboratory polysomnography. Simultaneous portable monitor and polysomnographic recordings can be obtained in-laboratory attended by a technologist and compared to portable monitor tests obtained in the home unattended setting. Differences in equipment and testing environments, intra-scorer reliability, and the known night-to-night variability in AHI, even on in-lab polysomnography, help explain why direct comparisons of results from portable-monitor testing and polysomnography are not closely correlated. Because Type 3 monitors cannot detect whether the patient is awake or asleep during the recording, the severity of the sleep-disordered breathing is quantified as the number of apneas and hypopneas per hour of recording, instead of per hour of sleep. The resulting measure is sometimes referred to as the respiratory disturbance index rather than the AHI (AHI is used for both determinations in this article). In patients with delayed sleep onset and low sleep efficiency, the calculated AHI from the Type 3 monitor recording will underestimate the AHI that would have been obtained by polysomnography. While the correlation between in-lab polysomnography and Type 3 monitor testing is generally acceptable when the recordings are performed simultaneously in the sleep laboratory, portable monitors need to be validated in the home environment, the intended location for their use. Comparison across nights and in different environments results in greater differences between in-lab polysomnography and Type 3 sleep studies. Patients are more likely to sleep in the supine position during in-laboratory polysomnography than during portable-monitor testing at home, and any positional differences between the 2 tests must be taken into account in the data analysis.

Another problem affecting the comparison of polysomnography and home portable-monitor testing is the known night-to-night variability of AHI, even on polysomnography (Fig. 1).[68-72] This variability has led to the recommendation that validation studies that directly compare the 2 types of testing should include multiple nights of both home portable testing and in-laboratory polysomnography, in order to factor out the night-to-night variability of the 2 testing methods.[73]

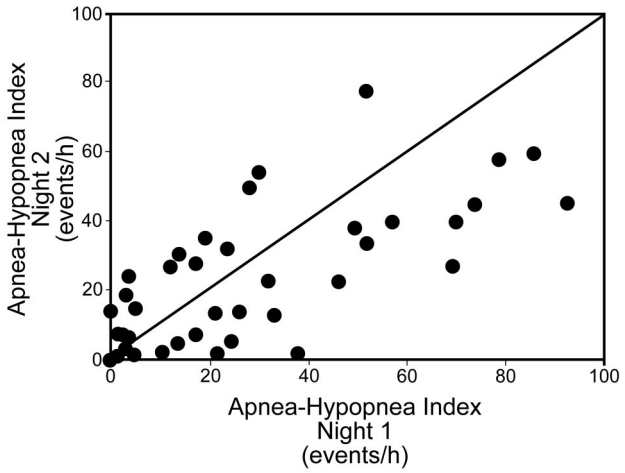

Fig. 1. Data obtained from 3 publications examining night-to-night variability of apnea-hypopnea index in individuals having 2 in-laboratory polysomnograms.[68-70] The diagonal line represents the line of identity.

Portable monitor recordings are more likely to be subject to data loss than in-lab polysomnograms. Losses of 4–33% have been reported in various studies.[47,52,74-79] The number of failed recordings will directly impact on the efficiency and cost of home testing. The more recent use of nasal pressure as the surrogate marker of air flow and improvement in artifact detection of pulse oximeters should help minimize this problem.[80]

Pilot Study Comparing Type 3 Monitor and Polysomnogram Results

A pilot study conducted at the Philadelphia Veterans Affairs Medical Center illustrates the potential effects of different equipment, different environments, and night-to-night variability when comparing the AHI obtained with a Type 3 portable monitor versus in-laboratory attended polysomnography (Fig. 2) (unpublished data). Thirty-nine adults (1 female) with suspected OSA (age 54 ± 9.6 y, body mass index 35.8 ± 7.0 kg/m^2, Epworth Sleepiness Scale score 13.6 ± 6.1) performed an overnight Type 3 portable monitor recording (Philips Respironics, Murrysville, Pennsylvania) at home. The following evening they performed an overnight in-lab polysomnogram with a simultaneous portable monitor recording. Table 3 shows the mean ± SD and median AHI on the in-laboratory and home testing. The lower mean and median AHI on both portable monitor recordings may in part be due to using recording time instead of sleep time to calculate the result. Figure 2 shows the results as identity (left panels) and

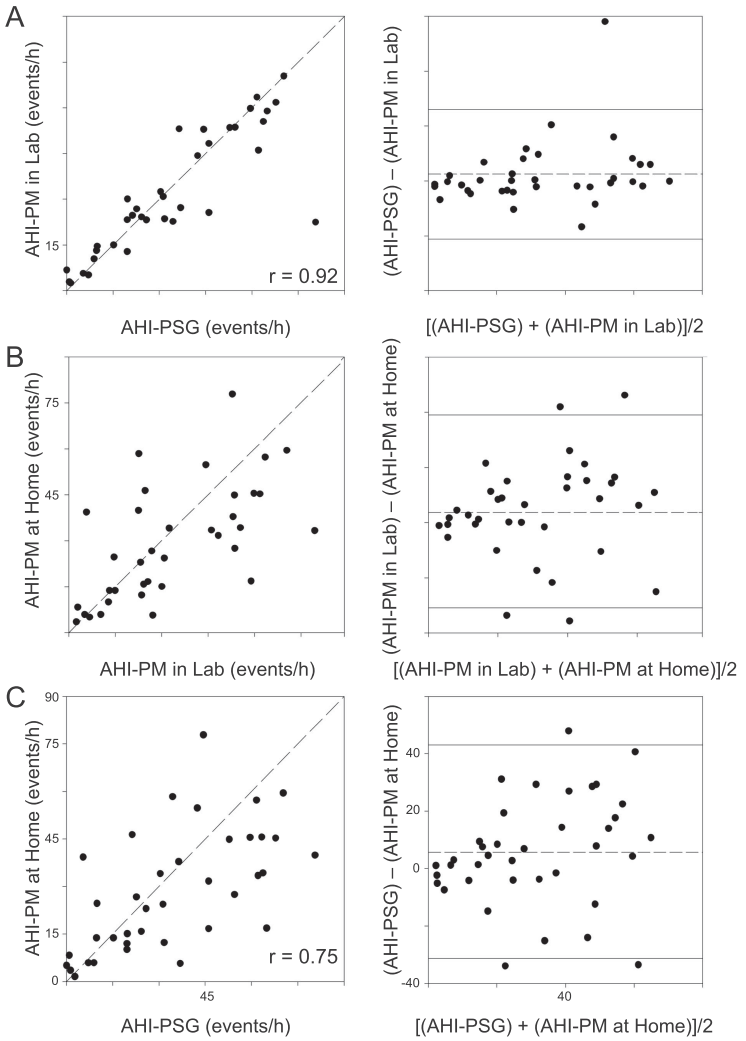

Fig. 2. Identity and Bland-Altman plots of apnea-hypopnea index (AHI) on an in-laboratory polysomnogram (PSG) and Type 3 portable monitor (PM) in 39 patients referred to a sleep laboratory with suspected obstructive sleep apnea (OSA). A: Simultaneous recordings (same night, same environments, different equipment). B: In-lab PM recording versus home PM recording (different nights, different environments, same equipment). C: Home PM recording versus in-lab PSG (different nights, different environments, different equipment).

Bland Altman plots (right panel).[81] The correlation coefficients on the identity plots reveal a relatively close correlation on the simultaneously recorded studies (different equipment, same environment, and same night). The correlation is lower when comparing in-lab polysomnography with home portable monitor recording (different equipment, different environment, and different nights), and similar variability is present when comparing the in-lab versus home portable monitor recordings (same equipment, different environment, and different nights). These results underscore the need to perform multiple night recordings to evaluate the night-to-night variability of both in-laboratory polysomnography and home testing when directly comparing performance of a home portable monitor recording with the in-laboratory polysomnogram.

A variety of statistical techniques have been applied to analyzing the data obtained in this type of comparison study.[73]

Table 3. Apnea-Hypopnea Index During Laboratory Polysomnograph Versus Portable Monitor Recording in 39 Patients With Suspected Obstructive Sleep Apnea

	Apnea-Hypopnea Index	
	Mean ± SD	Median
In Laboratory		
Laboratory polysomnograph*	40.6 ± 35.5	34.4
Portable monitor recording*	36.4 ± 27.7	27.2
At home study with portable monitor†	32.1 ± 27.4	27.5

* Simultaneous recording during in-laboratory polysomnography.
† Unattended home recording performed the night prior to laboratory polysomnography.

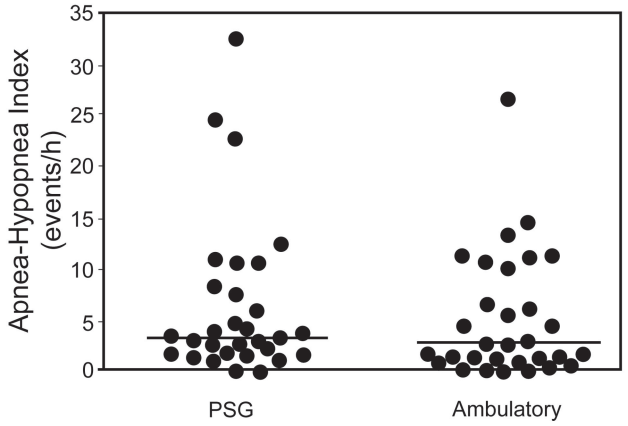

Fig. 3. Apnea-hypopnea index on continuous positive airway pressure after 3 months of treatment in patients with obstructive sleep apnea (OSA) randomized to polysomnography (PSG) (n = 30) versus ambulatory (n = 31) testing. (From Reference 5, with permission.)

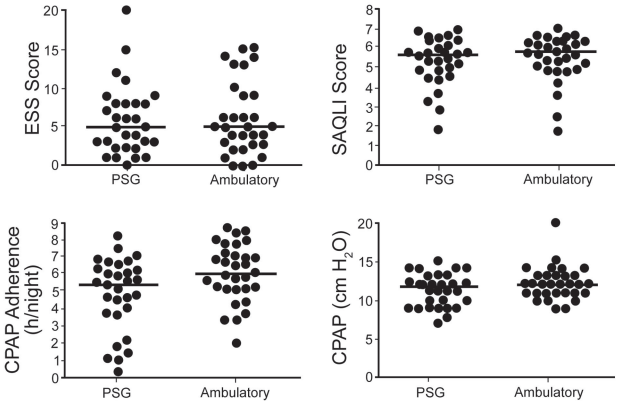

Fig. 4. Epworth Sleepiness Scale (ESS) score, adherence to continuous positive airway pressure (CPAP) therapy, Sleep Apnea Quality of Life Index (SAQLI) score, and continuous positive airway pressure (CPAP) setting in patients with OSA randomized to polysomnography (PSG) (n = 30) versus ambulatory (n = 31) testing. The horizontal bars are the median values. (From Reference 5, with permission.)

Although the use of correlation coefficients in the comparative study presented above is illustrative (see Fig. 2), this statistic is generally not recommended to evaluate the degree of agreement between 2 measurement methods.[73,81] Another approach is to present the data in terms of sensitivity, specificity, and likelihood ratios. These statistical methods require selection of a cutoff for AHI that classifies whether or not the patient has OSA. However, the unimodal distribution of AHI in cross-sectional epidemiological studies offers no rationale for selecting a particular cutoff value.[38,41,82] Debate continues as to whether different cutoffs should be selected for portable-monitor testing and polysomnography, given the differences in their AHI calculation. The weak relationship between AHI with daytime symptoms and treatment outcomes has also prevented acceptance of a specific cutoff. Indeed, different threshold values may be needed, depending on the physiologic outcome of interest. Future research may show that treatment to prevent systemic arterial hypertension and other cardiovascular consequences of OSA is beneficial only in patients with severe OSA (eg, an AHI > 30 events/hour), but that treatment is also indicated in patients with milder OSA who are sleepy. The AHI may not be the best polysomnographic outcome measure to fully predict the myriad health outcomes associated with OSA. It is generally believed that the excessive daytime sleepiness in patients with OSA is related to the number of arousals during sleep secondary to the sleep-disordered breathing, whereas the cardiovascular and metabolic consequences of OSA may be mediated by hypoxic stress and increased sympathetic activity.[37,83,84]

Validating Type 3 Portable Monitors Based on Clinical Outcomes of Ambulatory Management Pathways

Recognizing the challenges and limitations of studies that directly compare the performance of portable monitors to in-laboratory polysomnography, investigators are starting to perform comparative effectiveness research studies evaluating clinical outcomes of patients managed with portable-monitor testing at home versus those performing in-laboratory polysomnography. Instead of directly comparing sleep test results, these non-inferiority or equivalency trials compare improvements in quality of life and other outcomes in patients randomized to either ambulatory management using portable-monitor testing versus management using in-laboratory polysomnography. Several recent studies using this study design report no differences in clinical outcomes between the 2 management pathways.[3-5] All of these studies enrolled patients with a high pre-test likelihood of OSA, limiting their generalizability. Nevertheless, this study design represents an important alternative approach to validation of portable-monitor testing and is being used in other ongoing sleep research studies evaluating the use of portable monitors in OSA management pathways.

The study by Mulgrew et al[5] is an example of this alternative approach. Recruiting patients referred to a sleep laboratory for OSA evaluation, they combined standard clinical scales and overnight home oximetry to ensure at least a 90% probability of OSA. The standard clinical scales included the Epworth Sleepiness Scale, a questionnaire used to assess subjective daytime sleepiness, and the Sleep Apnea Clinical Score, a screening tool based on snoring, witnessed episodes of apnea, neck circumference, and systemic hypertension, that can be used to calculate likelihood ratios for the presence of OSA.[64,85] Sixty-eight patients were randomly assigned to usual care (polysomnography obtained before CPAP) or ambulatory management (CPAP started without doing polysomnography). To

determine the CPAP setting for treatment, patients randomized to in-lab testing who were diagnosed with OSA performed a manual CPAP titration polysomnogram and patients randomized to home testing used autoCPAP at home for one week. The CPAP setting selected in the latter group was the autoCPAP pressure below which the subject spent 95% of the time. Following 3 months of CPAP treatment, the AHI on overnight polysomnography using the prescribed CPAP settings was similar between the 2 groups (Fig. 3). In addition, following 3 months of treatment there was a slightly greater CPAP adherence in the home-tested group, and no difference in Epworth Sleepiness Scale score, score on a disease-specific quality-of-life questionnaire, or prescribed CPAP setting (Fig. 4). Aspects of the study that limit generalization were that it was performed in a single tertiary-care center and had highly selective inclusion criteria (ie, Epworth score $\geq$ 10 and Sleep Apnea Clinical Score $\geq$ 15).[64,85] Of the 2,216 patients referred to the sleep program during the recruitment period, only 81 were deemed eligible for enrollment.

These comparative effectiveness research studies must take into consideration that different testing modalities (portable-monitor testing vs polysomnography) are being used to diagnose OSA. For example, AHI on the baseline sleep study should not be used to determine if participants randomized to each arm have a similar severity of OSA, since the portable-monitor study (without sleep staging) tends to underestimate the AHI that would be obtained on polysomnogram. Another indicator of disease severity, such as the Multivariable Apnea Prediction Index,[65,66] could be used to assess disease severity at baseline across the 2 groups. Studies can attempt to compensate for these differences in diagnostic accuracy by performing polysomnography in those patients with negative home studies. This approach, however, is also potentially problematic. The option of a second diagnostic test in the home group and not the in-lab group may make it more likely, due to night-to-night variability in AHI, that the diagnosis of OSA will be established in patients randomized to home testing.

In order to compare the 2 management pathways using an intent-to-treat analysis, these comparative effectiveness research studies should select a primary outcome that evaluates all participants randomized to each arm of the study, regardless of whether they were diagnosed with OSA and initiated on CPAP treatment. CPAP adherence should not be the primary outcome measure, since different percentages of participants randomized to each arm may be diagnosed with OSA and treated with CPAP. CPAP adherence is an outcome of interest but is limited to a per protocol analysis.

When portable-monitor testing is used to manage a patient, the pathway must include the ability to perform in-lab polysomnography when clinically indicated, and insurance carriers should agree to cover the cost of that testing. Portable-monitor testing is not capable of diagnosing sleep disorders other than sleep apnea, and some patients are unable to perform this testing. In these cases, payer policy should recognize and accommodate in-laboratory polysomnography at the discretion of the physician and clinical needs of the patient. Guidelines should specify the selection of portable versus in-laboratory testing as the first test, and delineate the criteria for failure of portable-monitor testing requiring subsequent in-laboratory polysomnography.

Use of AutoCPAP to Determine the Pressure Setting Needed for CPAP Treatment

The use of home unattended portable-monitor testing to diagnose patients with OSA will be able to alleviate the growing demand for in-laboratory testing only if those patients diagnosed with OSA can be initiated on CPAP treatment without requiring polysomnography to establish the optimal CPAP setting. One alternative approach to in-laboratory CPAP titration has been to initiate CPAP treatment by selecting an arbitrary pressure based on measures such as body mass index and instructing the patient how to self-adjust the pressure setting at home.[86-89] A more common approach has been the use of autoCPAP machines that automatically adjust the level of positive airway pressure delivered to the patient in order to eliminate their sleep-disordered breathing.[90] The first-generation autoCPAP models used a pressure-adjustment algorithm based on the presence or absence of snoring and apneas, and were often unsuccessful in adequately controlling the sleep-disordered breathing. That problem has been corrected in newer-generation autoCPAP models that include the presence or absence of flow limitation in inspiration, a more sensitive detector of airway narrowing, in their pressure-adjustment algorithms. When pressure sensors in the machine detect the presence of snoring, apneas, periods of reduced flow, or inspiratory flow limitation, the pressure in the circuit is increased. Absence of these feedback signals leads to a decrement in pressure. Unfortunately, the algorithm for pressure adjustment is not standardized and varies across manufacturers.

Optimal Role of AutoCPAP Machines

No consensus exists regarding the optimal role of autoCPAP machines in the clinical management of patients with OSA. AutoCPAP has been used to titrate the fixed pressure setting needed for CPAP treatment in attended and unattended settings. Unlike the in-lab manual CPAP titration polysomnogram that determines the fixed CPAP pressure in one night (or half a night) in a strange environment, an autoCPAP titration can determine the optimal pressure setting by having a patient use an

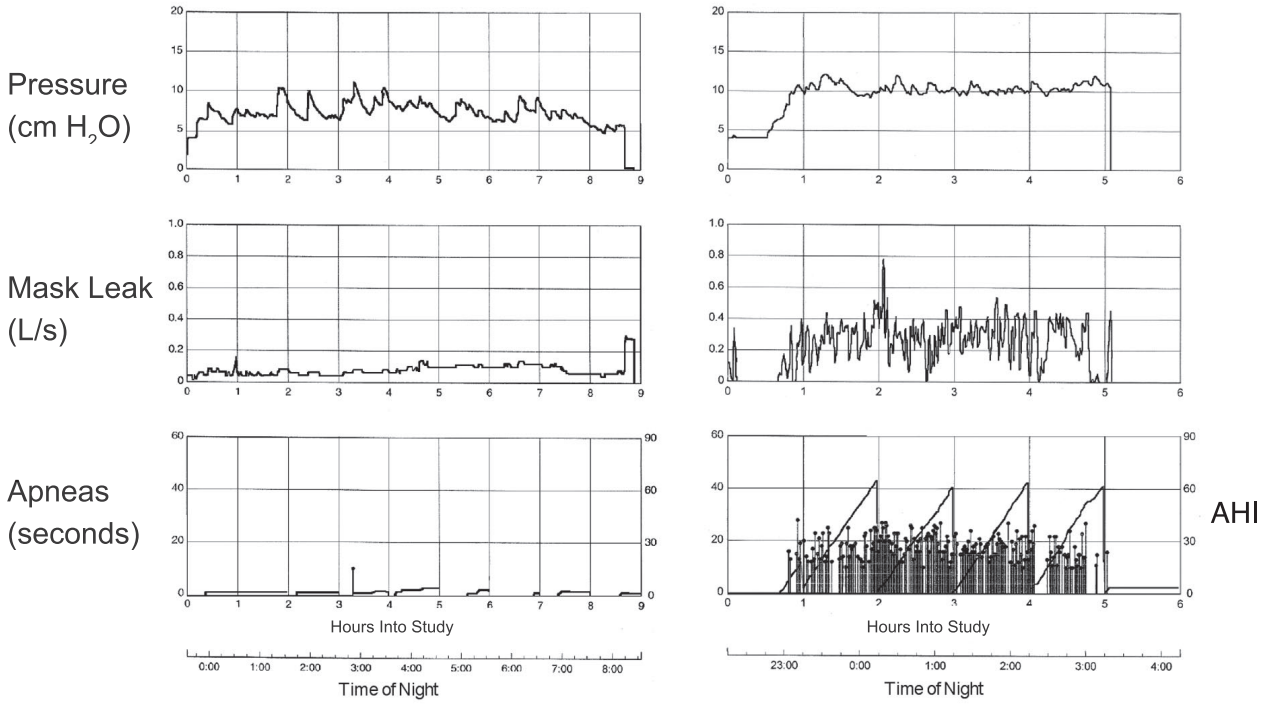

Fig. 5. Graphic reports of pressure profile, mask leak, and sleep-disordered breathing over one night of automatically titrated continuous positive airway pressure (autoCPAP) use in 2 patients with obstructive sleep apnea (OSA). In the lower panel of each graph, individual apneas are depicted as vertical lines (the height of the line indicating the duration of the event) and the running average of the apnea-hypopnea index (AHI) is represented by the solid line. In the example on the left, changes in pressure setting throughout the night were associated with a relatively small air leak and reduced the apneas and hypopneas to acceptable levels. In the example on the right, the machine was able to maintain a pressure of 10–11 cm H_2O despite a larger air leak but did not go to higher pressures, due to the persistent apneas. These apneas may have been obstructive or central. Patients with persistent apneas and an unacceptably high AHI (as indicated by the triangular waveform in the lower right panel) on unattended autoCPAP titration should be scheduled for an in-laboratory CPAP titration polysomnogram.

autoCPAP apparatus for one or more nights in his/her own home. AutoCPAP downloads report the daily pressure profiles delivered as well as the number of apneas and hypopneas, the AHI, and the amount of air leak from the mask (Fig. 5). The downloads also report the amount of time spent at given pressures and respiratory parameters at those pressures. The fixed pressure selected for CPAP treatment is the pressure below which the patient spends 90–95% of the time. An important drawback of the autoCPAP downloads is the paucity of published information validating the ability of autoCPAPs to detect apneas and hypopneas, and therefore the accuracy of their AHI determinations.[91,92]

AutoCPAPs are being used as regular treatment for some patients with OSA and appear to have particular utility in those patients who have difficulty tolerating high levels of CPAP throughout the night.[93] An arguable but untested approach might be to treat all patients with OSA with autoCPAP instead of CPAP, obviating the need for expensive in-laboratory CPAP titrations and eliminating the concern that a fixed pressure determined on in-lab polysomnography (or home autoCPAP titration) will be adequate over long periods of time despite fluctuations in nasal airway resistance, body position, and body weight. AutoCPAP machines are currently more expensive than CPAP machines, but, as the cost of autoCPAP machines declines this latter approach may become economically justifiable. Regarding the use of autoCPAP for home-unattended titration studies, many questions remain unanswered. For example, it is unknown how many nights autoCPAP should be used during home-unattended titration studies to obtain an optimal pressure setting.

AutoCPAP Features That Help Ensure Patient Safety

To prevent adverse events related to excessive pressure delivery, the autoCPAP machines are limited to a pressure range from 4 to about 20 cm H_2O. Some patients with OSA can develop central apneas while receiving positive-airway-pressure treatment, so-called complex OSA, and further increases in pressure after the appearance of central apneas only increase their occurrence.[94,95] AutoCPAPs are

unable to distinguish central from obstructive apneas. Therefore, to avoid the potential problem of increasing pressure in the presence of central apneas, autoCPAP algorithms uniformly prevent increases in pressure above 10–11 cm H_2O in the presence of persistent apneas (see Fig. 5, right panel). A patient with an unattended autoCPAP download showing persistent apneas should be scheduled for an in-laboratory positive airway pressure titration polysomnogram.

Some autoCPAPs are designed to interface with other monitors to help ensure the adequacy of pressure titration. To document that autoCPAP treatment is successful not only in controlling the apneas and hypopneas but also in restoring oxygen saturation to acceptable levels, some autoCPAPs can interface with pulse oximeter modules that record oxygen saturation and heart rate. Some autoCPAPs are also designed to interface with a Type 3 portable monitor, recording respiratory-related parameters but not sleep staging signals, for a verifiable documentation of AHI as well as oxygen saturation. The latest innovations in autoCPAP machines are allowing remote monitoring of their use and performance by either modem or wireless transmission of recorded data. Although no studies have investigated the use of this innovative technology, it is hoped that the ability to remotely track events during the home titration will lead to early interventions that can promote successful titration and initiation of CPAP treatment.

Validation of AutoCPAP Titration Studies

Validation of the home-unattended autoCPAP titration study faces similar challenges to those confronting validation of portable monitors for the diagnosis of OSA. Of particular concern to anyone who has interpreted manual CPAP titration polysomnograms is the relatively short amount of time that the patient may be on the "optimal pressure" selected for CPAP treatment, often preventing verification of its adequacy in all sleep positions and sleep stages. The time available to identify an optimal pressure may be particularly limited in split-night polysomnograms. Similar to the approach with portable monitors for the diagnosis of OSA, initial attempts to validate home autoCPAP titration studies directly compared the 90–95 percentile pressure setting to the optimal pressure determined on in-lab manual CPAP titration polysomnography. Differences in environment and equipment could explain why the 2 determinations did not have the same result. Although the night-to-night variability of the optimal pressure on in-lab manual CPAP titration polysomnography is unknown, it is likely that changes from one night to another also play a role in explaining discrepancies between the home autoCPAP and in-lab polysomnography determinations.

Randomized control trials[96-99] and case-based studies[100-102] report that autoCPAP selected a fixed CPAP level that reduced the AHI to less than 10 events/hour in 80–90% of OSA patients. The autoCPAP trials in all but 2 of these studies[97,102] were attended by a technologist or nurse in the laboratory. Depending on the method of selecting the pressure from autoCPAP and the manual CPAP titration protocol, the pressures from the 2 determinations were usually within 1 or 2 cm H_2O. One study suggested that using autoCPAP rather than traditional CPAP titration to determine a fixed effective pressure for treatment decreased the percentage of patients declining continuation of CPAP treatment at 6 weeks.[97] Almost all previous studies with autoCPAP have excluded patients with chronic heart failure and COPD. Future studies need to evaluate the performance of autoCPAP in these special populations.

Recognizing the inherent design weakness of studies that directly compare optimal pressure obtained by autoCPAP titration versus standard polysomnography, recent studies compared the 2 titration methods by evaluating the clinical outcomes following initiation of CPAP treatment in patients randomized to either home or in-lab testing.[5,89,97,103] Overall, the results report similar outcomes across titration methods. For example, the prospective study of Masa et al[89] randomized 360 naïve patients with OSA into 3 groups that received one of: standard CPAP titration polysomnography, unattended home autoCPAP titration, or CPAP treatment based on a predicted formula with home self-adjustment based on the bed partner's reports. Following 12 weeks of CPAP treatment on the determined pressure, an in-laboratory polysomnogram on CPAP was performed on all participants at their particular pressure setting. With CPAP treatment, the improvements in subjective daytime sleepiness (change in Epworth Sleepiness Scale score) and AHI were similar in the 3 groups. No differences were detected in the objective adherence to CPAP treatment or in the dropout rate of the 3 groups at the end of follow-up. Masa et al concluded that home autoCPAP titration and predicted formula titration with domiciliary adjustment can replace standard in-laboratory titration. In a similar study design, Cross et al[104] found no significant differences 3 months following initiation of CPAP treatment in CPAP adherence or functional outcomes (Epworth, Functional Outcomes of Sleep Quality, and the Medical Outcomes Study Short-Form 36-item questionnaire [SF-36] scores) in patients randomized to in-lab CPAP polysomnography versus home autoCPAP titration.

Study Populations That Need to Be Included in Portable Monitor Research

There is a paucity of data on portable-monitor testing in special populations, including diverse ethnic groups, the elderly, and among individuals with other cardio-respira-

tory and neurological diseases such as COPD, asthma, heart failure, and neuromuscular disorders. Studies are needed to determine whether portable-monitor testing is feasible and suitable for the screening and diagnosis of sleep disorders in these subgroups. Equally important are the advantages and limitations of these devices compared to attended in-laboratory polysomnography, and the difference between the sleep laboratory and home environment. Research on how portable-monitor testing can be adapted to specific comorbid medical and neurological conditions is needed. Individuals with COPD, asthma, heart failure, and neuromuscular disorders have a higher risk of developing sleep-related hypoventilation, OSA, and central sleep apnea. Ideally, portable-monitor testing in these patients should be able to distinguish these respiratory disorders. Studies on the relative feasibility, access, and convenience of portable-monitor testing versus in-laboratory polysomnography among community-dwelling older adults and nursing home residents are also needed. The most appropriate outcome measures for each study population need to be identified.

Critical Outcome Measures of OSA Management Pathways

Given the emphasis on outcomes-based assessment, investigators should carefully select and clearly define both clinical and cost-related outcomes in designing studies comparing ambulatory and in-laboratory management of patients with OSA. Ideally, both short-term and long-term outcomes should be evaluated. Categories of validated outcome measures to consider incorporating into study protocols include self-efficacy, general and disease-specific quality of life, symptoms, neurocognitive function, and surrogate measures of cardiovascular risk.

Differences between testing pathways may change a patient's attitudes and perceptions about OSA and CPAP, altering their subsequent adherence to CPAP treatment. This effect on clinical outcomes can be evaluated by measuring self-efficacy (ie, changes in a patient's attitudes and perceptions of OSA and CPAP treatment).[105-108] In-laboratory testing might result in greater self-efficacy than home testing, due to the greater amount of time healthcare providers interact with patients who spend the entire night in the laboratory with the sleep technologist.[109] The overnight-attended polysomnogram affords greater opportunities for education and immediate support, factors that have been shown to improve patient adherence to treatment.[110-114]

Examples of possible functional outcome measures include the Psychomotor Vigilance Task for objective assessment of daytime sleepiness, the Epworth Sleepiness Scale for subjective assessment of daytime sleepiness, disease-specific quality-of-life questionnaires such as the Functional Outcomes of Sleep Questionnaire and the Calgary Sleep Apnea Quality of Life Index, and general quality-of-life questionnaires such as the Medical Outcomes Study Short-Form 36-item and 12-item questionnaires.[85,115-122] There is almost no information on how much CPAP treatment is needed to improve functional outcomes, and it is possible that similar improvements are obtained despite differences in CPAP adherence.[123] Disease mastery and patient satisfaction with the care pathway should also be considered. Relative wait times and the number of lost, technically unsatisfactory, and/or equivocal studies should be recorded, together with the criteria for each of these categories. In patients diagnosed with OSA and initiated on CPAP treatment, objective measures of treatment response might include change in sleep quality, AHI, oxygenation, and objective adherence to CPAP treatment.

Studies comparing home portable monitor versus in-laboratory polysomnogram management pathways might evaluate their effect on surrogate measures of cardiovascular risk. These may include direct measures of cardiovascular function (individual or 24-hour blood pressure, ECG rhythm, heart-rate variability, and ischemic changes, echocardiogram, and cardiac magnetic resonance imaging) or documentation of clinical cardiovascular events (myocardial infarction, heart failure, angina, transient ischemic attack, stroke). Circulating or tissue biomarkers, measures of endothelial function, vascular intima-media thickness, and assessment of lipid metabolism and insulin sensitivity may also be relevant.

Critically important is the need to evaluate the cost-effectiveness of any ambulatory management pathway using portable-monitor testing. To date there is only one prospective cost-effectiveness study.[3] Antic et al compared a nurse-practitioner-led ambulatory management pathway to a physician-led management pathway, using in-laboratory testing.[3] They found similar changes in Epworth Sleepiness Scale score in the 2 groups following 3 months of CPAP treatment, but a lower study-related cost per patient ($1,000 Australian) in the nurse-practitioner-led pathway. Economic analyses should evaluate health resource utilization for the entire clinical management pathway, from diagnosis to treatment outcomes. Costs to consider include: sensor/supply costs and equipment purchase, maintenance and refurbishment/replacement due to damage from portable use and/or theft; laboratory space; personnel costs, including staff training/development as well as work load for equipment management, patient training, data download and scoring; costs associated with failed or inconclusive studies that need to be repeated, or for which polysomnography eventually has to be performed; the costs associated with incorrect or missed diagnosis of sleep-disordered breathing, failure to diagnose concomitant non-

respiratory sleep disorders, or with treatment failures, such as non-acceptance of CPAP.

Is Portable-Monitor Testing a Threat or an Opportunity for the Future Growth and Development of the Specialty of Sleep Medicine?

Portable-monitor testing for the management of patients with OSA is already well established in many countries. The recent decisions by CMS to approve coverage of portable-monitor testing for the diagnosis and initiation of CPAP treatment in patients with OSA is likely to result in a progressively greater role of portable-monitor testing in the United States. One can predict that 2 additional changes will occur in the United States in the near future: revision of current reimbursement fees for sleep testing, and coverage by insurers of autoCPAP units for home-unattended titration studies and/or treatment of OSA. Reimbursement fees are likely to be adjusted to narrow the current large difference in allowable charges between in-laboratory polysomnography and portable-monitor testing. Coverage of autoCPAP-related services will allow providers to supply this critical component of the ambulatory management pathway.

These predictions, if true, will have far-reaching consequences to the field of sleep medicine. The rapid growth of the specialty of sleep medicine over the past 3 decades has been largely driven and structured by the performance of the costly and technologically complex polysomnogram. The availability of the less costly and more user-friendly portable devices for management of patients with OSA is likely to lead to the development of clinical management pathways that can be implemented by non-sleep specialists, including primary care providers. Previous examples of such an evolution of disease management include asthma and diabetes mellitus. Patients with these diseases were originally cared for by allergists, pulmonologists, and endocrinologists. Today, the majority of these patients are managed by primary care providers. OSA is more common than asthma and diabetes and is acknowledged to be a major public health burden. But the clinical pathways to diagnose and treat patients with OSA using portable monitors still need to be developed and tested. Without well-developed clinical management algorithms, the premature, widespread application of these emerging new technologies by non-sleep-specialists carries the substantial risk of abuse and unacceptable quality of care.

The growing importance of portable-monitor testing may be of benefit from the societal and patient perspective, but is viewed by many sleep specialists as a threat to the viability of their specialty. Sleep specialists must recognize the inevitability of a prominent role for portable-monitor testing in patient care, embrace this new technology as a challenging opportunity, and perform the research needed to understand how these monitors should be best employed in patient care. Based on past experiences with other diseases and the knowledge that the vast majority of patients with OSA are undiagnosed, it can be argued that portable-monitor testing will increase rather than diminish the need for in-laboratory testing. For example, while portable spirometry has allowed primary care practitioners to diagnose and manage patients with asthma and COPD, the activity of pulmonary function laboratories has only increased.

As we learn how to manage patients with OSA with portable-monitor testing, measures taken by providers, insurers, and regulatory agencies to promote the ambulatory management of OSA should protect the quality of patient care and consider their potential impact on the growth and development of the specialty of sleep medicine. However future practice evolves, we need to continue to attract new investigators into this fledgling field. The continuing infusion of new talent into this specialty is vital for the generation of the evidence-based medicine that will guide and justify the use of the emerging technologies.

Summary

Pressure for alternative approaches to the current recommended in-laboratory management of patients with OSA apnea will continue to increase, given the cost of polysomnography, the limited number of laboratory facilities, and the growing clinical demand for more rapid access to testing. Ambulatory monitoring should be viewed as complementary rather than competitive technology to in-lab polysomnography. What roles will portable monitors assume and will this be imposed on providers based on market priorities, or will it be based on evidence-based medicine? While determining the role of portable-monitor testing we need to understand the substantial clinical limitations of polysomnography and work to further standardize the sensors, signal processing, and CPAP titration protocols used in the accepted standard test. Similar efforts are needed to standardize portable monitors. More prospective, high-quality clinical trials are needed to compare home versus in-laboratory testing in terms of treatment outcomes in diverse patient populations. Cost-effectiveness protocols should be routinely incorporated into these clinical trials to collect the data that will allow development of decision analysis models that are based on facts, not assumptions. Alternative approaches should also be made available to underserved and remote populations that do not have access to laboratory polysomnography. Finally, one can predict that the rapid evolution and expansion of the discipline of sleep medicine into a multidisciplinary specialty will help drive practitioners to alternative testing methods. As physicians in family practice and otolaryngology join pulmonologists, psychiatrists, and neurologists to specialize in sleep

medicine, the desire to test populations outside of the sleep center will increase and hopefully promote the research needed to systematically develop these alternative clinical disease management pathways.

REFERENCES

1. Ahmed M, Patel NP, Rosen I. Portable monitors in the diagnosis of obstructive sleep apnea. Chest 2007;132(5):1672-1677.
2. Collop NA. Portable monitoring for the diagnosis of obstructive sleep apnea. Curr Opin Pulm Med 2008;14(6):525-529.
3. Antic NA, Buchan C, Esterman A, Hensley M, Naughton MT, Rowland S, et al. A randomized controlled trial of nurse-led care for symptomatic moderate-severe obstructive sleep apnea. Am J Respir Crit Care Med 2009;179(6):501-508.
4. Berry RB, Hill G, Thompson L, McLaurin V. Portable monitoring and autotitration versus polysomnography for the diagnosis and treatment of sleep apnea. Sleep 2008;31(10):1423-1431.
5. Mulgrew AT, Fox N, Ayas NT, Ryan CF. Diagnosis and initial management of obstructive sleep apnea without polysomnography: a randomized validation study. Ann Intern Med 2007;146:(3):157-166.
6. Centers for Medicare & Medicaid Services. Decision memo for continuous positive airway pressure (CPAP) therapy for obstructive sleep apnea (OSA). CAG-00093R2.
7. Centers for Medicare & Medicaid Services. Decision memo for sleep testing for obstructive sleep apnea (OSA). CAG-00405N.
8. Kushida CA, Littner MR, Morgenthaler T, Alessi CA, Bailey D, Coleman J, et al. Practice parameters for indications for polysomnography and related procedures: An update for 2005. Sleep 2005; (28):499-521.
9. Kushida CA, Chediak A, Berry RB, Brown LK, Gozal D, Iber C, et al. Clinical guidelines for the manual titration of positive airway pressure in patients with obstructive sleep apnea. J Clin Sleep Med 2008;4(2):157-171.
10. Kushida CA, Littner MR, Hirshkowitz M, Morgenthaler TI, Alessi CA, Bailey D, et al. Practice parameters for the use of continuous and bilevel positive airway pressure devices to treat adult patients with sleep-related breathing disorders. Sleep 2006;29(3):375-380.
11. Patel NP, Ahmed M, Rosen I. Split-night polysomnography. Chest 2007;132(5):1664-1671.
12. Rodway GW, Sanders MH. The efficacy of split-night sleep studies. Sleep Med Rev 2003;7(5):391-401.
13. Fleury B, Rakotonanahary D, Tehindrazanarivelo AD, Hausser-Hauw C, Lebeau B. Long term compliance to continuous positive airway pressure therapy (nCPAP) set up during a split-night polysomnogram. Sleep 1994;17(6):512-515.
14. Strollo P, Sanders MH, Costantino JP, Walsh SK, Stiller RA, Atwood CW. Split-night studies for the diagnosis and treatment of sleep-disordered breathing. Sleep 1996;19:(10 Suppl);S255-S259.
15. Yamashiro Y, Kryger MH. CPAP titration for sleep apnea using a split-night protocol. Chest 1995;107(1):62-66.
16. Phillips B, Collop NA, Strollo P. Controversies in sleep disorders medicine. Pulmonologists respond. Chest 1996;110(6):1597-1602.
17. Iber C, Ancoli-Israel S, Chesson AL, Quan SF. The AASM manual for the scoring of sleep and associated events. Westchester, IL: American Academy of Sleep Medicine; 2007.
18. Rechtschaffen A, Kales A. A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Los Angeles: Brain Information Service/Brain Research Institute, University of California; 1968.
19. Redline S, Kapur V, Sanders MH, Quan SF, Gottlieb DJ, Rapoport DM, et al. Effects of varying approaches for identifying respiratory disturbances on sleep apnea assessment. Am J Respir Crit Care Med 2000;161(2 Pt 1):369-374.
20. Ruehland WR, Rochford PD, O'Donoghue FJ, Pierce RJ, Singh P, Thornton AT. The new AASM criteria for scoring hypopneas: impact on the apnea hypopnea index. Sleep 2009;32(2):150-157.
21. American Academy of Sleep Medicine Task Force. Sleep-related breathing disorders in adults: recommendations for syndrome definitions and measurement techniques in clinical research. Sleep 1999;22(5):667-689.
22. Adams N, Strauss M, Schluchter M, Redline S. Relation of measures of sleep-disordered breathing to neuropsychological functioning. Am J Respir Crit Care Med 2001;163(7):1626-1631.
23. Bennett LS, Barbour C, Langford BA, Stradling JR, Davies RJ. Health status in obstructive sleep apnea; relationship with sleep fragmentation and daytime sleepiness. Am J Respir Crit Care Med 1999;159(6):1884-1890.
24. Bennett LS, Langford BA, Stradling JR, Davies RJ. Sleep fragmentation indices as predictors of daytime sleepiness and nCPAP response in obstructive sleep apnea. Am J Respir Crit Care Med 1998;158(3):778-786.
25. Gottlieb DJ, Whitney CW, Bonekat WH, Iber C, James GD, Lebowitz M, et al. Relation of sleepiness to respiratory disturbance index: the Sleep Heart Health Study. Am J Respir Crit Care Med 1999;159(2):502-507.
26. Kingshott RN, Vennelle M, Hoy CJ, Engleman HM, Deary IJ, Douglas NJ. Predictors of improvements in daytime function outcomes with CPAP therapy. Am J Respir Crit Care Med 2000;161(3 PT 1):866-871.
27. Olson LG, King MT, Hensley MJ, Saunders NA. A community study of snoring and sleep-disordered breathing. Health outcomes. Am J Respir Crit Care Med 1995;152(2):717-720.
28. Barbé F, Mayoralas LR, Duran J, Masa JF, Maimo A, Montserrat JM, et al. Treatment of continuous positive airway pressure is not effective in patients with sleep apnea but no daytime sleepiness. Ann Intern Med 2001;134(11):1015-1023.
29. Roure N, Gomez S, Mediano O, Duran J, Pena Mde L, Capote F, et al. Daytime sleepiness and polysomnography in obstructive sleep apnea patients. Sleep Med 2008;9(7):727-731.
30. Bazzano LA, Khan Z, Reynolds K, He J. Effect of nocturnal nasal continuous positive airway pressure on blood pressure in obstructive sleep apnea. Hypertension 2007;50(2):417-423.
31. Haentjens P, Van Meerhaeghe A, Moscariello A, De Weerdt S, Poppe K, Dupont A, et al. The impact of continuous positive airway pressure on blood pressure in patients with obstructive sleep apnea syndrome: evidence from a meta-analysis of placebo-controlled randomized trials. Arch Intern Med 2007;167(8):757-764.
32. Marin JM, Carrizo SJ, Vicente E, Agusti AGN. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet 2005;365(9464):1046-1053.
33. Peker Y, Hedner J, Norum J, Kraiczi H, Carlson J. Increased incidence of cardiovascular disease in middle-aged men with obstructive sleep apnea. Am J Respir Crit Care Med 2002;166(2):159-165.
34. Buchner NJ, Sanner BM, Borgel J, Rump LC. Continuous positive airway pressure treatment of mild to moderate obstructive sleep apnea reduces cardiovascular risk. Am J Respir Crit Care Med 2007;176(12):1274-1280.
35. Campos-Rodriguez F, Pena-Grinan N, Reyes-Nunez N, De la Cruz-Moron I, Perez-Ronchel J, De la Vega-Gallardo F, et al. Mortality in obstructive sleep apnea-hypopnea patients treated with positive airway pressure. Chest 2005;128(2):624-633.
36. Doherty LS, Kiely JL, Swan V, McNicholas WT. Long-term effects of nasal continuous positive airway pressure therapy on cardiovascular outcomes in sleep apnea syndrome. Chest 2005;127(6):2076-2084.

37. Punjabi NM, Caffo BS, Goodwin JL, Gottlieb DJ, Newman AB, O'Connor GT, et al. Sleep-disordered breathing and mortality: a prospective cohort study. PLoS Med 2009;6(8):e1000132.
38. Shahar E, Whitney CW, Redline S, Lee ET, Newman AB, Nieto FJ, et al. Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. Am J Respir Crit Care Med 2001;163(1):19-25.
39. Kapur V, Strohl KP, Redline S, Iber C, O'Connor GT, Nieto FJ. Underdiagnosis of sleep apnea syndrome in US communities. Sleep Breath 2002;6(2):49-54.
40. Young T, Evans L, K., Finn L, Palta M. Estimation of the clinically diagnosed proportion of sleep apnea syndrome in middle-aged men and women. Sleep 1997;20(9):705-706.
41. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993;328(17):1230-1235.
42. Young T, Peppard PE, Taheri S. Excess weight and sleep-disordered breathing. J Appl Physiol 2005;99(4):1592-1599.
43. Flemons WW, Douglas NJ, Kuna ST, Rodenstein DO, Wheatley J. Access to diagnosis and treatment of patients with suspected sleep apnea. Am J Respir Crit Care Med 2004;169(6):668-672.
44. Sharafkhaneh A, Richardson P, Hirshkowitz M. Sleep apnea in a high risk population: a study of Veterans Health Administration beneficiaries. Sleep Med 2004;5(4):345-350.
45. Pack AI. Sleep-disordered breathing – access is the issue. Am J Respir Crit Care Med 2004;169(6):666-667.
46. Chesson AL, Berry RB, Pack AI. Practice parameters for the use of portable monitor devices in the investigation of suspected obstructive sleep apnea in adults. A joint project sponsored by the American Academy of Sleep Medicine, the American Thoracic Society, and the American College of Chest Physicians. Sleep 2003;26(7):907-913.
47. Ferber R, Millman RP, Coppola M, Fleetham J, Murray CF, et al. Portable recording in the assessment of obstructive sleep apnea: ASDA standards of practice. Sleep 1994;17(4):378-392.
48. Iber C, Redline S, Kaplan Gilpin AM, Quan SF, Zhang L, Gottlieb DJ, et al. Polysomnography performed in the unattended home versus the attended laboratory setting – Sleep Heart Health Study methodology. Sleep 2004;27(3):536-540.
49. Foster GD, Borradaile KE, Sanders MH, Millman R, Zammit G, Newman AB, et al. A randomized study on the effect of weight loss on obstructive sleep apnea among obese patients with type 2 diabetes: the Sleep AHEAD study. Arch Intern Med 2009;169(17):1619-1626.
50. Foster GD, Sanders MH, Millman R, Zammit G, Borradaile KE, Newman AB, et al. Obstructive sleep apnea among obese patients with type 2 diabetes. Diabetes Care 2009;32(6):1017-1019.
51. Goodwin JL, Kaemingk KL, Fregosi RF, Rosen GM, Morgan WJ, Sherrill DL, et al. Clinical outcomes associated with sleep-disordered breathing in Caucasian and Hispanic children - the Tuscon Children's Assessment of Sleep Study (TuCASA). Sleep 2003;26(5):587-591.
52. Redline S, Tosteson T, Boucher MD, Millman RP. Measurement of sleep-related breathing disturbances in epidemiological studies: assessment of the validity and reproducibility of a portable monitoring device. Chest 1991;100(5):1281-1286.
53. Redline S, Sanders MH, Lind BK, Quan SF, Iber C, Gottlieb DJ, et al. Methods for obtaining and analyzing unattended polysomnography data for a multicenter study – Sleep Heart Health Research Group. Sleep 1998;21(7):759-767.
54. Montserrat JM, Farré R, Ballester E, Felez MA, Pastó M, Navajas D. Evaluation of nasal prongs for estimating nasal airflow. Am J Respir Crit Care Med 1997;155(1):211-215.
55. Norman RG, Ahmed MM, Walsleben JA, Rapoport DM. Detection of respiratory events during NPSG: Nasal cannula/pressure sensor versus thermistor. Sleep 1997;20(12):1175-1184.
56. Thurnheer R, Xie X, Bloch KE. Accuracy of nasal cannula pressure recordings for assessment of ventilation during sleep. Am J Respir Crit Care Med 2001;164(10 Pt 1):1914-1919.
57. Ensuring adequate diagnosis and treatment: access, capacity, and technology development (Chapter 6). In: Colten HR, Altevogt BM, editors. Sleep disorders and sleep deprivation: an unmet public health problem. Washington, DC: The National Academies Press; 2006:261-280.
58. Elbaz M, Roue GM, Lofaso F, Quera Salva MA. Utility of actigraphy in the diagnosis of obstructive sleep apnea. Sleep 2002;25(5):527-531.
59. Westbrook PR, Levendowski DJ, Cvetinovic M, Zavora T, Velimirovic V, Henninger D, et al. Description and validation of the apnea reisk evaluation system: a novel method to diagnose sleep apnea-hypopnea in the home. Chest 2005;128(4):2166-2175.
60. Penzel T, Fricke R, Jerrentrup A, Peter JH, Vogelmeier C. Peripheral arterial tonometry for the diagnosis of obstructive sleep apnea. Biomed Tech (Berl) 2002;47(Suppl 1 Pt 1):315-317.
61. Pittman SD, Ayas NT, MacDonald MM, Malhotra A, Fogel RB, White DP. Using a wrist-worn device based on peripheral arterial tonometry to diagnose obstructive sleep apnea: in-laboratory and ambulatory validation. Sleep 2004;27(5):923-933.
62. Flemons WW, Littner MR, Rowley JA, Gay PC, Anderson WM, Hudgel DW, et al. Home diagnosis of sleep apnea: a systematic review of the literature: an evidence review co-sponsored by the American Academy of Sleep Medicine, the American College of Chest Physicians, and the American Thoracic Society. Chest 2003;124(4):1543-1579.
63. Collop NA, Anderson WM, Boehlecke B, Claman D, Goldberg R, Gottlieb DJ, et al. Clinical guidelines for the use of unattended portable monitors in the diagnosis of obstructive sleep apnea in adult patients. Portable Monitoring Task Force of the American Academy of Sleep Medicine. J Clin Sleep Med 2007;3(7):737-747.
64. Flemons WW, Whitelaw WA, Brant R, Remmers JE. Likelihood ratios for a sleep apnea clinical prediction rule. Am J Respir Crit Care Med 1994;150(5 Pt 1):1279-1285.
65. Maislin G, Gurubhagavatula I, Hachadoorian R, Pack F, O'Brien E, Staley B, et al. Operating characteristics of the multivariable apnea prediction index in non-clinic populations (abstract). Sleep 2003;26:A247.
66. Maislin G, Pack AI, Kribbs NB, Smith PL, Schwartz AR, Kline LR, et al. A survey screen for prediction of apnea. Sleep 1995;18(3):158-166.
67. Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin questionnaire to identify patients at risk for the sleep apnea syndrome. Ann Intern Med 1999;131(7):485-491.
68. Aber WR, Block AJ, Hellard DW, Webb WB. Consistency of respiratory measurements from night to night during the sleep of elderly men. Chest 1989;96(4):747-751.
69. Bliwise DL, Benkert RF, Ingham RH. Factors associated with nightly variability in sleep-disordered breathing in the elderly. Chest 1991;100(4):973-976.
70. Chediak AD, Acevedo-Crespo JC, Seiden DJ, Kim HH, Kiel MH. Nightly variability in the indices of sleep-disordered breathing in men being evaluated for importance with consecutive night polysomnograms. Sleep 1996;19(7):589-592.
71. Lord S, Sawyer B, O'Connell D, King M, Pond D, Eyland A, et al. Night-to-night variability of disturbed breathing during sleep in an elderly community sample. Sleep 1991;14(3):252-258.
72. Quan SF, Griswold ME, Iber C, Nieto FJ, Rapoport DM, Redline S, et al. Short-term variability of respiration and sleep during unat-

tended nonlaboratory polysomnography – the Sleep Heart Health Study. Sleep 2002;25(8):843-849.
73. Flemons WW, Littner MR. Measuring agreement between diagnostic devices. Chest 2003;124(4):1535-1542.
74. Ancoli-Israel S, Kripke DF, Mason W, Messin S. Comparisons of home sleep recordings and polysomnograms in older adults with sleep disorders. Sleep 1981;4(3):283-291.
75. Gagnadoux F, Pelletier-Fleury N, Philippe C, Rakotonanahary D, Fleury B. Home unattended vs hospital telmonitored polysomnography in suspected obstructive sleep apnea syndrome: a randomized crossover trial. Chest 2002;121(3):753-758.
76. Gyulay S, Gould D, Sawyer B, Pond D, Mant A, Saunders N. Evaluation of a microprocessor-based portable home monitoring system to measure breathing during sleep. Sleep 1987;10(2):130-142.
77. Kiely JL, Delahunty C, Matthews S, McNichols WT. Comparison of limited computerized diagnostic system (ResCare Autoset) with polysomnography in the diagnosis of obstructive sleep apnea syndrome. Eur Respir J 1996;9(11):2360-2364.
78. Pelletier-Fleury N, Gagnadoux F, Philippe C, Rakotonanahary D, Lanoé JL, Fleury B. A cost-minimization study of telemedicine. The case of telemonitored polysomngraphy to diagnose obstructive sleep apnea syndrome. Int J Technol Assess Health Care 2001; 17(4):604-611.
79. Whittle AT, Finch SP, Mortimore IL, Mackay TW, Douglas NJ. Use of home sleep studies for diagnosis of the sleep apnoea/hypopnoea syndrome. Thorax 1997;52(12):1068-1073.
80. Barker SJ. "Motion resistant" pulse oximetry: a comparison of new and old models. Anesth Analg 2002;95(4):967-972.
81. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1(8476): 307-310.
82. Whitelaw WA, Brant RF, Flemons WW. Clinical usefulness of home oximetry compared with polysomnography for assessment of sleep apnea. Am J Respir Crit Care Med 2005;171(2):188-193.
83. Caples SM, Garcia-Touchard A, Somers VK. Sleep-disordered breathing and cardiovascular risk. Sleep 2007;30(3):291-303.
84. Sulit L, Storfer-Isser A, Kirchnew HL, Redline S. Differences in polysomnography predictors for hypertension and impaired glucose tolerance. Sleep 2006;29(6):777-783.
85. Johns MW. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. Sleep 1991;14(6):540-545.
86. Coppola M, Lawee M. Management of obstructive sleep apnea syndrome in the home. The role of portable sleep apnea recording. Chest 1994;104(1):19-25.
87. Fitzpatrick M, Alloway C, Wakeford T, MacLean A, Munt P, Day A. Can patients with obstructive sleep apnea titrate their own continuous positive airway pressure? Am J Respir Crit Care Med 2003; 167(5):716-722.
88. Hukins CA. Arbitrary-pressure continuous positive airway pressure for obstructive sleep apnea. Am J Respir Crit Care Med 2005; 171(5):500-505.
89. Masa JF, Jimenez A, Duran J, Capote F, Monasterio C, Mayos M, et al. Alternative methods of titrating continuous positive airway pressure: a large multicenter study. Am J Respir Crit Care Med 2004;170(11):1218-1224.
90. Berry RB, Parish JM, Hartse KM. The use of auto-titrating continuous positive airway pressure for treatment of adult obstructive sleep apnea. Seep 2002;25(2):148-173.
91. Desai H, Patel A, Patel P, Grant BJ, Mador MJ. Accuracy of autotitrating CPAP to estimate the residual Apnea-Hypopnea Index in patients with obstructive sleep apnea on treatment with autotitrating CPAP. Sleep Breath 2009;13(4):383-390.
92. Ueno K, Kasai T, Brewer G, Takaya H, Maeno K, Kasagi S, et al. Evaluation of the apnea-hypopnea index determined by the S8 auto-CPAP, a continuous positive airway pressure device, in patients with obstructive sleep apnea-hypopnea syndrome. J Clin Sleep Med 2010;6(2):146-151.
93. Nolan GM, Doherty LS, Mc Nicholas WT. Auto-adjusting versus fixed postive therapy in mild to moderate obstructive sleep apnoea. Sleep 2007;30(2):189-194.
94. Gilmartin GS, Daly RW, Thomas RJ. Recognition and management of complex sleep-disordered breathing. Curr Opin Pulm Med 2005; 11(6):485-493.
95. Morgenthaler TI, Kagramanov V, Hanak V, Decker PA. Complex sleep apnea syndrome: is it a unique clinical syndrome? Sleep 2006;29(9):1203-1209.
96. Lloberes P, Ballester E, Montserral JM, Botifoll E, Ramirez A, Reolid A, et al. Comparison of manual and automatic CPAP titration in patients with sleep apnea/hypopnea syndrome. Am J Respir Crit Care Med 1996;154(6 PT 1):1755-1758.
97. Stradling JR, Barbour C, Pitson DJ, Davies RJ. Automatic nasal continuous positive pressure titration in the laboratory: patient outcomes. Thorax 1997;52(1):72-75.
98. Teschler H, Berthon-Jones M, Thompson AB, Henkel A, Henry J, Konietzko N. Automated continuous positive airway pressure titration for obstructive sleep apnea syndrome. Am J Respir Crit Care Med 1996;154(3 PT 1):734-740.
99. Teschler H, Farhat AA, Exner V, Konietzko N, Berthon-Jones M. AutoSet nasal CPAP titration: constancy of pressure, compliance and effectiveness at 8 month follow-up. Eur Respir J 1997;10(9): 2073-2078.
100. Berkani M, Lofaso F, Chouaid C, D'Ortho MP, Theret D, Grillier-Lanoir V, et al. CPAP titration by an auto-CPAP device based on snoring detection: a clinical trial and economic considerations. Eur Respir J 1998;12(4):759-763.
101. Gagnadoux F, Rakotonanhary D, Martind de Araujo MT, Barros-Vieira S, Fleury B. Long-term efficacy of fixed CPAP recommended by Autset for OSAS. Sleep 1999;22(8):1095-1099.
102. Sériès F. Accuracy of unattended home CPAP titration in the treatment of obstructive sleep apnea. Am J Respir Crit Care Med 2000; 162(1):94-97.
103. West SD, Jones DR, Stradling JR. Comparison of three ways to determine and deliver pressure during nasal CPAP therapy for obstructive sleep apnea. Thorax 2006;61(3):226-231.
104. Cross MD, Vennelle M, Engleman HM, White S, Mackay TW, Twaddle S, et al. Comparison of CPAP titration at home or sleep laboratory in the sleep sleep apnoea hypopnoea syndrome. Sleep 2006;29(11):1451-1455.
105. Aloia MS, Arnedt JT, Stepnowsky C, Hecht J, Borrelli B. Predicting treatment adherence in obstructive sleep apnea using principles of behavior change. J Clin Sleep Med 2005;1(4):346-353.
106. Stepnowsky CJ Jr, Bardwell WA, Moore PJ, Ancoli-Israel S, Dimsdale JE. Psychologic correlates of compliance with continuous positive airway pressure. Sleep 2002;25(7):758-762.
107. Weaver TE, Maislin F, Dinges DF, Younger J, Cantor C, McCloskey S, et al. Self-efficacy in sleep apnea; instrument development and patient perceptions of obstructive sleep apnea risk, treatment benefit, and volition to use continuous postive airway pressure. Sleep 2003;26(6):727-732.
108. Weaver TE. Predicting adherence to continuous positive airway pressure – the role of patient perception. J Clin Sleep Med 2005; 1(4):354-356.
109. Krieger J, Sforza E, Petiau C, Weiss T. Simplified diagnostic procedure for obstructive sleep apnea syndrome: lower subsequent compliance with CPAP. Eur Respir J 1998;12(4):776-779.

110. Hoy CJ, Vennelle M, Kingshott RN, Engleman HM, Douglas NJ. Can intensive support improve continuous positive airway pressure use in patients with the sleep apnea/hypopnea syndrome? Am J Respir Crit Care Med 1999;159(4 Pt 1):1096-1100.
111. Jean Wiese H, Boethel C, Phillips B, Wilson JF, Peters J, Viggiano T. CPAP compliance: video education may help! Sleep Med 2005; 6(2):171-174.
112. Lewis KE, Seale L, Bartle IE, Watkins AJ, Ebden P. Early predictors of CPAP use for the treatment of obstructive sleep apnea. Sleep 2004;27(1):134-138.
113. Means MK, Edinger JD, Husain AM. CPAP compliance in sleep apnea patients with and without laboratory CPAP titration. Sleep Breath 2004;8(1):7-14.
114. Popescu G, Latham M, Allgar V, Elliott MW. Continuous positive airway pressure for sleep apnoea/hypopnoea syndrome: usefulness of a 2 week trial to identify factors associated with long term use. Thorax 2001;56(9):727-733.
115. Dinges DF, Pack F, Williams K, Gillen KA, Powell JW, Ott GE, et al. Cumulative sleepiness, mood disturbance, and psychomotor vigilance performance decrements during a week of sleep restricted to 4-5 hours per night. Sleep 1997;20(4):267-267.
116. Dinges DF, Powell J. Microcomputer analyses of performance on a portable, simple visual RT task during sustained operations. Beh Res Meth, Instru & Comp 1985;17(66):652-655.
117. Johns MW. Sensitivity and specificity of the multiple sleep latency test (MSLT), the maintenance of wakefulness test and Epworth sleepiness scale; failure of the MSLT as a gold standard. J Sleep Res 2000;9(1):5-11.
118. Luo X, George ML, Kakouras I, Edwards CL, Pietrobon R, Richardson WS, et al. Reliability, validity, and responsiveness of the Short Form 12-item survey (SF-12) in patients with back pain. Spine 2003;28(15):1739-1745.
119. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996;34(3):220-233.
120. Ware JE Jr, Snow KK, Kosinski M, Gandek B. SF-36 health survey manual and interpretation guide. Boston: Nimrod Press; 1993.
121. Weaver TE, Laizner AM, Evans L, K., Maislin G, Chugh DK, Lyon K, et al. An instrument to measure functional status outcomes for disorders of excessive sleepiness. Sleep 1997;20(10): 835-843.
122. Flemons WW, Reimer MA. Development of a disease-specific health-related quality of life questionnaire for sleep apnea. Am J Respir Crit Care Med 1998;158(2):494-503.
123. Weaver TE, Maislin G, Dinges DF, Bloxham T, George CF, Greenberg H, et al. Relationship between hours of CPAP use and achieving normal levels of sleepiness and daily functioning. Sleep 2007; 30(6):711-719.

Discussion

Gay: Like so many things that have happened to us in the last several years, it seems that our care plans are being dictated by reimbursement rather than by good science. I see the crystal reimbursement ball saying care is being altered in many ways. To some extent we're already talking about how we're going to lose less money doing portable studies than doing in-lab studies. But my interest is really on the other end—the follow-up and care of these patients. Many primary care physicians now do not want to get involved in the complexity of seeing someone between 31 and 90 days. They don't have the various software programs for the different types of devices to get an objective download, and probably the biggest obstacle to this taking off more quickly is that we don't have an autoCPAP code, so how are we going to get the whole treatment covered, short of writing everybody an autoCPAP device and then doing the download and follow-up for next to nothing? That I think is the biggest obstacle.

Kuna: You bring up 2 very important points: any time you ask primary care providers, "Would you like to help manage patients with OSA?" they run away. They are so busy and so constrained within the limited time allotted to care for their patients' diabetes and asthma and other medical problems that to add OSA on top of that is daunting to them.

I agree that an ambulatory management program is not going to be feasible until there is some resolution of the autoCPAP question. There needs to be a reimbursement code for a home, unattended autoCPAP titration study. Furthermore, I would not be surprised if, as the cost of the autoCPAP units continues to come down, autoCPAP replaces CPAP as the standard of treatment. Perhaps patients will automatically be started on autoCPAP and followed carefully to make sure that they have an acceptable clinical response.

Patil: One question with respect to the gates being opened for portable studies is who should perform and interpret those studies. Is this something you think should be implemented within the primary care physician's office, or should third-party payers insist that sleep physicians read portable studies, to improve quality?

Kuna: That is a critical question. Should portable-monitor testing be used by non-sleep specialists? If so, how can one assure its appropriate use? I don't have the answers to those questions. We do not have the needed evidence.

It took 30 years to develop the current asthma algorithms being used in primary care practices. That took large clinical trials asking, "How does this work?" and "What treatments are of benefit?" Inhaled corticosteroids were not part of my asthma toolbox when I was an intern; today they are the foundation of asthma management—the first medicines a primary care provider will reach for to treat asthma.

The challenge to the field of sleep medicine is to develop those types of algorithms, to generate the evidence that tells us how to use portable-monitor testing and whether components of this management can be performed as effectively by non-sleep-specialists. I think Peter Gay is correct that these issues are being driven by reimbursement rules and not science. I was surprised that the CMS [Centers for Medicare and Medicaid Services] made the decision they did in 2008, because it was largely based on one study, the

Mulgrew study,[1] which was a relatively small study and very restrictive in its inclusion of participants.

We need studies that have more liberal inclusion criteria and that evaluate patients with comorbid conditions such as COPD and chronic heart failure. We need prospective studies assessing the cost-effectiveness of ambulatory management pathways. There is only one prospective cost-effectiveness study, and it considered only study-related costs, not total medical care costs.[2] We clearly need more evidence before deciding on best practice.

1. Mulgrew AT, Fox N, Ayas NT, Ryan CF. Diagnosis and initial management of obstructive sleep apnea without polysomnography: a randomized validation study. Ann Intern Med 2007;146(3):157-166.
2. Antic NA, Buchan C, Esterman A, Hensley M, Naughton MT, Rowland S, et al. A randomized controlled trial of nurse-led care for symptomatic moderate-severe obstructive sleep apnea. Am J Respir Crit Care Med 2009;179(6):501-508.

Quan: All the talk is about CPAP, but we know that only two thirds of people will use CPAP on a long-term basis, despite all the manipulations people do to get them to use the device. As more varieties of treatment will come up, I think that one of the flies in the ointment to having primary care doctors treat patients on a long-term basis is that, as the management gets more complex, they are going to be less qualified and willing to do this. You don't see a primary care doctor managing a patient with leukemia, for example, to any great extent, because it's complex, and that muddies the crystal ball as to what will ultimately happen for these patients.

As Sai has published,[1] a little bit of evidence suggests that sleep specialists do a better job than other caregivers in managing some of these patients. We have to look at those things.

1. Parthasarathy S, Haynes PL, Budhiraja R, Habib MP, Quan SF. A national survey of the effect of sleep medicine specialists and American Academy of Sleep Medicine Accreditation on management of obstructive sleep apnea. J Clin Sleep Med 2006;2(2):133-142.

Kuna: I agree. Ambulatory management is not ready for the primary care physician's office. They don't know how to do it, even if they had the time. It would require a lot more medical education and the development of relatively simple, well validated clinical algorithms.

I predict that it may require physician-extenders in primary care who are trained to do this, such as nurse practitioners with special training in sleep medicine that allows them to do patient intake, recognize patients with OSA, and provide follow-up CPAP care. Trained respiratory therapists may be able to coordinate the home unattended testing (providing patient instructions, distributing equipment, and processing the recorded files) at the primary care practice.

Communication with and referral to the sleep specialist will certainly be an essential element to provide the necessary backup. I don't know what primary care algorithm will be optimal, but the technology already available opens up a great many possibilities.

Kapur: Though you're using a simpler device whose output has less data and is easier to review, it may be more complex to manage a patient with it, because there are a lot more things you won't know about the patient. You have to be aware of the limitations. I think these protocols try to get around that by choosing patients with a very high probability of OSA and saying, "If you don't find OSA there, it's still probably there and you need to do another study." I would argue that you need more expertise if you're using portable monitoring on a less restrictive population, to make sure that it's used appropriately.

Kuna: Yes, it is very important that you know the strengths and weaknesses of whatever diagnostic test you use. When people ask me, "How should I start?" I say get a portable monitor, bring it into your lab and run simultaneous recordings with the polysomnogram. Compare the recordings and learn what information you are and aren't getting from the portable monitor. Understanding the performance of the portable monitor will help you to interpret the results of home unattended studies.

Kapur: Regarding the HomePAP study,[1] I see a problem in how it's designed. The group with an AHI of < 15 events/hour leaves the study. In clinical practice you'll obviously still be taking care of these people that we're not informing ourselves on in these studies. Though these folks are coming in with a very high probability of moderate to severe OSA, the studies are excluding a whole group that could end up having an AHI of 10 events/hour and is very sleepy. So we don't know what's happening in that group. Also, I think the exclusiveness of who gets into the studies may limit generalizability; what we found in HomePAP was that using an Epworth Sleepiness Score of ≥ 12 as an inclusion criteria made it very hard to recruit a large number of patients from general sleep clinics. Many patients were very sleepy by other subjective measures but didn't have high Epworth scores.

1. Rosen CL, Auckley D, Benca R, Foldvary-Schaefer N, Iber C, Kapur VK, Redline S, Schmotzer BJ, Zee P. A multi-site randomized trial of portable monitoring and positive airway pressure autotitration versus laboratory-based polysomnography for the diagnosis and management of obstructive sleep apnea: HomePAP study. Sleep 2010 conference. Abstract 0513. http://www.journalsleep.org/pdf/abstractbook2010.pdf. Accessed June 25, 2010.

Kuna: You raise an important issue. In my opinion, symptomatic patients with clinically suspected OSA who have a portable-monitor test that

is negative for sleep apnea should have polysomnographic testing in the sleep laboratory. That will rule out a false negative result on the portable study and look for a possible sleep disorder besides sleep apnea that might explain the patient's symptoms. Most of the protocols using a comparative effectiveness research design allow patients randomized to the home portable-monitor-testing arm to have in-laboratory testing if a home test is negative. Patients also cross over to in-lab testing if the portable study fails due to technical problems. Once the in-lab polysomnogram has been performed, the patient returns to the portable-testing arm and the results are included in the data from that arm in an intent-to-treat analysis.

I do not believe portable-monitor testing will prove useful for everyone. We need to develop better ways to identify which patients are best suited for portable-monitor testing. In my clinical practice, portable studies have been useful to rule in the diagnosis of OSA, not to rule it out. I think portable monitors will end up having a prominent role in managing patients with a high pre-test likelihood of OSA. We need to develop better recognition strategies to identify which patients are the best candidates for portable testing.

Kheirandish-Gozal: A few years ago I heard Colin Sullivan, who is the father of CPAP, say something surprising. He said, "It's been 30-something years and we're celebrating CPAP: isn't it about time to go on and use something else? Isn't it time to find a different solution?" So I'd like to put this challenge to the group: we are talking about perfecting an imperfect device or technique, a method where none of us can agree on the limits of it. We don't agree on normatives, and we don't agree on cutoffs. Everything is arbitrary right now. Isn't it about time that we move onto different diagnostic methods or pathways other than trying to perfect the imperfect sleep studies?

Kuna: The current technologies allow many different approaches to portable-monitor testing. Peripheral arterial tonometry and heart-rate variability are 2 examples of signals that go way beyond the traditional polysomnographic signals. We need to standardize the recordings and decide what signals are best to record. While I agree that sleep testing—even our accepted standard, polysomnogram—is imperfect, much of the current controversy is of our own doing. Most of the portable-monitor studies performed to date have been direct comparisons to polysomnographic testing, comparing one AHI to another. Many of these so-called head-to-head comparisons have been inadequately powered, have not considered the night-to-night variability in AHI, and have used older technology (ie, monitors without the nasal pressure signal). We have only just begun to conduct the comparative effectiveness research needed to evaluate portable-monitor testing.

But your question also proposes that we should be thinking beyond sleep testing and should consider very different approaches to the diagnosis of sleep apnea. I am aware of the innovative studies by your group[1,2] in children identifying specific gene and protein profiles that might provide a fingerprint for sleep apnea. Hopefully, these exciting approaches may eventually lead to a more perfect world. However, my personal opinion is that they will complement sleep testing, not replace it.

1. Gozal D, Jortani S, Snow AB, Kheirandish-Gozal L, Bhattacharjee R, Kim J, et al. Two-dimensional differential in-gel electrophoresis proteomic approaches reveal urine candidate biomarkers in pediatric obstructive sleep apnea. Am J Respir Crit Care Med 2009;180(12):1253-1261.
2. Khalyfa A, Capdevila OS, Buazza MO, Serpero LD, Kheirandish-Gozal L, Gozal D. Genome-wide gene expression profiling in children with non-obese obstructive sleep apnea. Sleep Med 2009;10(1):75-86.

Kheirandish-Gozal: The more we go on, the more the imperfect parts of it are showing; and the more we go on, the less we agree.

Kuna: I do not think we should throw out the baby with the bath water, but the thought has been considered. When CMS was evaluating whether to extend coverage of CPAP to portable monitors, part of that process was to form a Medicare Evidence Development and Coverage Advisory Committee (MedCAC) of independent experts to which CMS submitted questions about sleep apnea and CPAP management. A number of those questions to the MedCAC asked whether any testing was needed. CMS seemed very interested in considering the possibility of just starting patients with a high clinical suspicion of sleep apnea on CPAP treatment—an intervention with minimal risk—without any diagnostic testing! The committee did not recommend this approach, citing that there are no studies evaluating the feasibility of starting treatment without diagnostic testing. But the question is out there, and there were 3 or 4 questions submitted to the committee on that topic.

Maybe in the future we will develop recognition strategies that will allow us to proceed directly to treatment in a subset of patients. Those who show clinical benefit can be continued on treatment. Those who do not show benefit can be scheduled for diagnostic testing. This may not be as heretical as it seems! Case in point is the Sleep AHEAD Study that recruited obese adults with type 2 diabetes.[1] Home unattended polysomnograms at baseline in the 300 people enrolled across 4 different sites revealed that 87% had OSA using the AASM [American Academy of Sleep Medicine] recommended criteria for scoring hypopneas, which is the most restrictive of the hypopnea scoring criteria.[2] When I

show those results to epidemiologists they say, "Start these people on CPAP! Forget the diagnostic testing. You have an 87% probability of a positive test. What do you have in medicine with a higher yield than that? If an obese type 2 diabetic walks into your office, pull a mask off the shelf and start the treatment." Perhaps there will be subsets of patients who benefit from such a streamlined path to treatment.

1. Foster GD, Sanders MH, Millman R, Zammit G, Borradaile KE, Newman AB, et al. Obstructive sleep apnea among obese patients with type 2 diabetes. Diabetes Care 2009;32(6):1017-1019.
2. Iber C, Ancoli-Israel S, Chesson AL, Quan SF; for the American Academy of Sleep Medicine. The AASM Manual for the Scoring of Sleep and Associated Events. American Academy of Sleep Medicine; 2007.

Kheirandish-Gozal: We have done some radical changes. For patients who can't afford a sleep study or don't have insurance, we came up with the idea to do the sleep study *after* the adenotonsillectomy. Just make sure they get that and then get them back so that they can see, because if we have to choose between the two, we prefer to do the one after. However, in some countries I've heard from colleagues that they struggle with getting sleep studies done and it's very costly and it's very problematic. Some countries don't even have something called a sleep laboratory. Obviously, this is something that we need to think about. Just to put out a challenging question, are we going in the right direction? It's been so many years and we're still going to the same option.

Kuna: We'll come back in 20 years and find out whether we went in the right direction. Well conducted science has a way of correcting itself. Usually it will pull you back on course if you start going too far in the wrong direction. But we need science to take the lead and inform healthcare providers, insurance carriers, and health-system administrators on appropriate practices and policies.

Minkley:* When you're talking about a protocol, looking all the way to the end of efficacy and outcomes is important. There are places where the patients can fall through the cracks that become more problematic in portable testing. In the early days of home sleep studies one of the key problems was getting results. The studies showed that for the patients the simpler the device, the more likely they were not to get the results. Some of that responsibility falls on the patient. With a complex, expensive study like PSG [polysomnography] they kind of ask for results; the simpler it is, the more they assume, "Well, if it was something bad, they'd call me." I think it was around 50% in some of the earlier home studies, in contrast to PSG, didn't get results.

When we look at different ways to diagnose and treat OSA, one of the predictors of adherence to therapy is education. The more education a patient has, the more likely they are to remain adherent. A lot of education occurs before, during, and after a complex procedure such as PSG, and if that's not incorporated into a protocol with simpler testing, then our total outcome with adherence and efficacy might suffer.

Kuna: Excellent points. In assessing these pathways you have to do an intent-to-treat analysis, not a per-protocol analysis. You can't just look at the people who ended up on CPAP therapy: you need to look at everybody, even the people who fell out and did not end up on CPAP. CPAP adherence should not be used as the primary outcome. Rather, you should use some functional outcome, such as the Functional Outcomes of Sleep Questionnaire or blood pressure, and assess everybody who is randomized into the study in an intent-to-treat analysis.

Healthy-user bias is an important issue, and we recently published a paper[1] from the Philadelphia Veterans Hospital that looked at the fact that people who take their medications for lipids are more likely to adhere to their CPAP. People who follow the doctor's prescriptions and follow their diet and do their exercise are more likely to adhere to CPAP than people who do not follow these healthy behaviors. So study designs need to factor that in. A good randomization in a clinical trail should equally distribute adherers and non-adherers in all arms of the study.

Patient education is critical, and studies show that patient education improves CPAP adherence. The non-inferiority comparative effectiveness studies are trying to show that clinical outcomes of the portable-monitor testing and polysomnography pathways are equivalent, but we may find that in-laboratory testing produces better outcomes. Patients have greater opportunity to receive support and education about OSA and CPAP when they spend 12 hours in a laboratory with a PSG technologist, perhaps on 2 separate nights. In addition, the technologist can quickly intervene during the in-lab CPAP titration study and help the patient overcome a barrier that the patient may not be able to address at home. The greater support and education received on in-lab testing may result in better clinical outcomes.

1. Platt AB, Kuna ST, Field SH, Chen Z, Gupta R, Roche DF, et al. Adherence to sleep apnea therapy and use of lipid-lowering drugs: a study of the healthy user effect. Chest 2010; 137(1):102-108.

* Pamela Minkley RRT RPSGT CPFT, Home Healthcare Solutions, Philips Respironics, Monroeville, Pennsylvania.