Initial Public Comments for
NCA for Continuous Positive Airway Pressure (CPAP) Therapy for Obstructive Sleep Apnea
(CAG -00093R)
Public Comment Period (April 8, 2004 – May 8, 2004)

Comment #1:
Submitter: Asela M. Cuervo, Senior Vice President
Organization: American Association for Homecare (AAHomecare)
Date: May 7, 2004 5:57 PM
Comment:

The America Association for Homecare (AAHomecare) submits the following comments on the Centers for Medicare and Medicaid ServicesÆ (CMSÆ) reconsideration of the national coverage decision (NCD) on the use of continuous positive airway pressure (CPAP) devices for the treatment of obstructive sleep apnea (OSA) in adults. Currently, the NCD states that only a polysomnogram performed in a facility-based sleep study laboratory may be used to identify patients with OSA who will require CPAP. In response to a request from Dr. Terence M. Davidson, CMS has opened the NCD for reconsideration on whether CMS should permit the use of portable multi-channel sleep testing devices in the home site of service as an alternative to facility based polysomnography for the appropriate patient populations.

AAHomecare represents member companies in every line of service within the homecare community. Our members include home health agencies, and suppliers and manufacturers of durable medical equipment (DME) services and supplies and assistive and rehabilitative technologies. We support a revision to the current NCD to permit the use of portable multi-channel sleep testing devices in the home site of service as an alternative to facility based polysomnography for the evaluation of OSA. Many private sector payers currently recognize the use of home sleep studies for the diagnosis of OSA because this technology is reliable and affordable. Moreover,

it has been widely acknowledged by the medical community that a lack of access to facility based polysomnography presents a barrier to treatment for individuals with OSA. The Medicare program should follow the private sectorÆs lead in recognizing home sleep studies for the evaluation of OSA to improve the availability of sleep testing for patients with OSA.

Background

Sleep apnea is a disorder characterized by periods of apneas and hypopneas (breathing cessation and reduced breathing respectively). Obstructive sleep apnea is a common form of sleep apnea characterized by the partial or complete collapse of the upper airway during sleep. Symptoms of OSA include daytime sleepiness, fatigue, headaches, and cognitive impairment. OSA can lead to serious health risks for the individual, including for example, hypertension. OSA is commonly diagnosed by measuring the number of apneas and hypopneas during a defined period of sleep (the AHI index) and/or measuring the rate of oxygen desaturation during sleep in conjunction with the presence of other symptoms such as daytime sleepiness or hypertension.

While there are a number of treatment options for OSA, including surgery, the most prevalent form of therapy involves the use of a CPAP device. The CPAP forces a flow of air through the airways using a noninvasive nasal interface. The device maintains the airflow at a fixed pressure, forcing the airway to remain open. Since 1987, CMS has covered the use of CPAP devices for patients with ômoderate or severe OSA for whom surgery is a likely alternative.ö The NCD CMS issued in 1987 was consistent with the consensus opinion on the diagnostic criteria for OSA at that time.

In 2001, CMS revised the NCD for the use of CPAP for the treatment of OSA to reflect current diagnostic criteria for OSA. Medicare will cover and pay for CPAP for the treatment of adults with OSA who meet the following diagnostic criteria:

ò AHI > 15 events per hour, or
ò AHI > 5 and < 14 events per hour with documented symptoms of excessive daytime sleepiness, impaired cognition, mood disorders or insomnia, or documented hypertension, ischemic heart disease or history of stroke.

The NCD defines an apnea as the ôcessation of airflow for at least ten seconds.ö A hypopnea is defined as an ôabnormal respiratory event lasting at least 10 seconds with at least a 30% reduction in thoracoabdominal movement or airflow as compared to baseline, and with at least a 4% oxygen desaturation.ö

OSA is typically diagnosed via a laboratory based, attended sleep study (polysomnography) that measures at the least, sleep time through sleep staging and respiration. The Medicare NCD specifically states that the polysomnography used to diagnose OSA must be performed in a ôfacility-based sleep study laboratory, and not in a home or mobile facility.ö CMS is reconsidering this portion of the NCD to allow the use of portable multi-channel sleep testing in the home site of service as an alternative to facility based polysomnography.

Comments

It is widely acknowledged within the medical community that timely access to facility based polysomnography is a hurdle to treatment for patients with undiagnosed OSA. In the Wisconsin sleep cohort study, for example, 93% of women and 82% of men with moderate OSA did not receive a diagnosis. As CMS recognized in the decision memorandum for the NCD on the use of CPAP to treat OSA, the clinical literature establishes that sleep apnea is a risk factor for hypertension and cardiovascular comordbidity. CMSÆ decision memorandum references a number of randomized controlled trials that evaluated the use of CPAP for the treatment of OSA. These studies showed that individuals on CPAP devices had improved outcomes compared to those who

received other therapy. Untreated OSA results in a number of more serious health risks including hypertension as well as other behavioral and cognitive symptoms that can be reduced or avoided with appropriate treatment.

The current NCD for CPAP limits coverage for CPAP to those cases where the OSA was diagnosed during a facility based polysomnography, expressly excluding the use of portable multi-channel home sleep testing for the diagnosis of OSA. This policy is short sighted in light of the documented lack of timely access to facility based polysomnography and the serious health consequences of undiagnosed OSA. In contrast, the private sector, recognizing the importance of timely treatment for OSA, has adopted the use of portable multi-channel sleep studies in the home site of service as an effective alternative to facility based polysomnography. This policy allows payers to reduce both the costs associated with facility based studies and patient care inasmuch as individuals with OSA who are treated with CPAP have better health outcomes.

We are aware of one such program developed by a private sector health maintenance organization in response to backlogs of as much as four months for facility based sleep testing. The program has resulted in savings for the insurer, and its enrollees receive treatment within 30 days. We urge CMS to carefully consider the evidence in favor of adopting this alternative to facility based polysomnography. The available technology is reliable, effective and addresses the lack of timely availability to facility based studies for individuals with undiagnosed OSA.

Conclusion

Based on the foregoing, we reiterate our recommendation that CMS revise the current NCD for CPAP to include portable, multi-channel sleep testing in the home site opf service as an alternative to facility based polysomnography for the appropriate patient populations.

We appreciate the opportunity to submit these comments and remain available to discuss them with you at your convenience. Please feel free to contact me if you have any questions, or if we can be of further assistance.

OSA Diagnosis Bibliography

Peppard P, Young T, Palta M,Skatrud J, Perspective Study of the Association Between Sleep-Disordered Breathing and Hypertension, New England Journal of Medicine 2000; May 11; 342 (19): 1378-1384.

Pack, Allan I., M.D., Sleep-Disordered Breathing, Access Is the Issue, American Journal of Respiratory and Critical Care Medicine 2004; 169: 666-667.

Bahammam et al., Health Care Utilization in Males with Obstructive Sleep Apnea, SLEEP 1999; 22(6): 740-747.

Ip, Mary S.M. et al., Endothelial Function in Obstructive Sleep Apnea and Response to Treatment, American Journal of Respiratory and Critical Care Medicine 2004; 169: 348û353

Pelletier-Fleury, N., Meslier, M. et al., Economic arguments for the immediate management of moderate-to severe obstructive sleep apnoea syndrome, European Respiratory Journal 2004; 23: 53▒ 60.

Shamsuzzaman, Abu S.M. et al, Obstructive Sleep Apnea: Implications for Cardiac and Vascular Disease, Journal of American Medical Association, October 8, 2003; 290(14): 1906-1914.

Comment #2:
Submitter: Anthony Yonkers
Organization: Otolaryngology

Date: May 4, 2004 11:28 AM
Comment:

I agree with the letter sent to you by Dr. Terry Davidson regarding the cost effectiveness of the portable sleep testing devices that can be taken home with the patient.

Comment #3:
Submitter: Bob Ricker
Organization: Rex Healthcare
Date: May 3, 2004 8:38 AM
Comment:

The process of monitoring & managing OSA patients should be completed in an accredited Sleep Laboratory or Sleep Disorders Center. Patients monitored at home can not receive the real time interface with professionals to receive a quality study. It was only 6-8 years ago that the home study polysomnography abuse was laid to rest, please to not give credence to this study and dilute the value of the Sleep Disorders profession once again.

Comment #4:
Submitter: Buddy Marshall
Organization: Baptist Health Sleep Center
Date: Apr 30, 2004 11:37 AM
Comment:

The use of portable multi-channel sleep testing devices is not well defined. Does this mean an attended or unattended study? What parameters will be monitored? Although a cardio-respiratory sleep study may be adequate for identifying clear-cut OSA, it will not provide the information required to identify various sleep disorders such as PLMD, arousal disorders, UARS, and parasomnias. Therefore, if a patient with sleep-related symptoms is negative for OSA based on a multi-channel sleep test, he or she would need further polysomnographic testing. Therefore, testing cost would be increased for these patients as opposed to performing a PSG from the

begining.

In a center such as ours where the majority of patients undergo one split-night procedure for testing and treatment, use of this procedure would only increase the cost of testing. Upon identifying patients with OSA by multi-channel sleep testing, an attended polysomnogram would be required for adequate titration of positive airway pressure and/or oxygen. Again, this can usually be accomplished in one night of in-lab testing.

Comment #5:
Submitter: Jacalyn Courney
Organization: DCHS
Date: Apr 30, 2004 2:13 PM
Comment:

Sleep studies need to be done in a sleep facility. The patient needs to be observed during the study by a trained, competent technician who can make the necessary adjustments if leads are lose, etc. Performing the studies in the home environment will lead to diagnosis being made on poor quality studies, frequent repeat studies, lack of compliance with treatment modalities to name a few drawbacks.

Comment #6:
Submitter: David Polaski, RRT, RPSGT, Manager
Organization: Greenwich Hospital
Date: Apr 30, 2004 2:07 PM
Comment:

Response Re:Request to Allow Portable Sleep Testing in the Home
As Manager of a Sleep Laboratory Accredited by the American Academy of Sleep Medicine and a Registered Polysomnographic Technician, I am writing to express my views on the above proposal.

I do not agree that in-home portable sleep testing is equivocal to complete polysomnographic testing at a facility-based laboratory or center. The arguments proposed by Dr. Davidson are misleading in a number of areas.

First and foremost, patients sent to the Sleep Laboratory are assessed for the presence and severity of a sleep disorder or disorders (the International Classification of Sleep Disorders recognizes over 80 disorders) and not simply for confirmation of a diagnosis. Consequently, to automatically assume that a particular patient has a specific disorder, and that it is exclusive of all others, is somewhat presumptive. Many of these other disorders depend upon the EEG sleep staging for their assessment, otherwise they are missed. And if it turns out that the degree of disease does not correlate with the severity of symptoms and/or if multiple issues are suspected, then a second night of testing in an in-house, monitored facility will be necessary.

In regards to Dr. Davidsonæs comment that split night studies cannot be done effectively in a single night, I disagree. Because we use EEG for sleep staging, we can accurately assess 1-2 complete sleep cycles (REM and all non-REM sleep stages) with absolute certainty, and do this within 3 hours, leaving us with 3-4 hours for CPAP titration. We also have critical value triggers that allow us to intervene automatically when certain parameters are seen. The unattended in-home data cannot be analyzed on the fly, so there is no option to allow for timely intervention; the patient must get a second night of study regardless. That strikes me as inconvenient, at the least.

After seeing and reviewing thousands of PSG performed in a sleep laboratory, I also take exception to the implication that studies must be performed in the patientÆs own home and bed in order to accurately reflect sleep. Without monitoring EEG, one does not know objectively what the quality of sleep is, so that statement cannot be scientifically made. And since the patient is still connected to a number of wires, belts and electrodes, knows he is having a test done, and probably had a stranger in his home for the set-up (I truly hope that the patients would

not be getting ôtake-home do-it-yourselfö testing), this cannot hardly be construed as a ônormalö nightÆs sleep; yet, without EEG, we donÆt know that.

Frequently, during a sleep study, belts, electrodes, etc. must be repositioned, adjusted or replaced during the night. In an unattended home study, there is no way to address this. The data is lost or unusable. I am also familiar with the studies Dr. Davidson refers to. They were performed in by reputable laboratories using highly qualified technicians. Therein lies one of the major issues. It is implied that the high laboratory standards seen in these studies will also occur in the organizations doing portable studies in practice, and I can assure you that will not be the case. In my experience, individuals placing portable boxes in patientsÆ homes are marginally trained at best, because thatÆs the nature of the beast. The home-study companies are not going to be paying extra for qualified PSG technicians to do set-ups when they donÆt have to û therefore, this quality argument cannot be used here because the variables are entirely different.

I also do not agree with the notion that ôSBD is under-diagnosed in large part due to a limited number of sleep diagnostic facilitiesö. While SBD is indeed under-diagnosed, there are a number of reasons for this, including a lack of patient-education and failure of the patient to accept or act when confronted with the disease. If there are areas that do have long waiting lists for PSGs, I still do not think that the answer should be widespread proliferation of portable units. Issues in these local areas should be addressed locally. If more in-house sleep facilities must be created, so be it. The number of these facilities continues to increase, with many resourceful ideas to control costs without sacrificing quality. Allowing the placement of portable testing units should be neither the quick-fix nor the long-term solution.

Finally, I must take personal exception to the claim that arousal scoring has a high degree of ôinterpreter variabilityö. Arousal scoring has specific criteria defined by the American Sleep Disorders Association, and qualified scoring technicians will generally have a 95% rate of agreement.

The only way to guarantee a quality study, then, is to have it performed in a reputable sleep center or laboratory. While we urge all centers and laboratories to be accredited through he American Academy of Sleep Medicine, at least virtually any in-house sleep testing facility has some governing body overseeing the quality program, whether it is a State Agency, the Joint Commission of Hospital Accreditation, and/or internal review organizations such as their quality assurance departments.

I therefore strongly urge maintaining the standards as they are currently written. Thank you.

Comment #7:
Submitter: Greg Omlor
Organization: Akron Children's Hospital
Date: Apr 29, 2004 9:18 PM
Comment:

My comment is about the utility of portable multi-channel home sleep testing devices as an alternative to facility-based polysomnography in the evaluation of OSA. Any decision that is made should not be applied to pediatrics. There is not data that home testing in pediatric patients is accurate.

Comment #8:
Submitter: Harold Finn
Organization:
Date: Apr 30, 2004 7:39 AM
Comment:

I believe that it would make ALOT of sense to allow the studies to be performed in the homw. I

believe after many years of experience that the best results would be in the nnatural environment that the patient normally slepps in. We try in the labs to mimick the home enviroment, but it is VERY obvious that we are not. The home study would give us a much truer result.
EXCELLENT IDEA Thank you

Comment #9:
Submitter: Heather Highlander
Organization: Association of Polysomnographic Technologists
Date: Apr 30, 2004 7:59 AM
Comment:

Be careful here.
There are many "nonfacility" sites, which do an excellent job at accurately diagnosing and treating OSA (Neurologists for example, who have been diagnosing and treating OSA many years before "facility/accreditied sites" existed).

Excluding those sites will severely limit those Medicare recipients to potentially life saving care.

Also keep in mind that the National Board of Medical Specialties have never formally recognized the American Academy of Sleep Medicine. Limiting diagnoses and treatment to those AASM "approved" sites thus relies upon an organization with no real credibility in the medical profession.

Please make a very informed decision.

Comment #10:
Submitter: Lorelei Heineman
Organization: The Sleep Disorders Center
Date: Apr 30, 2004 1:02 PM
Comment:

Home study equipment for CPAP titration is still not reliable, and should be done under a technician's direct supervision. May be useful for retitration needs depending on the system.

Comment #11:

Submitter: Iain Boyle
Organization: Frisbie Memorial Hospital
Date: Apr 30, 2004 8:59 AM
Comment:

Home based diagnostic studies are no more comfortable than studies based in a sleep center. Also EEG patterns MUST be measured in a diagnostic study, it is after all a sleep study not a nocturnal breathing study. To even attempt to titrate CPAP without a SLEEP MEDICINE TECHNOLOGIST in attendance is so ridiculous a proposal that it does not even deserve commenting upon. If this group wishes to relook at criteria for diagnosis and treatment of SLEEP RELATED BREATHING DISORDERS, then revisit the need for a 4% drop in O2 sat for scoring a hypopnea, and make it either the drop in O2 sat or an arousal.

Comment #12
Submitter: Kevin Justice
Organization: Summit Medical Center - Center for Sleep Health
Date: Apr 29, 2004 7:17 PM
Comment:

Significant quality issues are well documented across the country regarding home sleep testing procedures, mainly those provided by inexperienced and/or unqualified labs and home care companies.
I submit to you it would be irresponsible for CMS to approve coverage for home testing for OSA, or any other sleep disorder, unless provided by an AASM accredited facility.

Only AASM accredited centers are held to a higher standard of maintaining quality & excellence within their respective programs. It is difficult enough to achieve & maintain quality in a home testing environment through experienced sleep programs, let alone allowing non-accredited, non-accountable progams & companies to provide this service.
Please consider carefully!... these are very expensive procedures, and left to those who are not held accountable to higher quality &

standards, mistakes will continue to be made, quality will suffer, and the expense of diagnosing & treating the millions with sleep disorders will continue to rise.

I also submit to you that strong consideration be given to approving coverage for all types of sleep testing, but only to those who have achieved AASM accreditation status.

Comment #13
Submitter: Camden McLauglin
Organization:
Date: May 2, 2004 8:03 PM
Comment:

Beleive that this is not in the best interest of

Comment #14
Submitter: Philip Becker, MD
Organization: Sleep Medicine Institute
Date: Apr 30, 2004 11:01 AM
Comment:

I DO NOT CURRENTLY SUPPORT the NCA that requests multichannel home recording for testing of sleep disordered breathing as proposed by Dr. Terence Davidson. There may be a qualified role for home testing of sleep disorders, but the issue is complex. It is not true in Dallas-Fort Worth that laboratory sleep testing is scarce. In fact, there is an over supply of testing beds since there are many new providers with little experience in the field of sleep medicine. As Chair of the Health Policy Committe of the AASM, I made the request of the AMA CPT Coding Committee, RUC, and HCFA in 1991-92 to allow various sleep testing codes, including ambulatory monitoring. It was the HCFA Medical Director, Dr. Bart McCann, who stated that home testing would be frought with the potential of abuse by unqualified practitioners.

Research to date more commonly demonstrates that patients SLEEP LESS when monitored at home. It is common to see the patient with the most

disturbed sleep to have the most significant difficulty with home monitoring.

Dr. Davidson also highlights the concept of sleep disordered breathing (SDB), rather than just sleep apnea. SDB encompasses subtle breathing events such as upper airway resistance-related arousals (UARA). UARA are defined by EEG AROUSAL, which requires brain electrical recording. It is my opinion that the sleeping EEG is an essential feature to record difficult patients and subtle breathing changes that lead to arousal.

The American Academy of Sleep Medicine has practice parameters that should be considered in any analysis of this request.

I also wish to point out that Dr. Davidson is a consultant to ResMed, a company that manufactures the home testing equipment described and will directly benefit from sales of their CPAP units. Dr. Davidson has done research and published a Sleep Primer on behalf of the company. Although Dr. Davidson is an experienced surgeon on faculty at a respected medical school, he is a fairly recent member of the American Academy of Sleep Medicine (Member # 5895 out of ~8500 members). I would think it prudent to determine the relationship and any conflicts of interest among the parties requesting the change.

This request represents a potential "sea change" in the manner of testing and in the provider of service. I would predict a 10-fold increase in the volume of testing for SDB in Medicare beneficiaries. The quality of tesing will also fall in view of the lack of qualification on whom might do the testing.

I recommend denial of this request until thorough study has been completed.

Comment #15
Submitter: Phillip Porte and Steven Zimmet, MD

Organization: Nat'l Ass'n for Med. Direction of Resp. Care
Date: May 8, 2004 5:14 PM
Comment:

The National Association for Medical Direction of Respiratory Care (NAMDRC) welcomes the opportunity to comment on the issue of portable sleep testing.

Conducting sleep studies in a patientÆs home raises numerous issues revolving around quality of testing, access, and costs.

- NAMDRC readily acknowledges that the clinical literature regarding home testing is not supportive, but many of these publications were based on outdated equipment and widely variable protocols. However, there is little doubt that as the technology capable of providing diagnostic information evolves, a payment system ought to be in place under appropriate circumstances. Those circumstances might include:

- A formal relationship with a facility based sleep laboratory that is accredited/approved by an appropriate body such as JCAHO, AASM, etc. to insure quality control. A care plan involving those appropriately trained and adept with the care of patients with sleep disorders is also a must.

We believe that the current technology associated with home sleep studies can generate important information that could appropriately shorten the time to access full, multi-channel sleep studies. There is no question that timely access to sleep laboratories is a significant problem, and that a reimbursement structure that would permit home sleep studies under some circumstances would address part of that access issue.

- Consideration should also be given to performing followup studies for patients already using equipment for sleep disorders to obviate the need for repeat studies in the lab.

We appreciate the opportunity to comment on this matter and certainly would be glad to offer our guidance and expertise to CMS.

Comment #16:
Submitter: Renee Meyer
Organization:
Date: Apr 30, 2004 2:29 PM
Comment:

Please be informed that the home testing equipment for OSA sleep studies is subject to many inaccuracies if not monitored by a polysomnography technician. This is very important to correct diagnoses.

Comment #17:
Submitter: Robert Garcia
Organization: Sleep Dynamics
Date: May 7, 2004 12:43 AM
Comment:

The use of multi-channel home sleep testing as an alternative method for determining OSA should be available for:
1. Patients with medically limitating diseases that prohibit travel to an overnight facility.
2. Single parents.
3. Patients with reported history of difficulty sleeping away from home.
4. Re-evaluation for patients with recurring symptoms of OSA.
5. Evaluation of patients needing readjustment of CPAP pressures.

Technology continues to produced smaller, lightweight portable multi-channel devices that are a significant improvement from early models.

Comment #18:
Submitter: Shawn Kimbro, RPSGT
Organization: Sleep Affiliates, LLC
Date: Apr 29, 2004 3:56 PM
Comment:

Please do not approve changes to CIM 60-17 without *valid* long-term scientific evidence. Current evidence does not support use of home based systems for CPAP titration. Our experience shows vast differences in titrated levels of patients tested outside an accredited diagnostic sleep testing facility. A bad decision in this regard could have life-threatening consequences.

Comment #19:
Submitter: Steve Riggs
Organization: Metroplex Health Systems
Date: Apr 29, 2004 5:12 PM
Comment:

I think with a little research that the complexity and the literal healthscape that is effected by OSA that doing studies in a sleep lab with an attending technician are warranted.

Having been charged with overseeing a sleep lab for three years I have come to appreciate that OSA can be masking overt central hypopneas along with a myriad of other sleep related disorders that will washout and not be attended to without a comprehensive sleep lab study. Along the lines of that thought the observations and interventions by a trained lab attendant is crucial.

While understanding that there are people and equipment suppliers looking for a healthy reimbursement along with minimal outlay for equipment and manpower wages I cannot support in good conscience studies at home that target a portion of the problems of sleepers that can only be unmasked in a sleep lab.

Comment #20:
Submitter: Susan Anderson, M.D.
Organization: Sleep Disorders Center & Neurology Practice
Date: Apr 29, 2004 10:08 PM
Comment:

It would be completely irresponsible and inadequate to do home studies for evaluating patients for sleep pathologies, including obstructive sleep apnea. Anyone who is appropriately traines/educated in this field is well aware of the variety of variables that can affect sleep, saturations, arousals, and sleep stages. There is no way that a home, unattended study can provide the needed information. Unfortunately, it can also allow patients to be assumed (incorrectly!) as NOT having a sleep pathology, or NOT having OSAS, when they really DO have it, because it will not pick up underestimated apneas, upper airway resistance, central vs obstr. pathologies, as well as other sleep pathologies. It will also grade zero for people who may not attain REM or delta sleep ! This is irresponsible !!!

Comment #21:
Submitter: Keith Thornton, D.D.S
Organization:
Date: Apr 30, 2004 1:10 PM
Comment:

One of the best papers on the problems and use of polysomnography was an abstract published in the abstract book of the American Professional Sleep Society by Milton Kramer, Bethesda Hospital, Cincinatti, Ohio. He did a follow-up on over 7000 patients referred to his sleep lab with a tentative diagnosis of sleep apnea by history. 25% refused the test (cost, etc?), 24% did not have sleep apnea bad enough to warrant cpap, 13% did not return for cpap titration, 10% chose another treatment, 8% rejected cpap at trial, 8% stopped wearing the cpap which leaves a yield rate of 12% of all those referred to a sleep lab. In numerous other studies the average use of cpap is about 4.5 hrs. per day, 5 days a week. The comments by Kramer wereô The diagnostic and treatment process in somnology , at the clinical level, needs to be more carefully and systematically scrutinized."
ôWe have an effective, but burdensome, treatment for OSA. Utilization of the treatment remains an enormous problem."
In this study, a minimum of 75 polysomnograms were done for the 12 that wore a cpap.
At present, I am using the Remmers Sleep

Recorder which has level 1 evidence comparing it to the polysomnogram (97% correlation). I am using it with the TAP oral appliance to treat cpap and surgery failures. I do both a before and after study to confirm efficacy. The device can be adjusted so that the jaw is maoved foward until the patient's apnea is below 15 with elimination of symptoms. The pertinant peer reviewed papers are as follows: Obstructive Sleep Apnea, Flemons, N Engl J Med, Vol.347, No.7, Aug 15, 2002; Automated Analysis of Digital Oximetry in the Diagnosis of OSA, Vasquez, Thorax 2000, 55:302-307; Evaluation of Variable Mandibular Advancement Appliance for the Treatment of OSA, Pancer et al, Chest/116/6/Dec. 1999.

Using this algorithm, I get a better than 90% success rate. In many cases, I have to do several studies to adjust the protrusion of the mandible to eliminate both the apnea and symptoms. The patients I treat include severe apnics. "Studies have shown that the TAP has stopped snoring in more than 96%* of patients who wear the appliance, making it more successful than any other oral appliance currently available. It is also the only oral appliance proven effective for the treatment of severe obstructive sleep apnea.

* Chest. 1999; Vol. 116, pages 1501-1503
"Treatment of Sleep Apnea"
by Peretz Lavie, PhD

The unfortunate issue is that Medicare does not cover oral appliances unless a patient has a polysomnogram and has failed cpap. In my experience, the failed cpap patients will not return for a follow-up polysomnogram and insurance does not pay for ambulatory monitoring. Virtually all my patients whom I treat, feel that the psg is a waste of time and will not go back to it. They would prefer to pay out of pocket the $150 I charge for the home study.

Probably the best algorithm would be to start people on an autocpap which could both diagnose

and treat people at the same time and would eliminate those that couldn't or wouldn't wear it.

Finally, Medicare should look into the effectiveness of oral appliances. If compliance is considered, the effectiveness (reduction in RDI times compliance) is considerably better with oral appliances than with cpap.

If you then consider the cost of diagnosis and treatment with the great numbers of people who can't wear cpap, oral appliance therapy using home monitoring bocomes just a fraction of the cost of psg's and cpap.

Comment # 22:
Submitter: Daniel Ventimiglia
Organization: Tampa General Hospital Sleep Disorders Center
Date: Apr 30, 2004 10:42 AM
Comment:

Although there are not enough centers to accomadate the growing population of OSA patients. I find it very concerning that we take the polysomnography and "water it down" to get as many people treated. It seems instead of allowing the professionals who are trained to review sleep, we will allow all persons who can see if a person has enough desats to be placed on CPAP. I have been trained and work with many board certified sleep doctors to know that the best diagnosis is one that takes into account the whole picture, not bits and pieces as to what is being proposed. I see a place in home studies but not on the large level that has been proposed. If this change is allowed to go through how can anyone be comfortable that there diagnosis is complete. I believe it would not instill the confidence people have in the present testing we have at this time. This test is a change in someones life for the rest of thier life in most cases. How can anyone feel it is okay to discount or reduce the necessary parameters to make such a life changing decision/treatment.

Comment #23:
Submitter: David Steward, MD

Organization: University of Cincinnati College of Medicine
Date: Thu, Apr 15, 2004 2:50 PM
Comment:

I am in favor of a change of policy regarding multichannel home sleep testing.

Comment # 24
Submitter: Bruce Reisman, MD
Organization:
Date: Wed, Apr 21, 2004 1:06 AM
Comment:

I am a practicing Otolaryngologist in California. I am intimately involved with the diagnosis, care and testing of patients with Obstructive Sleep Apnea (OSA). The past decade has seen an explosion of technology with regards to the diagnosis and treatment of OSA. The quality and validity of in-home testing has been improved by this advance of technology. I am quite confident that patients are only benefitted by the availability of in-home testing.

There are many instances where a polysomnogram done in a sleep lab has to be repeated because of the foreign nature of sleeping in a lab. In-home testing obviates this problem. The tests that are done in-home are frequently scored by board certified physicians and always by people highly trained in polysomnography.

There are limited accredited sleep labs in my area. Allowing patients to have the opportunity to have in home testing for OSA will help prevent access to care problems as the diagnosis of OSA becomes ever so increasingly common in our society. It need not be mentioned that in-home testing is much more cost-effective.

Please give this issue the high consideration it deserves.

Comment #25:
Submitter: Kent S. Wilson, M.D.
Organization: Midwest Eye & Ear Institute, Suite 120
Date: Thu, Apr 22, 2004 11:22 AM
Comment:

We hope you will modify Medicare policy to allow multichannel home unattended testing to diagnose OSA. We have employed the WatchPat 100 device and find it cost-effective, reliable, and easy to use. It achieves diagnostic results promptly at a low cost and allows rapid institution of treatment.

Comment #26:

Submitter: Woodson, B. Tucker, MD, FACS
Organization: Diplomat of the American Board of Sleep Medicine
Date: Tue, Apr 20, 2004 6:37 PM
Comment:

Dr Davidson's letter is clinically sound. Many of the arguments supporting full polysomnography as the only means of confirming the diagnosis of OSA border on scientific nihilism. One only needs to try to evaluate the recent position and review papers to realize the scientific argument is being manipulated. As the director of an accredited sleep center, I am fully aware that no test including PSG is perfect. Yet, there is ample evidence that many cardio respiratory devices can diagnose and assess severity in many subsets of OSA patients. There is also vast clinical experience that indicates that the addition of EEG and EMG data do not significantly alter diagnostic outcomes for sleep disordered breathing.

A major problem is that devices performance in patient populations and diagnostic environment widely differs. Although, many are likely adequate diagnostic tools, there is very scattered comparative information. Blanket acceptance of all OSA diagnostic devices is unsound but given the huge current and future need for such devices, all should not be excluded. I would support Medicare altering its policies on sleep studies.

Comment #27:
Submitter: M. Boyd Gillespie, MD
Date: Fri, Apr 23, 2004 10:15 AM
Comment:

I am an otolaryngologist in academic practice at the Medical University of South Carolina. I am writing in favor of home sleep testing by qualified physicians with an interest in sleep apnea. I do not perform these studies myself, but I have reviewed the literature with regards to home testing. I would like to share several observations with you:
(1) Home testing is less invasive and less expensive.
(2) Home testing is more natural, and therefore my provide a better picture of the patient's sleep disorder in the patient's normal sleep environment.
(3) The correlation between home testing and sleep lab polysomnography is excellent. Most of the major studies on sleep apnea (Wisconsin Sleep Cohort and Sleep heart Health Study) have used home testing devices.
Thank you for your consideration on this matter. I think it is important to give patients and their physicians as many options as needed in the evaluationa nd management of this chronic disorder.

Comment #28:

Submitter: W. Curtis Whisler
Organization:
Date: Wed, Apr 21, 2004 4:48 PM
Comment:

Dr. Sanders, I understand you have recently received a request from Dr. Davidson to reconsider the role of multichannel unattended sleep studies. I want to let you know I support this whole-heartedly.
We have been using the Watch-PAT system from Itamar since July 2003 with great success in our clinic. Not only have we performed over 40 studies in the patients home without a single problem reported from the patients, but we have significantly reduced the price of health care by going this route. By the time the patient has seen me for an initial visit, sleep study and follow-up visit, we are still costing the patients and insurance companies less than 1/4 of what a PSG costs.
In addition to cost savings, the procedure at our clinic keeps patient care in the primary care physician's office allowing us to coordinate care and follow-up efficiently. For example, I may see a patient on a Monday to discuss fatigue, snoring and obesity. If the screening questionnaire is positive, placing the patient at high risk for having OSA, I will then teach the patient how to use the Watch-PAT system. That night they will complete the study, return the unit to me on Tuesday for downloading and interpretation of the data. I will call them back in a couple of hours and as soon as that evening I can have them seen by the respiratory therapist and on an autotitration of CPAP
Because of this smooth flow and centrally located care our patients get follow-up at each and every visit regarding their sleep apnea.
The value of what I have discussed can't be underestimated. Our patients have been extremely pleased with the testing and treatment. I know that I have made a positive impact on each person I have tested and treated for OSA using the home based Watch PAT system.

Comment #29:
Submitter: Jose Loredo, MD, MS, FCCP
Organization: UCSD School of Medicine
Date: Tue, Apr 20, 2004 8:02 PM
Comment:

I am writing this letter to urge you to help change CMS policy so that it will accept the use of multi-channel unattended home sleep studies (Type 3 studies) for the diagnosis and the treatment with CPAP of obstructive sleep apnea(OSA) in patients with a high likelihood of the disease (history of chronic snoring, excessive daytime somnolence, observed apneas by family members, obesity).

The prevalence of symptomatic obstructive sleep apnea in the general

population is at least 2-4%, which probably a gross underestimation, and in some populations such as veterans and patients with chronic renal failure, can be as high as 40%-50%. I am sure that you are aware of the grave clinical and social consequences and the medical and social costs of not diagnosing and treating this condition. It is virtually impossible to timely diagnose and treat a condition with such a high prevalence in a tertiary care setting, as is in the attended sleep lab. The regulation that OSA can only be diagnosed in the attended lab by polysomnography has created a virtual bottle neck in helping these patients.

There are numerous studies, all of which have evaluated type 3 portable sleep recording equipment, looking at the accuracy of diagnosing OSA in patients referred because of symptoms suggestive of sleep disordered breathing. The correlation of the AHI with polysomnography ranged from 0.63 to 0.94 and the accuracy compared to polysomnography in diagnosing OSA was almost 100% in each study. What is also important from the CMS policy point of view is that unattended home sleep studies cost about 1/4 of the attended polysomnograms. The Sleep Heart Health Study has put to rest the idea that home sleep studies are not feasible or not acceptable to the patient or that the patient sleeps better in the lab in a strange bed (more than 6,000 subjects and more than 7,000 home unattended polysomnograms). I have taken the liberty to attach below a number of recent references that support the feasibility, accuracy, acceptance by the patient, and economical claims for unattended home sleep studies:

1. Redline S, Tosteson T, Boucher MA, Millman RP. Measurement of sleep-related breathing disturbances in epidemiologic studies. Assessment of validity and reproducibility of a portable monitoring device. Chest 1991;100(5):1281-1286
2. Coppola MP, Lawee M. Management of obstructive sleep apnea syndrome in the home. The role of portable sleep apnea recording. Chest 1993;104(1):19-25
3. White DP, Gibb TJ, Wall JM, Westbrook PR. Assessment of accuracy and analysis time of a novel device to monitor sleep and breathing in the home. Sleep 1995;18(2):115-126
4. Whittle AT, Finch SP, Mortimore IL, MacKay TW, Douglas NJ. Use of home sleep studies for diagnosis of sleep apnoea/hypopnoea syndrome. Thorax 1997;52(12):1068-1073
5. Ancoli-Israel S, Mason W, Coy TV, Stepnowsky C, Clausen JL, Dimsdale J. Evaluation of sleep disordered breathing with unattended recording: the NightWatch System. J Med Eng Technol 1997;21(1):10-14
6. Parra O, Garcia-Esclasans N, Montserrat JM, et al. Should patients with sleep apnoea/hypopnoea syndrome be diagnosed and managed on the basis of home sleep studies? Eur Respir J 1997;10(8):1720-1724
7. White DP, Gibb TJ. Evaluation of the Healthdyne NightWatch system to titrate CPAP in the home. Sleep 1998;21(2):198-204
8. Davidson TM, Do KL, Justus S. The use of ENT-prescribed home sleep

studies for patients with suspected obstructive sleep apnea. Ear Nose Throat J 1999;78(10):754-762
9. Fletcher EC, Stich J, Yang KL. Unattended home diagnosis and treatment of obstructive sleep apnea without polysomnography. Arch Fam Med 2000;9(2):168-174
10. Lloberes P, Sampol G, Levy G, et al. Influence of setting on unattended respiratory monitoring in the sleep apnoea/hypopnoea syndrome. Eur Respir J 2001;18(3):530-534
11. Golpe R, Jimenez A, Carpizo R. Home sleep studies in the assessment of sleep apnea/hypopnea syndrome. Chest 2002;122(4):1156-1161
12. Dingli K, Coleman EL, Vennelle M, et al. Evaluation of a portable device for diagnosing the sleep apnoea/hypopnoea syndrome. Eur Respir J 2003;21(2):253-259

I am acquainted with the recent review of the unattended home sleep study literature published in Chest and a distillation of it in Sleep 2003;26(7):907-913. The joint commission concluded that type 3 sleep studies were not adequate to diagnose OSA due to the lack of evidence after they disqualified most studies from consideration because they did not meet their level of evidence. They did not take into consideration that all of the current literature was designed to use Type 3 studies in patients at high likelihood of having OSA. I have recently been in meetings where some of the members of the joint commission were presenting these findings, and they had to agree, that the evidence that Type 3 studies are effective in diagnosing OSA in the suspected patient is strong. However, this evidence (references above), did not meet their prescribed scientific criteria.
Also, when pressured, most sleep clinicians will agree that once a study shows you an AHI of >15/hr in a patient who snores, has excessive daytime somnolence, observed apneas, and is obese, there is no need to have EEG recording of sleep as required by Medicare.

I am suggesting that unattended multi-channel home sleep studies (type 3) should be acceptable for diagnosing and treating with CPAP patients with a high likelihood of having OSA. These studies should be capable of full disclosure of at least 4 channels: oximetry, airflow by nasal cannula or thermistor or both, respirtory effort by impedance or piezoelectric band, and heart rate. Also all studies should be reviewed and scored manually to assess artifacts, and determine quality of the recording. Finally, the recording has to be interpreted by a Clinician (MD or PhD) with experience in the diagnosis and treatment of obstructive sleep apnea who would be qualified not just to make a diagnosis, but to make treatment decisions and recommendations.

Thank you very much for your help in helping us care for our patients.

Comment #30:

Submitter: Jimmie Daugherty
Organization:
Date: Mon, Apr 26, 2004 5:53 PM
Comment:

This will be a bad idea. These systems are much cheaper and this will allow more people to set up shop. The market will be flooded with bad companies. This also means that many dme providers will conduct these studies as well. I think this will open the door to more fraud in the future. I do not see how a patient can a sleep study performed in the home unattended and have the same quality. BAD IDEA!

Comment #31:
Submitter: Dee Clower
Organization: VitalCare HME, Inc.
Date: Tue, Apr 27, 2004 7:57 AM
Comment:

Medicare has stopped paying for these sleep studies, for various reasons. That is why there are a lot of patients that are not willing to go and get them done anymore. We hear more and more that "I wound up having to pay out of pocket for the sleep center to test me overnight, and I was not even sure I was sleeping well." This is not working well for the patients that do not have the money to do so. Word of mouth spreads fast when you are in a remote area as we are.

People are scared to go in and have this done at the sleep center and they are telling us that it would work better if someone could just come to their home. "How can the test be accurate, when I do not sleep anywhere but at home, normally?" The sleeping in a different bed is also a great issue. The PSG, I do believe, can not be 100% accurate when you are sleeping in a different bed then your own. How do you sleep when you are in a hotel room, or at someone else's house? I know that my patients and myself, sleep a whole lot different than what we would normally sleep. When I stay in a hotel, I wake up 4-5 times a night. I do not feel 100% rested at all. Please take at least this into consideration.

Comment #32:
Submitter:Duane_Ridenour
Organization: QS/1 Data Systems
Date: Mon, Apr 26, 2004 11:42 AM
Comment:

I believe it is a good idea to allow for home sleep studies in determining a diagnosis of OSA for patients who may need a CPAP. In home studies provide the beneficiary a familiar environment in which to sleep providing for a more accurate picture of how the patient sleeps. Studies performed in a sleep lab are not consistent with home sleep. Consider, for example, the fact that the beneficiary spends nearly an hour in being connected to the leads and then is awakened much earlier than they would normally arise.

Coupled with the fact that most people sleep better in their own bed, it is possible that beneficiaries are not getting the deep sleep that is necessary for a more accurate diagnosis.

Thank you for your consideration,

Comment #33:
Submitter: David Long, RRT
Organization:
Date: Tue, Apr 27, 2004 10:22 AM
Comment:

My name is Dave Long. I am a Respiratory Therapist from Rocky Mount, NC. I think home based sleep testing is a viable option that should be considered. There are pros and cons. I'm sure you would save a ton of money for one, and being a OSA patient myself, testing in my home enviornment would have made alot of sense for comfort reasons. I think many more people would have access to therapy this way. I understand that there will be a percentage of patients that would require a full labaratory work-up, but I beleieve that the majority of OSA can be non-invasively treated at home without ever visiting a lab. Thank you for reviewing my comments.

Comment #34:
Submitter: Jane C. Hodges, R PSG T
Organization: Doctors Hospital Center for Sleep Disorders
Date: Wed, Apr 28, 2004 10:11 AM
Comment:

This letter is in response to the request of Dr. Terence M. Davidson to include the use of portable multi-channel home sleep testing devices as an alternative to facility based polysomnography.

Being in sleep medicine for the past 15 years, I have dealt with both home sleep testing and facility based monitoring and feel that facility based monitoring should be the gold standard for the evaluation of OSA.

Home sleep testing has both advantages and disadvantages. The advantages include the patient sleeping in their own bed and the cost may be less, but that is all. The disadvantages include:
1. Wires falling off despite electrodes being secure during hookup. Once the wires fall off, information is lost and the study must be repeated.
2. Patients reliability in operating equipment. i.e. turning equipment on.
3. Pulse oximeters reliability for desaturations if probe becomes loose or patient is sleeping on arm.
4. Patient compliance. i.e. pulling off electrodes during the night and

deciding to quit procedure.

Dr. Davidson is also requesting that EEG and EMG recording not be used for home studies because of the high interpreter variability and that EEG and arousals make little difference.
I disagree with his statement.

Since I have scored thousands of studies over the past decade, I know the importance of EEG, EMG and arousals can make a difference in not only SDB but other disorders as well. Some patients with a suspicion of OSA may have other underlying sleep disorders that may go undetected without full polysomnography. Other disorders include Restless Leg Syndrome, Periodic Leg Movements of Sleep, seizure disorders, or REM Behavior Disorder. This physician may be treating one incidence of a sleep disorder but the patient's underlying daytime sleepiness may not be treated thus resulting in another full polysomnography at a facility or the patient may undergo Multiple Sleep Latency Testing.

At our facility, we discourage split night testing unless requested by the physician or insurance company. If the patient does not meet Medicare guidelines for the split night, then CPAP is not added and patient returns for a second night. We have 4 beds that operate 7 days a week. Our wait time is 10-14 days for scheduling and we provide a comfortable atmosphere for our patients. There are 9 other facility based sleep labs in our area which provide the same service.

Polysomnography studies should be interpreted by an MD, DO or PhD who is board certified by the AASM or had experience in a sleep lab facility. Allowing home sleep studies to be performed by a greater number of practioners will only jeopardize the sleep profession. If home based PSGs are allowed by CMS, then individuals who are not qualified or have a full understanding of sleep medicine will be performing these studies.

I ask that you please continue to use the national determination for diagnosis and treatment of OSA and NOT USE home testing.

Thank you for your time in this matter.

Comment #35:
Submitter: Dr. Martin Hopp
Organization: Cedars-Sinai Medical Center
Date: Tue, Apr 27, 2004 2:48 PM
Comment:

This letter is in support of Sr. Davidson's proposal in support of multichannel home sleep testing. This will enhance the health care of

many patients.

Comment #36:
Submitter: Lawrence E. Kline, DO, D.ABSM, FACP, FCCP
Organization: The Scripps Research Institute
Date: Thu, Apr 29, 2004 12:24 AM
Comment:

To my knowledge Dr. Davidson is not trained in sleep medicine and is an ENT surgeon on the board of ResMed a large manufacturer of CPAP and testing devices. There are much better sources of evidence based thinking on this issue that won't threaten care and elevate testing costs. A non conflicted scholarly review of options for diagnosis and treatment that serves patients in a cost sensitive manner is appropriate. Reliable testing that clearly is needed for therapeutic decision making is key. Allowing anybody to do testing promoted by manufactuers would likely create a problem for CMS costs and patient care. Well trained specialist who primarily do this work can apply these tools in an effective way. Organizing this outside of a facility based system where there are checks and balances may be difficult. To address this I would urge you to form an expert panel to review the issue and present their findings to you in a manner that serves the public good.

Thanks for your consideration.

Comment #37:
Submitter: Jed Black
Organization: Stanford Sleep Disorders Clinic
Date: Sun, May 9, 2004 5:43 PM
Comment:

This letter, sent to Dr. Phurrough on May 7, 2004, contains the view of the sleep medicine physicians at Stanford University Sleep Disorders Clinic in response to Dr. Davidson's letter regarding the national coverage determination for diagnosis and treatment of obstructive sleep apnea.

STANFORD
HOSPITAL & CLINICS
Stanford University Medical Center

MAY 11 2004

SLEEP DISORDERS CLINIC

May 4, 2004

Steve Phurrough, MD, MPA
Director, Coverage and Analysis Group
Office of Clinical Standards and Quality
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

Dear Dr. Phurrough,

We comprise the Stanford University sleep medicine physicians providing patient care at the Stanford Sleep Disorders Clinic and write to comment on Dr. Davidson's request for a review of "the national coverage determination for diagnosis and treatment of obstructive sleep apnea". While we agree that the regular review of Medicare/Medicaid policy regarding obstructive sleep apnea (OSA) is important as the rapid advancement of knowledge about OSA continues, we are concerned by the many factual errors and faulty logic Dr. Davidson presents. Ultimately, however, a modest modification of policy regarding the use of ambulatory diagnostic monitoring – which we describe below – may be timely.

Before proceeding, we must recognize the great strides in Medicare policy that have occurred already in the development of more appropriate guidelines, as we learn more about OSA and its health consequences.

It is true that health consequences of OSA are serious, have a significant impact on patients' lives, and result in increased health-care costs[1-3]. Yet, the prevalence data submitted by Dr. Davidson represent a misinterpretation of findings presented by researchers in Wisconsin who have rigorously followed a very large working adult cohort over many years[4]. Additionally, the assertion made by Dr. Davidson that OSA is under-diagnosed due to a dearth of "sleep-diagnostic facilities" is incorrect. The under-diagnosis of OSA largely stems from an improved but still inadequate fund of knowledge of this condition among physicians and other health practitioners. Finally, many inaccuracies are found in Dr. Davidson's perspective on polysomnography (PSG) versus ambulatory (in-home) monitoring. Specifically, a) home-monitoring equipment type, specifications and quality, as well as signal sensor type and number, vary substantially across manufacturers; b) in appropriate patients, particularly those with more severe OSA for whom a split-night study is a common approach, split-night PSG not only has the potential to be more cost-effective than diagnostic home-monitoring[5] but also reduces treatment delays because treatment is initiated the very night that the condition is confirmed; c) the overwhelming majority of home-monitoring validation studies have demonstrated some variance with PSG – frequently negatively affecting diagnostic sensitivity more than specificity[6]

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(This issue has been thoroughly explored multiple times by the American Academy of Sleep Medicine task force on testing for sleep-related breathing disorders[7]); d) much of what presents clinically as simple obstructive sleep apnea is complicated by co-morbid sleep disorders which require the multiple sensor signals PSG provides for accurate diagnosis. It is notable that many ambulatory monitoring systems are unable to distinguish periods of sleep from wakefulness.

Simply stated, Dr. Davidson's interpretations of the OSA literature are inaccurate and his experience inadequate. PSG provides critical and clinically essential advantages – in addition to potential economic advantages[3] - to home monitoring in a large percentage of sleep patients, and validation studies often demonstrate home monitoring to provide inadequate sensitivity in the less severe OSA patients, yielding false negatives. Patients in this category will be inappropriately characterized as "normal" and be denied treatment that we now know to not only reduce cardiovascular consequences and improve longevity[8] and quality of life, but also to reduce health care expenses[3].

All of the above caveats to home monitoring for OSA notwithstanding, judicious use of home monitoring may have an appropriate place in the ***diagnosis*** of OSA in patients suffering severe OSA who present with unambiguous clinical signs and symptoms of OSA. The majority of validation studies of home monitoring devices suggest adequate positive predictive values to warrant use in these unambiguous patients ***only if follow up PSG is provided, when the home study results are negative***, to confirm the absence of OSA. **A modification to Medicare policy for sleep testing coverage determination to include multi-channel home monitoring would be appropriate, if its use were restricted to patients presenting with unambiguous OSA, and if home studies were followed immediately by PSG when the home study findings were negative or equivocal for OSA.**

We thank you for your consideration of this important issue.

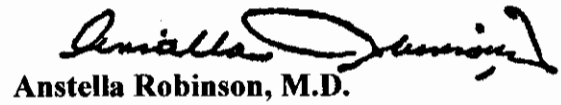
Sincerely,

Jed Black, M.D.

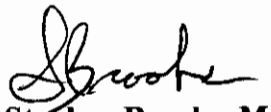
Christian Guilleminault, M.D.

Clete Kushida, M.D., Ph. D.

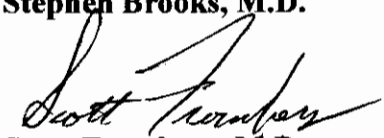
Rafael Pelayo, M.D.



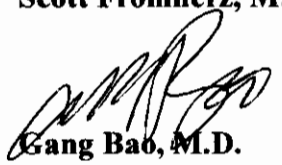
Anstella Robinson, M.D.



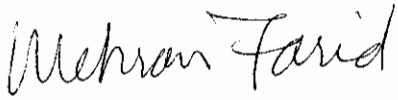
Stephen Brooks, M.D.



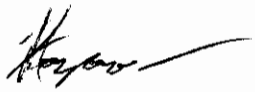
Scott Fromherz, M.D.



Gang Bao, M.D.



Mehran Farid, M.D.



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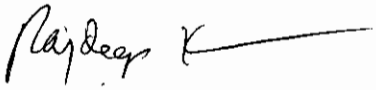
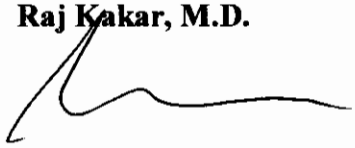


Raj Kakar, M.D.



Wynne Chen, M.D.

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Comment #38:
Submitter: Lawrence Lynn, FCCP
Organization:
Date: Sun, May 9, 2004 2:51 AM
Comment:

It is important first to recognize that sleep apnea is the only common disease for which there are no reimbursable testing which can be done by primary care. Sleep apnea is as common as insulin dependent diabetes and the symptoms of sleep apnea are often subtle and quite nonspecific. Like diabetes, the specificity and sensitivity based on history and physical alone is poor. Yet, in the USA there is no reimbursable simple test for detecting sleep apnea. Imagine how many patients would now be suffering in the US with undetected diabetes or hypertension if we required an expensive overnight stay in a laboratory to make the diagnosis of these disorders.

As presented by others, there is ample evidence that portable testing (for example including airflow, chest effort, and oximetry) is sufficient in a large percentage of the patients. It can be seen that portable testing is synergistic with the more complex in-lab PSG in much the way that simple office spirometry and complex in-lab pulmonary function testing are synergistic. In-lab PSG will likely always remain necessary for difficult titrations or complex patients. There will be plenty of business for the group of physicians who are presently financially dependent on in-lab testing. The pervasive fear of portable testing, which drives at least a portion of the aggressive "in-lab only" lobbying of the CMS, is misguided.

Portable testing would allow for ready detection preoperatively (important in view of the risk for post operative death due to narcotics in patients with undiagnosed OSA) and for improved case finding in the primary care setting. Portable testing would provide more affordable and ready access for the thousands of sleepy truck drivers, and for the tens of thousands of urban overweight minority patients with undetected OSA and significant comorbidities such as hypertension & coronary artery disease. To assure quality, and value for its money, the CMS should establish rigorous standards for portable testing, in-lab polysomnography, and CPAP compliance documentation.

As I discussed in my previous comment, previous reviews (such as the recent consensus statement published in Chest) have now been discredited since they were based on the fatally flawed premise that a portable test could be rendered invalidated if it could be established that the "AHI count" from the portable test was different than a comparison "gold standard in-lab AHI count". It is now well known that that there is no standard in-lab AHI definition therefore of course, there is no standard in-lab AHI count. Unfortunately, it is the same small group of vocal elite sleep scientists promulgating the critical need for increased access in the future who continue to lobby, based on the flawed argument above, for restricted access in the present.

In summary, OSA is morbid and, as common as insulin dependent diabetes. Yet, access to the detection of this disease is highly politicized and restricted in the US. Many well meaning "experts" in this field have engaged in an organized effort to support the "in-lab PSG only" position by promulgating the position that portable testing has an inadequate sensitivity and specificity for an in-lab AHI standard value. Given the gravity of the situation, before the CMS gives such an argument any weight, it is recommended that a formal investigation of the science and evidence supporting this AHI sensitivity-specificity issue be engaged.

OSA is too morbid to allow any room for political influence. For many reasons, the environment is too charged for portable testing to get a fair assessment by this discipline's elite. In the interest of the health of the nation --the CMS should engage this issue directly with its own group of medical scientists from outside this discipline.

Comment #39:
Submitter: Dave Walsh, RRT RCP
Organization: DRW&Associates Inc
Date: Sat, May 8, 2004 8:41 PM
Comment:

I find Dr. Davidson's request to be very appropriate and see no compelling reason not to initiate a thorough, fair and unbiased review of the criteria for diagnosis of sleep disordered breathing. I have been using four-channel multi-physiologic recording technology for over fifteen years now and have found it to be extremely accurate in identifying apnea and hypopnea.

After having worked with well over one thousand tracings, I am confident in the output of four channel devices (such as the Edentrace). However, I caution that this approach to diagnosing sleep apnea is specific to a subset of patients who present with high suspicion of sleep disordered breathing and low suspicion of other sleep co-morbidities. And I can validate Dr. Davidson's claim that the four-channel testing is but a fraction of the cost of complete lab polysomnography. I have conducted market surveys in the northern Illinois area and found that while a four-channel study is priced at $300, we have labs charging as much as $2800 for testing.

We cannot as a society afford to test the overwhelming number of patients with sleep apnea by sending them all to a sleep lab. We need to be open minded enough to consider using less expensive means to tackling this problem.

If I may be of service during your consideration of this issue, please let me know. I have been fortunate to have traveled across the country for the past ten years giving lectures and offering training to sleep physicians, respiratory therapists and home care specialists on the topics of sleep disordered breathing, the scoring and analysis of limited multiphysiologic recordings, and the pros and cons of the different levels of diagnostic approaches for sleep disordered breathing. I founded the first hospital based, in-home

unattended sleep apnea testing service at Swedish Covenant Hospital here in Chicago back in 1989 and have authored articles and have also been interviewed in several different health care industry magazines about this area of testing. I'm confident I can bring something valuable to the table in your future discussions.

One more thing: if you would, please, may I have a copy of the citations that Dr. Davidson mentioned in his letter? I cannot find them on the CMS website and would like to review the references he claims substantiate his position.

Comment #40:
Submitter: David Hudgel, M.D.
Organization: Hnery Ford Hospital
Date: Thu, May 6, 2004 3:57 PM
Comment:

I have read Dr. Davidson's request for CMS to consider reimbursement for unattended diagnostic polysomnograms. Unfortunately Dr. Davidson does not refer to a recent evidenced-based review of this topic. This review was the product of a comprehensive unbiased assessment that was jointly conducted by the American College of Chest Physicians, the American Thoracic Society, and the American Academy of Sleep Medicine. Rigorous grading of the scientific quality of the published papers available showed that monitoring devices that do not record sleep do not meet acceptable standards when used in an unattended setting. Thereby, use of these devices in the home can lead to incorrect diagnoses from either false positive or negative studies.

I encourage those who will review this topic for CMS to consult these manuscripts.

Chesson AL et al. Practice parameters for the use of portable monitoring devices in the investigation of suspected obstructive sleep apnea in adults. Sleep 2003; 26:907-13.

Flemons WW et al. Home diagnosis of sleep apnea: A systemic review of the literature. Chest 2003;124: 1543-1579.

I assume CMS is aware of the potential conflict of interest in that Dr. Davidson is a paid consultant for one of the CPAP manufacturing companies, who would benefit by an expanded marketplace of patients diagnosed inappropriately by potential inaccurate unattended sleep evaluations.

Therefore, based on the evidenced based reviews mentioned above, I do not recommend that CMS approve reimbursement for unattended sleep studies.

Comment #41:
Submitter: William Cary, President and CEO
Organization: WorkAlert, Inc.
Date: Wed, May 5, 2004 4:00 PM
Comment:

I am writing in support of Dr. Terance Davidson's request for CMS to modify its present National Coverage Determination pertaining to the use of multi-channel portal sleep diagnostic devices for the diagnosis of Obstructive Sleep Apnea (OSA) and coverage for Continuous Positive Airway Pressure (CPAP) therapy prescribed pursuant to a diagnosis using such multi-channel portal sleep diagnostic devices.

I am President of WorkAlert, Inc. Our company provides sleep apnea education, screening, in-home diagnosis, in-home CPAP titration and CPAP compliance monitoring to transportation and 24/7 safety sensitive companies. Based upon a review of the literature, interviews with clinicians at Kaiser Hospital in Denver and sleep physicians at the Veterans Administration hospital in Dallas, we selected the LifeShirt System (VivoMetrics, Inc.) as our in-home, multi-channel sleep diagnostic system of choice. The LifeShirt System monitors respiration, flow, thoraco-abdominal coordination, body position, ECG and pulse oximetry
through embedded respiratory inductive plethysmography (RIP) sensors. Since it doesn't require the use of oral-nasal flow canules or thermisters its ease of use is unmatched and the high resolution wave forms are equivalent to or exceed those derived from in-lab polysomnography. The LifeShirt System enables WorkAlert to diagnose large numbers of employees, in remote locations and quickly initiate appropriate CPAP therapy in a cost effective manner. Traditional insurance companies are reimbursing for both the in-home diagnostic procedure as well as the in-home CPAP titration procedure.

Technology has certainly advanced to the point where today, OSA can be effectively, safely and affordably diagnosed in the comfort and privacy of a person's home. In WorkAlert's case, the bed may be in a hotel, company owned dormitory or the sleeper cab of a truck.

While I am advocating for CMS to recognize and reimburse for portal ambulatory sleep diagnostic studies, I don't believe that all portal systems have the same sensitivity, specificity and ease of use and that criteria should be set before a particular sleep diagnostic technology would be approved and reimbursed.

Dr. Davidson also brings up a very valid point that traditional sleep physicians are negatively biased against home sleep diagnostic technologies because they represent a potential threat to the commercial viability of their centers. I trust CMS recognizes this conflict and will not allow biases of this nature to color its objective review of its NCD.

The facts are that obesity in the U.S. is at pandemic levels, the population is aging and OSA will rise porportionately. The present facility based sleep diagnostic industry can not meet the needs of this exploding population.

Dr. Sanders, once again, I want to urge CMS to recognize and reimburse multi-channel portable sleep diagnostic procedures and to cover CPAP therapy prescribed pursuant to the diagnosis obtained from in-home sleep studies.

Comment #42:
Submitter: Timothy Hiebert, MD
Organization:
Date: Thu, May 6, 2004 1:40 AM
Comment:

I am a Board Certified in Sleep Medicine, Pulmonary Disease and Critical Care Medicine. I am the director of an American Academy of Sleep Medicine accredited sleep diagnostic laboratory located in Ocean Springs, MS. A large proportion of my daily practice centers within the six intensive care units of the two hospitals in Jackson County Mississippi. We frequently have as many as nine Bipap machines in use at any one time. It is from this perspective that I feel qualified to make the following comments:

1) I have seen a significant number of patients with otherwise normal lungs who do not have significant oxygen desaturations but have severe sleep apnea, and would not be detected by trending nocturnal oximetry devices.

2) I have seen a significant number of patients with Obstructive Sleep Apnea who had severe (life threatining) and sustained hypoxemia when begun on cpap and bipap, These desaturation episodes frequently last for hours before the patients respiratory control center recovers enough to re-establish adequate ventilatory control. These desaturations are not detected by either airflow or respiratory effort sensors, and require active and immediate intervention by the monitoring technician to bleed in suplemental oxygen. This desaturation does not respond to cpap pressure augmentation alone as would possibly be done by "autotitrating" cpap macnines although a period of bipap with a timed backup rate will support the patients through this period of respiratory control center instability. The patient population at greatest risk of this phenomenon are those with hypercapnic respiratory insufficiency and obstructive sleep apnea.

3) The American Academy of Sleep Medicine has published a position paper regarding the use of unattended home sleep studies. The AASM web address is : aasmnet.org/practiceparameters.asp. Please review these recommendations as I agree with them.

4)Patient compliance with CPAP is strongly influenced by the patient's very first exposure to the equipment. If the patient has a bad experience with CPAP it is extremely difficult to reverse. They are very resistant to further attempts at CPAP therapy. I frequently perform empiric CPAP titration on hositalized patients who are otherwise too ill to go to an outpatient monitered sleep laboratory. Even with hours of physician time investment in each case, in my experience, patient compliance is much higher if they have their first experience in a controlled monitered environment in a sleep laboratory.

There is an advantage to having trained sleep technicians that can respond immediately to pressure, pain, intolerance, claustrophobic, and preference issues with each patient to the patient's satisfaction. Mask or CPAP interface leaking needs to be responded to immediately to provide adequate and safe CPAP administration.

5) Unattended home monitering encourages the untrained and perhaps unscrupulous physician/health care provider to make some quick, easy and if ordered enough - big money. Sloppy work is already being done and this will encourage more.

In summary, I could expound all day on the evils of unattended home sleep studies, but will leave this for another day. I would leave you with one suggestion, Medicare and Medicaid sleep studies should only be done in Accredited Sleep Labs or Sleep Centers under the direction of the AASM and sleep professionals.

Comment #43:
Submitter: Thomas Wiedel
Organization: COO, Pacific Sleep Medicine
Date: Thu, May 6, 2004 3:06 AM
Comment:

Regarding Dr. T. Davidson's letter asking CMS to approve home sleep studies:
1. He is incorrect in stating that all parallel reviews of polysomnograms vs. multiple channel screening devices typically used in home studies show a near perfect corelation.

2. He is incorrect in quoting the tremendous disparity of costs.

3. He misses the point that no matter what diagnostic device is used, the true result of the study, assuming the patient has obstructive sleep apnea, must be the proper titration of positive pressure (CPAP) levels to provide clinical benefit.

4. Overnight sleep studies in the home compromise the study due to an uncontrolled environment.

5. Home studies are typically unattended by a technologist, the sole contact who stands the best chance of properly fitting and titrating CPAP, and convincing the patient to actually use the device.

6. The relative cost of properly diagnosing and treating sleep disorders is very small in comparison the benefits accrued the patient and healthcare system, as when properly done, a healthier patient is the outcome, the result being a significant reduction in the use of the healthcare system.

Done correctly, sleep disorder testing and treatment saves money and qualtiy of life. It should not be compromised by introducing unattended, uncontrolled

home studies.

Comment #44:
Submitter: Lawrence Lynn, DO, FCCP
Organization:
Date: Wed, Apr 28, 2004 10:56 PM
Comment:

Thank you for opportunity to speak on the subject of sleep apnea testing, This issue is very important for the health of Americans. This issue particularly impacts the poor and the underserved, such urban minorities and rural patients. I will admit that I do not know the answer to the question as to whether or not the health of America will be improved by providing for home sleep apnea testing. I write this letter to assure that these issues are considered with complete scientific disclosure.

Throughout history we have learned that complex legal systems specifically developed to determine truth can be manipulated to define a false truth. It is not surprising that in the 21st century men and women will find unique ways to apply complex scientific analysis to define scientific truth in the manner which most suits them. A excellent analytic tool for finding real scientific truth is the Bland & Altman Plot. This widely accepted tool is very useful to compare the outputs of two devices. However, is it possible for very smart scientists to apply this tool in a way that assures that one device, no matter how good, will never be considered acceptable? The answer is, of course, yes.

Consider a situation, as is the case with in-lab polysomnography, wherein a "gold standard device" has an accepted output which varies 10 fold
depending on the definitions chosen to render the output (ref. 1-4). Then consider that, despite these known variances, all of these outputs are considered standards and any in-lab can chose to render any one of these outputs as their own standard, provided they do so in an "in-lab" setting. Perhaps to give the perception of measurement unity between these very different outputs, the scientist agree to call all of these outputs by one unifying name ("the AHI"). To further embellish these different outputs "The AHI" are all called "the gold standard output" rendered by "the gold standard test" (in-lab polysomnography).

Now suppose a scientist wanted to invalidate (or validate) a portable device in comparison with in-lab polysomongraphy. This scientist can choose from a wide range of accepted definitions to derive "the gold standard" in-lab AHI and the portable device must now match this output using a Bland & Altman Plot. If the portable device does not, it is considered invalidated. Since the scientist is free to choose in advance from a range of accepted definitions for "the gold standard" and the portable device will then have to match any one of them depending on the scientists choice, the portable device, no matter how perfect, has a very low chance of being validated. Indeed, if by chance the portable test matches one gold standard AHI it can be quickly invalidated against another gold standard AHI using the same in-lab PSG data set. Of course this also means that one in-lab "gold standard" has a poor sensitivity and specificity (and could be

invalidated) when compared against another in-lab "gold standard". However a Bland & Altman Plot between the AHIs derived of different in-labs or different AHI definitions form the same in-lab are never made (after all they are all "gold standards").

Indeed, this invalidation method is so perfect that it need not be deployed as a function of volition. The probability of a match between any specific a-priori selected in-lab AHI definition and the output of the candidate test is very low. This means that a well meaning researcher could seek to honestly compare "The AHI" which is used in his or her own sleep lab to the output of a portable test using Bland &Altman and never realize that they have pigeonholed the portable testing device in a manner which is almost certain to invalidate the device.

All this is so subtle. Of course it is hard to believe, these are all very smart scientist and many, perhaps most, are quite honest. Yet, patients are dying (6) and we need to be sure we are using good science to assess our testing options. Do the scientist writing consensus documents requiring that all portable tests be matched using Bland & Altman "the AHI" derived form in-lab PSG realize they have crafted the perfect invalidation method? We do not know, but we prefer to think that they are so smart and so much believe in their own brand of in-lab based science that they have fooled themselves. I respectfully request that those who argue that a given portable testing is invalid because of a limited sensitivity or specificity for a given preselected AHI, identify which AHI definition and number which defines the true gold standard for the diagnosis of this disorder.

Again I do not know what is best for the health of Americans but I believe it is critical that the decision be made with a complete understanding of the profound limitations of the embellished "science" commonly cited to discredit portable testing.

Addendum --Don't be fooled by those who say they apply "the" censuses definition for "the AHI". There is no such thing. Only a consensus range of definitions and this range varies depending on which consensus group is cited.

References:

1.Moser NJ, Phillips BA, Berry DT, Harbison L.

What is hypopnea, anyway? Chest. 1994 Feb;105(2):426-8

2. Redline S, et.al.

Effects of varying approaches for identifying respiratory disturbances on sleep apnea assessment.

Am J Respir Crit Care Med. 2000 Feb;161(2 Pt 1):369-74

3. Tang et.al

Identification of sleep-disordered breathing in children: variation with event definition.
Sleep. 2002 Feb 1;25(1):72-9.

5. Redline S, et.al.

Effects of varying approaches for identifying respiratory disturbances on sleep apnea assessment.
Am J Respir Crit Care Med. 2000 Feb;161(2 Pt 1):369-74

6" Sleep Apnea and Narcotic Postoperative Pain Medication: A Morbidity and Mortality Risk"

Comment #45:
Submitter: Kelvin Loh, MD
Organization:
Date: Thu, Apr 29, 2004 1:19 AM
Comment:

I concurre with Dr. Davidson. We need home lab.

Comment #46:
Submitter: Gwynne Aidala, CRT, RSPGT
Organization: TJ Sampson Community Hospital
Date: Thu, Apr 29, 2004 10:37 AM
Comment:

While I am not a researcher or physician who may offer "scientific input" realting to Home PSGs, I am a therapist who has had the opportunity to work in the DME field and
at accredited sleep disorders centers.

PSGs in the home have been deemed a more cost effective method by interested parties (DME providers and Home PSG equipment manufacturers). It is no suprise that their interest in this matter is financial. I agree Home PSGs may be cheaper, but at what expense.

As a person who has been both a PSG technician and a manager of PSG technicians, I can account for the unexpected happenings during an overnight PSG. Even in a controled sleep center environment, artifact may appear from sweat or loose leads. This artifact if left unattended can render a study useless. A patient at home may feel tied to the bed and unable to get up to go to the restroom, causing them to lie awake uncomfortable because of their inability to move. The vigilance of a night technician is required to prevent such occurrences.

Home environments are not designed for performing clinical testing. A spouses movements and even snoring may be detected by the monitoring devices causing a flawed or even false positive study. Even a household pet could interfere with the findings. There are reasons medical procedures are performed in controled environments.

Nationwide, states are dealing with how to regulate individuals who are performing PSG studies in laboratory settings. Licensure laws are addressing the qualifications of individuals who can and can not perform such tasks. The addition of pop-up Home DME sleep studies is only going to impair the states' ability to make their determinations.

Sleep Centers are more than just testing facilities, they provide support to both the patient and their families. Sleep Centers provide patient education before, during and after the PSG is performed. Sleep Centers also participate in community awareness.
Education, Support, and Community Awareness are key to early intervention and therefore less healthcare utilization in the long run.

When you consider the "big picture", Sleep Studies in the home don't equal quality patient care.

Comment #47:
Submitter: Laura Clapper, MD, MPPA
Organization: Health Net
Date: Thu, Apr 29, 2004 12:13 PM
Comment:

I would like to write in support of Dr. Davidson's letter to support home CPAP diagnostic testing for Medicare reimbursement. Based on the research noted, Health Net reimburses for home testing in our commercial population. Not only is home testing as effective but allows the patient to be in their own home and have less exposure to nosocomial infections.

I am writing on my own behalf and not on behalf of Health Net.

Comment #48:
Submitter: Anthony Magit, M.D., F.A.A.P.
Organization:
Date: Thu, Apr 29, 2004 10:22 AM

I support the proposed addition of home sleep studies as an approved method of determining the presence of obstructive sleep apnea.

Comment #49:
Submitter: Ashwin Gowda, MD

Organization: The Sleep Disorders Center of Central Texas
Date: Thu, Apr 29, 2004 2:22 PM
Comment:

I am writing to you in reference to the letter (CAG-00093R) submitted to CMS by Terence Davidson, MD. I believe as do many of my colleagues that there are inaccuracies in Dr. Davidson's letter. Polsomnography (PSG) is the gold standard in diagnosis and treatment initiation of CPAP.

SDB is grossly under diagnosed in the community; however that does not imply that you should lower the standard of care. As the awareness of the disorder has grown, and its implications on quality of life, cardiovascular and cerebrovascular disease; laboratories have seen a back log of patients. In our center we attempted the monitored use of a home study device in efforts to diagnose and treat patients quicker. During this 8 week period, there were numerous cases of individuals with mild to moderate sleep disordered breathing who were not given a diagnosis. Since the clinically history was consistent with sleep apnea a polysomnogram was completed verifying the diagnosis.

In situations where disordered breathing is severe; overnight oximetry or a home based study is likely sufficient. However in mild to moderate cases, these tests are insufficient. These patients will then remain symptomatic and not pursue further investigation since they were told that do not have sleep apnea. Detection of mild disordered breathing, including upper airway resistance and respiratory effort related arousals cannot be done via a home study or overnight oximetry.

In house PSG does have two drawbacks; it involves the patient sleeping away from home and the other is cost. The use of a PSG is superior to home sleep testing. Split night studies are effective in diagnosis and treatment with appropriately educated and trained sleep technicians. With CPAP initiation it has been clearly shown that the first impression a patient has with CPAP goes a long way in determining compliance. Also determining appropriate CPAP pressures at home with an auto-PAP device is extremely difficulty without adequate education and training for the patient.. Repeat studies with home studies are not uncommon and more importantly leads to inaccurate diagnosis or no diagnosis.

There are sleep laboratories in the community where polysomnography is conducted by non-medical staff (independent labs not accredited by the American Academy of Sleep Medicine). and interpreted by physicians. The quality of work there is already sub-standard. Home studies are more so.

There is no doubt that sleep related breathing disorders are grossly

under diagnosed in the community, including Medicare and Medicaid recipients. Missed diagnosis and poor care will only lead to a lower standard of care and inevitably lead to higher health care costs. However appropriate diagnosis, care and education is where the community will benefit the most. The American Academy of Sleep Medicine is striving to make this a reality.

Comment #50:
Submitter: Barry Alexander
Organization: Nelson Mullins Riley & Scarborough, L.L.P.
Date: Fri, Apr 30, 2004 9:15 AM
Comment:

I am working with a sleep testing company that would very much like to see a change in NCD relevant to home testing and have been advised that this issue is now under consideration by CMS. Our client is putting together a letter, but, I am wondering if you have a few minutes to chat about what types of issues we should address in our comments. Or, put another way, what are the major concerns of CMS with regard to the use of this new technology as it relates to sleep testing and, ultimately, CPAP medical device ordering.

Feel free to respond by e-mail if you feel more comfortable, or call me directly at the number below. Look forward to hearing from you.

Comment #51:
Submitter: Shahrokh Javaheri, MD
Organization: University of Cincinnati College of Medicine
Date: Mon, May 3, 2004 4:39 PM
Comment:

Home sleep studies should only be considered if there is a high probability of OSA as determined by a board certified sleep specialist in a face to face consultation with the patient. Criteria for identifying high probability of OSA includes obesity, habitual snoring, witnessed apnea, excessive daytime sleepiness, and waking up tired and unrested. Home sleep testing should be performed only by an accredited sleep facility and should not be considered for diagnosis of any other types of sleep disorders or if there are significant co-morbid disorders such as Congestive Heart Failure. If a facility does not have a board certified sleep specialist with extensive medical knowledge of cardio-respiratory disorders they should not be allowed to order in-home testing. In-home testing must be interpreted by a board certified sleep specialist and also reviewed with the patient in follow-up consultation with the board certified sleep specialist to discuss treatment options.

Any sleep facility must be accredited by the AASM and under the medical

guidance of a board certified sleep specialist physician. If the result of a home sleep study is negative or inconclusive but the patient is symptomatic, the patient must be tested by full night PSG in an accredited full service sleep disorders center. Only a board certified sleep specialist should be allowed to make a determination that a study is not falsely negative because some studies may include significant artifact that only a board certified sleep specialty physician can recognize.

Patients with suspected Central Sleep Apnea (predominant in CHF), Periodic Limb Movement, or Narcolepsy should only be tested in an accredited full service facility.

Comment #52:
Submitter: Lee Giddings, M.D.
Organization: Clinical Resource Management
Date: Tue, May 4, 2004 11:32 AM
Comment:

I am writing in support of Dr. Terry Davidson's proposal to consider allowing multichannel home sleep testing as an alternative to in-house polysomnography in the diagnosis of sleep disordered breathing. As Medical Director for Clinical Resource Management at UCSD, I believe this would represent a significant improvement in the utilization of healthcare resources. Of course, the first consideration is always the quality of patient care management. Dr. Davidson has certainly provided ample evidence of the clinical benefit for the patient. I believe the cost-efficiencies of home sleep testing coupled with the clinical appropriateness is a win-win situation for all. Thank you for your consideration.

Comment #53:
Submitter: George T. Simpson, M.D., M.P.H., FACS
Organization: VAWNYHS Medical Center
Date: Mon, May 3, 2004 3:45 PM
Comment:

I wish to write in support of reimbursement for home based sleep studies in diagnosing and evaluating Obstructive sleep apnea.

Considerable clinical experience has been accumulating in recent years to support the applicability and cost effectiveness of such studies. Given rising medical and medicare costs, cost effectiveness is gaining an ever increasing weight. Home studies should be far less expensive than Sleep Laboratory based studies. Most home studies can provide accurate effective data for interpretation and diagnosis without excessive costs for technician time.

Comment #54:
Submitter: Stuart J. Menn
Organization:
Date: Tue, May 4, 2004 8:13 PM
Comment:

It has come to my attention that a proposal is being considered to use portable equipment at home as a method to diagnose obstructive sleep apnea. As a sleep medicine professional (boarded in sleep medicine) who has evaluated well over 10,000 patients with OSA, I strongly recommend that you do NOT ACCEPT home-based portable studies as the standard of care in diagnosis. Many physicians still do NOT appreciate that sleep apnea is heavily influenced by both sleep state and position. One of the best ways of achieving a negative sleep study is to record a night
in which the patient did not enter into REM sleep or have very little actual sleep. I have seen many patients studied at home and told that they had minor sleep apnea, only to be seen by me, 1-2 years later with severe sleep apnea, when properly recorded with a full polysomnogram.

In many cases, things are not clear cut and the observations of a trained technologist is critical in deciding the causes of low O2 saturations or the difference between central and obstructive sleep apnea. A home study loses these valuable clinical observations that are currently present in the standard NPSG.

The sleep medicine field has spent 25 years trying to bring standards to the field of sleep scoring and diagnosis. Allowing portable home studies will open the gates to many, many kinds of devices (some of which may be good and some very bad) that are not standardized by any professional medical group. The manufacturers will be setting the standards for these patients (a dangerous idea).

Many of these measuring devices function as "black boxes" without any physician understanding of the assumptions made in projecting an event like an apnea.

Finally, as recently as 2003, the three leading medical societies in the sleep field (Amedican Academy of Sleep Medicine, American Thoracic Society, American College of Chest Physicians) reviewed the literature and came out with a position paper NOT SUPPORTING the use of portable home testing as the acceptable standard of care.

Comment #55:
Submitter: Hrair Koutnouyan, M.D.
Organization: ENT Associates
Date: Tue, May 4, 2004 10:12 PM

I support Dr. Davidson's recommendation. I have been using multi channel home studies for more than two years. I find them accurate and reliable to diagnose obstructive sleep apnea. The patients appreciate having the test in the comfort of their own beds.

Comment #56:
Submitter: Ronald D. Chervin, M.D., M.S.
Organization: Michael S. Aldrich Sleep Disorders Laboratory
Date: Tue, May 4, 2004 9:10 PM
Comment:

Issue The Centers for Medicare & Medicaid Services is reviewing its national coverage decision regarding the diagnosis of patients with OSA requiring CPAP therapy. Current national coverage guidelines specify that only a polysomnography done in a facility-based sleep study laboratory be used to identify patients with OSA requiring CPAP (CIM 60-17). CMS has received a Request from Dr Terence M. Davidson, MD, of the University of California San Diego, School of Medicine to modify this decision to include the use of portable multi-channel home sleep testing devices as an alternative to facility-based polysomnography in the evaluation of OSA.

The request was generated by a physician who is not a sleep specialist, and contains much misleading information. For example, home studies are typically called "cardiorespiratory" studies, not sleep studies, because they do not record sleep. Validation studies to which Dr. Davidson refers have been reviewed by the American Academy of Sleep Medicine and still found insufficient to warrant use of home studies except under limited circumstances. We published (around 1998) one of the few cost-effectiveness models of how to diagnose obstructive sleep apnea. We found that full laboratory polysomnography, rather than a home study system with the highest reported sensitivity and specificity, was most cost-effective, even after sensitivity analyses that used minimal costs for a home study (as low as $50).

Coverage for home studies in a very limited set of circumstances would be welcome. However, coverage at the discretion of any physician who orders it - sleep specialist or not - would likely harm more patients than it would help. We know, here in Michigan, because in the past some third party payers did cover home studies. Fly-by-night companies came into the state to set up home study shops that offered lucrative home testing without any physician evaluation or follow-up. The results disuaded us (those on the board of the Michigan Sleep Disorders Association) from readdressing possible coverage with Blue Cross/Blue Shield of Michigan when an opportunity to do so came up.

Comment #57:
Submitter: Julie A Yaeger,RRT
Organization: Sleep Services of Jasper, LLC
Date: Wed, May 5, 2004 5:49 PM
Comment:

I am writing you in response to the appeal made by
Dr. Terrance M. Davidson regarding in-home sleep testing. Before reading his letter,I was apposed to such testing, as it is inferior to in lab testing. I do,however, feel that Dr.Davidson made a few good points, mainly the lack of facilities to to treat the large volume of patients with SDB. I Think that SDB awareness and testing has grown so fast that many mistakes have been made. Sleep testing has become a money maker for many business men. Very cheesey labs exist with unqualified physicians overseeing testing. Most states currently have no state regulations over sleep labs. Alls that is required is a business licence. I am happy to see medicare and some other insurance carriers are mandating accreditation by the AASM. I fear that in-home testing is just going to become another opportunity for business men and othe non-qualified persons to profit from. I feel that if medicare is going to consider the proposal for in-home sleep testing, it should be mandated tat it is
overseen by an accredited sleep lab or center. Hopefully history will not repeat itself.

Comment #58:
Submitter: David A. Lewis, M.D.
Organization: Pulmonary, Critical Care & Sleep Medicine
Group Health Permanente
Date: Thu, May 6, 2004 8:14 PM
Comment:

I am writing to give my full support for the request by Timothy Davidson, MD to modify the current national guidelines for CPAP coverage to include the use of portable multi-channel home sleep testing devices as an alternative to facility-based polysomnography in the evaluation of OSA. I am the Service Line Chief for Group Health Permanente Pulmonary, Critical Care, & Sleep Medicine based in Washington State and previously directed the Sleep Laboratory at Harbor-UCLA Medical Center (1993-99). I am a Diplomate of the American Board of Sleep Medicine in addition to the American Board of Internal Medicine (Internal Medicine, Pulmonary Diseases, and Critical Care Medicine.) I do not have financial ties to any companies making equipment used for portable testing or for the treatment of sleep-related breathing disorders, nor any financial gain to be had by the use of either portable sleep monitors or facility-based polysomnography.
I have been involved in portable testing for the diagnosis of obstructive sleep apnea syndrome since my early fellowship training at Harbor-UCLA. As director of the Harbor-UCLA Sleep Laboratory, I continued to use portable testing to help keep up with the demand for sleep testing for this important disease in excess of the capacity of my polysomnography laboratory. As co-director of the Group Health

Cooperative Sleep Laboratory since 1999, I continue to find portable testing to be acceptable for the diagnosis of obstructive sleep apnea syndrome in the majority of patients we see. There are subtle presentations of sleep-disordered breathing that may be missed by portable testing, though false positive studies in patients suspected to have sleep apnea are very rare. We prefer to utilize our comprehensive polysomnography laboratory to ensure that negative home tests are, indeed, negative in patients with suspected sleep apnea; for the diagnosis of non-apnea sleep disorders (that do require EEG/EMG information); and for the titration of CPAP and BiPAP in patients diagnosed with OSA who do not find clinical improvement with home- or auto-titration of CPAP.

The Group Health sleep program based on portable testing has been operative since 1994 and has been highly successful in improving access to testing for patients with suspected sleep-disordered breathing. Patients are often seen for initial consultation and started on CPAP within one week (and sometimes within 24 hours), greatly reducing the wait time for treatment initiation compared to national and local averages using facility-based polysomnography testing. Our sleep medicine providers and patients are both very happy with the improved access. Unfortunately, our Medicare and Medicaid patients are required to wait for 1-2 months for a facility-based polysomnography study (a much more expensive and much less convenient test) before they can start therapy. As a healthcare professional, I am greatly concerned that this delay in diagnosis and treatment increases the risks of serious complications of this very common disease (traffic accidents, declining work performance, development of hypertension, exacerbation of heart failure, etc.)

I strongly support the use of portable monitors to greatly improve access to testing for the diagnosis of obstructive sleep apnea syndrome and sincerely hope that CMS will modify their requirements for CPAP coverage to include portable testing as an alternative to facility based PSG. Obstructive sleep apnea is a very common and potentially deadly disease that needs early treatment initiation to reduce complications and improve patient quality of life.

Comment #59:
Submitter: Richard L. Goode, M.D.
Organization: Stanford University School of Medicine
Date: Thu, May 6, 2004 7:50 PM
Comment:

I am an academic otolaryngologist at Stanford with a significant portion of my practice in the field of sleep disordered breathing. I strongly feel that Medicare and Medicaid should reimburse for multi-channel home sleep studies. There are several reasons for this. First, there is a great deal of data to support that these studies, when properly done with several of

the portable devices now available, correlate well with monitored in hospital studies. The absence of an EEG channel is not a reason to deny reimbursement. Second, a large number of patients do not need all the information that the monitored study provides--some do. In these cases a second study may be required but more often these patients can be screened out. A 325 pound male with heart disease and suspected sleep apnea needs a monitored study. Third, cost. The home tests are much cheaper. Fourth, delay. It takes weeks at Stanford to obtain an overnight monitored study. While they will do home studies, they know that they will not be reimbursed in Medicare/Medicaid patients for so they will schedule the in house study. Fifth, interpretation. Modern units provide computer generated, accurate data that can be classified by a variety of proven algorithms so that the severity of the OSA can be measured. Sixth, access. Independent of cost, the inconvenience of such a study turns off many patients. It is well known that there is a large number of undiagnosed OSA patients and the use of convenient testing would make it much easier to obtain patient compliance. Seventh, repeat testing. Some home units allow for testing on more than one night.This is helpful r.e. verifying borderline cases, role of drugs, alcohol, etc. as well as evaluation of dental devices, nasal opening devices, etc.

I am concerned that those physicians with a vested interest in overnight sleep studies have been able to convince Medicare/Medicaid that there is no role for home multi-channel sleep studies. The baby was thrown out with the bathwater. We need both and both should be reimbursed; the home studies should be reimbursed at a lower rate than the hospital studies, of course. It is time to correct this inequity and I do not feel there is evidence that standards will decrease or that the use of testing will be abused. It will obviously increase the amount of tests, as it should since the incidence is high and those with undiagnosed disease are at risk for major complications.

Comment #60:
Submitter: Edward M. Weaver, MD, MPH
Organization: University of Washington
Date: Fri, May 7, 2004 5:01 PM
Comment:

I strongly support Dr. Davidson s request for CMS coverage for portable multi-channel home sleep testing devices as an alternative to facility-based polysomnography in the evaluation of obstructive sleep apnea.

Home sleep testing offers several advantages:
1. It tests in the patients natural sleep environment. This important factor if often overlooked but should not be underestimated.
2. It is less cumbersome to patients. Fewer testing leads translate into less distraction in bed and more natural sleep.

3. Improved access to diagnosis and treatment, which ultimately reduces medical costs.
4. Less cost per patient.
5. It is adequate in 80-90% of patients who are thought to have sleep apnea.

Sleep physicians have demonstrated the cost-effectiveness of home sleep testing at Group Health Cooperative in western Washington [1]. Group Health Cooperative is a large health maintenance organization that realized in the mid 1990 s that it was not adequately managing sleep apnea in its >500,000 members. They realized that they could not succeed by simply trying to expand the in-facility polysomnography laboratory, because the number of tests required and the cost of the tests were both increasing exponentially.

Instead, they used a home sleep testing program (just like the proposal for which Dr. Davidson requests coverage) to increase access and reduce costs. They developed a program using a multi-channel home sleep test (cardiopulmonary test without electroencephalogram, electrooculography, electromyography, etc.), and they measured outcomes and costs.

After two years, they had impressive results. They completed 698 portable tests. Only 8% required repeat testing due to lack of diagnosis or a technical problem. Standard facility-based polysomnography was needed in just 11% of all patients. Overall testing rates increased 129%. The average cost per case of suspected sleep apnea decreased by 36%. The per-member, per-month health plan cost decreased by 13.5%. No deaths, hospitalizations, or Emergency Department visits occurred while undergoing portable testing or home CPAP titration.

A great proportion of sleep apnea patients remain undiagnosed, which translates into worse health outcomes and increased costs. Analysis of 147,000 Veterans Affairs patients with a diagnosis of sleep apnea revealed a 27% increased mortality risk for untreated compared to treated patients, after adjusting for age, race, gender, comorbidity, and year of diagnosis [2]. Sleep physicians at Group Health Cooperative showed that undiagnosed sleep apnea is associated with healthcare costs significantly higher (almost double) than age/gender-matched controls from the same population [3].

I anticipate that you will receive significant vociferous opposition to Dr. Davidson s proposal, especially among many sleep physicians that benefit financially from facility-based polysomnography. I ask you to consider their major, inherent conflict of interest and weigh their comments accordingly. I recognize that this conflict of interest exists even in some very prominent, highly respected sleep physicians.

As a final note, I wish to convey my background to provide a context for my support of Dr. Davidson s proposal. I am a clinical epidemiologist studying sleep apnea. I am also an Otolaryngologist Head & Neck Surgeon who specializes

in sleep apnea care as the Surgical Program Director of the Sleep Disorders Center at the University of Washington. I participate on several national committees: Chair of the Sleep Disorders Committee and Chair-elect of the Outcomes Research Subcommittee of the American Academy of Otolaryngology Head & Neck Surgery; member of the Research Committee of the American Academy of Sleep Medicine; and member-elect of the Research Committee of the Sleep Research Society. My own sleep apnea research is funded by NIH and by the American Geriatrics Society.

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Comment #61:
Submitter: Dominic A. Munafo, M.D.
Organization: Sleep Data, Inc.
Date: Tue, May 4, 2004 4:34 PM
Comment:

I am writing to express my strong support for Dr. Davidson's proposal that CMS cover type 3 monitors for the diagnosis of obstructive sleep apnea syndrome.

During the last seventeen years I have had an opportunity to see the practice of sleep medicine from a number of perspectives. Among these were sleep research associate, pulmonary fellow, university faculty, private practice, and medical director of a sleep diagnostic company.

While working as Pulmonary & Critical Care faculty at the University of California, San Diego, in the early 1990's I oversaw the care of many patients with severe sleep apnea. Unfortunately, we had little to offer them. There were no clinical sleep labs at either the University Hospital or the VA Medical Center then or now for that matter. Typically, we would have to use a piece of loaned diagnostic equipment from a manufacturer's representative, to do an ambulatory study. Once a diagnosis was made, we had no ability to manually titrate CPAP pressures in a lab. The result at the VA was that patients were sent home with a CPAP device, a pressure manometer, and a screwdriver! They were begun on an empiric amount of CPAP and instructed on the technique of adjusting the pressure based on symptoms, snoring and their bed partner's reports. Out of this necessity sprang the essentials of the program that is currently in place at both the University Hospital and the VA. The results have been remarkable. Instead of thousands of patients waiting months for a referral to a sleep lab, patients were efficiently diagnosed and begun on therapy. Fortunately, we now have access to ample numbers of portable recorders and CPAP devices. However, the principle remains unchanged. We found that patients were well served and that only a small fraction required referral to a sleep lab. Now we can use auto-titrating CPAP devices as well as symptom-based adjustments of CPAP pressures. In addition, with portable recorders we have the luxury of doing follow-up studies on the patients with severe disease so as to be assured that they are being adequately treated. Surely, this is a more appropriate use of precious clinical resources.

Amazingly, the University is just now committing the resources for a TWO bed clinical laboratory that may open this year. This is drop in the bucket if we are to insist that all patients undergo full polysomnography (PSG).

Fortunately, the medical literature is increasingly supportive of the ambulatory model. The article last year by Fitzpatrick et al., (1) confirmed results previously published by Coppola (2). Patients can be educated to assist in the titration of their own CPAP pressures. Once again, monies previously being spent on full PSG can be much better spent on the education and follow-up of patients with sleep apnea. Time and time again it has been shown that without aggressive education and follow-up, patient compliance with CPAP is poor. Why spend all of the resources on the diagnosis and leave nothing for the all-important aspects of therapy and patient education?

I would like to comment briefly on some of the literature that is often cited to criticize portable testing. The fundamental point often made is that portable testing fails to render an apnea-hypopnea index (AHI) equivalent to "the gold standard AHI" derived from PSG. Unfortunately, what is barely mentioned is that "the gold standard AHI" is not a single standard but actually varies considerably from lab to lab. Laboratory derived AHIs are, in fact, derived of many different combinations of methods and definitions (3,4,5). The literature clearly shows that an AHI determined in one sleep laboratory may have little if anything in common with an AHI determined in another laboratory using an alternate definition for hypopnea and/or a different method for detecting respiratory events. In fact, ranges between AHIs of at least ten-fold have been reported (4,5). If one cannot standardize the "gold standard" how can you possibly compare another technology to it and arrive at a scientific conclusion?

I fully realize that continuing work needs to be done to determine how best to implement portable diagnostic techniques in various patient populations and in different healthcare delivery systems. However, those of us with considerable experience have seen that far more good comes from improved access to care than from the ridiculous pursuit of an illusory diagnostic certitude.

I would also respectfully submit that no analysis of a diagnostic paradigm is complete without a careful consideration of the context in which it is placed. What of the cost in morbidity and mortality for the millions of patients who will remain undiagnosed and untreated in the absence of a more aggressive and integrated approach to sleep apnea? Young's seminal article demonstrated that over 80% of the patients with sleep apnea remain undiagnosed (6). Every day, hundreds of patients with undiagnosed severe sleep apnea have major surgery. Many will receive respiratory depressants and be placed at considerable risk (7). Countless Americans are on our roads with severe daytime sleepiness due to undiagnosed sleep apnea. There is not a single piece of evidence to support the contention that limiting sleep apnea testing to sleep laboratories ultimately benefits patients or the public health. In fact, I feel quite strongly that the public health is being harmed enormously by the limitation of care that results from the current guidelines.

From a strictly financial perspective, the increased access to heath care will no doubt increase the amount paid out for diagnosis and therapy. However, several analyses suggest that it is less expensive to treat sleep apnea than to manage all of its myriad complications (8). Large payers such as Blue Cross/Blue Shield, Cigna, CCN and HealthNet cover portable testing. Of course, from an ethical standpoint, financial factors should not be the primary driving force behind public policy anyway.

In the California health care system it is quite common to rely on portable diagnostics. Sleep Data, Inc. presently services major health care systems including Sharp Healthcare, Mercy Healthcare, Scripps Healthcare and elements of the Veteran's Affairs system. In addition, Kaiser Permanente, the University of California San Diego, and the San Diego Veteran's Affairs Medical Center all rely predominantly on portable studies, as does the Group Health System in Washington State. This says nothing of the fact that many other countries of the world rely in part or totally on portable diagnostic paradigms.

In summary, there can be little doubt that some form of portable testing will be the ultimate end point. The only issues are when and which techniques will prove best. The recent article by Flemons points out the fact that even with herculean efforts to increase the number of sleep labs and formal sleep physicians we will fall woefully short of the capacity necessary to adequately serve our patients (9). Dr. Pack's accompanying eloquent editorial distills the mater to its essentials, "Access is the issue."(10) We must proceed proactively to help insure that the overwhelming need of our patients is met in a timely and cost-effective fashion. To do less should not be an option.

While I acknowledge a financial interest in the use of ambulatory testing, I urge you to remember that those who have lobbied so hard to maintain the status quo have enormous financial, career and research interests at stake as well. The rapidly growing number of PSG labs is testament to their financial viability as cost centers for hospitals. Unfortunately, this is not the best use of our healthcare dollar.

Thank you in advance for your gracious attention and any consideration you may give this request. I would be delighted to meet with you at your convenience to further discuss the program we have found to be so successful.

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Comment #62:
Submitter: Kingman Strohl
Organization:
Date: Fri, 5/7/04 10:13PM
Comment:

Clinical decision making, not technology. Sleep apnea, like chest pain, requires a number of approaches to rule in the disorder. PSG is like cardiac catheterization as potable monitoring is to stress testing.

Scope of the Problem

In 1983, Coleman et al reported findings on approximately 3000 patient encounters in a survey of nine ASDA accredited laboratories; data were collected over 2 years. While some of participating centers had higher volumes (200-250 studies/year), the median number of studies among the 9 sites was 87/year/center; and sleep apnea accounted for 46% of the cases. In . During a one-month period of time in 1998, these centers reported doing a mean of 68 studies/month (annualized to over 800 studies/year/center); and 89% of studies were for evaluation of sleep apnea (Punjabi et al, 1999).

The End of the Technology Phase

There are number of reviews and reports on the role of testing focusing on issues of instrumentation and standardization (2-5). These publications have generally concluded that polysomnography as well as the more limited recording devices are biologically plausible and technologically feasible in both the unattended and attended mode. This includes portable and/or ambulatory monitors that permit testing outside the sleep center both with and without surveillance by a technician (5).

Portable monitoring of cardiopulmonary variables alone will detect sleep disordered breathing equally as well as attended studies, with the likelihood of an 8% or less failure rate. It should be noted that the failure rate for attended polysomnography is not published but is only believed to be lower. There have been several scholarly reviews of clinical utility of unattended cardiopulmonary testing suggesting that apneas can be detected (to the extent that a clinical decision can be made) without directly measuring sleep (3). Hence, controversy about the technology for monitoring sleep and breathing now focuses on application rather than methods, on use rather than instrument.

Two studies have examined compared the use of attended and unattended monitoring will all polysomnographic variables in patients with sleep disorders. Mykytyn et al (6) compared the use of the same polysomnographic equipment in the attended and unattended mode. Although there only 10 patient records examined, and no actual "home" testing, the results support the feasibility of doing "full"

sleep studies outside a center or fixed site, and without the need for constant attendance by an observer. In a study more consistent with clinical utility, Fry et al (7) studied 77 patients once in the laboratory and once at home. There was a very good concordance for indices of sleep disordered breathing but less so for the number of periodic leg movements. The differences observed between testing sites did not alter clinical decisions; however, twice as many patients preferred laboratory testing than home testing.

There are lessons to be gained about the use of unattended technology from the Sleep Heart Health Study (8). This epidemiologic study utilizes a 16 channel potable, unattended device for collection of polysomnographic data in the home, and has experience in the collection of data in over 6000 adults. In the course of this study there was installed a system for training and re-assessment of technical details of the patient set-up and a pre-determination of the quality of recording and for the interpretation of events (9,10). This body of information suggests that equipment failures occur but that the predominant problems are sensor failure, including senescence of sensors. Reliability among scorers can be maintained over time; however, the counting of respiratory events during sleep is highly dependent on definition of significant events. Reliability is poorest for arousals, but given a standard definition counting of respiratory events can be standardized among trained scorers.

The focus of attention in clinical sleep medicine should turn from technology to quality improvement protocols and issues of clinical utility (11). Millman, Newmeyer and Kramer (12) are, in my opinion, correct to use a perspective of clinical decision making in the understanding of the role of testing in the management of sleep apnea. The overall strategy is to identify people with sleep apnea in whom treatment of sleep apnea will improve the quality of life (reduce sleepiness and fatigue) and perhaps improve risk factors for cardiovascular disease (11,13,14).

Clinical Decision Making for Sleep Apnea Testing

The reality is that a test like poysomnography or portable monitoring comes after a patient encounter in which the best test is the one that results in a decision regarding the patient=s condition (15,16). After all, tests are of very little value clinically if a condition will not or cannot be treated. After any encounter, there is the decision by the doctor (and by the patient) if the clinical picture exceeds a Atest threshold@, ie. that point where a test will guide treatment. There is a second threshold where the physician will treat without testing. This circumstance arises most commonly when a patient with severe sleep apnea presents needing intensive care and therapy is initiated. This second senario is much less common than the first. The decision to test in the outpatient setting has been clearly articulated in consensus statements (15); however, the manner of testing has not (4,11).

Fortunately there is opportunity to begin to define the relationships among clinical presentation, testing modes, and clinical outcome the outpatient setting. A number of studies agree upon a profile upon which to base a Apre-test probability@ for sleep apnea (15,17). In unselected populations, answers to questions about the frequency of loud snoring, pauses in breathing during sleep, and functional sleepiness to predict the appearance of significant amounts of sleep apnea (13); inclusion of questions about body mass index and cardiovascular disease improved the predictive ability, but only modestly (14).

Table 1 summarizes the some of the issues that are addressed in the choice of testing for sleep apnea. These issues can be addressed by the creation of local pathways for patients who on presentation fall into mild, moderate, and severe forms of illness. At the present time I set my treatment threshold for sleep apnea above mild disease (18); as a consequence I offer patients with moderate and severe presentations of sleepiness or potential cardiovascular complications a test because I will then go on to treat.

Creating such pathways is only the first step in managing an illness as prevalent as sleep apnea. Implementation and assessment of outcome in a pathway permits process improvement (18). First, there is now the opportunity to link pre-test probability of testing to outcome of treatment. I suspect that any

number of strategies would reduce the need for attended polysomnography in patients with very high pre-test probability for apnea. These might include direct application of device that not only monitor breathing but also restore airway patency by adjusting the pressure in a nasal mask or restore minute ventilation. Second, in the low-probability individual the opportunity exists to reserve testing, institute conservative or behavioral measures to control symptoms, and observe. Third, determination of pre-test probability permits one to assess the importance of a negative test in a high risk individual or a positive result in a low-risk individual.

The Abest test@ is the one that improves the condition of the patient, leads to an effective treatment, or determines that no further therapy is needed. For some centers, portable monitoring fits these criteria.

In one managed care setting, between 1991 and 1994, the rate of new patients undergoing sleep studies increased 30% per year, resulting in recognition of perhaps 10-30% of individuals in the health management organization estimated to meet minimal criteria for OSA (James deMaine and Rob Sandblom, personal communication). This demand prompted a re-evaluation of the use of attended polysomnography and the institution of an in-home testing (and treatment) program to reduce the global cost of care.

If there becomes a time when a standardization of interpretation and clinical probabilities is used among centers multi-center trials could be used to refine clinical decisions and explore alternative strategies of care (19).

The Sleep Center of the Future

The APolysomnographic Age@ , as named by Patrick Strollo (1997) has ended for sleep medicine. The sleep center of the future will have to play a role in patient care that goes beyond the boundaries of the center because in many instances the diagnostic and intitation of treatment can be done in the home. For those patients who fit a high probability of sleep apnea, the center will play an advisory role to primary care practitioners in a care pathway; this may mean that the patient never sees a sleep specialist. For other patients, for instance those with snoring or hypoventilation syndromes, the sleep center will need to define its role in disease management along with specialists in otolaryngology and pulmonary medicine. For this to have Avalue", the level of expertise in designing and managing care pathways will have to be increased.

There will still be a need for polysomnography; however, I suspect that such efforts will be indicated for complex neurologic disorders and for the unusual disorders requiring a broad population base for patient referral. The personnel in the sleep center could have a role in education of patients and physicians and broaden its interest to prevention, chronopharmacology, and circadian disorders. In other words the sleep center will have to expand the application of technology and its scope of practice to increase its value the patient population and medical community.

ISSUES IN TESTING FOR SLEEP APNEA

QUESTIONS	POSSIBLE ANSWERS
What is the purpose of the study?	Initial diagnosis Evaluation of existing treatment Screening for prevention
What are the pre-test probabilities?	High, low, or intermediate probability for OSAHS Complicated presentation suggestive of two or more sleep disorders
Will recording of cardiorespiratory variables adequately reflect the patient=s problem?	Need apnea type and duration Need markers of gas exchange
Does sleep-wake cycle need to be measured?	Use of surrogate markers or time in bed is acceptable
What are the expectations for the patient?	Patient able to attach/arrange sensors Patient resists center environment
How clinically stable is the patient?	Requires observation, intervention, and/or assistance
What instrumentation is needed/available?	Single channel Multiple channels Video/Conferencing
What would be the response to an inadequate study? Or a study that is inconsistent with pre-test probabilities?	Can be easily repeated Cost/needs of second testing is understood
Are there special issues in the health care environment?	Rural/Urban resources Expectations of physicians or their ability to tolerate uncertainty Presence of a care pathway

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Comment #63:
Submitter: Nick Spanos
Organization:
Date: Thu, Apr 29, 2004 2:47 PM
Comment:

Thanks for reading this attachment and it's my opinion that Medicare doesn't change the current policy for the safety of many people who have sleep disorders.

I would like submit some commits on this issue. I'm currently a manager at a sleep disorder center and have been in sleep since 1998. I'll try to keep it short as possible.

1. I have witnessed several (fortunately not many) patients who have had home studies, later have a sleep study in the lab setting where the results are conflicting based on OSA. In addition other parameters of sleep such as limb movements and upper airway resistance syndrome are not evaluated by home studies, but can have similar outcomes as OSA.

2. To properly treat OSA patients as a result of home studies would lead to inadequate CPAP pressure determination and would not allow for the appropriate use of BIPAP.

3. The statement of the requestor for the policy change about recognizing sleep is uninformed. This information is extremely useful to allow for proper diagnosis as stated with Medicare's policy requiring 2 hours of documented sleep.

4. Another statement that home tests are less expensive is partially true, however costs in the long run because of misdiagnosis and improper treatment would increase substantially than allowing for the best diagnosis and treatment that occurs in a sleep center. Home studies are scored electronically which literature referenced in the American Academy of Sleep Medicine (AASM) lead to error. Manually scored studies by trained professionals is needed for proper interpretation.

5. One final statement to address, the requestor suggests that home studies would allow for a greater number of practitioners to perform the home studies. This would also contribute to misdiagnosis and improper treatment leading to increase medical costs. Education and training with a sleep background is important for evaluating sleep disorders.

There are other statements made by the requestor which don't seem validated. As far as the studies referenced in favor of home studies, I would refer to the Practice Parameters on portable studies by the AASM. In this guideline there are only select cases where an attended portable monitoring device is acceptable.

It is my opinion to allow for a correct diagnosis, treatment, and safety of many patients, Medicare doesn't change the policy to not allow portable home studies in the treatment of sleep disorders.

Comment #64:
Submitter: Gerald N. Rogan, MD
Organization:
Date: Tue, Apr 20, 2004 2:03 AM
Comment:

When I was the carrier medical director for NHIC CA, I wrote the LMRP not to cover home sleep testing principally because CMS required home sleep testing in CIM 60-17. The CPT code was 95806. I thought the technology was very good. I also thought that accurate home testing would be beneficial to patient care. I think OSA is underdiagnosed. When I practiced family medicine, I had a patient with SIADH and periodic V tach from OSA-cured with CPAP

http://www.medicarenhic.com/cal_prov/lmrp/lmrp_01_101.htm

By contrast, during this period Blue Shield of California did make a limited affirmative coverage decision.

Also, Practice Parameters for the Use of Portable Recording in the

Assessment of Obstructive Sleep Apnea ----

An American Sleep Disorders Association Report

Standards of Practice Committee of the American Sleep Disorders Association can be found at

http://www.aasmnet.org/PDF/PortableParameter.pdf

Comment #65:
Submitter: Michael Coppola, MD
Organization: Mercy Hospital Sleep Center
Date: Thu, Apr 22, 2004 10:39PM
Comment:

(See next page)

MICHAEL COPPOLA MD
PRESIDENT, SPRINGFIELD MEDICAL ASSOCIATES
MEDICAL DIRECTOR MERCY HOSPITAL SLEEP CENTER
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413-739-5676
May 20, 2004

re: NCA Tracking Sheet for Continuous Positive Airway Pressure (CPAP) Therapy for Obstructive Sleep Apnea (OSA) (CAG-00093R)

Dear Ms. Spencer and Dr. Sanders,

I am writing to urge you to give positive consideration to Dr. Davidson's proposal for CPAP coverage in patients who have had their need for CPAP documented in situations other than an attended facility-based study.

In 1988, I began utilizing unattended four-channel recording to establish the diagnosis of OSA for patients with a high pre-test probability of OSA. I embarked upon this out of sheer desperation, because of the lack of access to care. We found people could self-titrate quite well with proper education and follow-up. We published our preliminary uncontrolled series in 1990. [1]

We were met with not a small amount of criticism, but persisted because frankly our patients had little alternative. It became clear that economic forces were heavily in favor of attended testing and no one would step forward to fund a large-scale study. Group Health in Puget Sound (Seattle WA) bravely embraced our program and applied it across a patient population in the thousands as the preferred method for evaluating OSA and initiating CPAP. Their work was presented in abstract form but unfortunately was never presented in full publication, although their data was clean and the analysis was quite sophisticated. They clearly showed improved, lower-cost access to care with excellent patient outcomes. The success of positive pressure assist is not determined by the type of test, which documents the OSA, but by the care and support provided for the patient. We have successfully treated thousands of patients with CPAP as has Group Health and other programs with unattended non-facility based studies. Despite this our facility-based sleep lab is also booked for months. Recently Dr. Fitzpatrick in Canada, unaware of our previous work, published a paper documenting the same positive results with self-titration.[2]

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[1] Coppola, M., Lawee, M. Management of Obstructive Sleep Apnea in the Home: The Role of Portable Polysomnography. Chest, Vol. 104, 19-25.1993.

[2] Fitzpatrick MF, Alloway CE, Wakeford TM, MacLean AW, Munt PW, Day AG. Can patients with obstructive sleep apnea titrate their own continuous positive airway pressure? Am J Respir Crit Care Med. 2003 Mar 1;167(5):716-22.

I must ask, what would have happened to these patients who have had CPAP success for years if we had not done so? These people had little access to care with facility-based testing, so we devised a careful, thoughtful and supportive program which has stood the test of time. Our sleep lab and others in the area continue to grow, but as associations with other morbidities such as stroke, heart attack and diabetes are uncovered, awareness and demand is rising. We can not provide care to all these patients with the facilities we have. I have seen good results from home testing and poor results when patients have had a facility-based study with poor education and follow-up. I do not believe current CMS policy insures adequate care for our patients, but merely restricts care to those expensive and unavailable "sleep centers" who have successfully lobbied for their own interests in the guise of providing the "gold standard" of care. They have never shown that PSG improves outcomes with CPAP. Unfortunately they are a very powerful voice, while our millions of undiagnosed, symptomatic patients have no champion. I am afraid that those who have lobbied CMS in the past have had financial, career and research agendas, which biased them in demanding a certain approach to sleep. I support non-facility based testing even though I have a greater financial incentive to perform more attended facility-based studies. I know my colleagues at Group Health in Puget Sound who also have facility-based capacity and have three" boarded" sleep physicians also support my position. Other colleagues in San Diego, North Dakota and elsewhere have robust programs in unattended sleep management. We all have found that comprehensive disease management depends heavily on care and education with a de-emphasis on the diagnostic burden of polsomnography. The facility-based PSG requires a diagnostic burden completely out of proportion to the need given the safety of the therapy.[3] We have placed too much emphasis (and a disproportionate share of the dollars) on diagnostic testing and too little on therapy.

It is interesting to note that this anomaly is peculiar to the US. Most of the diagnostic testing in advanced European economies is done in portable scenarios. A recent article glaringly pointed out the disparity between the US and the rest of the world.[4] Access to care continues to be an issue in a common disease in which all estimates show we are not beginning to reach the millions of afflicted Americans. I am afraid that intense lobbying in the US by individuals whose bias is to grow and maintain high level tertiary care laboratories which generate millions of dollars in revenue and have a poor track record in providing care to their patients (follow-up rates < 50 % in some centers) has impacted on CMS's decision to limit CPAP coverage. As Dr. Pack, a well-respected sleep researcher, recently pointed out in an editorial: "It's all about Access".[5]

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[3] Kassirer JP, Our stubborn quest for diagnostic certainty. A cause of excessive testing. N Engl J Med. 1989 Nov 2;321(18):1272-3.

[4] 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 Mar 15;169(6):666-7.

[5] Pack, A. Sleep-disordered breathing: access is the issue. Am J Respir Crit Care Med. 2004 Mar 15;169(6):666-7.

I respectfully request CMS to reconsider its position on CPAP and allow us to manage our OSAS patients with safe, effective initiation of CPAP without the unnecessary burden of cumbersome testing. By devoting more resources to the therapy we can improve access to care and improve the quality of care provided our patients.

Respectfully submitted,

Michael P. Coppola MD

Comment # 66:
Submitter: Yosef Krespi, M.D. and Robert S. Lebovics, MD, FACS
Organization: St. Luke's Roosevelt Medical Center
Date: Wed, May 5, 2004 10:17 AM
Comment:

We are writing to express our strong support for a revision to the national Medicare coverage determination (60-17) under consideration by CMS that would permit Medicare beneficiaries to receive multichannel home sleep testing as a diagnostic alternative to attended polysomnography (PSG). Currently, Medicare only reimburses for Continuous Positive Airway Pressure (CPAP) devices if the polysomnography is performed in a facility - based sleep study laboratory, and not in the home or in a mobile facility.

While we recognize and are sensitive to historical concerns regarding the Medicare program?s payment of CPAP devices (particularly where DME companies furnish the testing), sleep disorder breathing (SDB), a.k.a. obstructive sleep apnea (OSA), continues to be a major health concern in our elderly population which includes Medicare beneficiaries. SDB is a chronic illness that significantly contributes to the progression of cardiovascular illness specifically heart attack and stroke. These diseases are among the leading killers in the USA today and significantly impact on the public health as well as on total Medicare spending. In addition, SDB in its milder forms cause untold losses in terms of work productivity and contribute to all types of mechanical accidents. Other well known associations to SDB include hypertension (both systemic and pulmonary), congestive heart failure, cardiac dysrhythmias, morbid obesity and diabetes mellitus. In 2003 alone, the estimated cost of cardiovascular disease and stroke was $351.8 billion. Of this amount, $209.3 billion is due to direct medical costs and $142.5 billion to lost productivity. *See*, http://www.cdc.gov/nccdphp/power_prevention/pop_spending.htm . Cost estimates for 2004 are projected to be around $368.4 billion - this figure also includes direct costs and costs of lost productivity. Suffice, cardiovascular disease is a major health care expense and early intervention will help to reduce long term expenditures even if there is an increase in sleep studies and CPAP therapies. You may also know that, The National Institutes of Health (NIH) has allocated nearly 1 billion dollars over the last decade to studying the science of OSA and this trend is increasing.

It is our view that, with the advent of new technologies, including that offered by Oxford BioSignals, Medicare?s restriction on sleep venues is an impediment to diagnosing and treating OSA and, ultimately, an impediment to beneficiary health. Specifically, the Oxford BioSignal BioSomnia device is a single channel ambulatory electroencephalogram (EEG) with a software package that has been approved by the FDA for use as an adjunct to a physician in the diagnosis of sleep disorders in the patient?s *home environment*. Although we do not promote or advocate the use of any particular device, we believe that CMS? should revise its coverage policies to permit home-sleep study testing for those multichannel diagnostic devices that include a

minimum 4 lead respiratory/cardiovascular recording. These parameters may include respiratory flow, pulse oximetry, respiratory effort, body position, and snoring. The option of including a single channel EEG measuring true sleep time is now a reality.

Devices, such as the BioSomnia, eliminate many of the previous objections to unattended home studies. First, the EEG component will confirm that the patient was actually in the proper phase of sleep while the cardiovascular/respiratory sensors are measuring their components. This is a major advance, in that the current gold standard of PSG uses human beings, usually with a limited medical background, to ascertain that a patient is in rapid eye movement sleep (REM) or even in any phase of sleep. Objective EEG recordings not subject to interpretive biases will define the time period for which the respiratory/cardiovascular data is analyzed.

Home testing for OSA also has a number of clinical and economic advantages for the patient and the Medicare program, in general. First, it is generally well recognized that patients sleep more comfortably in their own beds than in a sterile hospital or sleep lab facility environment. In fact, in some instances, it may be difficult to obtain reliable results in a sleep lab environment which bears no relation to the actual conditions encountered by the patient in the home setting. Second, in some areas of the country there is a paucity of sleep testing facilities and, as a result, patients experience delays in scheduling sleep studies which prevents timely diagnosis of OSA. Home studies should reduce and/or alleviate these delays.

Third, a home study using the BioSomnia (or other similar devices), will be substantially cheaper than a standard facility-based sleep study and the validation studies are available to substantiate the medical device?s diagnostic accuracy. As home testing equipment is significantly cheaper, physicians in multiple disciplines related to sleep medicine will find the testing equipment affordable and be able to offer these diagnostic services to those patients who medically require them. Such doctors might include, neurologists, cardiologists, pulmonologists, ENT surgeons, oral surgeons, in addition to family physicians and geriatricians. Fourth, home studies can produce virtually instant results for the treating physician; whereas, the ?class? sleep facility hand scoring report from ?attended? sleep labs may lead to a 10-14 day turn around time for results.

Reliable home testing, such as that we believe now exists through improved technology, will help a physician promptly diagnose a medical condition, such as OSA, leading to earlier intervention and, ultimately, to a better quality of life, decrease in long term disabilities and saving of health care resources. We believe that CMS must consider these important issues as it balances longstanding concerns over the appropriate types of sleep studies that can be relied upon for CPAP qualification. In our view, CMS should address ?who? can perform home testing (e.g., a physician, home health agency and/or DME supplier) separate and apart from whether this type of test should be covered. Clearly, as with all technologies, the potential for excess utilization exists?however, this

should not the form basis of coverage denial when, as in this case, the benefits of offering such technology can provide substantial improvements in the quality of life of patients.

In summary, we believe that home sleep testing will benefit the public health in multiple venues in addition to saving lives. As cardiovascular disease is a major Medicare expense, early intervention will act to reduce long term expenditures even if there some short-term increase in sleep studies and CPAP therapies. The technology has leaped forward and is now at a point where CMS can and should consider revision to its coverage rules to facilitate payment for such services.

Comment #67:
Submitter: Larry M. Higby
Organization: Apria Healthcare
Date: Fri, May 7, 2004 6:04PM
Comment:

(See next page)

APRIA HEALTHCARE

Lawrence M. Higby
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May 7, 2004

Tiffany Sanders, M.D.
Mail Stop C1-09-06
Office of Clinical Services and Quality
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, Maryland 21244

Re: CAG-00093R: Continuous Positive Airway Pressure (CPAP) Therapy for Obstructive Sleep Apnea

Dear Dr. Sanders:

I am writing on behalf of Apria Healthcare regarding the recent modified national coverage determination announced by CMS involving Continuous Positive Airway Pressure (CPAP) therapy for obstructive sleep apnea. Apria Healthcare is America's leading provider of integrated homecare products and services. Apria provides full-service homecare solutions in respiratory therapies and other clinical areas to over 1.2 million patients through 425 branch offices located throughout the United States.

We urge CMS to recognize the use of portable multi-channel home sleep testing devices as an alternative to facility-based polysomnography in the evaluation of obstructive sleep apnea (OSA). With the appropriate safeguards, in-home testing provides an accurate and cost-effective modality for evaluating whether or not patients suffer from OSA that would benefit clinically from the administration of CPAP therapy.

Although others are likely to describe the recent clinical literature in greater detail, we wish to highlight that investigations published during the past several years provide further support for the clinical appropriateness of home-based testing. Please consider the following:

- Golpe and Carpizo reported in *Chest* during 2002 on "a portable respiratory recording device used unsupervised in the patient's home" that can provide "useful assessment" for sleep apnea.[1]

- Also in 2002, Gagnadoux et al. compared home unattended polysomnography with polysomnography performed in the hospital setting to diagnose obstructive sleep apnea syndrome. The investigators concluded that the site of recording (home versus the hospital) had no influence on the polysomnographic indices relevant to diagnosing obstructive sleep apnea syndrome.[2]

- In 2003, Bar et al. compared the use of an ambulatory device for in-home testing to in-laboratory polysomnography, concluding that the ambulatory device provided "an accurate, robust and reliable ambulatory method for the detection of obstructive sleep apnea syndrome."[3]

It is important for the Medicare program to revisit the issue of in-home testing for OSA, especially due to the fact that home-based diagnostic devices have continued (and will continue) to evolve in this area. In practice, the current reliance on a finite number of sleep laboratories in the United States for polysomnography is resulting in *de facto* rationing of care and creating barriers to access to treatment, especially in rural areas. Home sleep testing provides a meaningful opportunity to address this problem and improve beneficiary care.

The recent clinical literature also highlights that in-home polysomnography is more cost-effective than laboratory polysomnography.[1,3] This is the case even when technologists are sent to the home to assist the patient in setting up the testing equipment.[1] In addition, there is significant and avoidable morbidity and financial costs associated with the current under-diagnosing of OSA.

Due to the relative cost-effectiveness of home testing and the well-documented shortage of sleep laboratories that perform polysomnography, private health plans have begun using in-home testing to evaluate patients for CPAP in the context of OSA. For example, we understand that Kaiser Permanente in California is using unattended in-home testing in patients who are suspected of having OSA. These patients are being screened, and after attending an educational session, they undergo unattended home testing followed by unattended auto-titration (if indicated) to accurately and effectively diagnose OSA and to initiate subsequent treatment with CPAP.

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[1] Golpe R, Jiminez A, Carpizo R. "Home Sleep Studies in the Assessment of Sleep/Hypopnea Syndrone (Clinical Investigations)." Chest, October 2002.

[2] Gagnadoux F, Pelletier-Fleury N, Philippe C, Rakotonanahary D, Fleury B. "Home Unattended vs. Hospital Telemonitored Poly somnography6 in Suspected Obstructive Sleep Apnea Syndrome; A Randomized Crossover Trial (Clinical Investigations)." Chest, March, 2002.

[3] Bar, A, Pillar, G, Dvir, I, Sheffy, J, Schnall, RP, Peretz, L. "Evaluation of a Portable Device Based on Peripheral Arterial Tone for Unattended Home Sleep Studies (Clinical Investigations)." Chest, March 2003.

We urge CMS to move forward in providing Medicare beneficiaries with access to in-home diagnostic testing for OSA. We believe that such a refinement to the current coverage policy is consistent with the best interests of the patients and the general trend toward identifying and employing cost-effective, home-based solutions for clinical diagnostics and treatments. Taking this step to help identify and treat patients with OSA is in the best interests of patients and the Medicare program.

Please do not hesitate to contact us if we can provide any further information or be of additional assistance. We hope to hear from you.

Sincerely,

Lawrence M. Higby

cc: Francina Spencer, CMS, OCSQ

::ODMA\PCDOCS\WSH\323026\1

Comment #68:
Submitter: Pamela Fry, BS, RRT and Susan Riley
Organization: AirLogix
Date: Fri, May 7, 2004 10:53 AM
Comment:

(See next page)

Medicare Coverage – CAG-00093R

The following is a submission for public comment on the national coverage determination for diagnosis and treatment of obstructive sleep apnea (OSA) to include multi-channel home sleep testing (HST) as an alternative to polysomnography (PSG).

- Obstructive Sleep Apnea (OSA) is one of many sleep related diseases which has fallen under the name sleep disordered breathing (SDB) and therefore is often confused with diseases of the airway which may be more complex in nature and require additional channel monitoring.

- The diagnosis of OSA starts with a history & physical, and should include an evaluation of the patient's performance related to daytime sleepiness and a risk assessment for sleep disorder. Several questionnaires are available to assist the physician in the patient evaluation. With this information the physician may determine the diagnosis, and choose to use a HST, home sleep test to verify that decision – similar to laboratory testing to confirm an infection. If the diagnosis appears more complex a sleep lab study would be indicated.

- When a diagnosis of OSA is suspected, sleep testing with multi-channel respiratory parameters is needed and can be completed with much success in the home as documented in several studies. The parameters for testing should include:
  - airflow for demonstration of apneas and hypopnea
  - oxygen saturation to determine the extent of oxygen injury associated with each event
  - position sensors and chest wall movement sensors to assist in diagnosis and determination of the type of apnea which will reflect in treatment options

- The results of the HST still require the rigors of evaluation with set standards related to total sleep time, apnea/hypopnea calculations and review by a physician trained in sleep medicine.

National coverage for multi-channel home sleep testing will allow patients to be tested and more importantly treated for a condition which has been associated with many co-morbid conditions. The treatment of OSA with CPAP therapy has been documented to improve hypertension and reduced stroke and heart failure – co-morbid conditions often associated with Medicare beneficiaries.

Looking at the cost of healthcare; research has identified significant increases in healthcare dollars spent on members in the 2-year period prior to a diagnosis of OSA. Kryger, M. Sleep 19 (1996)
In addition, OSA patients with cardiovascular and pulmonary disease experience reduced hospitalizations with CPAP treatment. Peker, Y. - Sleep 20 (1997)

The use of home sleep testing would allow patient diagnosis for those uncomfortable going to a sleep lab, reduce the time from diagnosis to treatment, and provide the physician a diagnostic tool to complete a care plan for OSA.

In a disease management model, the use of home sleep testing would allow the addition of patient education and compliance management to the CPAP treatment plan without any additional healthcare cost when compared to traditional polysomnography/CPAP treatment costs.

Thank you for the consideration,

Susan B. Riley
President and Chief Executive Officer

Pamela K. Fry BS, RRT
Director, Corporate Development
888.775.8676 ext2064

Comment #69:
Submitter: David Barone, M.Sc., MBA
Organization:
Date: Wed, May 5, 2004 9:30 PM
Comment:

(See next page)

Watch-PAT 100: Review of Evidence

David Barone, December 2003

TABLE OF CONTENT

The references presented in this memorandum do not address all portable sleep studies, but rather focus on the evidence associated with a new technology utilizing a measurement of peripheral arterial tone (PAT), in conjunction with other physiological parameters, to detect sleep apnea events. The specific technology addressed in this report was developed in recent years, and was not available during prior reviews of medical literature analyzing the evidence for reliability, efficacy and outcomes associated with unattended sleep studies.

Overview

Obstructive Sleep Apnea

Obstructive Sleep Apnea (OSA) is a recognized disorder of sleep, characterized by recurrent airway obstruction, identified as apneic and hypopneic episodes. In view of its high prevalence, serious associated morbidity and recently shown mortality, sleep apnea has been recognized as a major public health problem[1]. Persons with this disorder usually experience tiredness, fatigue, irritability and difficulty concentrating[2]. Worse still, they are more likely to fall asleep at inappropriate times and have a higher rate of vehicular crashes and work-related accidents than other people[3]. Sleep apnea also affects the cardiovascular system. It is associated with increased blood pressure, cardiac arrhythmias during sleep, and it may contribute to atherosclerosis leading to myocardial infarction[4], as well as to stroke[5]. The mortality among patients with severe untreated sleep apnea has been significantly higher than in patients with a mild sleep apnea[6]. The National Sleep Commission on Sleep Disorders Research estimated that sleep apnea may be responsible for 38,000 cardiovascular deaths per year[7].

OSA has been recognized as a clinical condition for over 25 years[8], and since then, diagnostic tests identifying OSA as well as treatments have increasingly been provided to patients complaining of excessive sleepiness and other related symptoms. The prevalence of OSA, most common among middle-aged adults, is estimated to be up to 5% of the U.S. population[9] (although some reports estimate the prevalence to be closer to 10%), and is in effect more prevalent than asthma. In certain high risk populations, the prevalence of OSA is even significantly higher. Over 50% of patients with CHF have been reported to suffer from sleep-disordered breathing[10], and among morbidly obese patients, the incidents of OSA are at least 12 fold higher than in the general population[11].

Shortcomings of current state of the art OSA diagnostics and treatment

Patients with obstructive sleep apnea benefit from a number of effective therapies, such as continuous positive airway pressure (CPAP), oral appliance, also known as an intraoral mandibular advancement device, and for those failing or refusing the non-invasive treatment options, surgeries such as tonsillectomy and adenoidectomy. Other treatment options, including surgeries, are available for patients failing or refusing CPAP treatment. In spite of the availability of effective treatments for OSA, results from the Wisconsin Sleep Cohort indicate that over 10 million patients with sleep apnea remain undiagnosed[12]. The major problem in the field is, therefore, not treatment but diagnosis: whom to test, how to identify the candidates for the test, how to test, and what are the implications of test results regarding the risk of serious clinical sequelae, as well as the economical related issues.

The most common diagnostic method for OSA is an overnight full polysomnography (PSG) test, which consists of measuring electroencephalogram (EEG), electrocardiogram (ECG), electrooculogram (EOG), electromyogram (EMG), respiratory airflow, chest and abdominal respiratory efforts, body position and blood oxygen saturation in a sleep laboratory. PSG is costly, and while considered as the “gold standard”, the interpretation of the data is complex and subject to significant variability[13]. The cost of full PSG for all suspected cases would be prohibitive, and will fall far short of providing an acceptable solution for

testing all patients suspected of sleep apnea. Thus, with so many people requiring testing for OSA, the availability of accurate, yet simpler and less costly alternatives for diagnosing sleep apnea, to augment the in-lab PSG, is highly desirable.

The PAT solution

On November 2001, the FDA approved a 510(k) application for the Watch-PAT100, a patient wrist-worn device to be used unattendedly during sleep in the home for the purpose of aiding in the diagnosis of obstructive sleep apnea syndrome. The device records a physiological measurement, Peripheral Arterial Tone (PAT) signal, which can be monitored non-invasively through a finger-mounted opto-pneumatic probe. In addition to the PAT probe, the device incorporates pulse oxymetry measurement and an embedded actigraph for sleep/wake differentiation. PAT signal is a measure of arterial pulsatile volume changes in the fingertip brought about by varying sympathetic nervous system activity. Since respiratory disturbances during sleep are associated with sympathetic surges, they cause changes in the PAT signal as well. The PAT device can identify respiratory disturbances during sleep, utilizing a computer analysis program used with the PAT signal to analyze fluctuations in sympathetic tone.

The Watch PAT 100 (WP100) is the first device to use PAT signal analysis to measure respiratory disturbance during sleep. A principal benefit of this measurement technique is its simplicity of use. Since PAT signal can be measured using a device worn comfortably on the wrist, it is ideal for studies performed outside of a sleep lab facility and does not require the full-night attendance of a technologist. Another primary benefit of the PAT measurement is the ability to detect and record even minute changes in peripheral vascular volume associated with arousals, and through this measurement, detect even subtle sleep disordered breathing events.

A further basic aspect of the PAT measurement that is of practical importance is that it also provides information about changes in pulse rate. While isolated spontaneous vasomotor tone and heart rate fluctuations are common and normal occurrences, it is in fact the specific combination of a characteristic pattern of vasoconstriction and a degree of transient relative tachycardia in close temporal proximity that serves as a highly sensitive and specific autonomic marker of OSA.

Despite the longstanding awareness that autonomic activation accompanies apnea termination, prior to the introduction of the PAT technology, a reliable noninvasive marker of this was conspicuously lacking. A number of autonomic parameters have been evaluated as potential markers of OSA but their performance has been disappointing. For example, Pitson and Stradling reported an R value of 0.65 for the pulse transit time (PTT), and 0.51 for heart rate changes relative to standard PSG criteria of sleep disordered breathing indices[14]. In sharp contrast to these modest levels of correlation, PAT has been consistently found to provide R values within the 0.85- 0.95 range in several independent studies[38,41,49].

In addition to the PAT probe, the WP100 device incorporates pulse oximetry and an embedded actigraph. The WP100 software automatic algorithms uses features of the PAT signal, blood oxygen desaturation and pulse rate for respiratory disturbances detection, and the actigraphy signal for sleep/wake state detection. The WP100 is the only non-EEG ambulatory device having the capacity to reliably detect sleep/wake states, providing for diagnostic capability closer to PSG, rather than any conventional cardio-pulmonary ambulatory device (which have been used in unattended sleep studies), as it allows the detection of the respiratory events during the relevant sleep periods only and the assessment of sleep fragmentation that is often caused by OSA.

PAT testing represents a substantial technological advancement from other devices currently marketed for ambulatory sleep tests. Some technologies previously used in the unattended setting require cumbersome sensors interface, and as a result, they are susceptible to unreliable and inconsistent data acquisition. Many devices have failed to demonstrate consistent sensitivity and specificity. The new PAT technology records some of the same physiological parameters as other unattended devices (e.g. arterial oxygen saturation and pulse rate) but (*i*) by including the PAT signal, instead of the cumbersome airflow and efforts measurements, and (*ii*) by adding actigraphy to identify sleep states, it performs unique physiological analysis, different from the parameters monitored and recorded by other devices.

By utilizing these new capabilities, the PAT device is able to provide a higher level of informative diagnosis value, and to achieve a high level of reliability and accuracy. Through a direct measure of the arterial pulse volume changes – a demonstrated surrogate of arousal and sympathetic activation, the PAT has the ability to provide an 'arousal context' to the measurement of apnea or hypopnea events,

matching the ability of the full PSG study to diagnose OSA in an unattended home testing environment. Furthermore, the unique nature of the PAT events enables the effective use of distinct computer programs, now well-validated, in the analytic parts of the PAT-based procedure.

The WP100 is mounted to the wrist, and connects to external sensors placed on two fingers. This configuration, with minimal discomfort, if at all, makes the device particularly convenient to the patient. Eliminating the patient's intimidation and physical interference factor, and allowing for the recording to be conducted at the patient's natural home environment, provide for a much better reflection of patient's typical sleep, and unimpaired recording of sleep patterns.

The Watch PAT100, which has been used clinically since early 2002, does not fit the definition of PSG, on one hand, but has clinical and technological features that are substantially advantageous to those associated with existing technologies for unattended sleep studies, on the other hand. CPT code 95806 describes unattended sleep studies, but the description of the service associated with this code refers to technologies predating the PAT. Due to certain limitations of such older technologies, some health plans have not reimbursed providers for conducting unattended studies. Approving reimbursement for sleep studies utilizing the PAT ambulatory technology, which represents significant improvement over prior devices, is consistent with the evolution of other medical practices. A number of procedures performed in the past only in a fixed facility setting, for example monitoring of cardiac and neurological parameters, have evolved to include home-based options, once ambulatory technologies for such applications have been properly validated. These ambulatory technologies have not replaced fixed site technologies, but rather provide additional diagnosis options for physicians and a valuable alternative for their patients. While the WP100 may not be appropriate for all patients being referred to the sleep lab, nor for the diagnosis of all sleep disorders, it will however, in the vast majority of cases, provide a definitive diagnosis to patients suspected of having sleep apnea.

Prior Guidelines for Unattended Sleep Studies

Various professional organizations, medical societies and health plans have assessed in the last ten years the use of unattended sleep studies for OSA. Since such reviews were based on literature predating the introduction of the peripheral arterial tonometry technology, they do not address the PAT technology specifically.

Blue Cross Blue Shield – TEC

A TEC Assessment of portable sleep studies for diagnosis of obstructive sleep apnea syndrome was presented to the Blue Cross and Blue Shield Associations' Medical Advisory Panel on May 1996[15]. The report recognized that "portable sleep studies have been used in the home setting for diagnosis of obstructive sleep apnea. Portable sleep studies may be used as an initial diagnostic tool to avoid the inconvenience of PSG in a sleep laboratory; as a means for evaluating treatment; or as an alternative to PSG for making a definitive diagnosis of sleep apnea", but indicated that (based on the scientific data reviewed for that report published prior to 1996) the evidence was not sufficient to quantify the probability of incorrect diagnosis, redundant testing, or the beneficial outcome of avoiding the inconvenience of an unnecessary polysomnography. Based on the report findings, many of the Blue Cross and Blue Shield plans determined that unattended sleep studies should be considered investigational and therefore, not eligible for reimbursement (since than a number of Blue Cross plans have decided to reimburse providers for unattended sleep studies).

Agency for Health Care Policy and Research (AHCPR)

MetaWork's systematic literature review conducted in 1998 on behalf of the U.S. Agency for Health Care Policy and Research (AHCPR)[16]. The report found evidence that a full PSG may not be necessary to diagnose sleep apnea, but determined, based on literature published prior to November 1997, that there was not sufficient evidence that sleep studies devices can be used reliably in the home setting.

American Association of Sleep Medicine (AASM)

The Practice Committee of the American Sleep Disorders Association (name changed to American Academy of Sleep Medicine, or AASM) stated in 1994[17] that unattended portable sleep recordings for OSA assessment is an acceptable alternative to PSG in the following situations:

- Patients with severe clinical symptoms indicative of OSA, when initial treatment is urgent, and standard PSG is not available.

- Patients unable to be studied in a sleep lab, such as non-ambulatory patients who cannot safely be moved. Such patients are likely to have disturbed sleep patterns, therefore the risk for false negatives and otherwise inaccuracy assessment is heightened.
- Evaluate response to therapy, using follow-up studies, when a diagnosis has been established by standard PSG, and therapy has been initiated.

Institute for Clinical Systems Improvement (ICSI)

The Minnesota-based organization, sponsored by the major health plans in the state, provides an evidence-based framework for the evaluation of treatment of patients. The 2003 ICSI guidelines[18] indicate that "selection of appropriate diagnostic tests, as in all clinical situations, must take into account the estimated pre-test likelihood (prior probability) of the patient having OSA, the availability of credible diagnostic tests, and the local expertise in interpreting these complex physiological tests". The guidelines state that in patients with a high pre-test likelihood of OSA, unattended portable recording for the assessment of obstructive sleep apnea is an acceptable alternative to standard polysomnogram in the same situations outlines by the AASM (above). The recommendation to reserve in-home ambulatory testing to patients for whom the probability of having moderate to severe obstructive sleep apnea is high, was justified by the number of false-negative results obtained by in-home studies when used in patients with mild to moderate apnea[19].

Validating the PAT Signal

OSA testing using the new physiological marker, peripheral arterial tone, has been studied and reported in the literature since 1999. There is a growing body of published evidence that demonstrates that measurement and analysis of peripheral arterial tone, in conjunction with pulse rate, blood oxygen Saturation, body movement and related physiological indicators, provides accurate assessment of OSA, comparable in most instances to that of in-lab PSG. The new procedure utilizing PAT technology can monitor and identify overnight patterns of arousal and cardio-respiratory pathophysiology, and provide the physician with reliable information to accurately diagnose sleep apnea and other subtle sleep disordered breathing pathologies in the patient's natural home setting

The studies of Schnall et al[20] and Lavie et al[21] based on 42 OSA suspected adults demonstrated that (*i*) terminations of apnea events are associated with marked attenuation of pulse wave amplitude and transient relative tachycardia; (*ii*) PAT attenuations were associated with alpha activity coinciding with the onset of the vasoconstriction phase of PAT; and (*iii*) mean Apnea-Hypopnea Index (AHI) score, as measured by conventional PSG and by the PAT, correlates well, with $R=0.92$ ($p<0.001$). Taken together, these studies showed that the use of the specialized PAT finger plethysmograph facilitates the non-invasive detection of peripheral vascular responses to arousals in sleep disordered breathing.

Ding et al[22] validated vasoconstriction response to apnea by the PAT signal, by measuring it simultaneously with PSG, while administering oxygen and intraarterial infusion of alpha-receptor antagonist (phentolamine) during sleep stages 1 and 2.

Grote, Hedner et al[23,24] concluded that PAT allows for a continuous and non-invasive measurement of digital blood flow changes, which are determined by adregenic alpha-receptor activation. The study validated the PAT's utility in detecting autonomic sympathetic nervous system activation, and showed that sleep disordered breathing induced an arousal-related attenuation of pulse wave amplitude. This study further demonstrated that vasomotion in the forearm vasculature is mediated by both alpha (constrictory) and beta (dilatory) sympathetic effectors, and is thus potentially capable of ambiguous and unpredictable response patterns during sympathetic activation due to the opposing vasomotor influences of the alpha and beta adrenergic effectors at the forearm. In contradistinction to this, the vascular bed of the finger is characterized by a tonic and phasic alpha-receptor mediated control, allowing accurate and unambiguous identification of arousals mediated sympathetic activation by pulse wave amplitude.

O'Donnell et al[25] conducted a validation study demonstrating that the magnitude of reduction in PAT signal amplitude is dependent on the degree of airflow obstruction during sleep, and thus, greater obstruction is reflected in a greater reduction in PAT amplitude. Furthermore, the study also demonstrated that the PAT signal shows marked attenuation during the arousal from sleep, immediately after nasal pressure is restored, while the signal amplitude shows non-significant decrease in the absence of arousal.

Summary of Evidence

Approval from the appropriate government regulatory bodies:

FDA has issued 510(k) clearance authorizing clinical use and commercial distribution of the Watch-PAT 100, consistent with its labeled indication. FDA's determination was issued on November 6, 2001, reference number K010739.

The approved indications for use are: *The Watch PAT 100 is a non-invasive home care device, intended for use as an aid in the detection of sleep related breathing disorders. It is indicated in cases of suspected sleep disorders. The Watch PAT 100 is not indicated for children less than 17 years old. The Watch PAT 100 is contraindicated for patients with latex allergy.*

The effect of the technology on health outcomes:

In a published position statement by the AASM[26], the authors refer to the many retrospective and matched control studies pointing to the fact that mortality appears to be related in a graded fashion to the severity of sleep-disordered breathing (SDB). Numerous papers reported that SDB also plays causal or contributing role in the development of co-morbidities, such as hypertension and cardiovascular events. Untreated OSA is also associated with increased risk of motor vehicle and work accidents.

In a two year study of 97 untreated sleep apnea patients, hospitalization days increased 2.8-fold compared to the control group. During that period, the OSA patients also incurred hospital costs of $100,000-$200,000 higher than the control group, and double the physician costs[27]. Another study of 238 patients with OSA, compared to age and gender matched control subjects, showed that the magnitude of medical costs correlated with the severity of OSA, with mean medical cost prior to diagnosis of $2,720 for sleep apnea patients vs. $1,384 for control subjects[28].

A study by Bahamman et al[29] analyzed saving realized following medical intervention in 344 patients with OSA. The author reported that in the two years following treatment, physician costs fell 33%, compared to the two years period prior to intervention, and that duration of hospital days for OSA patients dropped from 1.27 days per-patient-per-year to 0.54 days per-patient-per-year (p=0.01).

Positive diagnosis of OSA enables physicians to initiate treatment. The most common and first choice treatment for patients diagnosed with sleep apnea is CPAP, a highly effective, noninvasive treatment. CPAP has been shown to reduce physiological and psychological associated morbidities in patients with sleep apnea. A study at Yale[30] evaluated the impact of CPAP on quality of life of patients, showing marked improvement in vitality, social functioning and mental health. Other studies reported that treating OSA patients with CPAP may substantially reduce the negative effect on the cardiovascular system[31]. A recently published multi-center randomized clinical trial on 24 patients with CHF demonstrated improved heart function, decreased heart size, decreased blood pressure and decreased heart rate in the group treated with CPAP and medication, as compared to the group treated with medication alone, which showed no improvement at all[32]. Another study concluded that the magnitude of drop in blood pressure two months after starting CPAP treatment is predicted to reduce coronary heart disease event risk by 27% and the risk of cerebrovascular accident by 56%[33].

Chervin et al[34] analyzed the cost benefits of conducting sleep study for the detection of OSA. The study concluded that compared to other medical procdures, the advantage gained by sleep study seems to be well worth the cost. The use of PSG costs less than $40,000 per quality-adjusted-life-year (QALY), compared to the cost of screening asymptomatic patients for carotid stenosis at $120,000 per QALY, and the cost of renal dialysis at $47,200 per QALY.

Technology impact on health outcome

Various portable monitors, predating the PAT technology, have been reported to lose data in 9% to 33% of studies. Portier et al[35] reported that in a series of 103 patients undergoing PSG at home and in the lab, 20% of home studies recordings were voided because of lost, or due to poor quality of recorded data, compared to 5% of data collected in the lab, and that for 33% of patients, home sleep studies were not feasible. Another study reported on a more recent technology used in attended sleep studies, and pointed to the fact that the device limits the information available to the diagnosing physician to summary data only, without providing visibility to the specific breath-by-breath data[36].

Reporting on a study of 37 adults, randomly selected from a population based cohort of 400 subjects, Grote et al[37] reported a correlation of R=0.83 ($p<0.001$) between RDI measured by the WP100, and standard PSG. Sensitivity and specificity for the diagnosis of

OSA (defined in the study as AHI>20) by the PAT device were 92% and 70% respectively.

Another study by Pillar et al[38], including 35 OSA suspected patients, reported that the PAT can distinguish OSA with sensitivity of 100% and specificity of 80%. The correlation between the RDI measured by PSG and PAT was R=0.93 during Non-REM sleep and R=0.79 during REM sleep.

Pittman and Pillar[39] reported the results of a multi-center in-lab validation study of the WP100, including a sub-group of patients which was also evaluated in an unattended home setting. Data collected at patients' home was analyzed by the automatic algorithms built into the WP100 system. Each home study was followed by one PSG overnight study in the lab as a control. PSG scoring followed AASM criteria. The results showed that RDI measured by the PAT device in the home correlated well with RDI measured in the lab, using PSG (R=0.74, p<0.0001). This seemingly not very high R value should be considered in light of the inherent inter-night variability of the number of sleep disordered breathing events[40], and the fact that the in-lab PSG studies and the at-home PAT studies were conducted on different nights. Using RDI>12 to define OSA, sensitivity and specificity of the PAT device were 93% and 80%, respectively.

Benefit of the technology in comparison to established alternatives

Bar et al[41] studied 76 adults, including 69 previously diagnosed patients with OSA and 7 normal volunteers. Study consisted of simultaneous PSG and WP100 recorded in a sleep lab. The results showed high degree of correlation in RDI between the two modalities of sleep studies, with R=0.90 (p<0.0001).

Schnall et al[17] studied 42 adult patients with suspected OSA, and using an automatic analysis of the PAT signal and the pulse rate derived from the WP100, demonstrated high correlation between mean conventional AHI and mean PAT AHI, with R=0.92 (p<0.0001).

Ayas et al[42] compared indices of autonomic arousal derived from standard PSG variables, and those measured by the WP100, are found the latter to better predict (*i*) subjective day-time sleepiness, as measured by Epworth Sleepiness Scale, (*ii*) quality-of-life, as measured by Functional Outcomes of Sleep Questionnaire, and (*iii*) decrements in performance, as measured by Psychomotor Vigilance Test.

Pillar et al[43] studied 26 patients, presumably well treated with CPAP. Simultaneous recording of PSG and WP100 showed that (*i*) the WP100 accurately detected respiratory breathing disorders while the patient is on CPAP, and (*ii*) that 20% of the patients with moderate or severe OSA required a re-titration of their CPAP pressure. The authors suggested that considering the technical inherent difficulty in measuring nasal air flow while the patient is breathing through a CPAP nasal mask, the WP100 would be an ideal device to conduct reassessment of treatment efficacy.

Penzel et al[44] studied 20 adults with suspected OSA, comparing changes in the PAT signal to the World Health Organization (WHO) criteria, and reported that PAT signal followed closely apnea-related changes in blood pressure.

Pillar et al[45], following a study including 68 adult patients, confirmed that the automatic analysis of the PAT signal derived from the WP100 device identifies arousals during sleep. Simultaneous overnight recordings of PSG and PAT signal showed a correlation of R=0.87 (p<0.001) between arousals determined by sleep specialists analyzing PSG recordings using criteria defined by the AASM, and the arousals identified by the WP100.

In another study including 24 adults, Pillar, Shlitner et al[46] concluded that the PAT detects sympathetic activations associated with microarousals during sleep. Arousals identified by PSG, using AASM criteria, and arousals recognized by PAT, highly correlated with R=0.95 (p<0.01).

The improvement is attainable outside the investigational setting

Duntly et al[47] reported on a validation study using the WP100 device at the home setting. 56 subjects, tested in two separate centers, have undergone PSG and PAT study in a sleep lab (control), followed by unattended studies at home. PAT RDI was highly correlated to PSG RDI with R=0.87 (p<0.0001). Home studies were successfully collected in 91% of recordings, with Positive Predictive Value of 0.97 and Negative Predictive Value of 0.80.

Another study, reported by Ayas et al[48], compared the results of 28 randomly selected patients undergoing unattended home sleep study using the PAT device, to results obtained for same patients in both PSG and in-lab PAT studies. The study concluded that the WP100 provides an accurate method to differentiate patients with and without OSA. Using RDI>16 to

define OSA, sensitivity was 85% and specificity 87.5%. The study also documented 100% reliability of the PAT device, with no failure during data acquisition or data analysis.

Proposed Guidelines for Using PAT Technology to Diagnose OSA

Sleep studies can be done at patient's home, without a technologist in attendance, as long as the study incorporates the following elements:

1. Identification of respiratory disturbances through the monitoring of sympathetic activation and measurement of changes in peripheral arterial tone.
2. Simultaneous measurements of arterial oxygen saturation and heart rate.
3. Detection of sleep/wake states.

The PAT technology should be an acceptable method for conducting sleep studies in an unattended setting, in the following cases:

1. Rule out a questionable OSA diagnosis and thereby eliminate the need for polysomnography.
2. Affirmatively diagnose suspected OSA and refer a patient for immediate treatment.
3. When standard polysomnography is not readily available, and patient's symptoms are severe, strongly suggesting a diagnosis of OSA requiring immediate treatment.
4. When testing in a sleep laboratory is not possible because of the patient's condition (e.g., patient is non-ambulatory or obese).
5. As a follow-up study to evaluate the response to therapy after initiation of treatment or after a period of time to evaluate the stability of the treatment
6. When testing by a sleep laboratory is not readily available in the patient's locale.

Summary

The PAT technology has been studied extensively, with essentially all published studies reaffirming the efficacy of the technology in diagnosing OSA. Ten published studies, including a total of 743 patients, report mean correlation of R=0.86 between RDI measured by PSG and in studies using the WP100. The new technology has now been used in multiple clinical settings since its approval by the FDA in November 2001, demonstrating significantly better performance compared to previous devices used in unattended tests for OSA. Recording non-invasively Peripheral Arterial Tone (PAT) signal, together with simultaneous measurements of pulse oxymetry, heart rate and an embedded actigraph, enables reliable detection of sleep respiratory disturbances, as well as sleep/wake differentiation. These capabilities, coupled with a patient-friendly interface with the sensors and the device itself, have demonstrated in multiple reports close to 100% success in data acquisition in the unattended setting, with average reported sensitivity and specificity of 93% and 80%, respectively.

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May 3, 2004 VIA E-MAIL and US POST

Tiffany Sanders, MD
Lead Medical Officer
Centers for Medicare and Medicaid Services

Re: Review of Guidelines for Continuous Positive Airway Pressure Therapy (CAG-00093R)

Dear Dr. Sanders,

This letter is written in response to the pending review of the use of portable multi-channel home sleep testing devices as an alternative to facility-based polysomnography required to initiate treatment for obstructive sleep apnea (CIM 60-17).

I am the founder of a number of sleep diagnostic and treatment centers in Massachusetts, and continue to follow the sleep disorders and treatment field as a consultant to medical technology and healthcare organizations, including a number of companies directly involved in the field of sleep medicine. The facilities founded by myself, together with other clinicians, researchers and healthcare executives, are affiliated with a number of academic medical centers as well as community hospitals. Since the establishment of these facilities in 1998, we have successfully diagnosed and treated tens of thousands of patients; many of them are Medicare beneficiaries, with obstructive sleep apnea and other chronic sleep disorders. Our services entailed in-lab polysomnography studies, as well as using multi-channel sleep testing devices to diagnose patients at their homes. My specific experience in this area enables me to appreciate firsthand the benefits of treating affected patients, and the significant contribution of such services to public health.

The debilitating effects of obstructive sleep apnea on patients' quality of life, increased probability of accidents, increased cardiovascular disease and other morbidities, are well-documented. There have also been many studies documenting the economic impact of undiagnosed sleep disorders on individual patients, as well as on society at-large.

While the medical community and patients are now much more aware of sleep apnea, providers recognize that a large number of patients suspected of having sleep apnea are reluctant to undergo a study in a sleep lab. For many patients, especially Medicare beneficiaries, traveling to a sleep laboratory can also be a significant hardship, and as a result, they elect to refrain from following the orders to conduct such study. The prevalence of sleep apnea among aging patients is well recognized. Yet, partially due to current CMS guidelines, this patient population is under represented in the group of patients with sleep apnea actually treated for this disorder.

Numerous studies reported that the efficacy of diagnosing sleep apnea at patients' homes, using multi-channel testing devices (categorized by the American Academy of Sleep Medicine as "Level III Sleep Study"), is similar to the efficacy of studies conducted in a sleep laboratory. It is certainly appropriate to point out that a number of studies reported various quality problems with portable devices, especially due to a sensor falling off during the night, compromising quality of recorded data. Other studies have pointed out the lack of specific information of sleep quality when conducting a home study, as most of the multi-channel devices utilized for such studies lack the ability to identify sleep states and sleep fragmentation. Yet, a number of new technologies introduced in recent years for the specific function of home testing, overcome such limitations. Published studies report high level of sensitivity and specificity, and excellent reliability of such new technology. Many devices provide accurate and detailed data on all interruptions to airflow (apnea events), and some also provide information on sleep and wake states during the study, even when such studies are conducted at patients' homes, without the presence of a technician. A report summarizing the published evidence for one of such devices is enclosed with this letter. This report alone includes 48 relevant references. The cumulative body of information available within the literature provides ample support to the conclusion that we now have the tools to study accurately and reliably the presence and severity of sleep apnea in tests conducted at patients' homes.

Considering the available data, it is important that CMS modifies its current guidelines that require that any treatment for patients with sleep apnea follows a sleep study conducted in a sleep laboratory. This policy clearly restricts patients' access to care, depriving Medicare beneficiaries of the ability to undergo efficient diagnosis and treatment for their sleep apnea disorder.

The implications of current CMS policy on public health are very serious, as the agency directs beneficiaries to the most expensive testing modality. The significant amount of data published in recent years, and the introduction of technological advancements already approved by the Food and Drug Administration specifically for home studies, justifies the current review and supports revisions to current guidelines. In light of available data and cumulative experience gained by providers in recent years, I recommend that CMS modifies its guidelines to incorporate the following points:

1. Patients that have no symptoms of sleep disorders other than sleep apnea, or patients in which sleep apnea must be ruled-out, can be tested either in a sleep laboratory (undergoing polysomnography study) or tested at other settings, including homes, as long as the multi-channel devices used in such diagnostic evaluations record, at the minimum, the presence and duration of sleep apnea events, oxygen saturation and sleep fragmentation.

2. CPAP therapy or other treatments for sleep apnea will be covered following either polysomnography or a multi-channel sleep study, as long as patients do not present symptoms of other sleep disorders.

3. Patients testing negative for sleep apnea using a home test, but continue to present

symptoms of hypersomnolence, should be referred to a sleep laboratory for further evaluation.

4. Patients refusing tests in a sleep laboratory, or patients not able to undergo a diagnostic study in a sleep laboratory due to physical limitations, may undergo home studies, using multi-channel sleep testing devices that meet the requirements outlined above, including a determination of disruptions to airflow, oxygen saturations and sleep/wake states.

By modifying its current guidelines, CMS will enable Medicare beneficiaries to undergo sleep studies that are more cost effective and more compatible with their medical needs. Home studies using multi-channel devices, approved for this purpose by the Food and Drug Administration, complement well the diagnostic tools available in sleep laboratories. The various sleep testing modalities clearly augment each other, providing physicians with multiple choices to diagnose their patients. Allowing home-based sleep studies will enable sleep laboratories to allocate a larger portion of their resources to those patients who are clearly indicated for more elaborate tests and to the management of treatments. Sleep laboratories will expand their diagnostic capabilities, and in collaboration with primary care physicians and other specialists caring for the patients, will be in a better position to conduct the optimal diagnostic modality.

While the cost of conducting home studies is lower than in-lab polysomnography, it is extremely important that CMS does not create an economic disadvantage for providers offering home studies, and establishes reimbursement that recognizes the interaction required to properly evaluate and counsel the patient and to properly administer the sleep study, even when done at home.

As the number of patients requiring treatments for sleep apnea continues to rise, modifying current guidelines will allow CMS to diagnose and treat more of its beneficiaries, improving healthcare resources utilization, without compromising quality of patient care.

Sincerely,

David Barone, M.Sc., MBA

Encl.: Report “Watch-PAT 100: Review of Evidence”, Dec. 2003

Comment #70:
Submitter: Wallace Mendelson, MD
Organization:
Date: Mon, May 10, 2004 7:14 PM
Comment:

(See next page)

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Clinical research

Benefits of obstructive sleep apnoea treatment in coronary artery disease: a long-term follow-up study☆

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See page 709 for the editorial comment on this article[†]

KEYWORDS
Obstructive sleep apnoea;
Coronary artery disease

Aim The aim of this long-term prospective study was to evaluate the effect of treating obstructive sleep apnoea (OSA) on the rate of cardiovascular events in coronary artery disease (CAD).

Methods and results We prospectively studied 54 patients (mean age 57.3 ± 10.1 years) with both CAD (≥70% coronary artery stenosis) and OSA (apnoea–hypopnoea index ≥15). In 25 patients, OSA was treated with continuous positive airway pressure ($n = 21$) or upper airway surgery ($n = 4$); the remaining 29 patients declined treatment for their OSA. The median follow-up was 86.5 ± 39 months. The two groups were similar at baseline in age, body mass index, smoking history, hypertension, hypercholesterolaemia, diabetes mellitus, number of diseased vessels, left ventricular ejection fraction, and CAD therapy. Treatment of risk factors other than OSA was similar in the two groups. The endpoint (a composite of cardiovascular death, acute coronary syndrome, hospitalisation for heart failure, or need for coronary revascularisation) was reached in 6 (6/25, 24%) and 17 (17/29, 58%) patients with and without OSA treatment, respectively ($P < 0.01$). OSA treatment significantly reduced the risk of occurrence of the composite endpoint (hazard ratio 0.24; 95% confidence interval, 0.09–0.62; $p < 0.01$) and of each of its components.

Conclusions Our data indicate that the treatment of OSA in CAD patients is associated with a decrease in the occurrence of new cardiovascular events, and an increase in the time to such events.

☆ Presented in part at the European Society of Cardiology Congress, Vienna, Austria, September 2003.

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Introduction

Obstructive sleep apnoea (OSA) is a common disorder characterised by episodes of upper airway obstruction during sleep that lead to repeated episodes of apnoea or hypopnoea lasting 10 s or longer. A widely accepted definition of OSA is an apnoea–hypopnoea index (AHI) of 15 or more, AHI being the mean number of episodes of apnoea or hypopnoea per hour of sleep. In a prospective population-based study, 9% and 4% of middle-aged men and women, respectively, had an AHI greater than 15.[1] Several studies have found far higher prevalences, as much as 30–50%, in patients with systemic hypertension or coronary artery disease (CAD).[2–5] The association of OSA with CAD is not fully explained by known confounding factors such as obesity, age, and sex, and research is producing a growing body of evidence supporting a causal link between OSA and cardiovascular morbidity and mortality.

Treatment of OSA with nasal continuous positive airway pressure (nCPAP) has been shown to alleviate daytime sleepiness, a frequent complaint of OSA patients, and to improve quality of life. Some studies suggest that nCPAP may reduce morbidity and mortality.[6,7] In patients free of hypertension or other cardiovascular disease at the initiation of treatment for OSA, Peker et al.[8] recently reported a significant decrease in the occurrence of cardiovascular disease as compared to patients with untreated OSA. In addition, a recent double-blind randomised study found that diurnal and nocturnal blood pressures dropped by approximately 10 mm Hg after 9 weeks of nCPAP.[9] This blood pressure-lowering effect would be expected to significantly diminish CAD event rates. However, the long-term effect of OSA treatment on cardiovascular event rates in patients known to have CAD at the time of OSA diagnosis has not been evaluated.

We therefore studied the impact of OSA treatment on cardiovascular outcomes of patients with CAD. To this end, we compared rates of new cardiovascular events over a 5-year period in patients with treated versus untreated OSA.

Methods

Patients

Recruitment was prospective at our institution between September 1991 and June 1999. All patients admitted to the cardiology department for a selective coronary angiogram and found to have a stenosis of a major coronary artery of 70% or more were considered for the study. Revascularisation was performed by the attending cardiologist, if deemed necessary. The patients were eligible for the study if they were subsequently referred to our institution's sleep laboratory for evaluation of symptoms consistent with OSA and an AHI of 15 or more was found by overnight polysomnography, thus confirming the diagnosis. Polysomnography (PSG) was performed when the patient was in a stable clinical condition (at least 4 weeks after coronary angiography and hospital discharge). Polysomnography was recorded with either a 16-channel polygraph at a chart speed of 15 mm/s (Reega 2000, Alvar, France) or a computerised sleep recording system (Medatec, Belgium). The recordings included a two-channel electroencephalogram, electro-oculogram, electrocardiogram, chin electromyogram, body position, chest and abdominal excursions, nasal and oral airflow assessed by thermocoupling or a nasal cannula, and oxyhaemoglobin saturation (finger pulse oximetry). Sleep stages were scored manually. Apnoea was defined as a cessation of oronasal airflow lasting at least 10 s and hypopnoea as a reduction by at least 50% in oronasal airflow, as compared to the previous period of normal breathing, lasting at least 10 s and followed by a transient EEG arousal. Electroencephalographic arousals were scored according to standard criteria published by the American Sleep Disorder Association. The AHI was calculated as the mean number of apnoea or hypopnoea episodes per hour of sleep.

Risk factor definitions

"Hypertension" was defined as current use of antihypertensive medications and/or as recording during the hospital stay of a systolic blood pressure (SBP) value $\geq$140 mm Hg and/or a diastolic blood pressure (DBP) value $\geq$90 mm Hg being measured with a standard sphygmomanometer on three different occasions, with the subject in supine position. Hypertension was considered uncontrolled when SBP was $\geq$140 mm Hg and/or DBP $\geq$90 mm Hg at the end of the study follow-up period.

Hypercholesterolaemia was defined as current use of cholesterol-lowering medications and/or a total cholesterol value >5.2 mmol/l and/or an LDL-cholesterol value >3.4 mmol/l in a plasma sample drawn after an overnight fast. Uncontrolled hypercholesterolaemia was defined as a total cholesterol value >5.2 mmol/l and/or an LDL-cholesterol value >3.4 mmol/l at the end of the study follow-up period.

Diabetes mellitus was defined as a need for insulin or oral hypoglycaemic agents or as a fasting blood glucose concentration >7.0 mmol/l on two separate occasions.

Excess weight was defined as a body mass index (BMI) $\geq$25 but <30 and obesity as a BMI $\geq$30 kg/m^2.

The subjects were classified as current smokers, former smokers (defined as patients who stopped smoking at least 6 months before study inclusion), and nonsmokers.

Treatment of OSA

All the patients were offered treatment for their OSA. Either upper airway surgery or nCPAP was recommended, according to the severity of OSA and results of the otorhinolaryngologic evaluation. The patients were divided into two groups based on whether they accepted or refused treatment for their OSA. The treated group comprised all the patients who initially accepted treatment for OSA, including those who changed their mind later on and those who received nCPAP but complied poorly with this treatment modality. When nCPAP was recommended, titration was performed in our sleep laboratory, according to our usual manual standardised procedure, which includes nCPAP monitoring. Compliance with nCPAP was estimated based on the time counter on the device and on clinical effectiveness. The untreated group was composed of the patients who refused treatment for their OSA from the outset.

Follow-up

Follow-up started at the time of OSA diagnosis. Throughout follow-up, data were gathered at 6-month intervals, either during visits to the cardiologist or by phone calls to the patient, relatives, or general practitioner. The following information was

collected: cardiovascular death (i.e., sudden cardiac death or death due to myocardial infarction, unstable angina, heart failure, or cardiac arrhythmia), acute coronary syndrome (ischaemic symptoms and development of abnormal Q waves on the EKG, or EKG changes indicating ischaemia or total creatine kinase elevation to more than twice the upper limit of normal), hospitalisation for heart failure, and revascularisation procedures. When a patient had more than one coronary event during follow-up, only the first coronary event was used in the analysis. Cardiovascular treatments were administered at the cardiologist's discretion. Endpoint classification was made without knowledge of the OSA treatment group.

Statistical analysis

Continuous variables are presented as mean ± SD or median (first quartile–third quartile). Groups were compared for continuous variables using the Student's t test, or the Mann–Whitney nonparametric test when the frequency distribution was skewed. Categorical variables were compared using χ^2 statistics or the Fisher exact test. Cardiovascular event-free survival curves were calculated with the Kaplan–Meier method and compared with the log-rank test. All tests were two-sided. Prognostic factors associated with a P value of less than 0.2 were then introduced in a Cox proportional hazards model with descending stepwise procedure. Major interactions were explored. Final P values smaller than 0.05 were considered statistically significant. All analyses were performed with Statview 4.5 software (Abacus, Berkeley, CA).

Results

Between September 1991 and June 1999, 54 patients fulfilled our entry criteria and were included in the study. Among them, 25 accepted treatment for their OSA, either nCPAP (21 patients) or surgery (turbinectomy in 4 patients, complemented by ethmoidectomy in 1 patient and septoplasty in another), and 29 refused treatment. Reasons for refusal were concern that nCPAP would adversely affect quality of life and reluctance on the part of the general practitioner.

Clinical characteristics and cardiovascular features at the time of OSA diagnosis were similar in the two groups (Table 1). All the patients but one were men. Most patients had cardiovascular risk factors and the proportions of patients with a positive smoking history, hypertension, diabetes mellitus, hypercholesterolaemia, or obesity were similar in the two groups, as was the number of risk factors per patient (Table 2). In both groups, most patients had experienced several cardiovascular events; thus, 60% had a history of myocardial infarction and all but one had undergone percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass graft (CABG).The left ventricular ejection fraction (LVEF) at baseline was near normal in most patients in both groups, being below 35% in only 3 OSA-treated patients (3/25, 12%) and 3 OSA-untreated patients (3/29, 10%). Median time from the diagnosis of CAD to the diagnosis of OSA was 16.0 months (range 6.25–53.75 months) in the OSA-treated group and 19.0 months (range 10.75–33.75 months) in the OSA-untreated group (P>0.05). The median time between the last coronary event and OSA diagnosis was 4 months (range 1.75–13.25 months) and 6 months (range 1–13 months), respectively, in the treated and untreated groups ($P > 0.05$). The percentage of patients who underwent coronary revascularisation at this time did not differ significantly between the 2 groups, being 88% and 86% in the OSA-treated and un-

Table 1 Characteristics at the time of OSA diagnosis

	OSA-treated group, $N = 25$	OSA-untreated group, $N = 29$
Age, year	57.7 ± 10.1	57.0 ± 10.2
Sex, M/F	24/1	29/0
BMI, kg/m²	28.4 ± 4.2	28.2 ± 3.4
	No. of patients (%)	
Treatments		
Platelet inhibitor	24 (96)	28 (96)
Beta-blocker	18 (72)	24 (82)
Statin	11 (44)	9 (31)
ACE inhibitor	11 (44)	9 (31)
Calcium antagonists	8 (32)	11 (37)
Patients with previous		
Myocardial infarction	15 (60)	19 (65)
PTCA	20 (80)	28 (96)
CABG	8 (32)	7 (24)
LV ejection fraction	57.5 ± 14.7	54.6 ± 14.1
Number of vessels with CAD		
One	8 (32)	11 (38)
Two	6 (24)	10 (34)
Three	11 (44)	8 (27)

Plus/minus values are means ± SD. There were no significant differences between the two groups for any of the variables. Body mass index (BMI) is the weight in kilograms divided by the square of the height in meters. ACE, angiotensin-converting enzyme; CAD, coronary artery disease; PTCA, percutaneous transluminal coronary angioplasty; CABG, coronary artery by-pass graft; LV, left ventricle.

Table 2 Risk factors at the time of OSA diagnosis

	OSA-treated group, $N = 25$	OSA-untreated group, $N = 29$
	No. of patients (%)	
BMI >30 kg/m²	9 (36)	9 (31)
Current smoker	6 (24)	9 (31)
Hypercholesterolaemia	19 (76)	20 (68)
Diabetes mellitus	4 (19)	7 (24)
Hypertension	10 (40)	15 (51)
Family history of CAD	13 (52)	16 (55)
Number of risk factors		
One	7 (28)	7 (24)
Two	10 (40)	14 (48)
Three	2 (8)	3 (10)
Four	3 (12)	4 (14)

treated group, respectively. There was a nonsignificant trend toward a higher proportion of CABG in the OSA-untreated group (20% vs. 13.6%).

The severity of OSA at baseline was similar in the two groups: mean AHI was 33.7 ± 16.8 and 29.0 ± 12.8 ($P = 0.25$), the lowest O_2 saturation was $82 \pm 8\%$ and $85 \pm 8\%$, and the percent of nocturnal sleep time spent with an O_2 saturation below 90% was $8.1 \pm 11.5\%$ and $4.5 \pm 7.5\%$ in the OSA-treated and OSA-untreated groups, respectively. The oxygen desaturation ($\geq 4\%$) index did not differ between the 2 groups, with a median of 10/h (range 2.1–21.0/h) versus 2.15/h (range 0.4–12.9/h) in the OSA-treated and OSA-untreated groups, respectively. However, there was a nonsignificant trend toward a higher proportion of patients with severe OSA (AHI >30) in the OSA-treated group (52% vs. 44.8%).

Follow-up

The median duration of follow-up did not differ between the OSA-treated and OSA-untreated groups (median time: 86 months [range 62.75–96.00 months] and 90 months [range 49.50–99.75 months]), respectively ($p > 0.05$). During follow-up, 3 patients who initially used nCPAP stopped this treatment, 2 after 18 months and 1 after 5 years; these 3 patients were kept in the OSA-treated group for the initial analysis. In the remaining OSA-treated patients, nCPAP use was at least 3 h per night with a mean time of 5.7 ± 1.5 h per night for the entire group. The therapeutic effect of nCPAP was assessed in 20 of the 21 patients treated with nCPAP, all of whom had a mean AHI ≤ 10, with a decrease from 33.7 ± 16.8/h at baseline to 3.9 ± 2.9/h. Of the 4 patients treated surgically, one had an AHI of 0 and 2 had an AHI of 8; PSG could not be repeated in remaining patient. Polysomnography was not performed during follow-up in the group in which OSA was not treated.

At the end of follow-up, neither cardiovascular treatments nor risk factor control differed significantly between the two groups (Table 3). As shown in Fig. 1, at least one cardiovascular event occurred during follow-up in 6 (24%) OSA-treated patients and in 17 OSA-untreated patients (58%) ($P < 0.01$). The first cardiovascular event in the OSA-treated group was acute coronary syndrome in 5 patients and PTCA in 1 patient (for a positive stress test without symptoms); the first event in the OSA-untreated group was cardiovascular death in 1 patient, hospital admission for heart failure in 1 patient, PTCA in 2

Table 3 Risk factors and cardiovascular treatments at the end of follow-up

	OSA-treated group, $N = 25$	OSA-untreated group, $N = 29$
BMI, kg/m²	29.1 ± 3.9	28.2 ± 3.4
	No. of patients (%)	
BMI >25 kg/m²	21 (83)	21 (71)
Current smoker	4 (16)	6 (21)
Uncontrolled hypercholesterolaemia	7 (28)	4 (14)
Uncontrolled hypertension	2 (8)	5 (17)
Treatments		
Platelet inhibitor	23 (92)	29 (100)
Beta-blocker	15 (60)	19 (66)
Statin	17 (68)	22 (76)
ACE inhibitor	14 (56)	17 (59)
Calcium antagonists	10 (40)	13 (45)

Plus/minus values are means ± SD. There were no significant differences between the two groups for any of the variables. Body mass index (BMI) is the weight in kilograms divided by the square of the height in meters. ACE, angiotensin-converting enzyme.

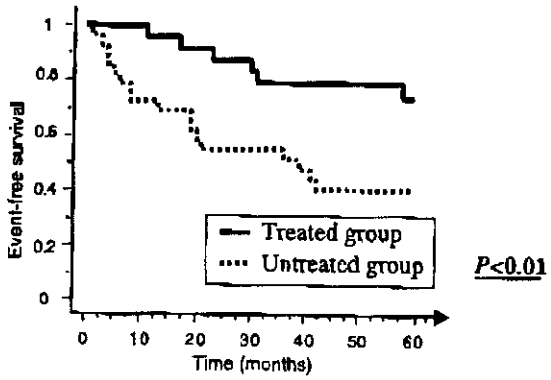

Fig. 1 Kaplan–Meier analysis: event-free survival in the groups with and without treatment for obstructive sleep apnea.

patients (for a positive stress test without symptoms), and acute coronary syndrome in 13 patients. The 3 OSA-treated patients (ages 41, 45, and 67 years) with none of the risk factors listed in Table 2 remained event-free during follow-up, whereas the only OSA-untreated patient (age 63 years) with no risk factors experienced unstable angina during follow-up. All 3 cardiovascular deaths observed during follow-up were in OSA-untreated patients, 2 being preceded by a first coronary event.

The time from OSA diagnosis to the first event was significantly longer in the OSA-treated group than in the OSA-untreated group (median time: 26.5 months [range 17–31 months] vs. 13.0 months [4.75–24.75 months], respectively, $P < 0.05$).

One of the patients who discontinued nCPAP after 18 months had a coronary event 13 months after stopping treatment. The other 2 remained free from a new cardiovascular event. When these 3 patients were excluded from the analysis, the difference between survival free from new cardiovascular event remained significant ($P < 0.01$).

We tested separately hypertension, current smoking, hypercholesterolaemia, diabetes mellitus, age >60 years, BMI >25 kg/m^2, AHI >30, LVEF <45% as predictors of coronary events. As the P-values were <0.2 for BMI, hypertension, hypercholesterolaemia, age, AHI, and OSA treatment, we introduced them in a Cox model in order to adjust treatment effect on these prognostic factors. In the final model, only treatment for OSA had a significant influence on the survival free of a new coronary event. The risk for experiencing a cardiovascular event during follow-up was significantly decreased in the OSA-treated group as compared to the OSA-untreated group (hazard ratio 0.24; 95% confidence interval, 0.09–0.62; $P < 0.01$).

Discussion

The main finding of our study is that the treatment of OSA in CAD patients was associated with a significant decrease in cardiovascular events, defined as cardiovascular death, acute coronary syndrome, hospitalisation for heart failure, or need for coronary revascularisation. In addition, the time to events was longer in the group of patients who accepted OSA treatment. These data strongly suggest that OSA has a deleterious effect on CAD outcomes and that this effect can be abolished by specific treatment.

That OSA is associated with an increased risk of cardiovascular events in CAD patients has been reported previously. Mooe et al.[10] observed a 62% relative increase and a 10.1% absolute increase in a composite endpoint of cardiovascular events (death, cerebrovascular events, and myocardial infarction) in patients with CAD and OSA during a median follow-up of 5.1 years. In a 5-year prospective follow-up study, OSA independently predicted cardiovascular mortality after an acute coronary syndrome and was associated with a 3-fold increase in the risk of death after adjustment for other risk factors.[11] Similarly, we found a 3-fold increase in cardiovascular events in patients with untreated OSA as compared to treated patients.

The worse cardiovascular outcomes in CAD patients with OSA cannot be entirely explained by the effects of risk factors associated with OSA, such as age and obesity. Each apnoeic episode is associated with arterial oxygen desaturation, which causes sympathetic system overactivity that is responsible for tachycardia and transient SBP elevation.[12] Thus, large oscillations in systemic blood pressure and episodes of hypoxia-reoxygenation occur repeatedly throughout the night. The increase in myocardial O_2 consumption due to tachycardia and SBP elevation at a time when the O_2 supply is decreased can be expected to be particularly deleterious in patients with CAD. Indeed, nocturnal myocardial ischaemic events commonly occur during the rebreathing phase in apnoeic patients with CAD.[13,14] Sympathetic activity, which remains increased during the day in OSA patients as compared to nonapnoeic obese subjects of similar age,[12,15] may contribute to the increased platelet activation and aggregation associated with OSA.[16–18] Treatment with nCPAP reduces sympathetic activity,[19,20] diminishes platelet activation and aggregation, and decreases nocturnal ischaemic events.[13]

Repeated episodes of hypoxia-reoxygenation may also result in oxidative stress causing abnormal lipid peroxidation.[21] In patients with severe OSA, oxidation of low density lipoprotein (LDL) particles normalises after nCPAP treatment.[21] Similarly, the increased production of reactive oxygen species in neutrophils and monocytes seen in OSA is normalised by nCPAP.[22] Altogether, these data point to increased oxidative stress in OSA, which may result in endothelial dysfunction[23,24] and enhanced atherogenesis, but responds favourably to nCPAP.

Circulating levels of C-reactive protein, fibrinogen, and IL-6 are elevated in apnoeic patients and decrease significantly with effective nCPAP.[25–28] Plasma levels of these markers for inflammation have been associated with mortality in patients with CAD. In addition, the expression of soluble adhesion molecules has also been found to be increased in OSA patients with or without CAD[29,30] and to be associated with an increased risk of

myocardial infarction in apparently healthy men. All these data are consistent with the hypothesis that the pathogenic effects of OSA may promote atherosclerosis but may be reversed by effective treatment of the breathing disorder.

However, direct demonstration of an independent role of OSA is difficult because cardiovascular risk factors such as obesity are associated with OSA. Moreover, OSA has been identified as an independent risk factor for the development of hypertension[31–33] and is common in patients with uncontrolled hypertension.[34] In addition, severe OSA predicts poor blood pressure control with medications[35] and nCPAP may significantly lower both day-time and night-time blood pressure values.[9] Interestingly, we found a trend toward better blood pressure control in OSA-treated patients, although this variable was similar in the two groups at baseline. Therefore, we cannot rule out the possibility that part of the reduction in cardiovascular events with OSA treatment was related to improved blood pressure control. This effect, together with abolition of the negative intrathoracic pressure swings that accompany apnoea, may have significantly reduced left ventricular afterload and myocardial O_2 requirement.

The main limitations of this study are the absence of randomisation and the small number of patients. However, using sham CPAP during the long period needed to allow assessment of clinical endpoints would be ethically questionable. The two groups did not differ significantly for known risk factors or treatment during follow-up, except for OSA therapy, but we cannot exclude that small differences failed to reach statistical significance because of the small size of the population. Nevertheless, our findings are strengthened by the fact that each component of the composite endpoint (cardiovascular death, acute coronary syndrome, hospitalisation for heart failure, PTCA, and bypass surgery) was less common in the treated than in the untreated group.

This is the first study, to our knowledge, indicating a beneficial effect of OSA treatment on event-free survival in CAD patients. Although not randomised, our study strongly supports the importance of recognising and treating OSA in this population.

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Controlled Trial of Continuous Positive Airway Pressure in Obstructive Sleep Apnea and Heart Failure

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Obstructive sleep apnea (OSA) is highly prevalent among patients with congestive heart failure (CHF) and may contribute to progression of cardiac dysfunction via hypoxia, elevated sympathetic nervous system activity, and systemic hypertension. Our aim was to assess the long-term effect of OSA treatment with nocturnal continuous positive airway pressure (CPAP) on systolic heart function, sympathetic activity, blood pressure, and quality of life in patients with CHF. Fifty-five patients with CHF and OSA were randomized to 3 months of CPAP or control groups. End points were changes in left ventricular ejection fraction, overnight urinary norepinephrine excretion, blood pressure, and quality of life. Nineteen patients in the CPAP group and 21 control subjects completed the study. Compared with the control group, CPAP treatment was associated with significant improvements in left ventricular ejection fraction (Δ 1.5 ± 1.4% vs. 5.0 ± 1.0%, respectively, p = 0.04), reductions in overnight urinary norepinephrine excretion (Δ 1.6 ± 3.7 vs. −9.9 ± 3.6 nmol/mmol creatinine, p = 0.036), and improvements in quality of life. There were no significant changes in systemic blood pressure. In conclusion, treatment of OSA among patients with CHF leads to improvement in cardiac function, sympathetic activity, and quality of life.

Keywords: congestive heart failure; obstructive sleep apnea; continuous positive airway pressure

Congestive heart failure (CHF) remains common in western communities and contributes significantly to the burden of morbidity and mortality (1). Cross-sectional results from the large Sleep Heart Health Study have shown a significant association between obstructive sleep apnea (OSA) and CHF (2). Moreover, the prevalence of OSA in a population with CHF has been shown to be as high as 40% (3–5). Factors associated with OSA, including systemic hypertension and obesity (2), are also associated with the development of CHF (6, 7)

Emerging data suggest that OSA may not only be associated with but may also contribute to the progression of CHF through several mechanisms. Large epidemiologic (8), animal (9) and human intervention studies (10) indicate that OSA contributes to the development of systemic hypertension, a precursor of CHF. Recurrent hypoxemia, hypercapnia (11), and baroreflex inhibition resulting from repetitive surges in nocturnal blood pressure (12) may contribute to elevated sympathetic nerve activity, which is known to be cardiotoxic in CHF (13). Hypoxemia may also independently lead to oxidative vascular wall injury (14, 15).

Although there is an increasing understanding of the physiologic consequences of OSA, until recently little was known of the clinical response to OSA treatment in patients with CHF. Small case series and uncontrolled trials suggest treatment of OSA with continuous positive airway pressure (CPAP) in patients with idiopathic cardiomyopathy led to significant improvements in heart function (16–18). Moreover, dogs exposed to simulated OSA develop left ventricular dysfunction (19). A recently published randomized controlled trial by Kaneko and coworkers demonstrated a significant improvement in cardiac function associated with a fall in systemic blood pressure with 1 month CPAP in patients with idiopathic and ischemic cardiomyopathy (20). There are several mechanisms by which this improvement may have occurred. In human intervention studies, the application of CPAP has been shown to reduce left ventricular transmural pressure gradient (21) and cardiac sympathetic tone (22) in patients with CHF and reduce systemic blood pressure (10) in patients with OSA.

The aim of this study was to measure the medium-term effect of treating OSA with CPAP on left ventricular systolic function, sympathetic nerve activity, and systemic blood pressure as well as functional outcomes including quality of life and exercise performance. Some of the results of this study were reported in the form of an abstract (23).

METHODS

Eligible patients aged between 18 and 80 years, under the care of a cardiologist, had a diagnosis of symptomatic, stable, and optimally treated CHF. CHF eligibility criteria included New York Heart Association Class II or greater and objective evidence of systolic dysfunction (left ventricular ejection fraction [LVEF] < 55%). Patients were questioned for symptoms of snoring and one or more of excessive daytime sleepiness, witnessed apneas, or nocturnal choking. Suitable patients were invited to undergo screening overnight polysomnography, and those with an apnea/hypopnea index (AHI) of more than 5 obstructive events per hour were eligible to participate and be randomized. Exclusion criteria included significant central sleep apnea (> 20% events central in type), clinical evidence of neurologic disease, renal disease with serum creatinine higher than 150 mmol/L, or spirometric confirmation of pulmonary disease with forced expiratory ratio of less than 70%. Patients with valvular heart disease were excluded.

Protocol

Consenting eligible patients were randomized to either 3 months of overnight nasal CPAP or to an untreated control group. All patients received lifestyle advice from the Australian National Heart Foundation guidelines (24) on diet, alcohol consumption, and on exercise for patients with CHF. The protocol was approved by the Alfred Hospital Ethics Committee (4/99), and all patients provided written consent.

Fixed-level CPAP was titrated manually during overnight polysomnography and continued at the optimally determined fixed pressure for 3 months (Autoset-T; ResMed, Sydney, Australia). All patients received one home visit and were contacted every second week by telephone. At 3 months, patients underwent repeat measurements at the same time

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of day. All patients underwent repeat overnight polysomnography: the treatment group on nasal CPAP.

Measurements at Baseline and 3 Months

At baseline and 3 months, patients underwent (*1*) right and left ventricular nuclear gated scans (Starcam 400AC; GE Medical Systems, Madison, WI), (*2*) symptom-limited incremental cycle ergometry (Sensormedics 2900; Sensormedics Corp., Anaheim, CA), and (*3*) overnight collection of urinary norepinephrine (UNE) and arterial blood gas sampling (Model 865; Ciba Corning, Medfield, MA) at the time of in-laboratory polysomnography (Somnostar; Sensormedics Corp.). Detailed methods for nuclear gated scanning, UNE determination, and polysomnography have been published elsewhere (25, 26). Quality of life was also assessed at baseline and 3 months using general (SF-36) and disease-specific questionnaires (Chronic Heart Failure questionnaire [27], New York Heart Association, Epworth Sleepiness Scale [28]). After a period of supine rest for 15 minutes, blood pressure was measured in a seated position using the average of three readings from a mercury sphygmomanometer.

Statistical Analysis

Statistical analyses were performed on the software package SPSS version 10 (SPAA Inc, Chicago, IL). All data were normally distributed and are expressed as arithmetic mean ± SE. The level of significance was accepted when the p value was less than 0.05. Outcomes were defined as the between-groups difference from baseline measurements and those recorded at 3 months. Two-way analyses of variance were completed for each of the independent variables. *Post hoc* analysis of covariants was performed for primary endpoints against AHI to measure effect of OSA severity on outcomes. Effect size was calculated from the difference in group changes divided by the pooled SDs of the groups at baseline.

RESULTS

One hundred fifty-six patients with a clinical diagnosis of CHF and a clinical suspicion of OSA underwent overnight polysomnography screening (Figure 1). Of the 156 patients, 35 did not have systolic heart failure with LVEF more than or equal to 55% and 43 failed to meet OSA criteria. Nine patients subsequently became unstable before randomization, and 14 declined participation. Fifty-five patients enrolled and were randomized (28 to CPAP and 27 to the control group (Table 1 and Table E1 in the online supplement).

TABLE 1. BASELINE CHARACTERISTICS

	Control Group (*n* = 27)	CPAP Group (*n* = 28)	p Value
Age, yr	57.5 ± 1.6	57.2 ± 1.7	NS
Sex, male:female	24:3	28:0	
BMI, kg/m^2	34.6 ± 1.2	33.5 ± 0.9	NS
LVEF, %	33.7 ± 2.4	37.3 ± 2.1	NS
$\dot{V}O_2$ peak, ml/kg/min	16.1 ± 0.7	19.1 ± 1.1	0.03
NYHA class	2.4 ± 0.2	2.5 ± 0.2	NS
Epworth Sleepiness Scale	9.2 ± 0.9	10.7 ± 0.7	NS
AHI, events/h	28.1 ± 3.9	28.3 ± 0.4	NS
Arousals, events/h	30.4 ± 4.3	42.2 ± 8.9	NS
Minimum overnight Sp_{O_2}, %	77.3 ± 3.2	79.3 ± 2.2	NS
TST oxygen saturation < 90%, %	5.5 ± 1.7	8.5 ± 3.0	NS
UNE, nmol/mmol creatinine	21.8 ± 1.8	20.6 ± 3.1	NS
BP mean, mm Hg	107 ± 3	99 ± 3	0.05

Definition of abbreviations: AHI = apnea/hypopnea index; BMI = body mass index; BP = blood pressure; LVEF = left ventricular ejection fraction; NS = not significant; NYHA = New York Heart Association; Sp_{O_2} = oxygen saturation (pulse oximetry); TST = total sleep time; UNE = overnight urine norepinephrine excretion.

Fifteen patients failed to complete the trial (9 from the CPAP and 6 from the control group), leaving 40 patients for complete analysis. Seven patients withdrew from the study. In the CPAP group, two patients were intolerant of CPAP and withdrew, and two patients withdrew for personal reasons. In the control group, three patients withdrew for personal reasons. Three patients in each group became unstable and required a new class of therapy. In the CPAP group, one patient received cardiac transplant and 2 patients received introduction of a new drug class likely to impact significantly on LVEF. In the control group, one patient received insertion of a biventricular pacemaker and two patients received introduction of a new drug class likely to impact significantly on LVEF. Two patients with ischemic cardiomyopathy in the CPAP group died. One patient suffered sudden death immediately after a game of tennis, likely due to an arrhythmia. The second patient developed pacemaker lead failure from a

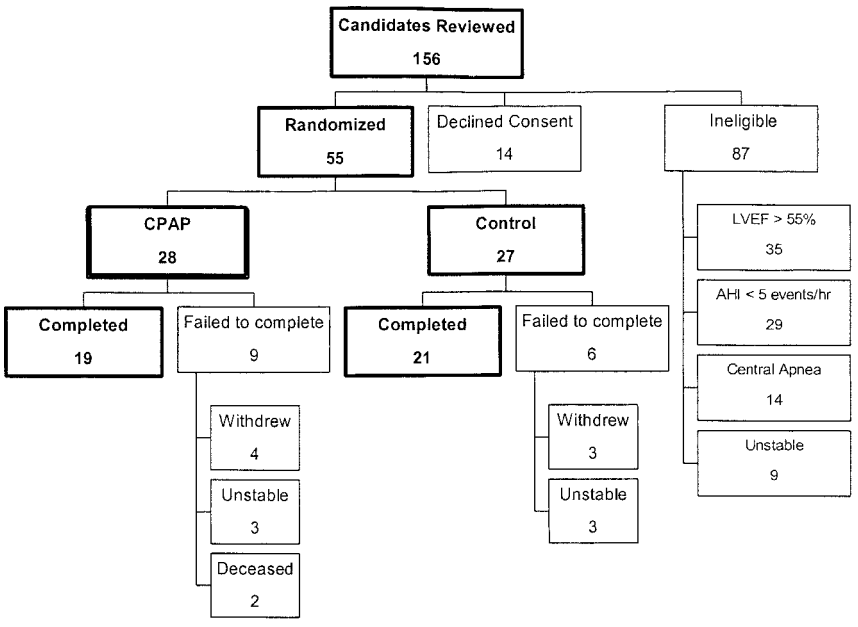

Figure 1. Fate of participating patients. Bold boxes represent the patients who completed the study.

previously inserted biventricular pacemaker and died of cardiac tamponade after reinsertion of a pacemaker lead. Both patients had been compliant with CPAP and had symptomatically improved. Thus, baseline versus follow-up data were available on 40 subjects who completed the study (Table 2 and Tables E2 and E3 in the online supplement). The severity of CHF and OSA were similar between the patients who completed the study and those who dropped out (Table 2 and Table E2 in the online supplement). Two patients (one in each group) in sinus rhythm at entry into the study were found to be in atrial fibrillation at the end of the study. They had not altered the drug class and were included in the final analysis.

The two groups were similar at baseline including age, sex, body mass index, LVEF, and AHI for both the patients who had enrolled in the study and for those who had completed the study (Table 1 and Tables E1 and E2 in the online supplement). Compared with the control group that completed the study, the CPAP group had a slightly greater $\dot{V}o_2$ peak at baseline (Table 2). The mean CPAP pressure was 8.8 ± 1.4 mm Hg, and the average nightly usage was 5.6 ± 0.4 hours. CPAP therapy was effective in the treatment of OSA as demonstrated by a fall in AHI and rise in minimum oxygen saturation (pulse oximetry) (Table 2 and Table E4 in the online supplement). There was an associated 42% reduction in UNE, and the Epworth Sleepiness Scale score improved by 27%. There was a small reduction in AHI in the control group over the 3 months ($p = 0.02$), which was not explained by changes in body weight, sleep quality, or positioning. This did not translate into changes in UNE or the Epworth Sleepiness Scale score (Table 2).

Figure 2 and Table 2 show a significant improvement in the LVEF in the CPAP group compared with the control group (Δ5.0 ± 1.0% vs. 1.5 ± 1.4% respectively, $p = 0.04$). There was however greater fluctuation in ΔLVEF in the control group resulting from one patient with idiopathic cardiomyopathy showing a spontaneous improvement of ΔLVEF of +14% and another (who developed atrial fibrillation) with ΔLVEF of −14% (Figure 2). In contrast, the LVEF of a CPAP-treated patient, who also developed atrial fibrillation during the study, fell by 2%. Otherwise, the CPAP group demonstrated a significant unidirectional shift to improvement (within-group comparison, $p < 0.001$). The analysis of covariants was unable to show that AHI severity impacted on ΔLVEF ($R^2 = 0.1$, $p = 0.3$).

The CPAP group demonstrated improvement in quality of life as measured by both SF-36 and the Chronic Heart Failure questionnaire (Figure 3), whereas the control group remained unchanged. Neither was there any change in patients' exercise performance determined by the cycle ergometry $\dot{V}o_2$ peak in either group nor was there any significant change in the New York Heart Association class of either group (Table 2 and Table E3 in the online supplement).

TABLE 2. ENDPOINT OUTCOME MEASURES

Control Group	(*n* = 21)	CPAP Group (*n* = 19)	p Value*
LVEF, %			
Baseline	33.6 ± 2.6	37.6 ± 2.5	
3 mo	35.1 ± 3.1	42.6 ± 0.3	
Δ	1.5 ± 1.4	5.0 ± 1.0†	0.04
UNE, nmol/mmol creatinine			
Baseline	21.3 ± 1.9	23.5 ± 4.8	
3 mo	22.9 ± 3.9	13.7 ± 2.5	
Δ	1.6 ± 3.7	−9.9 ± 3.6‡	0.036
Mean BP, mm Hg			
Baseline	105 ± 3	99 ± 3	
3 mo	99 ± 3	100 ± 2	
Δ	−6 ± 3	1 ± 3	NS
$\dot{V}o_2$ peak, ml/kg/min			
Baseline	16.4 ± 0.7	20.3 ± 1.2	
3 mo	16.3 ± 0.7	20.3 ± 1.3	
Δ	−0.2 ± 0.5	0 ± 0.8	NS
NYHA class			
Baseline	2.4 ± 0.2	2.2 ± 0.2	
3 mo	2.4 ± 0.2	2.3 ± 0.2	
Δ	0 ± 0	0.1 ± 0.1	NS
Epworth Sleepiness Scale			
Baseline	8.8 ± 0.9	9.5 ± 0.9	
3 mo	9.9 ± 1.0	6.9 ± 1.0	
Δ	1.1 ± 0.8	−3.1 ± 1.4Δ	0.01
BMI, kg/m^2			
Baseline	33.3 ± 1.2	33.6 ± 1.0	
3 mo	33.5 ± 1.2	33.9 ± 1.1	
Δ	0.2 ± 0.3	0.3	0.2
AHI, events per hour			
Baseline	26.6 ± 4.5	25.0 ± 4.1	
3 mo	18.2 ± 2.8	2.9 ± 0.8	
Δ	−8.4 ± 3.6	−21.1 ± 3.8†	< 0.001
Minimum Sp_{O_2}, %			
Baseline	77.2 ± 3.9	79.6 ± 2.6	
3 mo	77.2 ± 3.5	91.1 ± 0.9	
Δ	0.0 ± 1.6	11.5 ± 2.7†	0.001

Definition of abbreviations: AHI = apnea/hypopnea index; BMI = body mass index; BP = blood pressure; LVEF = left ventricular ejection fraction; NS = not significant; NYHA = New York Heart Association; Sp_{O_2} = oxygen saturation (pulse oximetry); UNE = overnight urine norepinephrine excretion.

* Degree of significance for Δ between groups.

† Within-group p value < 0.001.

‡ Within-group p value < 0.05.

DISCUSSION

We have demonstrated significant 3-month improvements in cardiac function and attenuation of sympathetic nerve activity associated with reduced hypoxemia with nasal CPAP treatment of OSA in patients with CHF, using a randomized controlled trial design. These physiologic improvements were associated with significant improvements in general and disease-specific symptoms of the quality of life.

The magnitude of the change in LVEF in the current study is similar to (29, 30) or greater than (30, 31) other large CHF pharmacologic intervention trials that have shown important

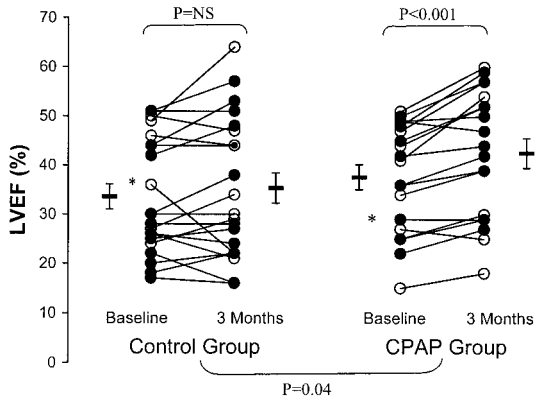

Figure 2. Display of left ventricular ejection fraction (LVEF baseline) and follow-up in control and continuous positive airway pressure (CPAP)–treated groups. *Open circles* represent idiopathic and *closed circles* the ischemic cardiomyopathies. There was significant improvement in LVEF in the CPAP group compared with the control group. Patients marked with an *asterisk* were in sinus rhythm at study commencement and found to be in atrial fibrillation at the end of the study.

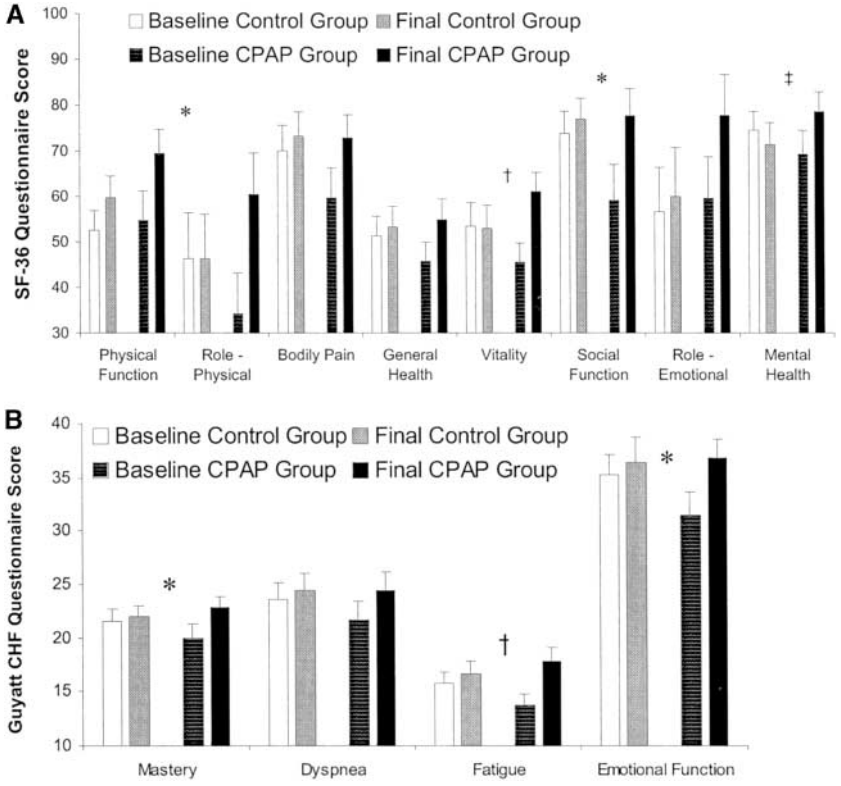

Figure 3. The SF-36 quality of life questionnaire. (*A*) Note improvements in the eight domains of the SF-36 questionnaire with significant improvements in the domains of physical role (*$p = 0.03$), vitality ($^{\dagger}p = 0.02$), social functioning (*$p = 0.03$), and mental health ($^{\ddagger}p = 0.01$). Note also the calculated treatment effect size of 0.31 for physical function, 0.62 for physical role, 0.37 for bodily pain, 0.38 for general health, 0.77 for vitality, 0.53 for social function, 0.36 for emotional well being, and 0.61 for mental health. (*B*) The Chronic Heart Failure questionnaire. Mastery scale 4–28, dyspnea scale 5–35, fatigue scale 4–28, and emotional function scale 7–49. Note significant improvements in three of four domains (fatigue, $^{\dagger}p = 0.01$; emotional well being, *$p = 0.02$; and disease mastery, *$p = 0.02$), with corresponding treatment effect sizes of 0.71, 0.46, and 0.47, respectively. The dyspnea domain did not significantly change, and the effect size was only modest (0.27).

mortality improvements. Given that the patients in the current trial were already on optimal medical treatment under the guidance of a cardiologist, our findings indicate an advance in the treatment of patients with CHF.

Our results confirm the recently published results by Kaneko and coworkers in which LVEF improved by 9% with CPAP in a 1-month controlled trial involving 24 patients with OSA and CHF (20). Our study included a larger sample size and was conducted on patients for a 3-month period. We explored mechanisms by which cardiac function may improve by measuring surrogate measures of sympathetic nerve activity and assessed functional outcomes in terms of quality of life and exercise performance.

The improvement in LVEF in the current study (+5%) was not as great as that in the study of Kaneko and coworkers (+9%). This could be explained by our group having less severe OSA (AHI, 26 vs. 42/hour) and higher baseline LVEF (35 vs. 28%). The mechanisms underlying the improvement in LVEF include the significant fall noted in sympathetic nerve activity, reflected by the 42% decrease in overnight UNE, in the CPAP group. Overnight UNE has been shown to correlate with plasma norepinephrine, mean sleep heart rate, hypoxemia, and sleep fragmentation (32). Sympathoexcitation is believed to have detrimental consequences on the failing heart (13). OSA contributes to sympathoexcitation through ventilatory inhibition (33), hypoxemia, and hypercapnia (11). Furthermore, effective treatment of OSA has been shown to attenuate sympathetic nerve activity in previous studies of patients without CHF (33), whereas the current study is the first to show a fall in UNE in the setting of CHF and OSA with CPAP. Given the abolition of hypoxemia and the nonsignificant change in arousals, it is likely that the fall in UNE is related to abolition of hypoxemia rather than alterations in arousal frequency.

An alternative mechanism through which OSA treatment with CPAP may improve LVEF is by inducing a fall in blood pressure. OSA has been causally linked to hypertension (10, 34). The current study, however, did not demonstrate a fall in awake blood pressure with CPAP treatment, suggesting that this mechanism may be less important in improving LVEF over the time frame measured. We also surmise that the changes to LVEF are likely to reflect improvements in systolic function *per se* rather than a potential effect of reduced afterload and more favorable hemodynamics secondary to lowered blood pressure. Our blood pressure findings contrast with those reported in OSA with the study of Kaneko and coworkers (20) and studies of patients without CHF (10, 34). In these three studies, blood pressure was measured over varying time frames from 15 minutes (20) to 24 hours (10, 34) with photoplethysmography (10, 20) or automated sphygmomanometry (34). In addition, all patients in the current study were on vasodilators, which may have blunted any additional effect of CPAP on blood pressure.

We were unable to demonstrate a significant improvement in maximal exercise capacity with CPAP. This may be explained by the high baseline $\dot{V}O_2$ peak, which would have limited the magnitude of any further improvement. Our group mean baseline $\dot{V}O_2$ peak of approximately 17.5 ml/minute/kg was similar to that reported in patient survivors with CHF (16.4 ml/minute/kg) and was significantly greater than that of nonsurvivors (13.2 ml/minute/kg) in a large prospective 3-year study (35). Alternatively, the lack of change in $\dot{V}O_2$ peak may simply have reflected the inflexibility of $\dot{V}O_2$ to change with therapies, as illustrated by recent large β-blocker studies in which several markers of exercise capacity did not change with β-blockers despite improvements in LVEF and survival (29, 36).

The responses to both quality of life questionnaires, the SF-36 and Chronic Heart Failure questionnaire, revealed significant improvements across most domains in the CPAP group. The effect size of CPAP on quality of life observed in the current study, approximately 0.3 to 0.8 indicates a clinically important treatment effect (37). This represents a substantial improvement

in symptomatology, given that our patient sample was recruited proactively through heart failure clinics rather than patients presenting of their own volition volunteering symptoms.

Study Limitations

First, although this was a randomized controlled trial, it lacked a placebo. Although placebo pills (37) and subtherapeutic or sham CPAP (38) have been administered in OSA trials other studies have used untreated control subjects (39), indicating a lack of consensus amongst clinicians conducting nasal CPAP trials. Given these difficulties and the fact that a recent metaanalysis suggested that placebo therapy has little benefit over untreated control groups (40), the control group in the current study was not offered placebo. As a result, the participants could not be blinded to treatment; however, the objective measurements (LVEF, UNE) were analyzed by scientists blinded to the patients' treatment status.

Our study included only three females. Although there is a consistent finding among prevalence trials of OSA in CHF (3–5) of a very high male predominance ($\sim$ 90%), caution should be taken when generalizing these results to all patients.

We included a higher LVEF cutoff than other heart failure trials. The objective of this trial was to measure effects of alleviating OSA on systolic dysfunction. Unlike CHF trials including mortality or hospitalization rates, in which low LVEF cutoffs were required to attain sufficient endpoints, our objectives could be satisfied at higher LVEF ranges. We acknowledge that left ventricular diastolic dysfunction may have coexisted with systolic dysfunction and possibly contributed to our patients' symptomatology, but it was not assessed.

We included patients with mild OSA (AHI, 5–15 events per hour) on the basis of the results of the Sleep Heart Health study (2), demonstrating a relationship between CHF, other cardiovascular diseases, and AHI more than five events per hour. Thus, our results not only confirm the findings of the Kaneko study but also demonstrate generalizability to a more mild and clinically prevalent population.

The study incurred a dropout rate of 27%. The reasons for dropouts are outlined in RESULTS. This dropout rate is similar to that experienced in other clinical trials of CPAP of 19 (34) to 47% (10). The study was limited by a higher than expected death rate and rate of other interventions initiated during the trial period that would have significantly impacted study endpoints. The latter outcome is explained by the vast array of therapeutic options available to clinicians for the management of CHF. In addition, clinical decision making was performed by cardiologists who were, in the main, not study investigators and were instructed in the study protocol that necessary additional interventions could not to be withheld for trial purposes.

In summary we have demonstrated that CPAP therapy for moderately severe OSA in patients with CHF augments systolic heart function, restores normoxia during sleep, reduces sympathetic nerve activity, and improves the quality of life. Further studies are required to assess the mortality benefits of this therapy.

Conflict of Interest Statement: D.R.M. has no declared conflict of interest; N.C.G. has no declared conflict of interest; D.M.K. has no declared conflict of interest; M.R. has no declared conflict of interest; P.B. has no declared conflict of interest; M.T.N. is a member of an Australian Medical Advisory Board for a device company that makes CPAP machines and as a result is paid a small stipend <$3,000 Australian to attend board meetings and has also been a recipient of an unconditional research grant of $50,000 Australian for two years to conduct this clinician initiated research project.

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ORIGINAL RESEARCH ARTICLE

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Insomnia, Health-Related Quality of Life and Healthcare Resource Consumption

A Study of Managed-Care Organisation Enrollees

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Abstract

Objective: Insomnia is a prevalent sleep complaint which has been reported to be greatly associated with reduced health-related quality of life (HR-QOL) and increased healthcare resource use. This study documents the prevalence of insomnia, and its impact on patients' HR-QOL and healthcare resource use in managed-care settings in the US.

Design and Setting: A multi-site survey of 5 American Medical Group Association® (AMGA) clinics was conducted. Each clinic mailed questionnaires to 1100 randomly selected individuals enrolled in its healthcare system and distributed questionnaires to 400 individuals during a clinic visit and prior to seeing a physician. The questionnaire was a form of the Health Status Questionnaire with the well-validated Medical Outcomes Study 36-Item Short Form (SF-36) Health Survey, a 3-question depression screen, a sleep questionnaire, demographic variables, and questions about medical encounters and prescription and over-the-counter (OTC) drug use.

Main outcome measures and results: Approximately one-third of managed-care enrollees in this study reported insomnia with daytime dysfunction. Individuals with insomnia reported lower HR-QOL scores and increased healthcare resource use compared with individuals with no insomnia. After controlling for demographic variables and comorbid conditions, the negative association of insomnia remained significant on all HR-QOL scores, emergency room visits, calls to the physician and OTC drug use.

Conclusions: Insomnia is significantly associated with reduced HR-QOL and increased healthcare resource use in enrollees of managed-care organisations.

Insomnia affects over 60 million Americans every year.[1] The condition has been reported to impact many areas of an individual's life, including self-perception of health.[2] Insomnia can negatively impact an individual due to its consequences during the day by decreasing quality of life in addition to diminishing length or quality of sleep. The disruptions of a person's functioning and well-being after nights of insomnia can be observed in physical fatigue and psychological impairment.[3,4] Independent of other disorders, insomnia has been documented to impact negatively on daily life and health-related quality of life (HR-QOL).[3]

To date, relatively little attention has been given to the impact of insomnia on the quality of an individual's daily life. Although many self-rated questionnaires are available for assessing insomnia, these questionnaires concentrate mainly on the clinical characteristics of sleep such as sleep latency and length of sleep rather than on HR-QOL. Rombaut et al.,[5] in a study to validate the Quality of Life of Insomniacs (QOLI) questionnaire, assessed individuals with no insomnia and untreated individuals with insomnia. The questionnaire measured 5 domains (quality of sleep, quality of waking, physical well-being, mood and mental state, and relationships) and assessed the overall quality of life. In all 5 domains, scores of untreated insomniacs were significantly different ($p < 0.0001$) from those of noninsomniacs, indicating that individuals without insomnia had a better quality of life than those with the condition.

Insomnia affects not only HR-QOL, but also healthcare resource consumption such as physician office visits. Individuals with insomnia frequently report persistent or recurring health problems and are hospitalised more often and for longer periods than individuals without insomnia.[6] Kales et al.[7] showed that patients with chronic insomnia, on average, had been hospitalised 2.7 times compared with 1.4 hospitalisations for the control group without insomnia. A longitudinal study reported that over a 4-year period, 53.2% of poor sleepers had been hospitalised 1 or more times compared with only 39.9% of good sleepers; and 24.8% of poor sleepers had been hospitalised 2 or more times compared with 14.2% of good sleepers.[8] Insomnia has also been demonstrated to constitute a major burden to primary-care physicians. One study showed that it caused a doubling of primary consultations from a mean of 5.25 per year for good sleepers to 12.87 per year for individuals with moderate to severe insomnia.[9] Simon and VonKorff[10] examined insomniacs in a primary-care setting and found that insomnia was associated with significantly greater functional impairment, more days of disability due to health problems and greater general medical use. These authors also showed that insomnia was associated with both depression and chronic medical illness, but adjustment for these factors only partially accounted for the associations between insomnia and healthcare resource use.

The present study surveyed a randomly selected population of several managed-care organisations and results were used to concurrently examine the impact of insomnia on HR-QOL and healthcare resource consumption. Our hypotheses were that insomnia is associated with a reduction in HR-QOL and that individuals with insomnia consume more healthcare resources [prescription and over-the-counter (OTC) drugs, visits and phone calls to physicians, laboratory testing, emergency room (ER) visits and hospitalisations] than those without insomnia.

Methods

Study Patients

This study was a multi-site survey of 5 American Medical Group Association® (AMGA) members: Lovelace Health System (Albuquerque, New Mexico); Lewis-Gale Clinic (Salem, Virginia); Cleveland Clinic (Cleveland, Ohio); Sutter/CHS (Sacramento, California); and Geisinger Clinic (Danville, Pennsylvania). Each clinic mailed questionnaires to 1100 randomly selected individuals

enrolled in its healthcare system and distributed questionnaires to 400 individuals during a clinic visit and prior to seeing a physician.

Survey Questionnaire and Data Compilation

The questionnaire was a 2-page, double-sided scan form of the Health Status Questionnaire with the well-validated Medical Outcomes Study 36-Item Short Form (SF-36) Health Survey,[11] a 3-question depression screen, a sleep questionnaire, demographic variables, and questions about medical encounters, prescription and OTC drug use. The data were compiled and analysed by the Quality Management and Research Department at AMGA.

Based on a preliminary analysis of data revealing similarities of findings, responses to mail surveys and clinic surveys were pooled for this study. The sleep evaluation section of the questionnaire contained 3 categories of questions dealing with sleep loss, daytime sleepiness, and night-time disturbances, each of which consisted of 5 items. Details of the questions have been described elsewhere.[12] Using the responses to the 5 questions in the sleep-loss category, 3 levels of insomnia were defined: no insomnia, level I insomnia and level II insomnia. Level I and level II insomnia were distinguished from one another by the presence of daytime dysfunction, i.e. level I insomnia was defined as difficulty attaining or maintaining sleep and level II insomnia was level I insomnia resulting in daytime dysfunction. The levels of insomnia were defined based on consensus by sleep experts, including one of the authors (W.B. Mendelson).

Responses to questions about prescription drug use were used as an index (proxy) for comorbid conditions. This comorbid index was divided into 9 categories:

- endocrine, nutritional, metabolic and immunity
- circulatory system
- respiratory system
- musculoskeletal and connective tissue
- genitourinary system
- digestive system
- brain, nervous system and sense organs
- infectious and parasitic
- other.

For drugs with multiple indications, the most common indication was used to determine the comorbid condition. Comorbid categories were selected based on the International Classification of Diseases, version 9 (ICD-9).

The frequency of medical encounters was determined by asking respondents how many times within the past 8 weeks they had been hospitalised, gone to an ER, visited their physician, called their physician for advice, had a prescription filled, bought OTC drugs and/or had a laboratory test.

Statistical Analysis

The various demographic and comorbid categories and insomnia levels were described in terms of percentages of respondents in each category. Mean scores in each of the 8 SF-36 domains and the 2 summary scores [physical component summary (PCS) and mental component summary (MCS)] were calculated for each level of insomnia, and these means were compared using the Student's t-test procedure.

Regression analysis was performed for all SF-36 domains and summaries using demographic, comorbid category, and level I and level II insomnia variables. If a respondent had missing data for a domain, the mean domain score calculated from the remaining respondents was used in place of the

Table I. Percentage of survey respondents (n = 3447) taking various categories of prescription drugs (comorbid category)

Comorbid category	% of respondents reporting
Endocrine, nutritional, metabolic, immunity	8.3
Circulatory system	21.4
Respiratory system	7.6
Musculoskeletal and connective tissue	8.6
Genitourinary system	13.2
Digestive system	4.9
Brain, nervous system, and sense organs	11.4
Infectious and parasitic	2.4
Other	5.2

Table II. SF-36 scores for respondents with no insomnia, level I insomnia, and level II insomnia

Domain/summary	Mean score		
	no insomnia (n = 1867)	level I insomnia (n = 464)[a]	level II insomnia (n = 1116)[b]
Physical functioning	86.80	83.07[c]	79.04[c,d]
Role physical	82.94	81.11	65.63[c,e]
Bodily pain	75.73	72.21[f]	60.93[c,e]
General health	76.84	73.47[c]	62.20[c,e]
Social functioning	88.83	88.39	70.58[c,e]
Vitality	64.30	64.43	44.64[c,e]
Role emotional	88.25	86.13	67.09[c,e]
Mental health	79.35	79.76	63.51[c,e]
Physical component summary (PCS)	50.50	48.72[c]	46.31[c,e]
Mental component summary (MCS)	52.80	53.37	43.57[c,e]

a Difficulty attaining or maintaining sleep.
b Level I insomnia resulting in daytime dysfunction.
c Significantly different from no insomnia, $p < 0.001$.
d Significantly different from level I insomnia, $p < 0.01$.
e Significantly different from level I insomnia, $p < 0.001$.
f Significantly different from no insomnia, $p < 0.01$.
SF-36 = Medical Outcomes Study 36-Item Short Form (health survey).

missing value. Similarly, mean income, age and education values calculated from the remaining respondents were substituted for these missing demographic values. If either gender or marital status data were missing, the respondent was not included in the analysis. Analysis of variance (ANOVA) was performed on the regression coefficients, and significance of F-test results was determined at the levels of $p < 0.05$, $p < 0.01$ and $p < 0.001$.

The frequency of medical encounters was cross-tabulated with insomnia level to determine the frequency and percentage of each type of medical encounter associated with each level of insomnia. Logistic regression analysis was performed to examine the impact of insomnia on each type of medical encounter when other variables were controlled. If the demographic variables of income, age or education were missing, the mean was substituted for the respondent. If gender or marital status data were missing, the respondent was dropped from the analysis. χ^2 analysis was performed on the regression coefficients and significance of results was determined at the levels of $p < 0.05$, $p < 0.01$ and $p < 0.001$.

Results

Demographics of Respondents

A total of 7500 surveys were distributed by mail and in the clinics between May 1995 and January 1996. Of the 5500 mailed surveys, 1740 responses were received, and of 2000 clinic surveys, 1707 responses were received. The majority of respondents were married (68.6%), women (61.9%) and Caucasian (80.9%); the largest age group represented was 41 to 55 years (32.3%). The demographic profile of the respondents is discussed elsewhere.[12] Table I shows the percentage of respondents in each of the comorbid categories. The most prevalent comorbid category was circulatory system problems followed by genitourinary and brain and nervous system problems. In the survey population, 54.2% (n = 1867) of respondents had no insomnia, 13.5% (n = 464) had level I insomnia and 32.4% (n = 1116) had level II insomnia.

Insomnia and HR-QOL

Table II presents mean scores for all SF-36 domains, the PCS and the MCS for respondents with each level of insomnia. When comparing indivi-

Table III. Standardised regression coefficients for SF-36 domains and variables (n = 3084)

Variables	SF-36 domain									
	physical functioning	role physical	bodily pain	general health	social functioning	vitality	role emotional	mental health	physical component summary (PCS)	mental component summary (MCS)
R^2	0.2097*	0.1540*	0.1874*	0.2221*	0.2121*	0.2406*	0.1278*	0.2467*	0.2085*	0.2356*
Demographics										
Age[a]	–0.2688*	–0.1412*	–0.0742*	0.0050	–0.0002	0.0448**	–0.0236	0.0949*	–0.1916*	0.1306*
Sex[b]	0.0824*	0.0118	0.0118	–0.0381**	0.0182	0.0627*	0.0273	0.0394**	0.0201	0.0326
Marital status[c]	0.0125	–0.0064	–0.0224	0.0205	0.0494†	–0.0092	0.0636*	0.0647*	–0.0244	0.0623*
Race[d]	0.0214	0.0265	0.0042	0.0320**	0.0550*	–0.0121	0.0629*	0.0339**	–0.0005	0.0377**
Income[a]	0.1281*	0.1051*	0.0864*	0.0934*	0.0851*	0.1036*	0.0470†	0.0748*	0.1169*	0.0561†
Education[a]	0.0869*	0.0254	0.0683*	0.1064*	0.0345	0.0244	0.0394†	0.0447**	0.0673*	0.0167
Survey type	0.0487†	0.1103*	0.1087*	0.0573*	0.0875*	0.0426†	0.0461**	0.0617*	0.0876*	0.0412**
Comorbid index categories[e]										
Endocrine	0.0071	–0.0240	0.0020	–0.0682*	–0.0084	–0.0069	–0.0121	–0.0105	–0.0250	–0.0062
Circulatory	–0.0515†	–0.0216	–0.0178	–0.1012*	0.0115	–0.0153	0.0333	0.0404**	–0.0849*	0.0441†
Respiratory	–0.0370**	–0.0402**	–0.0173	–0.0629*	–0.0150	–0.0283	–0.0250	0.0027	–0.0515†	–0.0079
Musculoskeletal	–0.1531*	–0.1523*	–0.2257*	–0.1156*	–0.1171*	–0.0783*	–0.0509†	–0.0331**	–0.2000*	–0.0075
Genitourinary	0.0333**	0.0170	–0.0112	0.0109	0.0345**	–0.0180	0.0109	0.0062	0.0102	0.0033
Digestive	–0.0582*	–0.0348**	–0.0581*	–0.0717*	–0.0159	–0.0364**	–0.0354**	–0.0415†	–0.0540*	–0.0242
Brain	–0.0605*	–0.0849*	–0.0701*	–0.1258*	–0.1446*	–0.1186*	–0.1148*	–0.1570*	–0.0536†	–0.1540*
Infectious	0.0074	–0.0554*	–0.0147	–0.0493†	–0.0474†	–0.0194	–0.0096	–0.0103	–0.0236	–0.0238
Other	–0.0467†	–0.0444†	–0.0157	–0.0570*	–0.0284	–0.0290	0.0200	0.0016	–0.0664*	0.0084
Insomnia										
Level I[f,g]	0.0259	0.0288	–0.0162	–0.0161	0.0104	0.0148	–0.0126	–0.0031	0.0108	–0.0027
Level II[f,h]	–0.1385*	–0.1874*	–0.2386*	–0.2853*	–0.3197*	–0.3820*	–0.2593*	–0.3587*	–0.1630*	–0.3528*

a Continuous.

b 1 = male; 0 = female.

c 1 = married; 0 = not married.

d 1 = Caucasian; 0 = non-Caucasian.

e For all categories, 1 = taking drug; 0 = not taking drug.

f 1 = has insomnia; 0 = has no insomnia.

g Difficulty attaining or maintaining sleep.

h Level I insomnia resulting in datime dysfunction.

SF-36 = Medical Outcomes Study 36-Item Short Form (health survey); * $p < 0.001$; ** $p < 0.05$; † $p < 0.01$.

duals with no insomnia and those with level II insomnia, individuals with level II insomnia had significantly ($p < 0.001$) lower scores in all domains and summary scores. Scores for individuals with level I insomnia were significantly lower than those for individuals with no insomnia in the Physical Functioning and General Health domains, the PCS ($p < 0.001$) and the Bodily Pain domain ($p < 0.01$). No significant differences between HR-QOL scores of noninsomniacs and level I insomniacs were found in any other domain.

Results of the HR-QOL regression analysis are shown in table III. The 3 most profound variables influencing HR-QOL were level II insomnia, the brain and nervous system comorbid conditions and levels of income. Level II insomnia was highly significantly ($p < 0.001$) associated with all SF-36 domains, the PCS and the MCS. The brain and nervous system comorbid conditions category was highly significantly ($p < 0.001$) associated with all SF-36 domains and the MCS, and significantly ($p < 0.01$) associated with the PCS. Income was highly significantly ($p < 0.001$) associated with the MCS and all SF-36 domains except role emotional and the PCS, for which it was significantly ($p < 0.01$) associated with. The musculoskeletal comorbidity category also had a significant association with HR-QOL. It was highly significantly ($p < 0.001$) associated with 6 domains and the PCS, and was significantly ($p < 0.05$) associated with 2 domains. This category did not, however, have an association with the MCS. Although the circulatory system and genitourinary comorbid categories were the 2 most commonly reported by the survey population, neither consistently influenced the HR-QOL.

Insomnia and Healthcare Resource Use

Figure 1 depicts the percentage of patients with each level of insomnia who experienced various medical encounters at least once in the previous 8 weeks. Individuals with level II insomnia were significantly ($p < 0.05$) more likely to have had an ER visit, physician visit, telephone contact with their physician, a laboratory test, a prescription filled and to have taken an OTC drug than were individuals with no insomnia. Furthermore, level II insomniacs were significantly ($p < 0.05$) more likely to have had an ER visit, physician visit and to have taken an OTC drug than were level I insomniacs. Level I insomniacs were also significantly ($p < 0.05$) more likely to have had a laboratory test or a

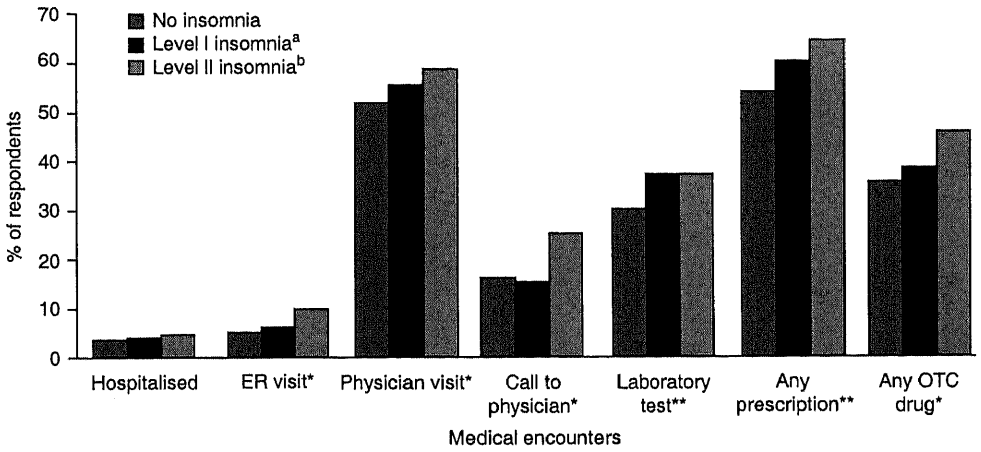

Fig. 1. Insomnia and medical care encounters. **a** = difficulty attaining or maintaining sleep; **b** = level I insomnia resulting in daytime dysfunction; **ER** = emergency room; **OTC** = over-the counter; * = significant difference between no insomnia and level II insomnia only, $p < 0.05$; ** = significant difference between no insomnia and both level I and level II insomnia, $p < 0.05$.

Table IV. Standardised regression coefficients for medical encounters and variables (n = 3084)

Variables	Medical encounter						
	hospitalised[a]	ER visit[a]	physician visit[a]	physician call[a]	laboratory test[a]	any prescription[a]	any OTC drug taken[a]
Demographics							
Age[b]	0.0425	−0.0567	0.0207	−0.0395	0.0844*	0.0346	−0.0785**
Sex[c]	0.0010	0.0493	−0.0820*	−0.1032*	−0.0622**	−0.0533†	−0.0773*
Marital status[d]	0.0605	−0.1470†	0.0004	0.0012	−0.0058	−0.0322	0.0436
Race[e]	−0.0202	−0.0703	−0.0258	−0.0479	−0.0252	−0.0348	0.1051*
Income[b]	−0.1429†	−0.0586	−0.0190	0.0092	0.0136	0.0444	−0.0258
Education[b]	−0.0055	−0.1024†	−0.0344	0.0726†	−0.0209	−0.0076	0.1313*
Survey type	−0.0285	−0.2083*	−0.1638*	−0.1036*	−0.0959*	−0.1146	−0.0310
Comorbid index categories[f]							
Endocrine	−0.0003	0.0910†	0.0100	0.0342	0.0851*	0.1438*	0.0020
Circulatory	0.1932*	0.1364**	0.1225*	0.0644†	0.1247*	0.3216*	−0.0092
Respiratory	0.0522	0.0811†	0.0370	0.0350	−0.0500**	0.1838*	0.0583**
Musculoskeletal	0.1623*	0.1396*	0.1144*	0.0505†	0.0786*	0.2035*	−0.0004
Genitourinary	−0.1840†	−0.1442**	−0.0081	0.0253	−0.0064	0.2383*	0.0654**
Digestive	0.0044	0.0541	0.0887*	0.0428	0.0468†	0.0482	−0.0110
Brain	0.0607	0.0552	0.1254*	0.0934*	0.0397	0.2496*	0.0086
Infectious	0.0190	0.0560	0.1274*	0.0619**	0.0762*	0.1805*	0.0094
Other	0.0574	−0.0544	0.0798*	0.0515†	0.0917*	0.1743*	0.0159
Insomnia							
Level I[g,h]	0.0031	0.0570	0.0178	0.0053	0.0269	0.0022	0.0559†
Level II[g,i]	0.0547	0.1604*	0.0288	0.1069*	0.0592**	0.0630**	0.1128*

a 1 = had this medical encounter at least once; 0 = did not have this medical encounter.

b Continuous.

c 1 = male; 0 = female.

d 1 = married; 0 = not married.

e 1 = Caucasian; 0 = non-Caucasian.

f For all categories, 1 = taking drug; 0 = not taking drug.

g 1 = has insomnia; 0 = has no insomnia.

h Difficulty attaining or maintaining sleep.

i Level I insomnia resulting in datime dysfunction.

ER = emergency room; **OTC** = over-the-counter; * $p < 0.001$; ** $p < 0.01$; † $p < 0.05$.

prescription filled compared with individuals with no insomnia.

Table IV shows results of the logistic regression analysis of medical encounters on variables including insomnia levels, demographic variables and comorbid categories. Level II insomnia had a significant association with the extent of ER visits, physician calls, the consumption of OTC drugs, laboratory tests and having a prescription filled. The strength of association between level II insomnia and ER visits was greater than that for all comorbid categories, except musculoskeletal. Level II insomnia was also associated with OTC drug use more than all of the comorbid categories.

Relationship Between HR-QOL and Healthcare Resource Use

Comparisons were made on each of the domain scores of the SF-36 between patients with at least 1 healthcare resource use encounter and those with no healthcare encounters. The results of the comparisons show that patients who had a healthcare

Table V goes as a landscape table here

encounter had significantly ($p < 0.05$) lower HR-QOL scores in all but 1 category (OTC, physical functioning) as compared to those who had no healthcare encounters (table V).

Discussion

By demonstrating that individuals with level II insomnia have significantly lower SF-36 scores than those without insomnia, this study confirmed that insomnia has a marked adverse association with HR-QOL. In addition, comorbid conditions that affect the brain and nervous system also have a negative impact on HR-QOL. This may provide additional support for the often observed link between insomnia and mental health problems such as depression, although the causal relationship could not be explored in this study.

The difference in HR-QOL impact between insomnia levels I and II could be attributed to daytime dysfunction associated with level II insomnia. This observation provided further support to earlier observations that the most serious consequence of insomnia is the loss of well-being during the day rather than loss of sleep itself.[3,4]

The hypothesis that insomniacs are greater users of healthcare resources than noninsomniacs was also confirmed. Level II insomniacs were shown to be significantly more likely to have had medical encounters, with the exception of hospitalisation, than noninsomniacs. Level I insomnia did not have such a pronounced association with healthcare resource consumption except in cases of laboratory tests and prescriptions filled, where level I insomniacs were more likely than noninsomniacs to have had an encounter. Because daytime dysfunction differentiates level II from level I insomnia, the implication here is that the daytime impact of sleep loss corresponds with the perception of having sleep problems, thus warranting a visit with the physician for this purpose.

The use of prescription drugs as a proxy for comorbid conditions provided an unobtrusive and convenient means to establish the general health conditions and profiles for the surveyed popula-

Table V. Mean SF-36 scores for respondents with and without medical encounters

	Hospitalised		ER visit		Physician visit		Physician call		Laboratory test		Any prescription		Any OTC drug	
	yes	no	yes	no	yes	no	yes	no	yes	no	yes	no	yes	no
PF	68.69*	84.65	75.01*	84.77	80.01*	88.69	77.65*	85.54	78.73*	86.64	80.01*	89.45	83.53	84.26
RP	38.03*	78.84	54.46*	79.20	68.81*	87.62	58.69*	81.78	66.64*	83.01	69.56*	88.11	74.92**	78.99
BP	51.99*	71.26	54.48*	71.77	64.85*	77.38	59.17*	73.28	64.27*	73.91	65.40*	77.79	67.10*	73.02
GH	61.03*	72.08	57.79*	72.68	67.79*	76.29	63.37*	73.58	67.07*	74.11	67.44*	77.77	69.53*	73.11
SF	59.00*	83.81	65.58*	84.18	78.87*	87.70	71.12*	85.61	77.88*	85.41	79.08*	87.97	80.95*	84.07
VT	47.19*	58.35	46.15*	58.83	54.44*	62.17	50.06*	59.85	54.10*	60.01	54.73*	62.43	55.46*	59.64
RE	69.54**	81.45	66.50*	82.16	77.75*	85.24	71.33*	83.28	76.25*	83.65	77.29*	85.90	79.19†	82.27
MH	70.67†	74.35	65.30*	74.85	72.63*	76.20	69.00*	75.48	72.84*	75.10	72.69*	76.54	72.87*	75.28
PCS	39.32*	49.30	42.94*	49.40	46.45*	51.87	44.52*	49.99	45.89*	50.50	46.59*	52.17	48.14*	49.49
MCS	47.48†	49.90	44.85*	50.17	49.03*	50.80	46.81*	50.53	49.09*	50.29	49.01*	50.95	49.00*	50.43

BP = bodily pain; **ER** = emergency room; **GH** = general health; **MCS** = mental component summary; **MH** = mental health; **OTC** = over-the-counter; **PCS** = physical component summary; **PF** = physical functioning; **RE** = role emotional; **RP** = role physical; **SF** = social functioning; **SF-36** = Medical Outcomes Study 36-Item Short Form (health survey); **VT** = vitality; * $p < 0.001$; ** $p < 0.01$; † $p < 0.05$.

tions. Relying on patient self-reports takes into account what drugs the patient is actually using and represents a trade-off to the rather more complex means of reviewing actual drug use from existing databases or medical charts. The latter normally underestimates the actual prescription drug use to the extent the patient might have gone outside the insurance drug plan to purchase prescription drugs. Also, although the study involved random sampling of 5 managed-care organisations, the results may not be generalisable to the general health maintenance organisation (HMO) population. Additionally, the response rate for the mailed questionnaire was low compared with the clinical survey responses. These limitations need to be considered while interpreting the study results.

Conclusion

This study corroborates earlier findings regarding the impact of insomnia on reducing HR-QOL and increasing healthcare resource use. In addition, individuals who have increased medical encounters and lower HR-QOL scores not attributed to other medical conditions may have insomnia, thus warranting further exploration by healthcare providers. The results of this study support that appropriate diagnosis and treatment of insomnia can have a positive impact upon the patients' quality of life and may reduce patients' consumption of healthcare resources.

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Place of chronic insomnia in the course of depressive and anxiety disorders

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Abstract

Background: Insomnia is frequent in the general population and is often related to a psychiatric illness. However, little is known about how the chronicity of insomnia affects this relation and how often subjects with chronic insomnia have antecedents of psychiatric disorders. *Methods*: A total of 14,915 subjects aged from 15 to 100 years representative of the general population of the United Kingdom, Germany, Italy, and Portugal were interviewed by telephone using the Sleep-EVAL system. The questionnaire assessed current psychiatric disorders according to the DSM-IV classification and a series of questions assessed the psychiatric history. Insomnia was considered as chronic when it lasted for 6 months or more. *Results*: The prevalence for insomnia accompanied with impaired daytime functioning was 19.1% and significantly increased with age. More than 90% of these subjects had a chronic insomnia. About 28% of subjects with insomnia had a current diagnosis of mental disorders and 25.6% had a psychiatric history. A DSM-IV insomnia disorder was found in 6.6% of the sample. Presence of severe insomnia, diagnosis of primary insomnia or insomnia related to a medical condition, and insomnia that lasted more than one year were predictors of a psychiatric history. In most cases of mood disorders, insomnia appeared before (> 40%) or in the same time (> 22%) than mood disorder symptoms. When anxiety disorders were involved, insomnia appeared mostly in the same time (>38%) or after (> 34%) the anxiety disorder. *Conclusions*: The study shows that psychiatric history is closely related to the severity and chronicity of current insomnia. Moreover, chronic insomnia can be a residual symptom of a previous mental disorder and put these subjects to a higher risk of relapse.

Keywords: Epidemiology; Insomnia; Anxiety disorder; Depressive disorder

1. Introduction

Insomnia is a distressing and disabling condition that affects up to one third of the general population. Epidemiological and clinical studies have shown that a high number of insomnia subjects also suffer from a concomitant mental disorder mainly depression or an anxiety disorder: between 40 and 60% of insomnia complainers fall into this category (Breslau et al., 1996; Buysse et al., 1994; Coleman et al., 1982; Ford and Kamerow, 1989; Hohagen et al., 1993; Mellinger et al., 1985; Ohayon, 1997; Ohayon et al., 1997a; Schramm et al., 1995; Tan et al., 1984). Retrospective studies that examined whether the insomnia resulted from a sleep disorder or was a symptom of some other mental disorder have shown that the insomnia is mostly an associated symptom of the mental disorder and does not warrant a separate diagnosis of insomnia (Ohayon, 1997).

However, how the chronicity of insomnia affects this relationship and how often chronic insomniac subjects have previously suffered from a mental disorder has been only minimally investigated. Results of longitudinal studies with individuals with insomnia suggested that the maintenance of insomnia problems over the time increases the likelihood of developing a concomitant mental disorder (Breslau et al., 1996; Hohagen et al., 1993; Ford and Kamerow, 1989). However, the past history of the subject was not specifically investigated in order to understand how chronic insomnia impacted psychiatric pathology.

In this perspective, we investigated the psychiatric history of insomniac subjects in the general population.

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2. Methods

2.1. Sample

Subjects of the general population from four European countries were queried via the telephone about their sleeping habits, sleep symptoms and mental health status. To this end, four representative samples were drawn from the non-institutionalized population aged 15 years or older of United Kingdom, Germany, Italy and Portugal. The targeted population consisted of 166,990,882 inhabitants. All the samples were drawn in a similar fashion using a two-stage design. At the first stage, phone numbers were randomly pulled according to the geographic distribution of the population of each country using official census data available at the time. At the second stage, a controlled selection method was applied to maintain the representation of the sample according to age and gender. The Kish method (Kish, 1965) was used to this end and served to select one respondent in each household. The interviewers collected the age and gender of all eligible household members. The Sleep-EVAL system designated which family member should be interviewed using one of the eight Kish tables that was previously assigned to the household with respect to the prescribed proportions by Kish. If the household member thus chosen refused to participate, the household was dropped and replaced by another, and the process repeated.

The surveys were conducted with the help of Poll Service Companies: British Poll Service (UK), Teleperformance (Germany), Grandi Numeri (Italy) and Action (Portugal). The studies were approved by ethical and research committees of the Imperial College (London, UK), Regensburg University (Germany), the San Rafaele Hospital (Italy) and the Hospital de Sta. Maria (Portugal). All these studies were strictly controlled by the research team of the P.I. (MMO).

Verbal consent was required before interviewing the subjects. For subjects younger than 18, the verbal consent of the parents was also requested. Individuals with insufficient fluency in the national language, with a hearing or speech impairment or with an illness precluding the feasibility of an interview were excluded. The participation rate was 79.6% in the UK (4972 of 6249 eligible subjects), 68.1% in Germany (4115 of 6047 eligible subjects), 89.4% in Italy (3970 of 4442 eligible subjects) and 83% in Portugal (1858 of 2234 eligible subjects). Overall, 14,915 subjects were interviewed.

2.2. Instrument

Lay interviewers performed the interviews using the Sleep-EVAL expert system (Ohayon, 1995a, 1999; Ohayon et al., 1997b). Sleep-EVAL is a non-monotonic, level-2 expert system. It has a causal reasoning mode and is capable of formulating diagnostic hypotheses that are validated or discarded through further queries and deductions. It is specially designed to conduct epidemiological studies of sleep habits and sleep and mental disorders in the general population. Interviews typically begin with a standard questionnaire composed of sociodemographic information, sleep/wake schedule, physical health, and a series of questions related to sleep symptoms and mental disease symptoms. From the answers provided on these questions, the system elicits a series of diagnostic hypotheses (causal reasoning process) that are confirmed or rejected through further questioning and by deductions of the consequences of each answer (non-monotonic, level-2 feature). The system allows concurrent diagnoses in accordance with the Diagnostic and Statistical Manual of Mental Disorders, forth edition (DSM-IV) (APA, 1994) and the International Classification of Sleep Disorders (ICSD) (Diagnostic Classification Steering Committee, 1990) classifications. The differential diagnosis process is based on a series of key rules allowing or prohibiting the co-occurrence of two diagnoses in accordance with the classifications implemented in the system. The interview ends once all diagnostic possibilities are exhausted.

The system has been tested in various contexts; in clinical psychiatry, overall kappas between the diagnoses of four psychiatrists and those of the system ranged from 0.44 with one psychiatrist to 0.78 with two psychiatrists ($n=114$ cases) (Ohayon, 1995b). In another study that involved 91 forensic patients, most of the patients (60%) met criteria for a diagnosis in the psychosis spectrum. The kappa between diagnoses obtained by the system and those given by psychiatrists was 0.44 for specific psychotic disorders (mainly schizophrenia). The latest validation studies were conducted with 105 patients at the Sleep Disorders Centers at the Stanford University (USA) and at the Regensburg University (Germany). Patients attending the Sleep Disorders Centers were interviewed twice: (1) by a physician using the Sleep-EVAL system. These physicians were blind to the diagnoses given by the Sleep-EVAL system, (2) by a senior sleep specialist clinician using his/her usual practice and the results of polysomnographic examination to give one to three main diagnoses and one to ten main symptoms for each patient. This specialist was blind to the diagnoses made by the Sleep-EVAL system. The Sleep-EVAL diagnoses were later compared to those of the sleep specialists. A kappa of 0.93 was obtained between the Sleep-EVAL system and the sleep specialists for the diagnosis of Obstructive Sleep Apnea Syndrome. The sensitivity of Sleep-EVAL for OSAS was 92.5% and the specificity was 100%. For all types of sleep-disordered breathing, the sensitivity of Sleep-EVAL was 98.2% and the specificity was 95.1%. Agreement for insomnia diagnoses

was obtained in 96.9% of cases (kappa 0.78) (Ohayon et al., 1999). Another similar study was done with 72 patients at the Sleep Disorders Center of the Toronto Hospital (Canada) (Hosn et al., 2000). The agreement between Sleep-EVAL and sleep specialists for obstructive sleep apnea syndrome attained a kappa of 0.92. The kappa on insomnia diagnoses was of 0.71.

The duration of interviews ranged from 28 to 150 minutes. The longest interviews involved subjects with sleep disorders associated with mental disorders. Interviews were completed over two or more sessions if the duration of a session exceeded 60 min.

2.3. Variables

Participants were submitted to an extensive interview that examined current mental health and explored DSM-IV mental diagnoses. Current use of psychotropic and other medications were also probed. Psychiatric history was investigated including questions about past use of medications to help sleep, to treat anxiety or depressive mood. A series of questions about past professional consultations for a mental health problem and the type of problem were also asked. The sleep questionnaire instrument covered questions about sleep/wake schedule, sleeping habits, sleep quality, sleep symptoms (insomnia, hypersomnia, daytime sleepiness, snoring breathing pauses during sleep, leg symptoms, etc.) daytime consequences of insomnia and daytime sleepiness, hypnagogic and hypnopompic hallucinations, use of medication to improve sleep, medical consultations for sleep problems and explored DSM-IV sleep disorders diagnoses and ICSD diagnoses.

2.4. Group definitions

To facilitate the presentation of the results, the insomnia subjects were divided according to the duration of their insomnia. An insomnia lasting for more than six months is considered as chronic condition. Non-chronic insomnia (lasting less than 6 months) was compared with chronic insomnia. The cut-off duration of 6 months for chronic insomnia was chosen based on the ICSD classification that divided the duration of most of its insomnia diagnoses in acute (less than 1 month); subacute (1–6 months) and chronic (6 months or longer). The DSM-IV requests only an insomnia duration of at least one month without reference to a duration criterion for chronic insomnia.

Insomnia was considered as present when the subject reported (1) difficulty in initiating or maintaining sleep or a complaint of nonrestorative sleep and (2) the insomnia was associated with impaired daytime functioning.

Insomnia severity was assessed as a function of number and intensity of daytime consequences on functioning. Severe insomnia refers to almost daily severe impairment of the functioning; moderate insomnia refers to almost daily mild or moderate impairment of the functioning and mild insomnia refers to little or no impairment related to insomnia.

2.5. Data analyses

The data were weighted to compensate for disparities between the sample and the national census figures for the non-institutionalized population aged 15 or over. Descriptive and qualitative variables were analyzed using the chi-square. Ninety-five percent confidence intervals (95% CI) were calculated for prevalences. Logistic regression was performed using the SUDAAN software that allows an appropriate estimate of the standard errors from stratified samples by means of a Taylor series linearization method. Reported differences were significant at 0.05 or less.

3. Results

The total sample was comprised of 14,915 European subjects, 52.1% are women. The mean age for men was 42.99 ($\pm$17.89) and 45.88 ($\pm$19.07) for women. Young adults (15–24 year old) represented 17.5% of the sample. Individuals between 25 and 44 years of age accounted for 35.2% of the sample; those between 45 and 64 portrayed 28.7% of the sample and those 65 years and older represented 18.5% of the sample.

Overall, 19.1% (95% confidence interval: 18.5–19.7%) of the sample reported to have at least one insomnia symptom and to experience daytime consequences related to that symptom. The highest rate was observed in Germany (21.1%) and the lowest in Portugal (17.3%). Women more frequently reported to have insomnia than men (23.2 vs. 14.6%; odds ratio 1.8 [95% confidence interval: 1.6–1.9]). The prevalence increased with age: it was 16.1% in subjects between 15 and 24; 16.4% for those between 25–44; it increased to 21.0% in those between 45 and 64 years of age and reached 24.1% in those 65 years of age and older ($P<.0001$). The prevalence of DSM-IV insomnia disorders diagnoses was 6.6% (95% confidence interval: 6.2–7.0%).

The duration of insomnia symptoms and resultant consequences was less than 6 months for 1.5% ($n=229$) of the entire sample; 17.6% of the sample had a chronic insomnia (lasting at least 6 months). As can be seen in Fig. 1, nearly 8% of the population had insomnia for more than 10 years. Longstanding insomnia (more than 5 years) was more prevalent in the subjects 45 years of age and older while insomnia of less than 6 months in duration was more frequent in subjects 15–24 years of age (Table 1).

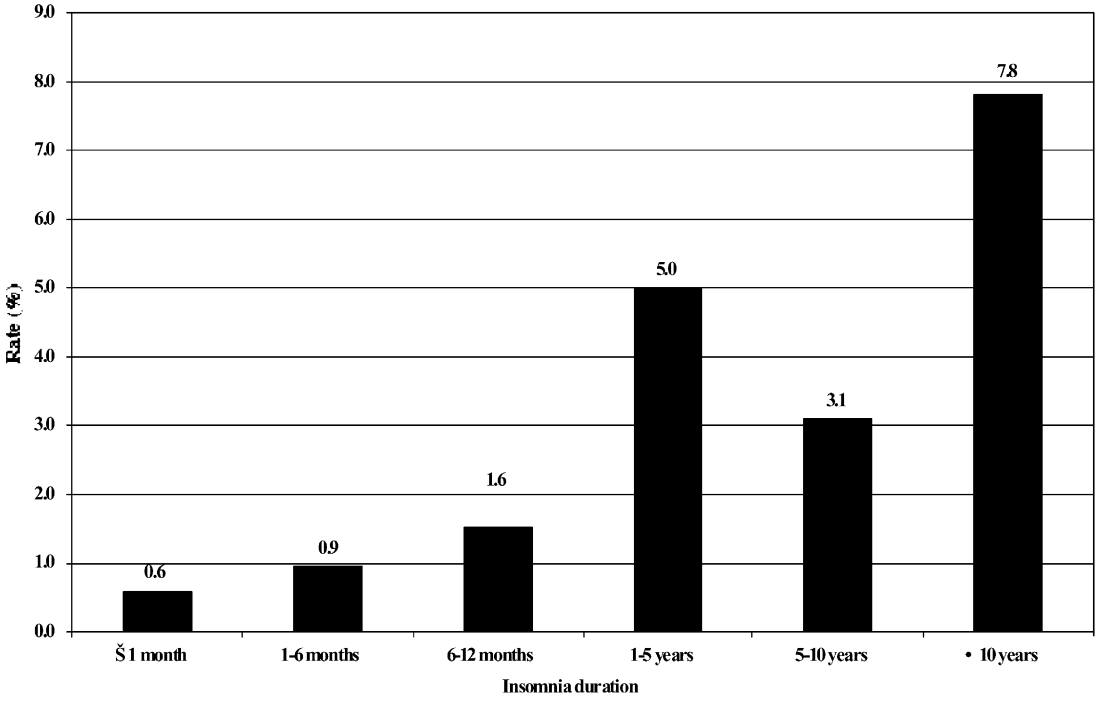

Fig. 1. Prevalence of insomnia by its duration.

Table 1
Prevalence of insomnia and its duration by age groups and gender

	Duration of insomnia		
	<6 months% [95% CI][a]	6 months to 5 years% [95% CI]	>5 years% [95% CI]
Age groups			
15–24	3.5 [2.8–4.2]*	7.3 [6.3–8.3]	5.3 [4.4–6.2]
25–44	1.4 [1.1–1.7]	6.3 [5.6–7.0]	8.7 [7.9–9.5]
45–64	1.0 [0.7–1.3]	6.6 [5.9–7.3]	13.3 [12.3–14.3]*
⩾65	0.8 [0.4–1.2]	6.3 [5.2–7.4]	17.0 [15.6–18.4]*
Gender			
Male	1.1 [0.9–1.3]	4.8 [4.3–5.3]	8.7 [8.0–9.4]
Female	1.9 [1.6–2.2]*	9.2 [7.6–8.8]*	13.1 [12.3–13.9]*

[a] CI = confidence interval.
* $P < 0.05$ with the lowest value in the same column.

3.1. DSM-IV diagnoses

When examining the duration of insomnia according to the DSM-IV diagnoses, it appeared that when the insomnia lasted less than 6 months, in 32.3% of cases a mental disorder was present (insomnia related to a mental disorder: 8.2%; DSM-IV mental disorder diagnosis: 24.1%). Twenty-eight percent of subjects for whom the insomnia lasted between 6 months to 5 years and 25.8% of subjects for whom the insomnia lasted more than 5 years ($P < .05$) had a psychiatric diagnosis. Short-term insomnia (<6 months) issuing in a DSM-IV diagnosis of mental disorder was more likely to occur in the youngest subjects. Insomnia lasting more than 5 years was more likely to result in an insomnia disorder without mental disorders or in no diagnosis in the older subjects.

Severe insomnia was more frequent in subjects with comordid major depressive disorder and anxiety disorder (44.6%) compared to subjects with only one mental disorder diagnosis (33.6%) or an insomnia disorder diagnosis (20.9%; $P < 0.001$).

3.2. Past psychiatric history

Past anxiety and/or mood disorders were most frequently observed in subjects with a current diagnosis of Insomnia related to another mental disorder (49.4%) or in those with a mental disorder diagnosis (mainly Major depressive disorder: 64.6%; Panic disorder: 60.6% and

generalized anxiety disorder: 43.6%). Subjects with a sleep disorder diagnosis not involving a mental disorder most frequently reported a history of previous sleep problems.

Overall, 25.6% of insomnia subjects had a past psychiatric history. This proportion was higher in insomnia subjects with a current mental disorder (47.7%) as compared with insomnia subjects without current mental disorder (17.2%; $P<0.001$); only 8% of subjects without insomnia had a past psychiatric history. The duration of the insomnia complaint was related to the presence of a past psychiatric history only when a current mental disorder was present (Table 2). Subjects with only insomnia symptoms (i.e. without current sleep or mental disorders diagnosis) had the lowest rates of past psychiatric history (Table 2).

We also verified the order of appearance of current symptomatology. When it was a first episode of mood disorder, insomnia symptoms appeared before the mood disorder symptoms in 41% of cases; they appeared in the same time in 29.4% of cases and the mood disorders symptoms appeared first in 28.9% of cases. When there was a relapse of the mood disorder; insomnia was present before the relapse in 56.2% of cases; both symptoms appeared in the same time in 22.1% of cases; insomnia appeared after in 21.6% of cases.

When we examined for anxiety disorders, the figures were slightly different. When there was no previous history of anxiety disorders, the insomnia appeared before the current anxiety disorder in 18% of cases, anxiety and insomnia appeared about in the same time in 38.6% of cases and anxiety appeared before insomnia in 43.5% of cases. When past history and current anxiety disorder were present, insomnia appeared first in 23.2% of cases, anxiety and insomnia appeared together in 42.5% of cases and anxiety appeared first in 34.3% of cases.

Next, insomnia variables (diagnoses, severity, duration) were entered into a multivariate model to determine which of them are more likely to determine if there was a past psychiatric history. Results show that currently having a severe insomnia was the strongest factor indicating a past psychiatric history with an odds ratio of 5.8 (95% CI 2.4–14.0). The second strongest factor was having a diagnosis of primary insomnia or insomnia related to a medical condition [OR: 5.6 (2.3–13.8)]. Thereafter, it was having a moderate insomnia (i.e., nightly or almost nightly insomnia interfering moderately with the daytime functioning) [OR: 4.1 (1.7–10.0)]; having insomnia lasting for more than 12 months [duration between 1 and 5 years and between 6 and 10 years had each an OR of 1.3 (1.0–1.6); more than 10 years: OR 1.4 (1.2–1.8)]. Finally, age [25–44 OR 1.9 (1.6–2.3); 45–64 OR 2.7 (2.2–3.3); $\geqslant 65$ OR 1.6 (1.4–1.8)] and being a woman [OR 1.9 (1.6–2.3)] were also significant factors related to the presence of a previous psychiatric history.

4. Discussion

Our study with a European sample of 14,915 subjects shows insomnia symptoms causing daytime consequences occurred in 19.1% of the sample. In about 85% of cases, the insomnia was chronic, lasting at least six months. Interestingly, chronic insomnia is observed in 12.6% of subjects between 15 and 24 years of age; 5.3% of the young adults have insomnia for more than 5 years. For many of these young subjects, the insomnia problem begun in the adolescence: one out of three said insomnia began in the adolescence and about one in ten said it began in the childhood.

The question about the reliability of data collected by telephone could be raised. Previous studies using this methodology for data collection indicate that, in general, telephone interviews are satisfactory, have good inter-rater reliability and have provided comparable results to that of other interview techniques (Rohde et al., 1997; Slutske et al., 1998). It should be kept in mind, however, that psychiatric history information is derived from cross-sectional data and therefore, it relies on the memory of the subjects.

The results indicate also that nearly half of subjects with chronic insomnia have a past or a current mental disorder. Acute and sub-acute insomnia is more often related to a current mental disorder than chronic insomnia. However, subjects with chronic insomnia (lasting more than one year) more often have a psychiatric history. Importantly, when a diagnosis of mood disorders is involved, insomnia appeared first in more than 40% of cases; when it is a relapse of the mood disorder, insomnia appeared first in 56% of cases. This is not the case with anxiety; in about 80% of cases, anxiety and insomnia symptomatology appeared either in the same time (about 40% of cases) or insomnia appeared after the anxiety disorder was developed (about 40% of cases). This is in line with results reported by the three longitudinal epidemiological studies on insomnia. These studies have shown the increased risk of developing a major depressive illness, within a 12-months interval in two studies (Ford and Kamerow, 1989; Roberts et al., 2000) and within a 3.5 years interval in another study (Breslau et al., 1996), when the insomnia complaint is persisting over the time; the risk ranging from four to 40 times. Persistent insomnia was also associated with an increased risk of developing an anxiety disorder and abuse or dependence to alcohol or drugs (Breslau et al., 1996; Ford and Kamerow, 1989). These results are also in line with clinical observations of natural course of insomnia, which often begins with anxiety to finally results in clinical depression.

A previous history of a mental disorder is closely related to the severity and the chronicity of current insomnia. The likelihood was near six times higher in subjects with a severe insomnia; four times higher in

Table 2
Past psychiatric history by current DSM-IV diagnoses in participants with insomnia symptomatology and duration of insomnia

Current DSM-IV diagnoses	Insomnia duration	Past psychiatric history[c]			History of sleep disturbances% (*n*)	No past history% (*n*)
		Anxiety disorder% (*n*)	Mood disorder% (*n*)	Other mental disorder% (*n*)		
Insomnia disorder diagnoses without mental disorders[a] (n = 816)	< 6 months (n = 56)	9.5 (5)	10.8 (6)	1.2 (1)	20.6 (11)	75.4 (42)
	6 months–5 years (*n* = 305)	8.7 (26)	7.9 (24)	1.5 (5)	10.3 (32)	80.7 (247)
	> 5 years (*n* = 455)	10.2 (46)	6.0 (27)	1.1 (5)	19.0 (87)	75.7 (344)
Insomnia related to another mental disorder (n = 161)	< 6 months (*n* = 19)	16.2 (3)	16.2 (3)	0 (0)	7.9 (1)	75.9 (14)**
	6 months–5 years (*n* = 60)	43.5 (26)	36.7 (22)	10.8 (6)	23.8 (14)	44.8 (27)
	> 5 years (n = 82)	47.2 (39)**	31.5 (26)	5.5 (4)	21.5 (18)	47.6 (39)
Diagnoses of mental disorders (n = 612)	< 6 months (*n* = 55)	17.7 (10)	28.9 (16)	1.5 (1)	13.4 (7)	65.6 (36)
	6 months–5 years (*n* = 215)	26.6 (57)	25.9 (56)	1.9 (4)	18.1 (39)	61.4 (132)
	> 5 years (*n* = 341)	40.9 (140)*	39.1 (133)*	6.1 (21)	24.0 (82)	45.4 (155)*
Major depressive disorder	< 6 months (*n* = 55)	25.0 (7)	44.4 (12)	3.7 (1)	14.8 (4)	48.1 (13)
	6 months–5 years (*n* = 85)	42.4 (36)	44.7 (38)	5.8 (5)	17.6 (15)	47.7 (41)
	> 5 years (*n* = 147)	57.1 (84) *	61.0 (89) *	6.1 (9)	30.6 (45)*	30.8 (45)*
Bipolar disorder	< 6 months (*n* = 16)	25.0 (4)	25.0 (4)	0	23.5 (4)	62.5 (10)
	6 months–5 years (*n* = 62)	37.1 (23)	27.4 (17)	8.1 (5)	27.4 (17)	54.8 (34)
	> 5 yrs. (*n* = 79)	49.4 (39)	41.0 (32)	10.3 (8)	16.7 (13)	43.6 (34)
Generalized anxiety disorder	< 6 months (*n* = 6)	33.3 (2)	40.0 (2)	20.0 (1)	0	60.0 (3)
	6 months–5 years (*n* = 28)	35.7 (10)	37.0 (10)	3.7 (1)	7.4 (92)	53.6 (15)
	> 5 years (*n* = 46)	39.1 (18)	37.0 (17)	8.7 (4)	19.6 (9)	54.3 (25)
Obsessive-compulsive disorder	< 6 months (*n* = 2)	33.3 (1)	50.0 (1)	0	33.3 (1)	50.0 (1)
	6 months–5 years (*n* = 20)	50.0 (10)	45.0 (9)	15.0 (3)	30.0 (6)	50.0 (10)
	> 5 years (*n* = 25)	24.0 (6)	24.0 (6)	4.0 (1)	16.0 (4)	64.0 (16)
Panic disorder	< 6 months (*n* = 11)	18.2 (2)	36.4 (4)	9.1 (1)	36.4 (4)	40.0 (4)
	6 months–5 years (*n* = 55)	56.4 (31)	41.8 (23)	9.3 (5)	32.7 (18)	32.7 (18)
	> 5 years (*n* = 88)	76.1 (67)*	63.2 (55)*	18.2 (16)	31.8 (28)	19.3 (17)
Post-traumatic stress disorder	< 6 months (*n* = 9)	11.1 (1)	11.1 (1)	0	11.1 (1)	70.0 (7)
	6 months–5 years (*n* = 36)	25.0 (9)	27.8 (10)	5.6 (2)	19.4 (7)	61.1 (22)
	> 5 years (*n* = 36)	55.6 (20)*	52.8 (19)*	25.7 (9)	33.3 (12)	30.6 (11)*
Any phobia disorder	< 6 months (*n* = 35)	2.9 (1)	5.7 (2)	2.9 (1)	11.4 (4)	88.2 (30)
	6 months–5 years (*n* = 102)	27.5 (28)	25.5 (26)	4.9 (5)	11.8 (12)	65.7 (37)
	> 5 years (*n* = 130)	36.9 (48) *	28.5 (37)*	5.4 (7)	24.6 (32)*	50.8 (66)*
Insomnia symptoms and other DSM-IV sleep disorders[b] (*n* = 175)	< 6 months (*n* = 11)	0 (0)	0 (0)	0 (0)	0 (0)	95.7 (10)
	6 months–5 years (*n* = 48)	6.9 (3)	5.2 (3)	0 (0)	18.5 (9)	76.5 (37)
	> 5 years (*n* = 115)	6.1 (7)	2.8 (3)	1.8 (2)	11.5 (13)	84.9 (98)
No diagnosis, insomnia symptoms only (*n* = 1024)	< 6 months (*n* = 85)	4.7 (4)	6.7 (6)	0 (0)	4.8 (4)	87.8 (75)
	6 months–5 years (*n* = 327)	4.4 (14)	5.3 (17)	0.5 (2)	7.1 (23)	86.9 (284)
	> 5 years (*n* = 612)	4.5 (28)	3.5 (21)	0.9 (6)	7.9 (48)	87.2 (533)
No insomnia (*n* = 12,127)		4.5 (528)	3.8 (452)	0.5 (56)	3.6 (439)	91.9

[a] This category includes Primary insomnia, Substance-induced Sleep Disorder (insomnia type) and Sleep Disorder due to a general medical condition (insomnia type)

[b] This category includes: Dysomnia not otherwise specified, Breathing-related sleep disorder, Circadian rhythm sleep disorder, Narcolepsy, Parasomnias

[c] A subject may have multiple past disorders.

* $P < 0.01$.

** $P < 0.05$.

those with a moderate insomnia and about 1.4 times when the insomnia lasted for at least 12 months. Insomnia lasting for more than five years with a current mental disorder is more likely to be associated with a past history of mental disorder. The results suggest that, for these subjects, insomnia may have persisted after the remission of the mental disorder. It may also indicate that subjects with a chronic insomnia and a past history of mental disorder are at risk of relapse for the mental disorder. Furthermore, most of subjects with a current mental disorder (insomnia related to another mental disorder or a mental disorder diagnosis) do not take any medication for the mental disorder (about 80%). A consequence of this situation is the increased risk of relapse when the disorder remits spontaneously and a longer duration of the illness when not treated.

The results show insomnia and psychiatric disorders interact in multiple ways. This is evidenced by the fact that "pure" insomnia is infrequent: only 2.4% of our sample met the DSM-IV diagnostic criteria of insomnia

and has no current or past history of mental disorders. Yet, the causal relationship between insomnia and psychopatholgy is not fully understood. Two points need to be raised. First, insomnia is part of the mood disorder symptomatology and of some anxiety disorders. Consequently, there is the possibility that insomnia could be the most apparent manifestation of the disorder and that its presence or absence would not change the evolution of the psychiatric disorder. Second, some clinical studies that investigated sleep changes in the course of affective disorders have found interesting results. Some findings indicated that persisting abnormalities in the EEG of remitted depressed individuals could be good indicators of a relapse (Grunhaus et al., 1994; Kupfer et al., 1990, 1991). In addition, self-reported sleep disturbances could be a prodromal symptom of a first or a recurrent depressive episode (Fava et al., 1990; Perlis et al., 1997).

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Validity of a Portable Cardio-Respiratory System to Collect Data in the Home Environment in Patients with Obstructive Sleep Apnea

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ABSTRACT

Study Objectives: As part of the development of a portable cardio-respiratory system for detection of sleep-disordered breathing in the home, data gathered from the LifeShirt® (LS) system were compared to that from traditional polysomnography (PSG) in a laboratory environment and then again in the home to ascertain (1) the degree of concordance between the two and (2) to verify whether or not reliable data could be collected outside the laboratory.

Setting: Tertiary care sleep center and in-home.

Patients: Ten subjects were recorded for one night each during three different conditions, PSG in the lab (PSG), LS and PSG in the lab (LS-L), and LS at home (LS-H).

Measurements and Results: Total sleep time ($p = 0.097$), time in stage 1+2 sleep ($p = 0.245$), time in stage 3+4 sleep ($p = 0.633$), REM sleep time ($p = 0.157$), and total awakenings ($p = 0.364$) were not different between PSG and LS-L. No significant difference between the apnea/hypopnea index (AHI) as determined by PSG (28.2 $\pm$ 21.1/hr) LS-L (30.8 $\pm$ 16.3/hr) and the LS-H (27.3 $\pm$ 21.4/hr.) was observed. Oximetry data were not significantly different between the two devices (mean: PSG, 93 ± 5%; LS-L, 92 ± 3%; and LS-H, 92 ± 3%; $p = 0.41$). There was a strong linear relationship between PSG and LS-H and PSG and LS-L for AHI ($r = 0.96$; $p < 0.0001$ and $r = 0.82$; $p=0.004$, respectively). Agreement for AHI was determined using the method of Bland-Altman (bias = 0.848, SD = 6.41), as well as the concordance correlation coefficient ($?_c = 0.96$). Sensitivity and specificity for detection of OSA were high, but varied slightly with the threshold definition used. For an AHI of > 5/hr, sensitivity and specificity were both 100%; for an AHI > 15/hr, they were 87.5% and 100%, respectively.

Conclusions: In summary, a high degree of concordance between LS and traditional PSG was observed, suggesting that LS may be a viable option for the physicians to consider for home detection of OSA.

KEY WORDS: Polysomnography, Home Monitoring, Monitoring, Physiologic, Sleep, Sleep-Disordered Breathing, Cardio-Respiratory, Portable, Validation Studies

INTRODUCTION

Obstructive sleep apnea (OSA) is a common disorder, reported to affect 4% of the adult population [1], and is associated with daytime sleepiness, systemic hypertension, and cardiovascular morbidity [2]. Usually diagnosed by polysomnography (PSG) in the sleep laboratory, many individuals with OSA likely remain undiagnosed because of the costs and limited access associated with sleep laboratory analysis. Additionally, most sleep laboratories operate during the night and are, therefore, unavailable to accommodate individuals who do shift work. Thus, in-home sleep apnea tests have become increasingly available in response to the desire to reduce the cost and time to diagnosis of OSA.

LifeShirt® (LS, VivoMetrics, Inc; Ventura CA) utilizes respiratory inductance plethysmography [3, 4] and pulse oximetry incorporated into a comfortable Lycra shirt to collect respiratory and saturation data from patients sleeping in their home. The LS utilizes established technologies such as fingertip pulse oximetry, for data collection, but needs to be shown to provide as effective an evaluation of OSA in the home setting as polysomnography provides in the sleep lab. While less expensive, in-home data collection is potentially vulnerable to variability in equipment set-up, protocol compliance, and patient behavior when compared to data collection in the more controlled environment of the laboratory. The present study was undertaken to compare the results for standard measures of sleep time and OSA related disturbances obtained from traditional polysomnography with the LifeShirt® in the laboratory and at home.

In practice, the development of an inexpensive and reliable system that can be used in the home may help increase detection and treatment of sleep related breathing disorders in the general population. The LifeShirt® is such a system, employing the well-

recognized technique of respiratory inductance plethysmography (RIP) to assess changes in lung volume, and provide values for calibrated minute ventilation [5]. In order to determine the validity of this system for identification of OSA, we compared sleep related breathing patterns in patients known to display OSA recorded by polysomnography in the laboratory and by the LS at home.

METHODS

Subjects

Ten patients (8 men and 2 women; age, 48.8 ± 14.2 yrs; BMI, 32.4 ± 5.6 kg/m^2; neck circumference, 41.4 ± 4.3 cm) who were clinically suspected of having obstructive sleep apnea (Table 1) were invited to participate from consecutive patients scheduled to undergo routine polysomnography during February and March 2002 at the clinic of the Sleep Disorders Center at the Dallas Veterans Affairs Medical Center (VAMC). All patients scheduled for polysomnography were suspected of experiencing sleep disordered breathing. Their clinical complaints of sleepiness were documented by the Epworth Scale [6] (13.4 ± 4.5).

Protocol

Subjects suspected of having OSA underwent sleep analysis under three conditions: (1) traditional polysomnography (PSG) carried out in the sleep laboratory; (2) modified polysomnography in the laboratory, in which LS was substituted for the chest and abdominal expansion belts used in polysomnography (LS-L); and (3) sleep recording by use of the LS at home (LS-H). All three procedures were performed in random sequence and study nights were not separated by more than two weeks for any patient. Details of each testing session are below. Study procedures were explained to

the subjects, who gave written informed consent for participation in accord with the Institutional Review Board of the Dallas VAMC.

Study Procedures

Apnea/Hypopnea Identification

Respiratory events for PSG and LS studies were scored according to the criteria set forth by the American Academy of Sleep Medicine (AASM) [7]. An apnea event was defined as an airflow or tidal volume amplitude reduction of >75% from baseline with a duration of at least 10 seconds; or a less significant reduction in airflow or tidal volume amplitude, but the presence of an oxygen desaturation = 3%. A hypopnea event was defined in the same manner but utilizing a reduction of >25% from baseline in airflow or tidal volume amplitude. Apnea-hypopnea index (AHI) was the rate of apneas and hypopneas per hour of sleep.

Laboratory PSG

Laboratory PSG was performed in accordance with the standard operating procedures at the Dallas VAMC Sleep Laboratory overseen by an American Board of Sleep Medicine (ABSM) certified physician. Data collected included: two EEG channels (C3-A2 or C4-A1 and O1-A2 or O2-A1), two electro-oculographic channels (right outer canthus and left outer canthus), submental electromyogram (genioglossus), ECG, oronasal (thermistor) air flow, thoracic and abdominal effort, body position and pulse oximetry (Ohmeda, Biox, model 3700, Boulder, CO, USA). Polysomnographic recordings were scored manually and interpreted by a board certified polysomnographer for total sleep time (TST), total number of night time awakenings, and sleep staging at the Dallas VAMC Sleep Laboratory according to Rechtschaffen and Kales [8].

Home LifeShirt

The LifeShirt system (LS, VivoMetrics, Ventura, CA, USA) is a portable system that incorporates two respiratory inductance plethysmographs (RIP) (thoracic and abdominal) sewn into a Lycra vest, a pulse oximeter (Nonin, Adult Flexi-Form II, Model 7000A, Plymouth, MN, USA) an ECG, and an accelerometer. (FIGURE 1 ABOUT HERE) The rib cage-abdominal volume-motion coefficients for RIP signals were determined by the qualitative diagnostic calibration procedure (QDC) [9]. The sum of rib cage and abdominal signals were calibrated in absolute volume units (L) by a fixed volume calibration procedure. Overnight data from these sources were stored on a memory card in a small recorder unit. In the morning, the data were transmitted via the Internet to a data processing center, where it was checked for technical quality, then assessed clinically using proprietary software (VivoLogic®) which calculates values for traditional measures of sleep-related ventilation, including the apnea/hypopnea index (AHI) and measures of oxygen saturation. Time from "lights out" to "lights on" as recorded by the patient via the LS electronic diary was used as sleep time for the calculation of AHI for the LS at home night. A registered sleep technologist and a physician certified by the ABSM then reviewed the data.

Statistical Analyses

Statistical comparison of the scoring was performed by use of SPSS for Windows 11.5 (SPSS, Inc., Chicago, IL, USA). The Pearson product-moment was used to evaluate the relationship between the calculations of AHI between the two devices. Agreement was assessed via the concordance correlation coefficient ($?_c$), as validated by Lin [10], as well as, by the method of Bland and Altman [11]. Sensitivity and specificity were also determined. In consideration of the possibility that sensitivity and specificity might vary with the severity of the sleep-disordered breathing, the

determinations were carried out using two different thresholds for a diagnosis of obstructive sleep apnea (AHI values of >5/hr and >15/hr). Linear regressions were performed to demonstrate relationships between the various conditions tested.

RESULTS

EEG

Total sleep time (TST), number of night time awakenings and sleep stage results for PSG and LS-L are contained in Table 2. Simultaneous and synchronized EEG, EOG, EMG, and pulse oximetry were recorded during LS-L as described in condition 2 above. Sleep scoring from the in-lab PSG and in-lab LS-L were compared. This comparison revealed no significant difference in total sleep time (PSG, 362.4 ± 40.6 min; LS-L, 327.1 ± 64.8 min, p = 0.097) and number of awakenings (PSG, 38.7 ± 24.4; LS-L, 44.4 ± 35.7, p = 0.364)

Apnea/Hypopnea/AHI

Table 3 contains the absolute respiratory and EEG data for PSG, LS-L, and LS-H. No significant difference between the apnea/hypopnea index (AHI) as determined by PSG (28.2 ± 21.1/hr), LS-L (30.8 ±16.3/hr) and the LS-Home (27.3 ± 21.4/hr) was observed.

As seen in Figure 2, a regression analysis indicated a highly significant relationship between the AHI as determined by PSG and LS-Home (r = 0.96). Spearman rank correlation (non-parametric correlation) revealed similar results (? = 0.97). When agreement was expressed as a function of mean AHI in a Bland-Altman plot, 8 of the 10 points fell within 1.0 SD of the mean bias, and there was no relationship between degree of agreement and the severity of sleep-disordered breathing when comparing PSG vs. LS-L (Figure 3A), LS-L to LS-H (Figure 3B), or PSG to LS-H (Figure

3C). Sensitivity and specificity for determining a diagnosis of OSA varied slightly as a function of the AHI threshold utilized. For a value of >5/hr, sensitivity and specificity were both 100%. At AHI >15/hr, sensitivity and specificity were 85.7% and 100%, respectively. Consistency of the AHI analyses in the three conditions can be observed in Figure 4 where the regression results for each individual test are presented together.

There were also no observed differences in mean pulse oximetry between PSG and LS-L (mean S_pO_2: PSG, 93 ± 5%; LS-L 92 ± 3%; p = 0.41).

DISCUSSION

There was a high degree of agreement between sleep disordered breathing results from recordings by laboratory polysomnography and the LifeShirt® in this population of mostly middle-aged, somewhat obese patients selected because of a history suggestive of OSA. The accuracy of LS did not vary with the severity of sleep-disordered breathing (AHI) as demonstrated with Bland-Altman analysis. Additionally, sleep time and distribution of sleep stages were similar suggesting that the LS provides equivalent results for these analyses.

In considering the design of the study, there were several possible approaches for comparing the two systems. Ideally, one would record using both systems simultaneously. This would eliminate the possibility of spurious results due to night-to-night variability in degree of sleep-disordered breathing. We chose not to do so, because of the physical difficulty of placing respiratory belts for polysomnography and LS on the patient together, and because of the possibility that in this situation (which would not be used clinically) the two might somehow interact. Rather, we chose to record on two different nights in two different settings (laboratory and home, respectively) in order to gain the advantage of testing the systems as they would be used in practice. This decision allowed the possibility that night-to-night variability in

severity of sleep-disordered breathing might result in a spuriously low agreement between the two methods. However, there was a high degree of agreement between the two systems, in two different settings suggesting consistency in both sleeping pattern and performance of the LS and PSG. It is unlikely that the error rates and direction would have coincidently occurred in such a way as to result in an inappropriate appearance of agreement.

The night-to-night variation in OSA has been assessed in several studies. In one series, 46 patients with a mean age of 50 who were found to have an AHI > 5/hr were re-recorded; the rate of discordance between the two nights was 8% (4). The correlation coefficient for AHI between the two nights was 0.86. In middle aged volunteers, the correlation coefficient of the desaturation index (number of desaturations per hour) was found to be 0.79 (5). In healthy elderly subjects, the discordance rate, using a cutoff of AHI > 5/hr, has been reported to be 43% in a three night study (6). Thus, the degree of variability between the laboratory polysomnographic recordings and LS at home was substantially less than the expected night-to-night variability. These comparisons show that the LifeShirt® can be a useful addition to the physician's armamentarium by allowing the detection of OSA in the home setting, thus avoiding the scheduling difficulties and inconvenience of using a traditional PSG sleep lab.

Summary

PSG and LifeShirt in the laboratory setting showed similar values for the main measures of sleep architecture. Similarly, PSG in the laboratory was concordant with both LS in the laboratory and LS at home for measures of sleep-disturbed respiration. While the LS didn't incorporate EEG in the home condition (e.g., LS-H) at the time of the study it provided similar results for sleep disordered breathing utilizing patient recorded approximate sleep time. Also, the LS did not appear to cause any sleep disturbance

relative to the other conditions tested. The LifeShirt appears to provide a reasonable alternative to the traditional PSG sleep lab for the assessment of sleep disordered breathing.

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Table 1 – Characteristics and symptoms of subjects who completed the study. All values expressed as mean (±SD) unless otherwise stated.

Characteristic	***Mean (SD)***
Age (yr)	48.8 (14.2)
Weight (kg)	102.4 (19.1)
Height (cm)	178.3 (14.2)
BMI (kg/m^2)	32.4 (5.6)
Neck size (cm)	41.4 (4.3)
ESS	13.4 (4.5)
Symptoms	***# of patients reporting***
Loud snoring	9
Witnessed apneas	9
Non-refreshed sleep	9
Night time arousals	3
EDS	8
Morning headaches	8

n = 10 (8 men, 2 women)
BMI = Body Mass Index
ESS = Epworth Sleepiness Scale
EDS = Excessive Daytime Somnolence

Table 2 – Sleep time

Comparison		Mean (minutes)	Std. Error of Mean	P value
TST	PSG	362.4	13.55	0.097
	LS-L	327.1	21.59	
# of Awakenings	PSG	38.7	8.13	0.364
	LS-L	44.4	11.88	
Stage 1+2 Sleep	PSG	243.7	9.48	0.245
	LS-L	222.4	17.47	
Stage 3+4 Sleep	PSG	60.9	11.56	0.633
	LS-L	64.9	12.26	
REM Sleep	PSG	62.6	7.06	0.157
	LS-L	46.2	8.92	

TST – Total sleep time

NOTE: all comparisons included 10 pairs, except Stage 3+4 sleep which was based on 9 pairs.

Table 3 – Individual respiratory and EEG data for PSG, LS-L and LS-H

	Subject	APNEA events	HYPOP events	AHI events/hr	S_pO_2 %	TST min	Stage1+2 min	Stage 3+4 min	REM min	Awks total #
PSG										
	1	110	117	34.4	90.7	278.0	242.5	3.0	32.5	30
	2	131	328	64.6	93.2	418.0	258.0	80.5	79.5	12
	3	48	297	49.3	87.0	362.0	232.0	81.5	48.5	25
	4	7	167	24.5	97.9	353.0	222.5	77.5	53.0	55
	5	183	246	55.0	94.0	383.5	302.5	N/A	68.0	49
	6	1	1	0.3	99.9	413.5	230.5	91.0	92.0	15
	7	122	85	24.9	86.8	360.5	279.0	20.5	61.0	101
	8	14	21	4.5	89.8	319.5	217.5	72.5	29.5	40
	9	25	35	8.2	96.4	343.0	250.0	25.5	67.5	32
	10	57	59	16.1	96.9	393.0	202.5	96.5	94.0	28
	Mean	**69.8**	**135.6**	**28.2**	**93.3**	**362.4**	**243.7**	**60.9**	**62.6**	**38.7**
	SD	**59.4**	**112.4**	**21.1**	**4.3**	**40.6**	**28.4**	**32.7**	**21.2**	**24.4**
	SE	**19.8**	**37.5**	**7.0**	**1.4**	**13.5**	**9.5**	**12.3**	**7.1**	**8.1**
LS-L										
	1	70	289	40.8	90.7	303.0	229.5	17.5	56.0	22
	2	247	184	49.5	91.0	450.5	338.0	47.0	65.5	18
	3	39	194	31.5	89.3	365.0	233.0	100.5	31.5	19
	4	89	209	42.0	91.3	310.5	177.0	95.5	38.0	43
	5	101	289	53.4	90.4	282.0	258.0	N/A	24.0	100
	6	5	28	4.5	96.3	366.0	149.5	122.0	94.5	17
	7	255	31	39.7	87.1	204.5	182.5	21.5	0.5	125
	8	99	77	24.1	95.4	268.0	169.5	43.5	55.0	39
	9	36	50	10.1	93.6	368.5	239.5	54.0	75.0	38
	10	45	51	12.3	93.2	352.5	247.5	83.0	22.0	23
	Mean	**98.6**	**140.2**	**30.8**	**91.8**	**327.1**	**222.4**	**64.9**	**46.2**	**44.4**
	SD	**81.6**	**99.2**	**16.3**	**2.7**	**64.8**	**52.4**	**34.7**	**26.8**	**35.7**
	SE	**27.2**	**33.1**	**5.4**	**0.9**	**21.6**	**17.5**	**11.6**	**8.9**	**11.9**
LS-H										
	1	117	239	37.9	90.3	N/A	N/A	N/A	N/A	N/A
	2	196	43	62.9	91.2	N/A	N/A	N/A	N/A	N/A
	3	52	236	34.3	88.5	N/A	N/A	N/A	N/A	N/A

4	29	128	20.7	95.4	N/A	N/A	N/A	N/A	N/A
5	293	211	63.0	91.0	N/A	N/A	N/A	N/A	N/A
6	1	10	1.3	96.8	N/A	N/A	N/A	N/A	N/A
7	183	69	29.6	88.8	N/A	N/A	N/A	N/A	N/A
8	17	22	4.1	95.3	N/A	N/A	N/A	N/A	N/A
9	27	46	9.2	94.3	N/A	N/A	N/A	N/A	N/A
10	56	63	10.3	92.3	N/A	N/A	N/A	N/A	N/A
Mean	**97.1**	**106.7**	**27.3**	**92.4**					
SD	**92.1**	**85.5**	**21.4**	**2.8**					
SE	**30.7**	**28.5**	**7.1**	**0.9**					

Hypop = total number of hypopneas
AHI = apnea hypopnea index
Mean SpO2 = mean arterial saturation as estimated by finger pulse oximetry
TST = total sleep time
Awks = total number of night time awakenings
PSG = polysomnography in the lab
LS-L = PSG in lab with LifeShirt®
LS-H = LifeShirt at home
n = 10

Figure 1 - A model wearing a LS system, which consists of a Lycra garment with two embedded respiratory inductance plethysmography bands, 3-lead single channel ECG, 2-axis accelerometer and pulse oximetry. NOTE: this person was not an actual subject in the study. The figure is meant to give the reader a visualization of the portable device.

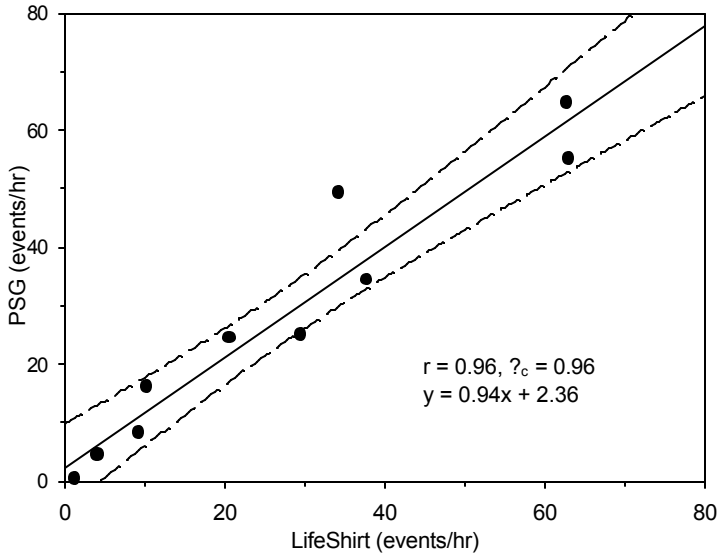

Figure 2 - Regression analysis depicting relationship between PSG (lab) and LS (home) with respect to the apnea/hypopnea index. Solid line represents the regression line. Hatched lines represent the 95% confidence intervals.

n = 10
r = Pearson-product moment
$?_c$ = concordance correlation coefficient

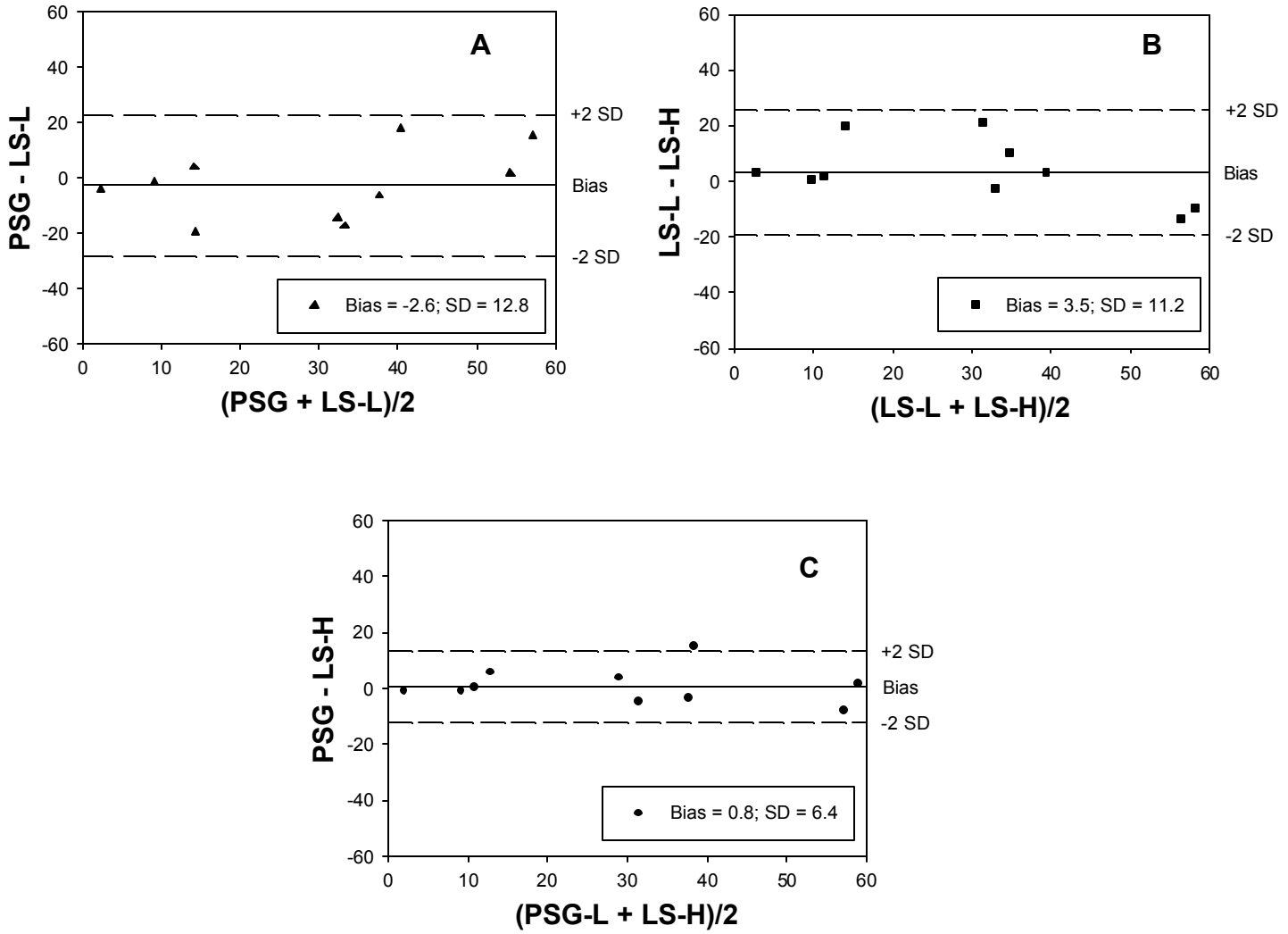

Figure 3. Mean against difference plots for PSG, LS-L and LS-H.
LS-L = LifeShirt® and PSG in lab
LS-H = LifeShirt® at home
n = 10 for each comparison

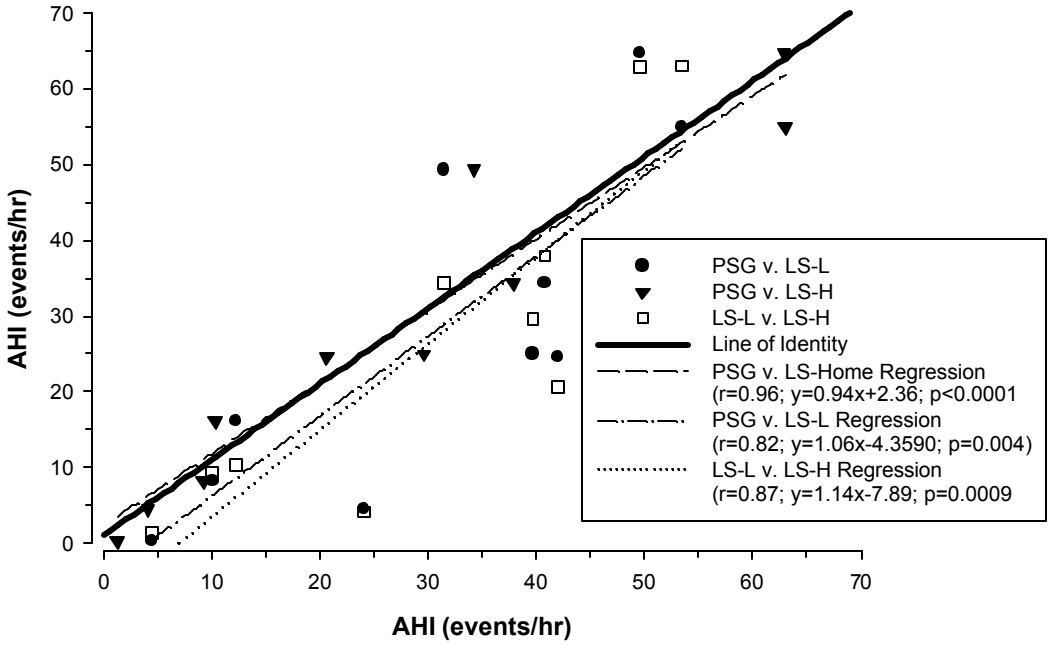

Figure 4 - Regression analysis depicting relationship between PSG (lab) LS-L and LS-H with respect to the apnea/hypopnea index. Solid line represents the line of identity.

LS-L = LifeShirt® and PSG in lab
LS-H = LifeShirt® at home
n = 10 per comparison

Sleep in the Laboratory and Sleep at Home II: Comparisons of Middle-Aged Insomnia Sufferers and Normal Sleepers

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Study Objectives: The study compared adaptation responses and sleep pattern differences shown by normal sleepers and insomnia sufferers during lab (LPSG) and home (HPSG) polysomnography.

Design: A counter-balanced, matched-group design was used. Participants underwent 3 consecutive nocturnal LPSG's and 3 consecutive nocturnal PSG's in their homes (HPSG's).

Setting: The sleep disorders laboratories at affiliated VA and university medical centers.

Participants: Thirty-five (18 women) middle-aged (40 to 59 years) non-complaining normal sleepers and an age-matched sample of 33 (17 women) individuals who met structured interview criteria for persistent primary insomnia were the study participants.

Measurements and Results: A series of multivariate and univariate analyses were conducted with 9 common sleep parameters to address study objectives. Bed partner influences were controlled by conducting separate sets of analyses for those with and without routine home bed partners. The interaction of participant type (normal vs. insomnia), sleep setting, and PSG sequence (HPSG 1st vs. LPSG 1st) affected first night values of sleep efficiency and stage 2 sleep among those without routine bed partners, and REM latency and sleep efficiency among those with routine bed partners. Analyses which controlled for first night and sequencing effects showed a significant participant type x sleep setting interaction among those with bed partners. These latter analyses suggested that LPSG's may underestimate the home sleep time of insomnia sufferers and overestimate the sleep continuity of normal sleepers, at least among those who routinely sleep with a bed partner.

Conclusions: The nocturnal recording site may influence adaptation effects and sleep pattern differences noted between insomnia sufferers and normal sleepers.

Key words: Home- and laboratory-based polysomnography; insomnia; first night effects

INTRODUCTION

INSOMNIA IS A HIGHLY PREVALENT FORM OF SLEEP DISTURBANCE THAT COMPROMISES THE HEALTH STATUS, occupational pursuits, and social functioning of countless individuals worldwide.[1-6] Whereas insomnia commonly results from medical, psychiatric, and substance-abuse disorders, a substantial subset of insomnia sufferers experience sleep problems which develop and persist independent of such causes. Many who suffer such persistent primary insomnia (PPI) enjoy reasonably satisfactory mental and physical health, yet they incur significant morbidity in association with their sleep complaints. Even when insomnia persists in the absence of co-morbid psychiatric, substance abuse, or medical disorders, it may significantly enhance subsequent risks for various psychiatric illnesses.[7-10] Furthermore, PPI may contribute to reduced productivity, work-related accidents, chronic hypnotic dependence, substance abuse, and increased health care costs/utilization.[11-15] Unfortunately, many studies conducted to improve our understanding of this form of sleep difficulty have produced rather perplexing results.

Over the past several decades, numerous studies have assessed the nature and extent of sleep pathology associated with PPI. These studies compared results of laboratory polysomnographic (LPSG) recordings derived from individuals with PPI complaints and matched non-complaining normal sleepers.[16-24] Most such investigations excluded depressed, medically ill, and apneic patients, and derived sleep data from multiple LPSG nights. Although such studies typically found sleep differences between PPI and control samples, the magnitude of the differences observed consistently appeared rather modest. For example, the mean difference in total sleep time between these groups was less than 38 minutes across these studies whereas the average difference in total nocturnal wake time was less than 42 minutes. These differences seem particularly unimpressive in view of previous research which suggests that normal sleepers can endure extended periods wherein they reduce their sleep by one to two hours below their customary amounts without evidence of any daytime alertness/performance decrements.[25] Indeed, we are left to wonder whether we are missing something in our laboratory study of those with PPI complaints.

In this regard, it seems important to question the potentially powerful influences the sleep laboratory setting may have on comparisons of insomnia sufferers and normal sleepers. Since normal sleepers and PPI sufferers differ markedly in their reported satisfaction with their usual home sleep patterns, the novelty and routines of the sleep laboratory may have contrasting effects on these two groups. Among normal sleepers, usual bedtime rituals and the familiar home sleeping environment provide a sense of stability and serve as powerful conditioned cues which facilitate a restorative sleep process. The absence of these cues in the laboratory setting may adversely affect the sleep of these individuals when, as has been the case in most research protocols, they complete only a few recording nights in the novel laboratory setting. Conversely, among those with PPI, aberrant sleep

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habits occurring at home and conditioned stimuli present in the home bedroom may obviate a regular sleep/wake routine and elicit bedtime arousal which perpetuate sleep disturbances.[26,27] In addition, many insomnia sufferers may view the sleep laboratory as a setting where poor sleep is expected and understood by those professionals conducting the sleep recordings. This view, in turn, may reduce the conditioned bedtime arousal which typically confounds their sleep attempts at home. Given this rationale, it seems reasonable to speculate that insomnia sufferers may appreciate some sleep improvements when they are monitored in the sleep laboratory. Hence, LPSG might underestimate the degree of sleep difficutly such individuals typically experience in their home sleep settings.

Support for these contentions come from previous studies of sleep laboratory adaptation effects as well as investigations which have scrutinized insomnia sufferers and normal sleepers in their home sleeping environments. Various studies of the so-called "first night effect" (FNE) have shown that normal sleepers show more disrupted sleep (e.g., longer sleep onset latencies, longer REM latencies, greater sleep fragmentation, etc.) on the first laboratory recording night than they do on subsequent nights whereas a reversed FNE, characterized by improved sleep on the first laboratory night (relative to subsequent nights), has been noted among insomnia sufferers.[28-32] In contrast, a few studies have suggested that neither normal sleepers nor insomnia sufferers show these pronounced adaptation responses when monitored in their homes.[33-35] Moreover, in our previous work we found that home-based PSG (HPSG) recordings showed older (ages>60 yrs.) insomnia sufferers and normal sleepers had similar mean values of sleep measures across lab and home PSGs although the insomnia group showed significantly greater night-to-night sleep variability than did the normal sleepers only during HPSGs.[35]

The current investigation was conducted as extension of our previous HPSG studies of insomnia. We conducted this study with the global premise that HPSG is relatively unencumbered by adaptation effects inherent in the sleep laboratory setting and, hence, should be more likely than LPSG to show sleep differences between insomnia sufferers and normal sleepers. In the current project we chose to enroll a middle-aged cohort inasmuch as we suspected that age-related sleep changes (i.e., sleep fragmentation, reduced slow-wave sleep, etc.) among the older controls enrolled our previous study[35] may have served to minimize the degree to which their sleep differed from matched insomnia sufferers. Given these considerations, our specific study hypotheses for the current project were: 1) both normal sleepers and insomnia sufferers would show less pronounced FNEs (i.e., significant differences between sleep measures derived on the first recording night vs. similar measures from subsequent nights) during HPSGs than during LPSGs; and 2) mean values of sleep measures averaged across HPSG nights would suggest greater sleep differences between insomnia sufferers and normal sleepers than would averaged sleep measures derived from LPSG.

METHOD

Participants

Research participants were recruited via posted advertisements at the Durham (NC) VA Medical Center, via letters mailed to persons in the Duke University Center for the Study of Aging and Human Development Subject Pool, and via face-to-face solicitations of patients presenting to the Duke University Sleep Disorders Center. All participants completed an informed consent prior to entering the study and were compensated financially for their participation. Participants first underwent multiple screening procedures including a Structured Interview for Sleep Disorders[36] and, once enrolled, they completed self-report questionnaires and multiple nights of sleep monitoring. The insomnia sufferers recruited for this study were middle-aged adults (ages 40 to 59 years) who reported sleep complaints consistent with current criteria[37] for Primary Insomnia. These prospective participants were considered for inclusion if they: 1) reported chronic (i.e., of >6 months duration) difficulty initiating or maintaining sleep or noted chronic poor sleep quality (i.e., nonrestorative sleep) which, on average, minimally occurred at least three times per week; and 2) reported associated daytime deficits related to their nocturnal sleep difficulties. We also recruited a comparable sample of middle-aged, non-complaining adults. These normal sleepers had no identified major medical or psychiatric condition that might have contributed to an unreported, occult sleep disorder.

Using thorough screening procedures we excluded prospective participants if they: 1) had a terminal illness; 2) had a medical condition (e.g., rheumatoid arthritis, thyroid disease) that compromises sleep; 3) had abnormal TSH levels on a screening thyroid panel; 4) had a history of psychiatric illness; 5) met criteria[37] for a current major psychiatric (Axis I) condition on the basis of a Structured Clinical Interview for Psychiatric Disorders;[38] 6) were substance abusers; 7) showed sedative hypnotic dependence and were unwilling/unable to abstain from these medications while in the study; 8) were taking anxiolytics, antidepressants, or any other psychotropic medication; or 9) had objective evidence of clinically significant sleep apnea (i.e., and apnea/hypopnea index - AHI >15) on nights 1 or 2 of the objective sleep recordings described later herein. In addition, we excluded prospective insomnia sufferers if they met SIS-D criteria[36] for another sleep disorder in addition to PPI whereas we excluded normal sleepers who met SIS-D criteria[36] for any sleep disorder.

A total of 76 (35 women, 41 men) prospective participants underwent the study's screening procedures. Of these, three of the male self-described normal sleepers and five men with insomnia complaints were dropped because they had AHI's >15 during their initial PSG studies. The remaining group comprising our final sample consisted of 33 (17 women) insomnia sufferers and 35 (18 women) non-complaining, normal sleepers.

The normal sleepers retained had an average age of 46.5 years (SD=5.0 yrs.) and had completed an average of 16.2 years (SD=2.5 yrs.) of formal education. Twenty-seven (16 women) of these individuals were Caucasians, seven (one woman, six men) were African Americans, and one (woman) was an Asian American. Independent sleep interviews and medical exams suggested that none of these individuals had medical conditions that contributed in any way to sleep difficulties. However, a number of these volunteers reported histories of common medical conditions and symptoms including mild arthritis (n=6), coronary artery disease (n=1), hypertension (n=3), sinusitis (n=7), occasional heartburn (n=6), and intermittent headaches (n=3). Medical and sleep history evaluations conducted during screening suggested that these conditions/symptoms either were con-

trolled with ongoing treatment or were not present at the time of study entry.

The average age of the insomnia sufferers was 49.9 years (SD=5.8 yrs.) and their average years of formal education was 14.9 years (SD=2.8 yrs.). Of these individuals, 21 (11 women) were Caucasians and the remaining seven (six women) were African Americans. Most of the insomnia sufferers were research volunteers who were recruited via solicitation announcements/letters. However, three of the insomnia sufferers were sleep clinic patients who agreed to become study participants. Like the normal volunteers, these insomnia sufferers endorsed histories of medical symptoms and conditions including mild arthritis (n=11), coronary artery disease (n=1), diabetes (n=2), hypertension (n=5), sinusitis (n=7), occasional heartburn (n=8), and intermittent headaches (n=8). Nonetheless, as was the case among the normal volunteers, our screening evaluations suggested that these conditions/symptoms either were controlled with ongoing treatment or were not present at the time of study entry. Moreover, both the self reports of these individuals and our screening evaluations suggested that these medical conditions were not significant contributors to their reported sleep difficulties.

Although most of the insomnia sufferers enrolled were not clinical patients, they collectively appeared to suffer from long-standing sleep difficulties inasmuch as they reported having suffered from insomnia for an average of 9.5 years (SD = 7.6 yrs.). Three (9.1%) of the insomnia sufferers reported exclusively sleep onset difficulties, 14 (42.4%) reported only sleep-maintenance difficulties, 14 (42.4%) reported mixed onset/maintenance problems and two (6.1%) reported concerns in regard to chronic poor sleep quality. At the time of enrollment, 24 (72.7%) of the insomnia sufferers reported no current use of prescription or non-prescription sleep aids, four (12.1%) reported use of such sleep aids less than one time per week, and the remaining five (15.1%) reported use of sleep aids two or more times per week. Twenty-eight (84.8%) reported no use of alcohol as a sleep aid whereas four (12.1%) used low dose (one to two alcoholic beverages) alcohol as a hypnotic less than one time per week. Only one (3.0%) of the insomnia sufferers reported nightly reliance on one to two alcoholic beverages to aid sleep. However, all of these individuals agreed to totally abstain from the use of sleep aids during the time periods prescribed by the study (see details below).

Polysomnography

Each participant underwent six nights of polysomnographic (PSG) sleep monitoring. Three consecutive PSG recordings were conducted in the Duke Medical Center's Sleep Laboratory and the other three consecutive PSG studies were conducted in participants' homes.

All participants underwent both home and lab PSGs in order to address this study's specific research objectives. The order of studies (lab vs. home) was randomly determined so that roughly one-half of the men and women in each group underwent lab recording first, whereas the other half completed home monitoring first. So that PSG measures would be reasonably contemporaneous, we scheduled each participant's home and lab PSGs a minimum of four and a maximum 30 days apart.

All PSGs were conducted using Oxford Medilog® 9000 series ambulatory cassette recording devices. The recorders have the capability of recording eight channels of electro-physiological data as well as digital time in one-second intervals. They also include an event marker which participants used to electronically mark both the time they retired to bed at night and their subsequent final rising time on the following morning. Various studies conducted at our center[39-40] and elsewhere[41,42] have attested to the technical acceptability of the Oxford system and have shown that sleep measures derived from this form of monitoring are comparable to those obtained from standard laboratory polygraphs. The specific PSG-monitoring montage used in the current study included two electroencephalogram (EEG) channels (C3-A2, Oz-Cz), bilateral electrooculogram (EOG), submental electromyogram (EMG), two channels of anterior tibialis EMG (right and left leg,) and a nasal-oral respiration thermistor.

Prior to scheduling PSG recordings, participants were throughly interviewed to determine their customary bedtimes and rising times. Once these times were discerned for each participant, she/he was instructed to adhere to these customary bedtimes and rising times on all six nights (lab and home) that PSG recordings were scheduled. On dates home PSG studies were scheduled, participants reported to the sleep laboratory between 14:00 and 17:30 for electrode attachment before returning home where they were encouraged to follow their usual evening routines and pre-sleep rituals. Each individual was also instructed to sleep in her/his usual bedroom with her/his usual bed partner if such an individual was typically present. In the morning, they returned to the sleep laboratory for removal of electrodes.

On the nights of laboratory studies, participants reported to the sleep laboratory without bed partners approximately 60 to 90 minutes before their reported usual bedtimes for electrode placement. As a consequence of this scheduling, electrode attachment was routinely completed just prior to each participant's target bedtime so, shortly after completing of this process, the individual was placed in a sleeping room, the lights were turned off, and the recording was started. For both home and lab studies, participants kept written records of their bed and rising times. These records were used to assist our research staff in finding the electronically marked bed and rising times when scoring the Medilog recordings.

All Medilog recordings were scored directly on the screen of the Medilog scanner by experienced scorers using standard criteria.[43] This screen scoring procedure was used since it allows for both rapid scanning of sleep data and screen by screen editing for those recordings which prove difficult to score. Moreover, we have found screen scoring produces estimates of standard sleep parameters that are comparable to those obtained from conventional epoch by epoch scoring of records on paper.[44] To minimize biases in scoring, scorers were kept blind to the date of each recording and the type of participant from whom each PSG study was obtained. Since HPSG electrode attachments occurred between 14:00 and 17:30, these recordings began well before the individuals' bedtimes in the home settings. As a result, it was not possible to totally blind scorers to the setting wherein recordings were obtained.

Results of sleep-stage scoring were used to derive measures of total sleep period (TSP—time between "lights out" and final rising time) and several sleep parameters which previously have proven useful either for detecting FNE's[28-32] or for discriminating insomnia sufferers from normal sleepers.[16-24] The specific sleep

parameters we chose to use included total sleep time (TST), sleep efficiency (SE%—[total sleep time/ sleep period] x 100%), latency to the onset of sustained sleep (SOL—time between "lights out" and the first 10 minutes of sleep containing no more than two minutes of wake time, stage 1 sleep or movement time), wake time after sleep onset (WASO—all wake time after SOL and before the final AM awakening), stage 1 time (STG1), stage 2 time (STG2), slow wave sleep time (SWS), REM time, and REM latency (RLMA—time between SOL and the first three consecutive minutes of REM minus intervening wake time) for each study night. For the purpose of this investigation, time and latency measures were expressed in minutes.

Procedure

All consenting persons who met inclusion criteria underwent the six PSG studies previously described. Following their first series of three consecutive PSGs (home or lab), participants underwent daytime sleepiness and performance testing which are to be described in a future report.[46] All HPSG studies were scheduled for nights when subjects planned to have no overnight house guests. Participants who reported recent use of sleep medications were required to abstain from these medications for at least two weeks prior to their first series of studies and to not resume these medications until they completed both series of PSGs. Finally, they were instructed to abstain from alcoholic beverages and to not consume caffeinated substances after 18:00 on study nights.

RESULTS

Sample Comparability and Effectiveness of Randomization

Prior to conducting tests of our study hypotheses, we first conducted several analyses to compare our samples in regard to their demographic characteristics. Fisher Exact tests showed the samples of insomnia sufferers and normal controls were well balanced in terms of their females/males (p=1.00) and Caucasians/Non-Caucasians (p=1.00) ratios. Results of a 2 (insomnia sufferer vs. normal sleeper) x 2 (genders) ANOVA showed that the insomnia sufferers (M_{age}=49.9 years), on average, were slightly, albeit significantly ($F_{1,64}$=7.33, p=.009), older than were the normal sleepers (M_{age}=46.5 years). A similar analysis showed that the normal sleepers ($M_{education}$=16.2 years) had slightly, albeit significantly ($F_{1,64}$=4.23, p=.04), more years of education than did the insomnia sufferers ($M_{education}$=14.9 years). These statistical differences were consistent across genders inasmuch as the gender and type x gender effects were nonsignificant (p's>.05).

In addition to these initial comparisons, we conducted preliminary analyses to test the effectiveness of our randomization procedures. As noted previously, we enrolled a total of 76 participants in the study and retained 68 participants. Since all subjects were randomized at the time of study enrollment, we reviewed participant assignments to determine if roughly equal numbers of men and women within each sample of our final cohort were assigned to each sleep monitoring sequence (i.e., HPSG 1st vs. LPSG 1st). This review showed that 18 (10 women) insomnia sufferers and 16 (8 women) normal sleepers underwent HPSG first whereas the remaining 15 (7 women) insomnia sufferers and 19 (10 women) normal sleepers underwent LPSG first. Chi-square analysis confirmed that the four subgroups were proportionally assigned to the contrasting sequences of PSG studies (χ^2_3=0.81, p=0.85).

Technical Acceptability of Medilog Recordings

Of the 408 PSGs conducted on our final cohort, 397 were technically acceptable and scorable. The remaining 11(2.7%) were not scorable either because the clock module inside of the Medilog recorders malfunctioned or critical electrodes became dislodged during the study. All but one of these unscorable recordings occurred on nights 2 or 3 in the one or the other of the recording sites (home or lab). Single nights (two HPSG and three LPSG) were lost from five (four women and one man) normal sleepers and four (three men, one woman) insomnia sufferers (one HPSG and three LPSG's). In addition, data were lost from a female normal sleeper from night three in the lab and night one in the home. The unscorable LPSG recordings were lost because we chose not to tether subjects to an online recording apparatus in the lab; this decision assured that the recording procedures used in both recording sites were identical. Because of data loss, results reported herein are based on the 397 scorable recordings.

Pattern and Reliability of PSG Scoring

A total of three scorers participated in the scoring of the PSGs obtained in this study, and except for those records used in the reliability checks, each PSG was scored by only one of these individuals. However, all (98%) but eight of the scorable records were scored by one of the two main scorers who participated in this project. For 52 of the 68 participants, the task of scoring the multiple nights of PSG recording was split between the two scorers with one scorer reviewing some of the six nights and the other scoring the remainder. Scorer 1 scored 44 HPSGs and 46 LPSGs from the normal sleepers and 51 HPSGs and 52 LPSGs from the insomnia sufferers. Scorer 2 scored 56 HPSGs and 54 LPSGs nights from normal sleepers, and 44 HPSGs and 42 LPSGs from the insomnia sufferers. An overall chi square test showed that the four specific types of records were equally distributed across these two main scorers (χ^2_3=3.64 p=.30).

To test for inter-scorer reliability, 10 randomly selected PSG's were independently scored by each of the two main scorers. Epoch-by-epoch comparisons showed an overall agreement rate of 90% between scorers. This highly acceptable agreement rate suggested little variance due to scorer differences.

Adherence to Prescribed Bed and Rising Times

Despite instructions to the contrary, study participants varied their prescribed bed and wake times across the six PSG nights. For the normal sleepers, the mean bedtimes across the three LPSG and three HPSG studies respectively were 23:02, 23:07, 23:12, 23:11, 23:01, and 22:44. For the insomnia group these respective times were 22:54, 22:51, 22:52, 22:41, 22:44, and 22:35. The LPSG and HPSG mean rising times across nights for the normal sleepers respectively were 6:08, 6:13, 6:14, 6:16, 6:13 and 5:57; these respective mean times for the insomnia group were 6:18, 6:17, 6:17, 6:08, 6:27, and 6:26. Analyses via 2 (normal sleeper vs. insomnia sufferer) x two (LPSG vs. HPSG) x

Table 1—Differences between first nights and the means of the subsequent two PSG nights in each setting.

Study Participants with No Bed Partner

	Normal Sleepers		Insomnia Sufferers	
	Lab PSG	Home PSG	Lab PSG	Home PSG
Measure+	Nt 1-Nts 2/3	Nt 1-Nts 2/3	Nt 1-Nts 2/3	Nt 1-Nts 2/3
TST	-14.7 (10.7)	-4.2 (18.2)	4.7 (10.8)	-21.7 (20.4)
S2 Onset	14.2 (5.7)	6.3 (8.3)	15.0 (6.4)	-14.5 (9.3)
WASO	-6.2 (10.2)	4.5 (12.8)	-8.6 (11.4)	5.6 (14.3)
SE %	-1.0 (2.4)	-3.0 (2.5)	1.0 (2.7)	0.7 (2.8)
Stage 1	0.2 (3.5)	2.9 (3.8)	1.2 (4.0)	7.1 (4.2)
Stage 2	-0.78 (10.8)	-1.9 (17.1)	7.8 (12.2)	-5.8 (19.3)
SWS	-1.0 (5.3)	1.5 (7.4)	-6.1(6.0)	-10.3 (8.3)
REM	-13.1(8.2)	-6.8 (5.2)	1.9 (9.3)	-12.7 (5.9)
RLMA.	17.4 (10.6)	-4.0 (13.2)	8.0 (11.9)	8.8 (14.8)

Study Participants with a Bed Partner

	Normal Sleepers		Insomnia Sufferers	
TST	-1.1 (9.2)	-13.4 (12.9)	-25.3 (8.9)	-53.8 (12.5)
S2 onset	5.3 (5.6)	5.8 (3.2)	13.9 (5.5)	3.8 (3.1)
WASO	2.5 (6.9)	1.2 (8.1)	8.2 (6.7)	26.4 (7.9)
SE %	-1.1 (1.5)	-0.8 (2.1)	-4.4 (1.5)	-7.7 (2.1)
Stage 1	-0.4 (3.5)	-1.3 (3.2)	0.7 (3.4)	1.7 (3.1)
Stage 2	-2.1 (8.0)	-0.9 (9.2)	3.2 (7.7)	-24.7 (8.9)
SWS	0.5 (6.2)	-5.4 (5.4)	-17.3 (6.0)	-16.4 (5.3)
REM	1.0 (5.1)	-5.8 (5.9)	-11.9 (5.0)	-14.4 (5.7)
RLMA.	9.0 (5.7)	1.3 (9.6)	5.9 (5.6)	10.9 (9.3)

+Note: Full definitions for the abbreviations used for sleep measures in this table can be found in the portion of Method section labeled. "Polysomnography." The differences shown represent minutes for all sleep measures except sleep efficiency which is expressed as differences in %. Data presented are means and (SE's). Nt. = night. Data from one female normal sleeper without a bed partner was excluded due to PSG recorder failure on the first home PSG night. Thus, data for the group without bed partners are from 11 (8 women) normal sleepers and 9 (5 women) insomnia sufferers; data for the subgroup with bed partners are from 23 (9 women) normal sleeper and 24 (12 women) insomnia sufferers.

three (night) repeated measures ANOVAs showed the participants' rising times were statistically similar across nights and settings but the bedtimes of both groups were significantly ($F_{1, 328}$=4.02, p=0.05) earlier in their homes (M_{time}=10:50 PM) than they were in the lab (M_{time}=11:00 PM). Normal sleepers tended to choose a later rising time on night 1 in their homes than they did on subsequent nights in that setting. In contrast, the insomnia sufferers arose earlier on HPSG night 1 than they did on subsequent HPSG nights. Finally, ANOVA results showed that average total sleep periods—TSPs (times in bed) of the insomnia sufferers (M_{TSP}=452.4 min., SD=58.0 min.) were significantly ($F_{1, 66}$=6.13, p = 0.02) longer than those of the normal sleepers (M_{TSP}=427.3 min., SD=57.8 min.) and both groups had significantly ($F_{1,328}$=5.34, p=0.02) longer TSPs in their homes (M_{TSP}=444.5 min., SD=67.4 min.) than they did in the sleep lab (M_{TSP}=434.6 min., SD=49.4 min.).

Tests of Normality and Data Transformations

Prior to conducting planned tests of FNEs, we inspected each sleep measure to determine if its distribution approximated normality. In doing so, we computed Shapiro-Wilk tests[46] of normality and constructed frequency histograms with each measure so that we could statistically as well as visually evaluate each distribution. Results of these procedures showed that the majority of these measures had distributions that were normal or approached normality (W values >0.95). However, the distributions of the sleep onset latency, sleep efficiency, stage 1 time, WASO, and REM latency were somewhat skewed. As a result, we used arithmetic data transformations (e.g., Logarithm) to normalize these measures before conducting any tests of study hypotheses.

First Night and Sequencing Effects

We predicted that both groups would show less pronounced differences between first and subsequent night values of each sleep parameter in their homes than they would in the lab. To test this prediction, we first computed the difference between values of each sleep parameter derived from the first recording night in each setting and mean values of these respective sleep measures for nights 2 and 3 in each setting. Combining data from nights 2 and 3 in these computations seemed justified since preliminary comparisons showed no significant differences between these two nights for any of the sleep measures in either of our samples.

To conduct our comparisons of these resultant difference scores, we first used an omnibus 2 (normal sleeper vs. insomnia sufferer) x 2 (recording site: lab vs home) x 2 (PSG sequence:

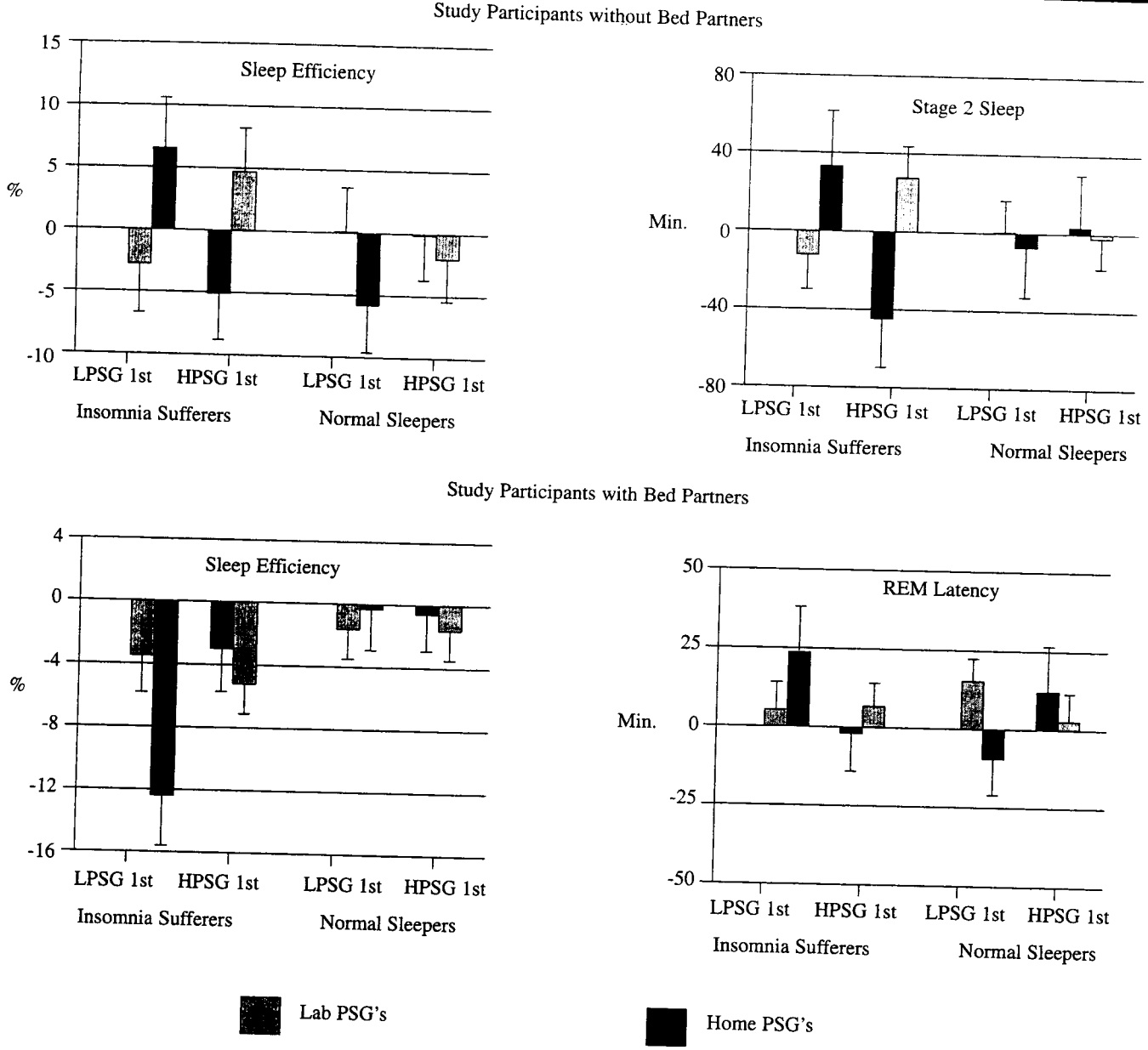

Figure 1—Differences between first nights and subsequent nights across participant types, recording sites, and PSG sequences.

HPSG 1st vs. LPSG 1st) x 9 (sleep parameters) repeated measures multivariate ANCOVA model.

To control for demographic and gender differences, we included age, educational level, and gender (female = 0; male = 1) as covariates in this model. Also included as covariates were measures which corrected for the previously noted differences in bed times and times in bed (TSPs) across nights and settings. Furthermore, in anticipation of potential influences of routine bed partners, we performed separate analyses for the subgroups with and without routine home bed partners. Finally, these analyses were conducted both with raw and normalized values of our dependent measures so as to determine the effects of data transformations on the results obtained.

Since the analyses of raw and normalized dependent measures produced similar results, only the results for the raw data are presented herein *to simplify data interpretation*. Table 1 shows the adjusted mean differences between initial and subsequent PSG nights (i.e., First night value—Mean of Nights 2 &3) and standard error terms for these differences scores. Our omnibus ANCOVA comparisons of FNEs showed significant participant type x recording site, x PSG sequence x sleep measure interactions among both those without routine home bed partners ($F_{8,88}$= 4.20, p=0.003) and those who had routine home bed partners ($F_{8,304}$=2.20, p=0.03). Follow-up univariate tests showed significant participant type x recording site x PSG sequence interaction effects for the measures of sleep efficiency ($F_{1,11}$=7.89, p=0.02) and stage 2 sleep ($F_{1,11}$=5.59, p=0.04) among those without routine bed partners, and for the measures of sleep efficiency ($F_{1,38}$=4.68, p=0.04) and REM latency ($F_{1,38}$=5.68, p=0.02) among those with routine bed partners.

Figure 1 shows the trends in the night 1 vs. nights 2/3 difference scores which contributed to these interaction effects. Each

Table 2—Adjusted means and standard error terms for the combined night 2/3 data across settings and subgroups

	Insomnia Sufferers		Normal Sleepers	
Measure+	**Lab PSG**	**Home PSG**	**Lab PSG**	**Home PSG**
Participants without Bed Partners				
TST	355.0 (15.7)	339.5 (17.3)	399.2 (13.2)	380.4 (14.6)
SOL	14.5 (4.4)	38.7 (11.5)	16.8 (3.7)	22.1 (9.7)
WASO	72.5 (10.3)	71.8 (16.7)	41.4 (8.6)	61.2 (14.1)
SE %	81.5 (2.6)	78.1 (3.8)	88.4 (2.1)	84.8 (3.2)
Stage 1	20.3 (5.0)	19.2 (3.6)	19.1 (4.2)	20.8 (3.0)
Stage 2	190.9 (12.2)	187.5 (15.4)	196.0 (10.3)	203.1 (13.0)
SWS	66.0 (9.4)	61.9 (10.2)	94.4 (7.9)	73.5 (8.6)
REM	78.1 (7.3)	70.9 (7.5)	89.7 (6.2)	82.9 (6.3)
RLMA	61.8 (4.6)	52.3 (9.6)	67.8 (3.9)	78.2 (8.1)
Participants with Bed Partners				
TST*	365.4 (9.0)	389.1 (10.3)	376.5 (9.2)	377.6 (10.5)
SOL	15.4 (1.8)	20.4 (2.7)	10.4 (1.8)	15.6 (2.7)
WASO*	65.4 (5.0)	55.9 (3.4)	26.3 (5.1)	38.8 (3.5)
SE %*	82.7 (1.2)	84.5 (1.1)	92.3 (1.2)	88.6 (1.1)
Stage 1	17.7 (2.9)	19.3 (2.3)	17.3 (2.9)	20.2 (3.3)
Stage 2	178.0 (6.4)	203.4 (7.2)	179.5 (6.6)	188.8 (7.4)
SWS	92.2 (6.5)	80.8 (5.3)	92.2 (6.6)	82.3 (5.4)
REM	77.5 (4.9)	85.7 (4.9)	87.6 (5.0)	86.3 (5.0)
RLMA	71.9 (4.9)	72.9 (6.4)	67.5 (5.0)	72.0 (6.6)

Note: Values in the tables represent minutes except for values of sleep efficiency which are %'s. Data are rounded to 1 decimal place. Values are means and (SE's). Data for those without bed partners, are from 12 (9 women) normal sleepers and 9 (5 women) insomnia sufferers; data for those with bed partners are from 23 (9 women) normal sleepers and 24 (12 women) insomnia sufferers. Asterisks (*'s) denote variables showing significant group (insomnia vs. normal) x sleep setting effects.

+Because the multivariate ANCOVA conducted for the subgroup without bed partners showed no significant main or interaction effects, no follow-up univariate statistical tests were conducted with the individual sleep measures obtained from this subgroup.

graph in this figure shows the differences between the first night and subsequent nights in each recording site. Negative values imply that first night values of the sleep parameter were lower than values obtained for subsequent nights, whereas positive values suggest first night values were higher than those shown on subsequent nights. Among the subgroup without bed partners, post-hoc statistical tests showed the above-noted interaction effects were due to significant recording site x PSG sequence (HPSG 1st vs. LPSG 1st) interaction effects within the insomnia group. As the figure implies, those insomnia sufferers who underwent HPSGs first, showed standard FNE's in sleep efficiency and stage 2 sleep in their homes and reverse FNEs in the lab. However, those insomnia sufferers who underwent LPSGs first, showed just the reverse of this trend. In contrast, post hoc tests showed normal sleepers had statistically similar FNEs for these measures across recording sites regardless of the order in which home and lab PSGs were conducted.

Results of those who had routine home bed partners showed somewhat different first night and sequencing effects. Among these participants, contrasting patterns of FNEs were found between the normal sleepers and insomnia sufferers who were first monitored in the sleep lab. Within this group, the normal sleepers showed more pronounced FNEs in sleep efficiency and REM latency (i.e., reduced sleep efficiencies and higher REM latencies on the first night relative to subsequent nights) in the lab than they did at home whereas the insomnia sufferers in this subgroup showed a reverse of this trend across both measures. In contrast, the normal sleepers and insomnia sufferers who underwent HPSG first did not statistically differ from each other in regard to the pattern of FNEs they showed for these measures across settings. Hence, conducting LPSGs prior to HPSGs seemed to heighten the laboratory FNE's of normal sleepers and home FNEs among the insomnia sufferers.

Results of Group Comparisons

To determine if, as predicted, home PSG recordings showed greater differences between our two samples than did LPSGs, we conducted a series of analyses which controlled for the above-noted first night and sequencing effects, and allowed us to isolate setting-specific effects of the two recording sites on our two samples. To do so, we eliminated first night data and used participants' averaged values of the nine sleep measures derived from nights two and three in each setting. Subsequently, we conducted an omnibus 2 (normal sleeper vs. insomnia sufferer) x 2 (recording site: lab vs home) x 9 (sleep parameters) repeated measures multivariate ANCOVA model to analyze these data. Included as covariates in this model were such variables as age, educational level, gender (female = 0; male = 1), as well as measures which corrected for the noted differences in bed times and times in bed (TSPs) across settings. Also, we included a dichotomous covariate (LPSG 1st = 0; HPSG 1st = 1) in our statistical model so as to partial out PSG-sequencing effects from our final results. As was the case in our tests of PSG-adaptation effects,

we conducted these analyses with both raw and normalized data and performed separate analyses for the subgroups with and without routine bed partners.

The analyses of raw and normalized dependent measures produced similar results, so, once again, only the results for the raw data are considered in order to simplify data interpretation. Table 2 provides descriptive statistics concerning the combined sleep data from nights 2 and 3 for the various participant subgroups. Results of our omnibus ANCOVAs showed no significant effects among the subgroup without routine home bed partners. However, among those with routine bed partners, a significant participant type x recording site x sleep measure ($F_{8,312}$=2.82, p=0.005) interaction effect was obtained. Follow-up univariate ANCOVA's showed significant participant type x recording site interactions for measures of total sleep time ($F_{1,39}$=5.95, p=0.02), WASO ($F_{1,39}$=6.62, p=0.01), and sleep efficiency ($F_{1,39}$=6.61, p=0.01) among this subgroup. Post-hoc tests showed the normal sleepers and insomnia sufferers had statistically similar values of total sleep time within each sleep setting. However, the insomnia sufferers slept significantly longer in their homes than they did in the sleep lab. In contrast, the insomnia sufferers had significantly more WASO and significantly lower sleep efficiencies than did the normal sleepers within each recording site. Nonetheless, these group differences were less marked during HPSGs than during LPSGs. Moreover, whereas the insomnia sufferers had statistically similar values of WASO and sleep efficiency across settings, the normal sleepers had statistically higher values of WASO and lower sleep efficiencies in their homes than they did in the sleep lab. Thus, contrary to predictions, these findings suggest that LPSGs may imply greater relative sleep disturbances among insomnia sufferers than do home-based recordings.

DISCUSSION

The current investigation was conducted, in part, to test our prediction that both insomnia sufferers and normal sleepers would show significantly less pronounced FNEs during HPSG than they would during LPSG. Our findings both failed to support this hypothesis and suggested the few FNEs observed seem dependent upon the particular sequence in which PSGs are conducted, the type of individual undergoing monitoring, and the individual's habit of sleeping with or without a routine home bed partner. Among those without bed partners, FNEs in sleep efficiency and stage 2 sleep were more pronounced among the insomnia sufferers than among the normal sleepers but the nature of these effects seemed influenced more by the order of recording sites than by the sleep settings themselves. These individuals showed standard FNEs during their first series of recordings and reverse FNEs during their second series of PSGs. Among those with routine home bed partners, differences in FNE's were most pronounced in comparisons of the normal sleepers and insomnia sufferers who underwent LPSG prior to HPSG. Within this group, the normal sleepers showed reduced FNE's in sleep efficiency and reverse FNEs in REM latency on their subsequent HPSGs whereas the insomnia sufferers undergoing the same PSG sequence showed much more marked standard FNE's in these measures during HPSGs than during LPSGs.

Although PSG adaptation effects varied as a function of setting, study sequence, and usual sleeping arrangement, a number of generalities are suggested by these data. First, for most of the sleep parameters examined, FNEs were not more pronounced in the lab than they were in the home. In addition, the FNEs observed appeared minimal among our normal sleepers. Furthermore, regardless of their usual sleeping arrangement, insomnia sufferers did not show a reduced first night adaptation response in their second series of studies relative to their first series. Instead these individuals seemed reactive to change in PSG monitoring venue particularly when switching from lab to home-based monitoring. Finally, the home-lab differences in FNEs observed varied between those who did and did not have a routine home bed partner. This observation seems noteworthy inasmuch as the influence of a companion in the home sleeping environment has generally been ignored in studies of lab and home FNEs. Indeed, our data would suggest that more systematic scrutiny of this factor's influence on FNEs seems warranted.

As an additional study objective, we tested our prediction that HPSG's would show greater differences between insomnia sufferers and normal sleepers than would LPSG's. When conducting analyses pertinent to this prediction, we eliminated first night data and employed a multivariate model that isolated sleep setting effects via statistically controlling for demographic differences, varying sleep scheduling across recordings sites, and PSG sequencing effects. Our results did suggest that LPSG and HPSG provide somewhat distinctive views of the sleep differences between insomnia sufferers and normal sleepers. However, these results were limited to the subgroup of participants with home bed partners and were not in the direction anticipated. Within this cohort, LPSGs generally suggested greater relative sleep difficulties (lower sleep times and sleep efficiencies, more wake time) among the insomnia sufferers than did HPSGs. Whereas both LPSG and HPSG showed the insomnia sufferers had more WASO and lower sleep efficiencies than did the normal sleepers, the group differences were less dramatic during the HPSGs. Furthermore, whereas the average total sleep times of the two groups were statistically similar in both sleep settings, the insomnia sufferers slept significantly longer in their homes than they did in the lab. Moreover, the normal sleepers had significantly less consolidated sleep in their homes than they did in the sleep lab. Hence, contrary to prediction, these findings suggest that LPSG may actually overestimate insomnia sufferers' relative disruption, at least among those with routine bed partners. These data also suggest normal sleepers may have somewhat less consolidated sleep in their homes than we have been led to expect from laboratory studies.

Overall, these group comparisons might be considered disappointing in the sense that our HPSG studies failed to show much more marked differences between our study samples than did the LPSG comparisons. In fact, like many previous studies,[16-24] both our lab and home PSGs suggested rather modest relative sleep deficits among our insomnia cohort. Given the level of daytime distress often reported by PPI patients as well as the apparent morbidity associated with insomnia, per se, it may well be that standard Rechtshaffen and Kales[47] parameters provide a very limited view of disease severity among many who suffer from this form of sleep difficulty. What our findings do suggest in this regard is that much more research concerning the nature of insomnia is needed before we understand the relationship between insomnia's objective sleep dysfunction and its eventual untoward consequences.

In view of our results, it seems useful to consider the relative merits of HPSG and LPSG. First, it appears that, for the types of individuals studied herein, LPSG does not appear to have more pronounced FNEs then HPSG, at least for the majority of the sleep measures we employed. As a result, expectations for reduced FNE's does not appear to be an adequate justification for choosing HPSG over LPSG. However, since we used relatively unobtrusive ambulatory recorders for home and lab recordings, our findings may underestimate differences that would be found between ambulatory and more traditional LPSG in which individuals are tethered to a large, stationary recording apparatus. Secondly, since our night 2/3 data showed no recording site effects for those without routine bed partners, HPSG, which requires no in laboratory bedrooms and no over-night technologist, may, for practical reasons, be favored over LPSG for studies in this subgroup, particularly when strict experimental control is not essential. For those who typically sleep with bed partners, HPSG and LPSG clearly give distinctive views of differences between normal sleepers and insomnia sufferers on sleep measures that are thought to be very relevant to insomnia complaints. In studies of such individuals, HPSG may be favored in naturalistic studies focused on capturing "typical" sleep patterns. In contrast, LPSG may remain the gold standard for group comparisons when the goals of PSG monitoring require a standardized, controlled sleeping environment. For example, studies concerned with basic sleep physiology or the endogenous circadian system may require LPSG.

In reviewing our results, it is important to consider this study's limitations. Our sample was moderate in size and consisted of only middle-aged normal sleepers and non-clinical insomnia sufferers who presented to us as research volunteers. Whether our findings apply to normal sleepers in general, younger age groups, and clinical samples of insomnia patients remains to be determined. Also, the small number of participants without bed partners may have prevented us from detecting group and setting differences that would be apparent in a larger cohort of this nature. In addition, we attempted to achieve comparable bedtimes and rising times for our subjects during LPSG and HPSG studies, but, in no way did we intrude into subjects' homes to enforce these prescriptions. Although we attempted to statistically control for the sleep scheduling variability seen across participant types and sleep settings, replication of this investigation with more rigidly controlled sleep schedules may be beneficial. Despite such limitations, our findings suggest that HPSG may provide an alternative view of the sleep differences between insomnia sufferers and normal sleepers.

AKNOWLEDGMENTS

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Comment #71:
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Comment:

(See next page)

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Attention: Ms Francina Spencer

05 May 2004

Dear Ms Spencer

CPAP Therapy for Obstructive Sleep Apnea, Project Number (CAG-0093R)

As part of the national Medicare and Medicaid coverage determination (60/17) which is under consideration by the CMS, we are writing to express our full support for the revision that would permit Medicare beneficiaries to receive multichannel home sleep testing as an alternative to attended polysomnography (PSG) sleep studies.

We are writing on behalf of Oxford Biosignals Limited, a technology company based in Oxford, United Kingdom, with a specialist knowledge in sleep diagnostics in relation to Sleep Disordered Breathing (SDB) and the identification of Obstructive Sleep Apnea (OSA). We believe our technology can provide significant clinical and economic advantages for the patient and Medicare program, especially in relation to identifying SDB and its contribution to the progression of cardiovascular disease.

Oxford Biosignals has developed a technology which uses single-channel electroencephalography (EEG) to overcome the shortcomings currently experienced by respiratory-only technology in the assessment of OSA and sleep disturbance in the patient's home. We believe that the technology can be used as a valuable addition alongside the other respiratory channels in the accurate diagnosis of sleep disorders.

We have developed an FDA-approved device called BioSomnia to facilitate the assessment of sleep EEG in the home environment. The device has 3 leads (versus the normal PSG minimum of 8 for EEG, EOG and EMG) allowing easy patient set-up and operation. It provides an automated and secure analysis of a patient's sleep statistics (Appendix 2) We are also developing a next generation 'wireless' device for optimum patient ease of use.

The technology has been proven to be as accurate as the existing PSG technologies (see Appendix 1), but more importantly allows the determination of wake and sleep times enabling the precise calculation of a patient's Apnea/Hypopnea Index (AHI). The AHI index is vitally important in assessing the severity of OSA, high AHI values corresponding to severe OSA. Policy 60-17 on CPAP therapy for OSA states clearly that "AHI is equal to the averaged number of episodes of apnea and hypopnea per hour and *must be based on a*

minimum of 2 hours of sleep". It is therefore vitally important to know when the patient is asleep and hence be able to calculate the Total Sleep Period (period of time from sleep onset to final awakening) and the Total Sleep Time (Total Sleep Period less movement and awake time). Both of these parameters have been shown in comparative studies with full PSG to be accurately calculated by the BioSomnia software (see Appendix 1).

Home testing of our technology has also identified several other benefits including:

- A patient's ability to sleep comfortably in their home environment
- A reduced delay in the scheduling of sleep clinic studies
- The reduced cost of sleep studies, whilst maintaining diagnostic accuracy
- Faster turn around of results

We have extensive support for our technology ranging from home monitoring trials through to sleep validation assessment against the existing PSG monitoring benchmarks and believe that our technology will facilitate the advent of multichannel sleep monitoring in the home.

In summary, we request that the Centers for Medicare and Medicaid Services consider our technology as a valuable addition to the 'physician toolkit' in enabling the accurate assessment of OSA and in reducing the longer term cost expenditure in relation to cardiovascular disease.

We would welcome the opportunity to discuss the content of this letter with you and/or present our technology more fully to any of your experts.

We will contact you shortly, in the meantime please do not hesitate to contact us if you have any questions.

Yours sincerely

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Appendix 1

Validation of BioSomnia with respect to full PSG – A Summary

The BioSomnia device is a single-channel ambulatory EEG analysis device which has been approved by the FDA as an adjunct to a physician in the diagnosis of sleep disorders in the patient's home environment. It has been assessed against full polysomnography (PSG) in a number of clinical studies carried out by independent expert.

The main study is that of Schweitzer *et al.* (2004) and the paper reporting its findings has been accepted for publication. Schweitzer *et al.* obtained 64 all-night sleep recording from 36 patients suffering from OSA (35 male, 1 female), with an age range from 35 to 77 years. They compared the values of sleep parameters calculated by the BioSomnia software with visual analysis of the PSG data by experienced sleep experts according to the Rechstaffen and Kales (R&K) criteria. They found no statistical differences between the BioSomnia and PSG analyses for the major sleep parameters of Sleep Latency (time period measured from "lights out" to sleep onset), Total Sleep Period (period of time from sleep onset to final awakening), Intermittent Time Awake and Number of Micro-Arousals. The average of Total Sleep Time (Total Sleep Period less movement and awake time) computed by BioSomnia for all recordings was within 3.2% of that determined by visual R&K analysis of the PSG (323 minutes versus 334 minutes). They conclude by describing BioSomnia as "a useful and sufficiently valid screening method to differentiate between sleep and wakefulness in ambulatory sleep medicine".

This conclusion is also reached by Stores *et al.* (2002) who report that the BioSomina software "provides reliable results of clinical value". In a study with six healthy adult volunteers in their own homes, they found that Total Sleep Time and Total Sleep Period estimates from BioSomnia were within 4% and 1%, respectively, of those obtained from PSG and R&K analysis. Similarly, Buchanan *et al.* (2003), in a study of 26 OSA patients, found no statistically significant differences between the values of Total Sleep Time, Sleep Efficiency and Intermittent Time Awake calculated by the BioSomnia software and those obtained from PSG plus R&K analysis. They conclude that BioSomnia "provides a simple computerized scoring of overnight sleep studies, a more sensitive analysis of the sleep continuum and reduces the overall time of analysis of sleep studies as compared to the traditional R&K analysis."

Finally, Minto and Espie (2004) have investigated the use of BioSomnia for home studies of patients with persistent primary insomnia. They recruited 14 male and 16 female subjects into their study and recorded single-channel EEG at home for two consecutive nights. They comment that "BioSomnia provides several benefits for sleep investigation. It provides output that mimics both R&K analysis and American Sleep Disorders Association (ASDA) arousal analysis. It is convenient and simple to use. It can therefore be used in the home environment with minimal disruption and is likely to generate reliable data. Collecting data at home helps eliminate the "first night effect" of laboratory-based experiments." They found that data loss in their clinical studies as a result of electrode problems was minimal. In more recent work (yet to be published) with 63 patients who provided 122 recordings, there were only 5 recordings lost as a result of problems with the EEG electrodes (i.e. 4% data loss).

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Prof. Lionel Tarassenko
May 2004

Bio Somnia

Bringing sleep lab expertise to all

- *Single channel EEG*
- *Simple patient hook up*
- *Instant results*
- *Ambulatory for home studies*
- *Validated algorithm*

OXFORD Bio Signals

BioSomnia "A Revolution in Sleep Monitoring"

Who needs BioSomnia?

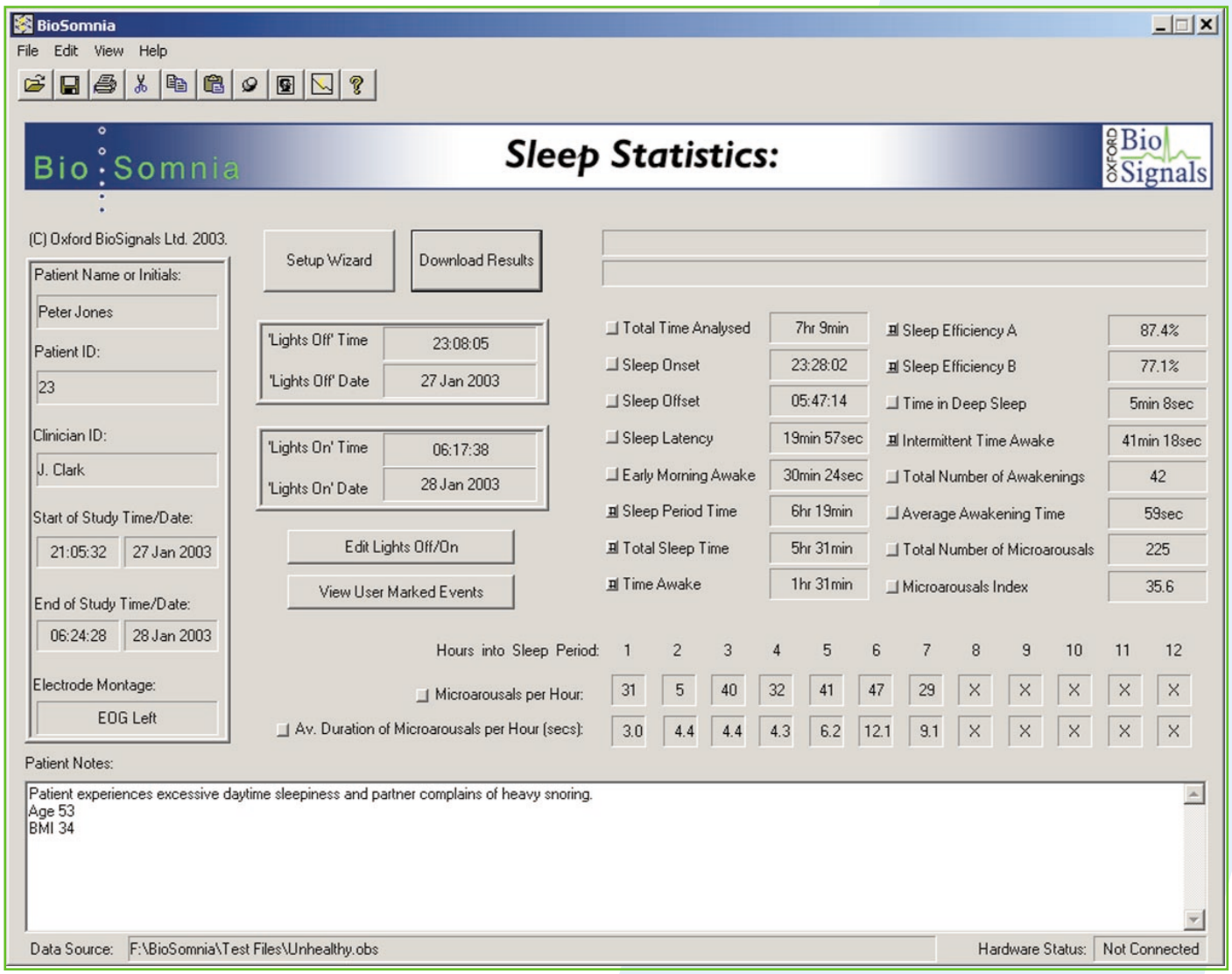
At any one time, some 10 per cent of the population suffer from a sleep disorder such as obstructive sleep apnoea (OSA), characterised by repeated microarousals throughout the night.

Insomnia, the western world's most common and costly sleep complaint, affects around half of the adult population at some point in their life. Quality of sleep has an impact on quality of life and sleep disturbance is now associated with cardiovascular disease and stroke.

What is BioSomnia?

BioSomnia is the first portable sleep system to automatically quantify patients' sleep habits and help evaluate treatment.

This lightweight, battery-powered monitor processes a single channel of EEG overnight. The system analyses the signal in real time, on a second by second basis, using Oxford BioSignals' patented neural network technology.



BioSomnia software report highlighting a patient with a sleep disorder

The BioSomnia product family

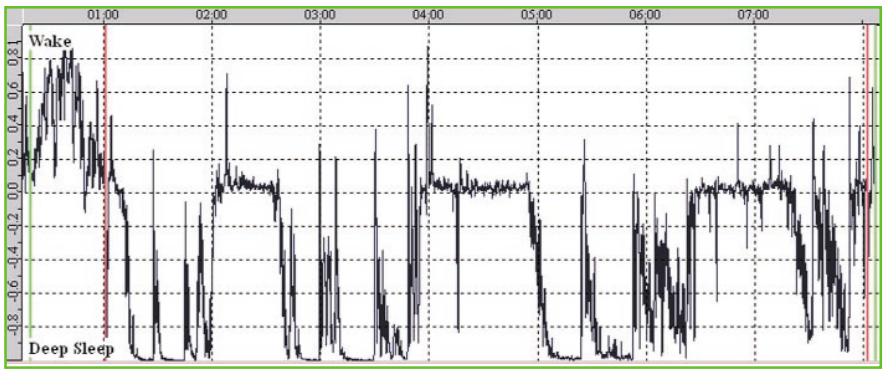
BioSomnia

- Single-channel EEG recorded using 3 leads.
- Includes automated microarousal detection.
- Disposable electrodes positioned below the hairline for easy application.
- Small, lightweight and ambulatory.
- Easy to operate, unobtrusive overnight recording
- Instant results on download, no need for manual scoring of EEG.

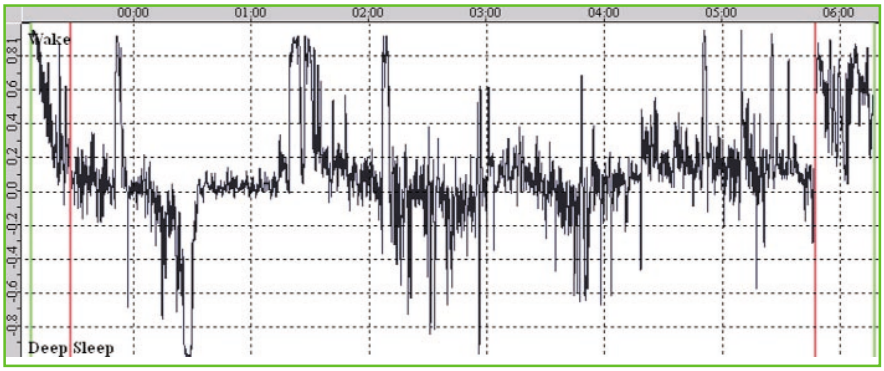
- Results validated against expert scoring.
- Single patient-operated push button to mark events.
- Affordable system for lab or home studies.
- Wizard-driven BioSomnia software installed in host PC.
- Can be used with standard or rechargeable 'AA' batteries.

BioSomnia PLUS

- BioSomnia Plus builds on the strength and reputation of BioSomnia.
- BioSomnia Plus adds a depth of Sleep Hypnogram for increased clinical information and visualisation of the sleep profile.
- The BioSomnia Plus Hypnogram displays, on a second by second basis throughout the study, the probability of the patient being awake, in light sleep/REM or in deep sleep.
- Data can be exported for further statistical analysis.



A typical BioSomnia Plus Hypnogram



Hypnogram of patient diagnosed with OSA

BioSomnia and BioSomnia Plus Specifications

Functional

- **BioSomnia Set-Up**

  Simple Wizard driven software to be completed while BioSomnia is connected to a host PC

- **Input Channel**

  Red connector – Active EEG electrode

  Black connector – EEG reference electrode

  Green connector – Neutral/ indifferent electrode

- **Recording Duration**

  Up to 24 hours

- **Recording Medium**

  Non-volatile solid state memory chips

- **Display**

  Two lines of twelve characters

- **User Control**

  Single user push button control for event marking

- **Electrode Impedance**

  Automatically monitored by BioSomnia device

Physical

- **Dimensions**

  120mm long x 78mm wide x 37mm deep

- **Weight**

  241g with batteries

Environmental

- **Operating Temperature**

  +10°C to +40°C

Power Supply

- **Battery Powered**

  Two 'AA' disposable or rechargeable cells

Results

- **Display of Results**

  Automatically displayed on host PC when connected to BioSomnia device

BioSomnia Plus with accessories and software	251-A-0
BioSomnia with accessories and software	250-A-0

BioSomnia Accessories

PC interface cable	SA 250003-01
Battery compartment tool	CM 15001
Monitor pouch and shoulder strap	SA 25001-01

BioSomnia Consumables

EEG Electrodes – Disposable (Pack of 10)	CA 11001
Batteries – Disposable (Pack of 2)	CM 16001

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Comment #72:
Submitter: Lawrence Lynn
Organization:
Date: Thu, May 13, 2004 10:58 PM
Comment:

(See next page)

From: "Lawrence Lynn" <lyntek@iwaynet.net>
To: <FSpencer@cms.hhs.gov>
Date: Thu, May 13, 2004 10:58 PM
Subject: CMS and portable sleep apnea testing

Thorax -- Schlosshan and Elliott 59 (4): 347RE: CMS Portable testing reimbursment
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Thorax 2004;59:347-352

REVIEW SERIES

Sleep . 3: Clinical presentation and diagnosis of the obstructive sleep apnoea hypopnoea syndrome

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ABSTRACT

Patients with OSAHS may present to a sleep clinic or to other specialists with symptoms that are not immediately attributable to the condition. The diagnostic methods available are reviewed.

Keywords: sleep apnoea hypopnoea syndrome; diagnosis; clinical presentation

Abbreviations: AHI, apnoea/hypopnoea index; EDS, excessive daytime sleepiness; ESS, Epworth sleepiness scale; MSLT, multiple sleep latency test; MWT, maintenance of wakefulness test; ODI, oxygen desaturation index; OSAHS, obstructive sleep apnoea hypopnoea syndrome; PSG, polysomnography; RIP, respiratory inductance plethysmography; SDB, sleep disordered breathing

The obstructive sleep apnoea hypopnoea syndrome (OSAHS) has been described as a public health problem comparable to smoking in its effects upon society.1 However, it is largely unrecognised and undiagnosed.2 Young et al estimated that 93% of women and 82% of men with moderate to severe OSAHS are not diagnosed.3 Yet these patients are being seen by doctors on a regular basis; a telephone survey in the UK of approximately 5000 individuals aged 15-100 years found that 31% of those with breathing pauses during sleep had sought medical help more than six times in the previous 12 months compared with 12% of snorers and 11.9% of non-snorers. They sought medical treatment from their GP for a variety of physical complaints-not obviously related to a sleep problem-more than twice as often as patients without OSAHS.2 The failure to recognise the syndrome is in part due to lack of training in sleep medicine (a study of all UK medical schools showed that students received a median of 5 minutes teaching in all aspects of sleep medicine throughout their training4) and a general lack of awareness. Many of the symptoms are non-specific and have other possible causes.5 Failure to recognise OSAHS is costly both to the individual and to society; underdiagnosis is thought to cost the USA $3.4 billion in additional medical costs per year.6 To this figure must be added the cost of losses in productivity, accidents, etc.7,8

Because OSAHS is so common, has considerable effects upon patients and their partners, increases the risk of other diseases, can be effectively treated, and is so often unrecognised, it is important to improve the way these patients are diagnosed. The first step is to increase awareness among doctors and the general public and for a simple sleep history to become part of the normal systems review taught at medical school.

This review will focus both on how patients present to sleep clinics and how they may present to other specialists with symptoms that are not immediately attributed to OSAHS.

PRESENTATION TO SLEEP CLINICS

CONCLUSION
REFERENCES

Patients are predominantly referred to a sleep clinic because they complain of excessive daytime sleepiness (EDS) or their partner complains about the noise of their snoring or expresses concern about witnessed apnoeas.9

Snoring
Snoring is very common in the general population; 35-45% of men and 15-28% of women report habitual snoring.2,10 Loud intrusive snoring affects bed partners, family, and even neighbours. Noise pollution and its resulting social disability, relationship disharmony and threatened marriage break up11 is an important reason why the patient, often pressurised by their partner, seeks medical help. In this case the "patient" is often more correctly the partner as the individual concerned is not aware of any adverse affects from his/her snoring other than the irritation reported by others. Snoring is also the most frequent symptom of OSAHS, occurring in 70-95% of patients,12 but because it is so common in the general population it is a poor predictor of OSAHS.13 However, the absence of snoring makes OSAHS unlikely; only 6% of patients with OSAHS do not report snoring,14 but it should be appreciated that a patient's perception of his/her snoring may be inaccurate. Three quarters of patients who deny snoring turn out to snore when this is measured objectively.15 Whenever possible, an account from a third party should be obtained.

Excessive daytime sleepiness
Excessive daytime sleepiness is caused by fragmented sleep related to frequent arousals. Like snoring, it is common and a poor discriminator of the patient with OSAHS. 30-50% of the general population without OSAHS report moderate to severe sleepiness.10,16 It is important to differentiate true sleepiness (the urge to sleep) from various forms of tiredness such as lethargy, malaise or exhaustion. Patients themselves may underreport their sleepiness,17 either because they are not aware of it or because there are social pressures to deny that it is a problem. They may not have considered other obvious causes of EDS such as drugs and shift work, and these should always be asked about in the history. The possibility of dual causes such as shift work and OSAHS should also be considered.

Several tools are available for measuring sleepiness both subjectively and objectively. There is no gold standard, but the easiest and most practical is the Epworth sleepiness scale (ESS).18 Drawbacks include poor correlation with the severity of OSAHS and the disadvantages that accompany any self-evaluated test such as misperception of sleep episodes and the possibility of cheating. The input of the partner is very useful.19 The major advantages of the ESS are that it is simple, quick, inexpensive, and has a high test-retest reliability.20 Objective tests have obvious advantages but are time consuming and may not reflect everyday activity. They include the multiple sleep latency test (MSLT),21 the maintenance of wakefulness test (MWT),22 and the Osler test.23 Patients may also have neurocognitive deficits and psychological problems such as difficulty concentrating, poor memory, cognitive performance and personality changes with irritability and mood swings.9 These problems may be of greater consequence to the patient than EDS, but routine psychometric assessment is not practical in clinical practice.

Witnessed apnoeas and nocturnal choking
Concern by the bed partner about breathing pauses witnessed during sleep is the third common reason for referral to a sleep clinic. However, bed partners rarely give a reliable account about apnoeas during sleep and even trained medical staff are poor at diagnosing respiratory events in patients with OSAHS through clinical observation.24 Female patients with OSAHS are less likely to report nocturnal apnoeas25,26 and witnessed apnoeas may be reported in up to 6% of the normal non-apnoeic population.25 The patient may report waking up with acute panic and choking. These episodes usually only last for a few seconds but can cause considerable distress, both to the patient and the partner. They have to be differentiated from other causes of nocturnal breathlessness such as paroxysmal nocturnal dyspnoea in the patient with left ventricular failure, nocturnal asthma, acute laryngeal stridor, or Cheyne-Stokes respiration in patients with heart failure. Episodes of breathlessness in these conditions usually last longer and/or there is other evidence of the condition in question.

The pathophysiological consequences of OSAHS can affect almost every organ in the body and patients can present to other medical specialties with symptoms related to, caused by, or exacerbated by OSAHS.27 It is important that clinicians are aware of the various ways in which OSAHS may manifest in their specialty, as in some cases treatment of the OSAHS results in an improvement in-or even complete resolution of-these symptoms.28-30 Furthermore, treatment of some conditions such as hypothyroidism31 and acromegaly32 may result in resolution of OSAHS. It is beyond the scope of this review to describe in detail the presentation to various medical specialties but an overview is given in table 1.33,34

View this table:
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Table 1 How OSAHS might present to non-sleep specialists

The diagnosis of OSAHS is based on the characteristic clinical features together with objective demonstration of sleep disordered breathing (SDB). The American Sleep Disorders Association (ASDA) has proposed guidelines and a classification of severity of OSAHS (box 1).20 This emphasises that the diagnosis of OSAHS is not based solely on the detection of respiratory events, but equally includes clinical factors such as sleepiness and impairment of social or occupational functioning.

Box 1 American Sleep Disorders Association (ASDA) classification of OSAHS

a.. Sleepiness

a.. Mild: unwanted sleepiness or involuntary sleep episodes occur during activities that require little attention

b.. Moderate: unwanted sleepiness or involuntary sleep episodes occur during activities that require some attention

c.. Severe: unwanted sleepiness or involuntary sleep episodes occur during activities that require active attention

b.. Sleep related obstructive breathing events (apnoea, hypopnoea, and respiratory effort related arousals):

a.. Mild: 5-15 events/hour of sleep

b.. Moderate: 15-30 events/hour of sleep

c.. Severe: >30 events/hour of sleep

Clinical assessment

Clinical assessment alone is not sufficient to make the diagnosis of OSAHS. Even sleep experts have been reported to be wrong in 50% of cases when making the diagnosis on history and examination alone.14,35 None of the common presenting symptoms alone has sufficient discriminatory value to make an accurate diagnosis.13 Combining constellations of symptoms can improve diagnostic accuracy. Loud snoring and witnessed apnoeas identified OSAHS with a sensitivity of 78% and a specificity of 67%.36 In a large study of 5000 subjects, those reporting habitual loud snoring and frequent breathing pauses were 3-4 times more likely to have an apnoea/hypopnoea index (AHI) of >15 than those who did not have any of these symptoms.37 These findings are in keeping with results from previous studies.13,14,36,38,39 Although obesity is an important risk factor for OSAHS, 50% of patients are not clinically obese (body mass index >30 kg2).40 Location of fat deposition, especially anterolateral to the upper airway, is more important.40 Neck circumference has consistently been shown to be a strong predictor of OSAHS,41,35 values of <37 cm and >48 cm being associated with a low and high risk, respectively. Certain craniofacial abnormalities are associated with OSAHS. Tonsillar hypertrophy, retrognathia, micrognathia, and certain facial configurations have been detected by cephalometry, MRI, or CT scans to be present in some patients with OSAHS,42 but are of little predictive value. However, some are potentially amenable to surgical correction. Routine upper airway imaging is not currently recommended.

Clinical prediction models

Prediction models for both primary and secondary care that calculate the probability of a patient having OSAHS using self-reported symptoms combined with demographic and anthropometric data have been developed to try to improve the predictive value of clinical variables. With increasing recognition of OSAHS, the demand for diagnostic services is rising and such models may help to select patients for further evaluation. One author claimed that the number of polysomnographic investigations could be reduced by nearly 40% using one such model.43 They are low cost and can be performed in the clinic; however, when tested prospectively, they have a high sensitivity (76-96%) but a low specificity (13-54%).43 Furthermore, most have not been validated in populations such as the elderly, ethnic minorities, and in the primary care setting, in all of which the presentation of OSAHS may be very different from that seen in a sleep clinic.44 Further validation of the clinical usefulness and cost effectiveness of such an approach is required.

Tests for sleep disordered breathing

Full polysomnography (PSG) is traditionally regarded as the gold standard for the diagnosis of OSAHS. Typically, it requires admission to hospital with a trained technician present throughout the night. It is time consuming, expensive, and the large variety of techniques, equipment, and diagnostic criteria used by

different sleep centres make evaluation and comparison of PSG data difficult.45 Redline et al showed that the respiratory disturbance index can vary 10-fold depending on the definitions of the respiratory variables used for the diagnosis of OSAHS. This could lead to a situation where the same patient could be diagnosed and treated in one centre and be declared not to have OSAHS in another.46 Furthermore, PSG has not undergone the rigorous evaluation of accuracy, reliability, and validity expected for a "gold standard" diagnostic test.45 The AHI, the primary index extracted from PSG, is poorly correlated with EDS, increases in normal people with age,47 and has not been shown to predict short or long term morbidity or mortality. This leads some authors to question whether PSG can be regarded as a gold standard and reference tool when evaluating alternative diagnostic tests.48,49

There are two different aspects to full PSG-monitoring of various parameters reflecting respiration and monitoring cortical brain activity to assess the presence or absence of sleep and its stage. The constraints of space preclude a comprehensive review of all the various devices available for the investigation of SDB, but the most important issues will be addressed.

Monitoring of respiration
The diagnosis of SDB rests upon detecting changes in oronasal airflow and respiratory effort to define apnoeas and hypopnoeas. However, increased work of breathing usually, but not always, associated with loud snoring alone can lead to sleep disruption and daytime symptoms. This has been described as the upper airway resistance syndrome.50 Whether it is part of the OSAHS spectrum or presents a distinct syndrome is controversial.51,52 Classically, it requires measurement of changes in oesophageal pressure.20,50 The definition of apnoeas and hypopnoeas is arbitrary and other respiratory effort related events20 and episodes of inspiratory flow limitation may be important.

In patients with moderate to severe OSAHS the reproducibility of the respiratory parameters from night to night is good.53 For milder OSAHS a single negative study may not exclude OSAHS and a second study should be considered.54,55 Sleep position, acclimatisation to a foreign sleep environment, concurrent respiratory tract infections, and variable alcohol and drug use are thought to be responsible for night to night variability in both respiratory and sleep parameters. Most airflow sensors detect apnoeas reliably, but the detection and quantification of decreased flow needed to diagnose hypopnoeas depends on the type of sensor used. Hypopnoeas make up the majority of obstructive respiratory events46 and therefore measurement needs to be reliable. Oronasal airflow can be measured using thermistors which detect changes in temperature with respiration. Unfortunately, the response is not linear and therefore they cannot be used to determine hypopnoeas reliably. Furthermore, their accuracy varies greatly depending on the position of the sensors, the sleep position of the patient, the presence of nasal obstruction, and the make of the thermoelement used.56 For these reasons the ASDA Task Force does not recommend thermoelements for the detection of obstructive respiratory events.20 Despite this, they continue to be used for flow detection in many commercially available sleep diagnostic systems. Nasal pressure sensors connected to the nose via nasal prongs are more accurate than thermoelements in detecting hypopnoeas.57 However, nasal pressure is falsely increased in the presence of nasal obstruction and there is a non-linear relation between nasal pressure and nasal flow. Square root linearisation of nasal pressure greatly increases the accuracy for quantifying hypopnoeas and detecting flow limitation.58,59 Mouth breathing can affect the measurement but pure mouth breathing is uncommon.60

Respiratory effort can be assessed in a number of different ways. Chest and abdominal wall motion can be measured by strain gauges, pressure transducers, or by measuring the impedance of wires placed around the chest and abdomen. This allows the distinction between central events, characterised by a reduction in respiratory effort, and obstructive events in which efforts continue, usually with a phase shift between chest wall and abdominal wall motion; as the diaphragm descends the abdomen moves out but, because of upper airway obstruction, the thorax is subjected to large negative pressures and is sucked in. Respiratory inductance plethysmography (RIP) detects changes in the volume of the chest and abdomen during inspiration and expiration and, when properly calibrated, the sum of the two signals can provide an estimate of tidal volume.61 However, calibration may be difficult to maintain throughout the night.62 RIP allows an acceptable semi-quantitative measurement of ventilation and therefore hypopnoeas. The ASDA Task Force recommends the use of RIP or measurement of nasal pressure using nasal cannulae to detect airflow and ventilation.20

Monitoring of sleep
Sleep quality and stage is monitored by electroencephalography (EEG), electro-oculography (EOG), chin electromyography (EMG) and analysed by criteria agreed in the 1960s.63 These have been modified subsequently, in particular with the recognition that much shorter periods of arousal (so called "micro arousals") may be important. Electrophysiological monitoring allows confirmation that sleep has taken place, gives data about the amounts of different sleep stages and sleep quality, and can quantify the number of arousals which might reasonably be expected to be a good predictor of one of the most important symptoms of obstructive sleep apnoea-namely, EDS. Unfortunately, a number of studies have failed to show any relationship between the arousal index or any other of the sleep quality variables with daytime symptoms.49,64,65 Furthermore, there is poor reproducibility of the scoring of arousals.66 Douglas et al67 showed that the addition of electrophysiological analysis of sleep did not alter the diagnosis in 200 consecutive patients being investigated for possible OSAHS. It could be diagnosed as accurately by measuring the number of apnoeas + hypopnoeas per time in bed as by the number of apnoeas + hypopnoeas per time asleep (AHI).

Despite its widespread use and many advocates, the evidence does not support the need for full PSG in the routine diagnosis of OSAHS. One other approach to the recording of sleep is wrist activity monitoring. Although it is not recommended routinely in the diagnosis, it may be a useful adjunct to a detailed history in the assessment of sleep disorders.68

Objective confirmation of OSAHS
Various different approaches have been developed. These range through attended full PSG, unattended full PSG, limited PSG to oximetry, or movement detectors alone. Split night studies have been used; in patients with an AHI of >40 recorded in the first 2 hours of PSG the diagnosis of OSAHS can be made reliably without proceeding to a full night study. The second part of the night can be used for continuous positive airway pressure (CPAP) titration with accurate CPAP estimation.45 There is a trend for studies to be performed in the patient's home rather than hospital. Home studies have the theoretical advantage that patients can sleep in their own environment without occupying a hospital sleep laboratory bed, providing more representative data in a cost effective way.69 Failure due to technical problems can occur in 5-20% of cases.45,70 Repeat testing increases costs. Factors such as patient disability or transportation problems make home studies impractical for some.71 Further validation and evaluation of the cost effectiveness of home studies is required.

Limited sleep studies usually quantify obstructive respiratory events without recording sleep. They typically include the measurement of oronasal airflow, chest wall and abdominal effort, ECG and oxygen saturation (SpO_2). In addition, leg and eye movement, body position, and snoring may be recorded. The systems are usually portable and can be used at home. The potential advantages of these systems are that they are cheaper, less labour and time intensive, and technically less challenging. The main disadvantage is that the lack of sleep recording leads to uncertainty when deciding if respiratory events occur during wakefulness or sleep. Surrogates of sleep such as motion detectors72 and static beds73 attempt to estimate times of wakefulness but are poorly validated and do not appear to improve sensitivity or specificity.45 Furthermore, the study by Douglas et al45 suggests that documentation of sleep does not affect the final diagnosis. Generally, there is good correlation between the AHI obtained from limited channel devices and PSG.74 The sensitivities and specificities of limited in-laboratory devices are 82-94% and 82-100%, respectively.75,76 A systematic review in 1997 concluded that full PSG may not be necessary to diagnose OSAHS and that limited in-laboratory cardiorespiratory studies in patients with a clinical suspicion of OSAHS may suffice.77

Newer techniques
The effects of the large intrapleural pressure swings during obstructive respiratory events on the autonomic nervous system, pulse, and blood pressure have given rise to the development of newer non-invasive techniques to measure apnoea or hypopnoea.

Indirect measurement of peripheral vasoconstriction and transient tachycardia through a finger plethysmograph,78 analysis of very low frequency components of heart rate variability,79 and the

measurement of the change of pulse transit time80 during apnoeas have revealed promising results. Furthermore, pulse transit time can be used to differentiate between obstructive and central events.81

Pulse oximetry
Transcutaneous nocturnal pulse oximetry is increasingly being used for initial screening for OSAHS as it is inexpensive and can be simply applied and interpreted.47 Oxygen desaturations are common with obstructive apnoeas but can be absent with hypopnoeas or in events with increased upper airway resistance. They also occur frequently in other cardiovascular and respiratory conditions unrelated to airway obstruction, resulting in false positive results. The parameters reported vary widely but include total number of desaturations, oxygen desaturation index (ODI), desaturations per hour, highest, lowest and mean SpO2, and cumulative time SpO2 spent below 90%. A 4% desaturation is most commonly considered to be significant, but 3% and 5% desaturations are also used. As with the AHI criteria, there is no consensus as to the ODI which represents a normal or abnormal result but commonly used thresholds are ODI >5, >10, and >15. Nocturnal artefacts, inaccurate readings in obese patients, and the presence of hypotension and haemoglobin abnormalities can limit the accuracy of the results. Devices with low sampling rates, used in some home pulse oximeters to preserve memory, can significantly underestimate oxygen dips.82 Furthermore, it is important for there to be a visual print out of the oximeter trace; artefacts are more easily seen and the pattern of oximetry may indicate that the calculated AHI may be an underestimate-for instance, if the patient did not sleep for a period of the night.

The sensitivity of nocturnal pulse oximetry in the diagnosis of OSAHS ranges from 31% to 98% and specificity from 41% to 100%. This wide range of reported sensitivities and specificities results from the great diversity in criteria definition, populations studied, and devices used.83 In the study by Douglas et al 66% of patients with OSAHS could be diagnosed with oximetry alone, but many of the patients undiagnosed by oximetry had moderately severe OSAHS and benefited from treatment.67 Nocturnal pulse oximetry performed prospectively in 275 patients suspected of OSAHS in the laboratory and compared with full PSG reported sensitivities of 80%, 71% and 63% and specificities of 89%, 93% and 99% for ODIs of >5, >10, and >15, respectively.84 The authors argued that the number of full PSG recordings could be reduced by up to 50% using nocturnal pulse oximetry.

Pulse oximetry is probably most useful in patients with a high suspicion for OSAHS based on clinical features.83,85,86 The combination of a high ODI and high pretest clinical suspicion can be regarded as sufficient to make a diagnosis of OSAHS. Patients with suspected OSAHS who have a negative pulse oximetry trace or have significant concurrent respiratory or cardiovascular disease need further investigation.47 It may also be useful in excluding sleep apnoea in snorers with a low clinical suspicion for OSAHS.87 The 4% dip rate has been shown to be the best oximetry derived variable predicting symptomatic benefit from CPAP.88

The history and examination are key to making the diagnosis of OSAHS and are sometimes overlooked in the debate about which technology is most appropriate. The history should be targeted towards making the diagnosis, but also assessing disease severity, the impact on social and occupational function, as well as on the patient's quality of life. The presence of significant cardiovascular, respiratory, and neurological co-morbidity should also be determined. This assessment should include the bed partner's report whenever possible. In a significant proportion of patients the diagnosis can be made by oximetry alone, and in most of the remainder by limited PSG although close attention needs to be given to the parameters

recorded and the instruments used. Full PSG remains useful in research and for occasional patients who cannot be diagnosed using the simpler strategies. The future lies in the development of less intrusive systems to identify accurately those patients most likely to benefit from treatment.

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CC: <dmunafo1@san.rr.com>

Comment #73:
Submitter: Yury Furman, MD
Organization: Pacific Sleep Medicine Services, Inc.
Date: May 3, 2004
Comment:

(See next page)

PACIFIC SLEEP MEDICINE SERVICES, INC.
LOS ANGELES CENTER
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Phone: (323) 782-9894 Fax: (323) 782-0687
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05-03-2004

To: Centers of Medicare and Medicaid Services

Re: Approval of ambulatory studies for Medicare and Medicaid patients Proposed by Terence Davidson, MD

As a Sleep Medicine specialist practicing for past ten years I am very disturbed by Dr. Davidson's' proposal of approving home based sleep testing for Medicare and Medicate. I personally have had extensive experience with limited sleep monitoring over past ten years. Unfortunately, after extensively field testing most if not all, available systems I can definitively state that home testing in elderly population is totally inappropriate as it is fraught with unacceptable failure rate and does not provide adequate data to form medical conclusions as far as diagnosis and treatment are concerned. We also have not found it to be cost effective. With high failure rate and necessity of at least two recording sessions (one diagnostic and one treatment) home studies proved to be vastly inferior to sleep center based recordings. Facility based recordings have virtually no failure rate and most of the tome require only one night for diagnosis and treatment thus making it significantly better from technical and cost savings point of view. We are privileged to have close working relationships with majority of Southern California Health Maintenance Organizations. Over the years various models were tried and closely evaluated for quality and cost effectiveness. As of now all HMO covered patients are being evaluated in facility based sleep centers for above-mentioned reasons.
Furthermore Medicare and Medicaid patients usually require close observation and technician involvement to produce quality study, which would not be available during home-based recordings thus further increasing failure rate and driving up cost and utilization.

Should you have any questions, please do not hesitate to contact me.

Sincerely,

Yury Furman, MD
Diplomate, American Board of Sleep Medicine

Comment #74:
Submitter: Board of Directors
Organization: New England Polysomnographic Society
Date: May 17, 2004
Comment:

(See next page)

From: New England Polysomnographic Society
250 Pleasant Street
Concord, NH 03301

To: Steve Phurrough, MD, MPA

Director, Coverage and Analysis Group

Centers for Medicare and Medicaid Services

From: Board of Directors

New England Polysomnographic Society

Re: Home Polysomnography Coverage

Dear Dr. Phurrough,

As providers of medical services in the field of sleep medicine, we are writing you this letter to voice our opposition to home polysomnography coverage. We had an opportunity to read Dr. Davidson's position paper regarding the purported "benefits" of home sleep studies, and wholeheartedly disagree with many of his points. Dr. Davidson states that not only is it an advantage to patients to have this study at home, but that it would be less expensive. While initially it may be slightly less expensive, we believe that in the long term, it would be more expensive and provide poor care for patients with sleep disorders.

There is no substitute for having an attended sleep study in a lab environment. Technologists do not simply apply electrodes and turn out the lights. A great deal of information is gathered from the patient through observations and conversations while in the lab. Also crucial information is disseminated to the patient regarding not only the test, but also treatment. We have found that this opportunity to educate the patient while in the lab greatly influences CPAP compliance. Unfortunately, patients who have been poorly educated and have had minimal medical contact will be much less likely to use CPAP treatment after their study. (Making this a complete waste of time and money)

While home testing does monitor similar parameters, its reliability must be questioned. A trained polysomnographer in a lab setting has the ability to determine if equipment is malfunctioning or is giving accurate information. (A poorly placed or loose sensor can easily give the impression that a person has a sleep breathing disorder, and these sensors frequently become displaced during the night) A laboratory sleep study is a "controlled" environment that eliminates the possibility of misdiagnosis due to environmental factors or patient behaviors.

Dr. Davidson made a point suggests that "home sleep studies are sufficient for routine sleep apnea/ SDB cases". We would argue that there are few "routine" sleep apnea cases with the older and disabled populations. Many patients report symptoms that are consistent with sleep breathing disorders, but turn out to be something completely different. Within the realm of sleep-disordered breathing, OSA, CSA, Cheyne-Stokes breathing and obesity hypoventilation can be difficult to differentiate simply from digital waveforms. Observations in the lab help interpret the subtle differences between these disorders, and direct the appropriate course of treatment.

One area in particular of Dr. Davidson's proposition made us very concerned. This is point 7E: "Multichannel home sleep diagnostic dispensing and titration is far easier than PSG lab setups and therefore can be performed by a greater number of practitioners, such as ENT surgeons, cardiologists, PCP's and others". Sleep is a very unique field and sleep boarded physicians and polysomnographers are uniquely trained and experienced to handle the task. If any physician is allowed to order and interpret this data it will be a great disservice to the patient.

Surgeons may not offer CPAP as an option to their patients, opting for surgical intervention instead. (Estimates show 50% of operations performed do not control SDB) PCP's often still are unaware or less than knowledgeable about CPAP therapy. Ultimately this will lead to unsuccessful treatments and outcomes for many patients. Home titration (especially if considered with an auto-titrating machine) is in our opinion irresponsible and ineffective.

Please consider these factors when evaluating home diagnostic testing in the field of sleep medicine. We could go on and on regarding the benefits of laboratory testing versus a home study, but we know you are very busy. Thank you very much for your time. If you have any questions please feel free to email blund@crhc.org.

Sincerely,

The Board of Directors

New England Polysomnographic Society

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Comment #75:
Submitter: William C. Dement, MD, Ph.D.
Organization: Stanford University
Date: May 8, 2004
Comment:

(See next page)

SLEEP RESEARCH CENTER

William C. Dement, M.D., Ph.D., Director

STANFORD UNIVERSITY

School of Medicine
Department of Psychiatry
and Behavioral Sciences

May 8, 2004

VIA FACSIMILE: (410) 786-9286

Ms. Francina C. Spencer
Lead Analyst
Obstructive Sleep Apnea Coverage Determination
Coverage and Analysis Group
Office of Clinical Standards and Quality
Centers for Medicare and Medicaid Services

Dear Ms. Spencer:

I am writing to support a national coverage decision for the diagnosis and treatment of obstructive sleep apnea to include multi-channel home sleep testing and auto-CPAP titration as an alternative to polysomnography (PSG).

1) Numerous scientifically sound studies reveal that obstructive sleep apnea (OSA) contributes to hypertension, heart attack, stroke, heart failure, cardiac arrhythmia, nocturia, gastroesophageal reflux disease, asthma, obesity, diabetes, and early death. It is a modifiable risk factor for motor vehicle accidents. Its adverse impact on quality of life is treatable. The term sleep disordered breathing (SDB) is now used synonymously with the older term OSA. SDB can be identified in 4% of adult males and 2% of adult females using an AHI $\geq$ 15.

   SBD occurs in 80% of Medicare patients with congestive heart failure, and they benefit substantially from CPAP therapy.

2) Medicare patients with SBD are under-diagnosed because they experience impaired access to care.

3) Sleep medicine is not well integrated into medical practice. Medicare patients have previously had to rely on diagnostic polysomnographic testing that could only be done in sleep laboratories. The capacity for performing polysomnography is limited, and recent advances in technology now allow for the accurate diagnosis of routine sleep apnea/SDB cases at home within a continuum of care.

4) Multi-channel home sleep testing and auto-titration CPAP offer the opportunity to improve access to care for the treatment of SBD.

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5) A large and growing body of evidence demonstrates excellent correlation between multi-channel home sleep testing and PSG.
   a) Multi-channel home sleep testing uses the same respiratory equipment, oximetry monitoring, and chest and abdominal monitoring equipment as PSG.
   b) The outputs from PSG and multi-channel home sleep tests are very similar. (Although sleep stages and efficiency are useful information, they are not required to diagnose the presence of a sleep-related breathing disorder.)

6) Advantages of multi-channel home sleep testing are:
   a) Lower costs than traditional PSG testing
   b) Test is performed in the privacy of the patient's own home and bed
   c) Simplicity of testing, with wires and leads being less numerous than traditional PSG and can be completed by an unattended patient.
   d) Multi-channel home sleep diagnostics and titration is easier and faster to accomplish than PSG.

7) Multi-channel home testing and auto-CPAP titration will allow primary care practitioners, cardiologists, ear nose and throat (ENT) surgeons, and other healthcare providers to rapidly and accurately diagnose and begin therapy, thus helping to alleviate the enormous lack of access that Medicare patients experience in the treatment of this condition.

Thus, it is proposed that multi-channel home sleep testing and auto-titration CPAP be used as an alternative to polysomnography to improve access to care for Medicare patients with OSA.

Very truly yours,

William C. Dement

William C. Dement, M.D., Ph.D.
Lowell W. and Josephine Q. Berry Professor of Psychiatry and Sleep Medicine in the Department of Psychiatry and Behavioral Sciences
Director, Sleep Disorders Clinic and Research Center
Stanford University

Comment #76:
Submitter: Emmanuel Mignot, MD, Ph.D.
Organization: Sleep Research Society
Date: May 7, 2004
Comment:

(See next page)

Sleep
Research
Society

May 7, 2004

Steve Phurrough, M.D., MPA
Director, Coverage and Analysis Group
Office of Clinical Standards and Quality
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244-1850

Dear Dr. Phurrough:

We have been made aware of the recent request for modification of policy CIN6017 forwarded to CMS by Dr. Terrance Davidson. It is our understanding that this application includes a request for the approval of portable home monitoring evaluation as an alternative to facility-based polysomnography for the diagnosis of obstructive sleep apnea in Medicare patients.

The Sleep Research Society is a society of approximately 1,000 members working in the area of basic and clinical sleep research. Many of our members work in the area of sleep apnea research and also practice clinical sleep medicine. We disapprove of the suggested change of policy based on currently available research findings and the acceptable standard of practice within the sleep medicine field.

Whereas home portable monitoring diagnosis may in some cases be helpful to the diagnosis of sleep apnea under highly controlled experimental conditions, it is impossible with the current level of heterogeneity in the type of systems/monitors used to recommend this practice. Additionally, it is almost certain these readings will be frequently evaluated by untrained staff and not by trained sleep professionals, leading to many errors. In fact, current publications do not support the use of home portable monitoring without professional attendance. High rates of diagnosis misclassifications and errors have even been reported in one study evaluating the use of a limited-channel home recording monitoring device. A state-of-the-art in-laboratory study remains the best way to make a definitive diagnosis that will allow proper long-term treatment.

The Sleep Research Society is concerned that the uncontrolled use of home portable monitoring can at best be used for screening in the context

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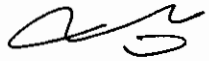
of epidemiological studies and will miss a significant number of real sleep apnea cases in clinical practice. Additionally, it is our experience that many patients have complex pictures with combined diagnosis; for example, narcolepsy and sleep apnea, and these patients will be ill served with a hasty evaluation and diagnosis. Only in the context of a proper clinical evaluation by a trained sleep physician, can any diagnostic test be properly interpreted.

In summary, we feel patient evaluations and therefore subsequent treatments will not be well served by reducing the standard leading to a proper diagnosis. At the research level, peer-reviewed publications indicating that unattended home monitoring can replace attended laboratory sleep testing are simply not available and thus moving in this direction will be haphazard and scientifically unacceptable.

We will be very happy to provide you with additional information if need be. Please do not hesitate to contact the Sleep Research Society if you have any additional questions on our position.

Sincerely,



Emmanuel Mignot, M.D., Ph.D.
President, Sleep Research Society

Comment #77:
Submitter: Conrad Iber, MD
Organization: American Academy of Sleep Medicine
Date: May 5, 2004
Comment:

(See next page)

American Academy of Sleep Medicine

May 5, 2004

Steve Phurrough, MD, MPA
Director, Coverage and Analysis Group
Office of Clinical Standards and Quality
S3-26-27
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore MD 21244-1850

Re: NCA Tracking Sheet for Continuous Positive Airway Pressure (CPAP) Therapy for Obstructive Sleep Apnea (OSA) (CAG-00093R)

Dear Dr. Phurrough:

The American Academy of Sleep Medicine would like to comment on the request for modification of policy CIM 60-17 forwarded to CMS by Terence M. Davidson M.D. It is our understanding that this application incorporates a request for the approval of portable home monitoring (unattended portable monitoring) as an alternative to facility-based polysomnography (attended monitoring) in Medicare patients with (suspected) obstructive sleep apnea for the purpose of prescribing CPAP.

For the purposes of clarity, previously established definitions for attended and unattended will be used throughout this discussion (1): a) in attended monitoring, personnel are physically present throughout recording session b) in unattended monitoring, trained personnel are not physically present throughout recording session.

To summarize the position of the American Academy of Sleep Medicine, there is insufficient evidence to support the use of home portable monitoring as it is currently applied in clinical practice to confirm or exclude the diagnosis of sleep apnea prior to initiating CPAP or for the titration of CPAP in the treatment of sleep apnea. A careful evidence-based analysis does not support the use of portable home monitoring for this purpose. There also is no compelling evidence that the welfare of the patients would be improved by encouraging the use of portable home monitoring to diagnose sleep apnea by practitioners who have limited training in sleep medicine. To the contrary, the Academy feels that extensive use of non-standardized techniques for portable home monitoring, especially by practitioners with little or no training in the evaluation and treatment of sleep disorders, may increase the likelihood of inaccurate diagnosis and treatment, and may contribute to an escalation of unnecessary health care costs. This increase in incorrect diagnosis would be expected to substantially increase unnecessary prescription of CPAP.

The utility of unattended portable monitoring in the diagnosis of the sleep apnea syndrome rests on more than the recording accuracy of a somnographic device. Historically, the field of Sleep Medicine has placed a high priority on the provision of

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comprehensive clinical care to patients with sleep disorders. Specifically, the standards for care emphasize that polysomnographic evaluation should only occur within the context of a full evaluation of the patient by a trained expert in Sleep Medicine. Thus, the evaluation process includes comprehensive clinical assessment, accurate somnographic evaluation, appropriate diagnosis based on polysomnography and consultation, selection of appropriate treatment and demonstration that the chosen therapy is effective. Each component has standardization and quality assurance components to ensure optimal patient care. The demonstration of effective therapy is most often incorporated into patient management in sleep laboratories and is recognized under the current Medicare coverage policy which requires a facility-based polysomnography (CPT codes 95810 or 95811) in order for CPAP to be covered.

One of the common paradigms for management of sleep apnea syndrome is to provide these components through a sleep center that can ensure quality for all or some of the components. This commonly includes clinical reassessment when a referring physician has not provided a comprehensive clinical evaluation with respect to the patient's sleep-related complaint, clinical attention to multiple problems that contribute to or complicate the presenting complaint, and administration of multimodal therapy. Centralizing this complex patient management paradigm helps to ensure high quality, efficient, and cost-effective patient care by linking appropriately educated, trained, and qualified practitioners to the tests being ordered and the therapy provided. Degrading this paradigm by disseminating a myriad of monitoring instruments to be used in a non-standardized method by practitioners who do not have the appropriate skill set runs the substantial risk of similarly degrading the quality and efficiency of patient care. On the other hand, centralization of patient management arguably creates obstacles to access to care.

Before considering a change in CMS policy, three questions need to be carefully addressed regarding the use of home portable monitoring in obstructive sleep apnea. These questions will be discussed in the context of the request for modification of policy CMI 60-17.

Do sleep centers meet the current needs for diagnosis and management of sleep apnea?

Inadequate access to sleep laboratory diagnosis has recently been cited as a potential rationale for the use of home portable polysomnography (2, 3). Certainly marked regional variations in the number of laboratory polysomnographies performed (3) suggests that in some areas either identification of clinical disease or access to laboratories or both may be restricting the initiation of appropriate therapy for sleep apnea.

Currently, sleep laboratories in the United States are performing an estimated 1.5 to two million polysomnographies a year. Based on a 16% sample from an unpublished survey of the 728 AASM accredited sleep centers in the fall of 2003, there are

approximately 1.8 million patients being seen and 980,000 polysomnographic studies performed per year in accredited facilities. Among the multidisciplinary practitioners seeing these sleep patients are 2,656 board-certified sleep specialists. The number and volume of unaccredited laboratories likely far exceeds that of accredited laboratories. Integrating the aforementioned information results in a very conservative estimated volume of polysomnographies of 1.5 to 2 million per year. This is well within the range of previous estimates.(3)

Though previous estimates of disease prevalence for sleep apnea would suggest that a large proportion of patients were undiagnosed (4), it is not clear that there are prohibitive delays to scheduling patients for necessary evaluation and treatment in the current setting of rapidly expanding laboratory resources. The metric most often utilized for determining the effect of limited laboratory availability on diagnosis and treatment is the time patients wait for laboratory diagnostic procedures. Unfortunately, accurate assessments for these delays are not available on a national basis. Nevertheless, it is clear that, with the exception of the VA system where market forces are not in effect, in many areas patients wait for diagnostic procedures for less than one month for a condition that is usually stable for many years.(2) Sleep laboratories should and do exercise the option to prioritize patients who have more substantial and immediate risks so that performance of polysomnography is expedited in such patients.

Is unattended portable monitoring an accurate way to assess the severity of obstructive sleep apnea?

Decisions regarding medical policy should rely, when possible, on evidence based medicine rather than references to case series or uncontrolled clinical trials. The process of evidence grading should include guideline construction based on the highest levels of evidence performed by those with expertise in the process of evidence grading and familiarity with the content area. An extensive and broad-based evidence review and guideline paper has just been completed on portable monitoring (5) with participation and endorsement from three professional organizations: the American Academy of Sleep Medicine, the American Thoracic Society, and the American College of Chest Physicians. Evidence was graded according to a standardized process and recommendations were based on levels of evidence. (6, 7)

This guideline paper on portable monitoring detailed the range of monitoring from single parameters to multichannel recording and portable polysomnography. Based on clinical evidence grading of 49 articles, this published guideline does not recommend portable monitoring without direct supervision of a technician (i.e., unattended portable monitoring), thus *home portable monitoring is not recommended.* Eight of the fourteen articles cited in Dr. Davidson's request are included in this evidence review. One of the articles cited by Dr. Davidson has not yet been reviewed or published by a peer-reviewed journal. Additional articles included with the request by Dr. Davidson are include in a subsequent evidence-based review below.

Are there newer studies which would justify a change in the guideline recommendations since its publication? A supplemental literature review was conducted to capture any studies published after the literature review for the original guideline paper on portable monitoring. A total of 59 new articles were captured in this supplemental search. Of these articles, 6 met the inclusion criteria for the literature search described in the original guideline paper, and were classified as follows. Four of the 6 articles described studies using a Type 3 monitor (minimum of 4 channels monitored, including ventilation or airflow, heart rate or EKG, and oxygen saturation), 1 article described a study using a Type 2 monitor (minimum of 7 channels monitored, which is similar to in-laboratory polysomnography), and 1 article described a study using a Type 4 monitor (1-2 channels, including oxygen saturation or airflow). The addition of four studies of Level II evidence grade to the Type 3 monitor group discussed in the original paper does indicate that higher-level evidence is beginning to accumulate for Type 3 monitors. However, the variability in the false negative results confirms the original conclusion that the reliability of the Type 3 monitors for making patient-care decisions is below acceptable standards. Similarly, the addition of one study apiece (each of Level II evidence grade) to the Type 2 and Type 4 monitor groups discussed in the original paper, does not change the conclusion that these type of monitors should not be used in an unattended setting. Thus, despite the addition of the studies derived this supplemental literature review, the original conclusion from the prior guideline paper is unchanged: *home portable monitoring is not recommended.*

In contrast to the evidence-based process above, the request in section 9 refers to a limited number of studies without evidence review. In addition, the comment in this section: "There are ***no reports*** of poor correlations, error in diagnosis or adverse events as a result of multichannel home sleep testing in these studies" is an inaccurate representation of the published limitations of portable monitoring. In three investigations, poor quality necessitated exclusion of 5 to 20% of polysomnographic recordings performed in the home.(8-10) One study noted a four-fold higher rate of failure in home vs laboratory polysomnography.(8) Disease misclassification rates have recently been reported in up to 65% of patients with limited channel home recordings. (11) The Academy is concerned that the literature review provided by Dr. Davidson is cursory and overstated and provides no new information beyond already published practice parameter papers.

It could be argued that in single research studies with very large cohorts such as the Sleep Heart Health Study (12-14), polysomnography demonstrated highly reproducible results that were similar in the attended laboratory setting and with unattended portable monitoring. These studies, however, have highly standardized processes of technician training, quality assurance, and standardization of procedures (15) that exceed the requirements of accredited sleep laboratories. These standards are never duplicated for portable home monitoring procedures performed for clinical purposes. Extrapolation from the results in large research studies would suggest that any clinical practice paradigm incorporating home monitoring would need to include a credentialing process requiring standards and instrumentation similar to those used

in these studies. Such standards would likely exceed those currently in effect for full laboratory polysomnography. The converse of standardization, i.e., non-standardized techniques and equipment, can result in serious errors in ascertainment. Varying the criteria for the definition of respiratory events can result in differences in disease prevalence ranging from 11% to 83% in the same population.(10)

Is it appropriate to have home portable monitoring ordered and performed by surgeons, cardiologists, and primary care physicians [or dentists] as part of the clinical evaluations of sleep apnea?

Obstructive sleep apnea is a syndrome that often presents with an array neurocognitive, behavioral, and cardiovascular consequences. In many cases, the presenting symptoms may be quite subtle. A correct decision for performing any polysomnographic study is based on an appropriate clinical evaluation of patient complaints and identification of any alternative or contributing causes for symptoms as diverse as daytime sleepiness, depressed mood and increasing peripheral edema. These symptoms may reflect etiologies as diverse and common as insufficient sleep, restless legs syndrome, depression and venous insufficiency. The ability of the practitioner to determine whether a respiratory disturbance index of 9 on a polysomnographic study in a symptomatic patient is clinically significant will depend on the clinician's skill set. (CPAP therapy for an RDI of 9 is currently reimbursable in symptomatic patients and this RDI was the median value in an unselected random patient population in the Sleep Heart Health Study).(10) The skill of the clinician making the determination of when to order a polysomnographic study and how to act on the results is variably determined by type of training and clinical experience. Thus, the greatest expertise will be exemplified by those clinicians who are certified as Sleep Medicine specialists.

Increasingly, outcomes research has demonstrated that care for a number of common conditions is better delivered by specialists in that field. For example, Go et al concluded that "Patients with coronary disease or heart failure in the United States who are treated by cardiologists appear more likely to receive evidence-based care and probably have better outcomes" in comparison to generalist physicians.(16) For critically ill patients, it is now generally accepted that care given in a "closed" ICU format by intensivists results in improved clinical outcomes.(17) As a consequence, the Leapfrog group now recommends that ICU's be staffed around the clock by intensivists.(18) There has been less evidence validating the effectiveness of sleep specialists. Nevertheless, emerging data in the field of Sleep Medicine does support the premise that specialists deliver better and more cost effective care than non-sleep specialists.(19) This conclusion with respect to sleep apnea and polysomnographic monitoring has been formalized by both the Canadian and American Thoracic Societies as well as the American Academy of Sleep Medicine.(20-22)

Sleep Medicine is a specialty of medicine. The purpose of having specialty training and certification in Sleep Medicine is to offer the highest quality of care to patients. Sleep Medicine has had an established certifying examination since 1978 and the

American Board of Sleep Medicine was founded in 1991. There are currently 2,656 board-certified sleep specialists. Furthermore, the Accreditation Council for Graduate Medical Education recently has established requirements for fellowship training in Sleep Medicine.

Most Sleep Medicine specialists practice within the context of sleep disorders centers or laboratories. Many such facilities are accredited by the American Academy of Sleep Medicine indicating that they have met the Academy's standard for delivery of safe and high quality care for sleep disorders patients. In contrast, purveyors of ambulatory limited channel recordings are often poorly trained, unregulated and not subject to any quality assurance standards. As noted previously, in order to obtain useful data from such recordings, stringent quality standards need to be enforced. Thus, CMS's current requirement that the diagnosis of sleep apnea be made in laboratory-based facilities is both reasonable and prudent. Accepting the argument made by Dr. Davidson that cardiologists and other practitioners (such as dentists) untrained in Sleep Medicine are competent to interpret any level of sleep study, much less unattended and often technically poor limited channel studies, would lead to poor quality of care, over-utilization of resources and increase the probability of inaccurate or missed diagnoses. Such a scenario would be analogous to an otolaryngologist interpreting an echocardiogram to diagnose valvular heart disease. Hospital credentialing committees would never approve such privileging and it is unreasonable that CMS should consider acquiescing to it either.

The Academy appreciates the opportunity to provide you with these comments and we look forward to meeting with you and your staff later this month. Please feel free to contact our Executive Director Jerry Barrett, 708-492-0930 if you would like any further information on this matter.

Sincerely,

Conrad Iber, MD

Conrad Iber, MD
President, American Academy of Sleep Medicine

CC: Jesse Polansky, MD, MPH
Tiffany Sanders, MD
Francina Spencer

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Practice Parameters for the Use of Portable Monitoring 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

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Background: A variety of devices are used to evaluate patients with a potential diagnosis of obstructive sleep apnea (OSA). A committee comprised of members of the American Academy of Sleep Medicine, American Thoracic Society, and American College of Chest Physicians systematically evaluated data on the use of these devices and developed practice parameters.

Devices reviewed: Three categories of portable monitoring (PM) devices were reviewed with regard to assessing the probability of identifying an apnea-hypopnea index (AHI) of greater or less than 15 in attended and unattended settings. Type 2 (minimum of seven channels, including EEG, EOG, chin EMG, ECG or heart rate, airflow, respiratory effort, oxygen saturation), Type 3 (minimum of four channels, including ventilation or airflow (at least two channels of respiratory movement, or respiratory movement and airflow), heart rate or ECG and oxygen saturation) and Type 4 (most monitors of this type measure a single parameter or two parameters) devices were evaluated, and in-laboratory, attended polysomnography was used as a reference.

Specific recommendations:

(1) Insufficient evidence is available to recommend the use of Type 2 PM devices in attended or unattended settings.

(2) Type 3 PM devices appear to be capable of being used in an attended setting to increase or to decrease the probability that a patient has an apnea-hypopnea index greater than 15.

(3) The use of Type 3 PM devices in an unattended setting is not recommended to rule in, rule out, or both rule in and rule out a diagnosis of OSA.

(4) There is some evidence that the use of Type 3 PM devices in an attended in-laboratory setting may be acceptable to both rule in and rule out a diagnosis of OSA if certain limitations are in place. These limitations include manually scoring the records, using the devices only in patients without significant comorbid conditions, having an awareness that symptomatic patients with a negative study should have a Type 1 study, and not using these devices for titrating positive airway pressure or conducting split-night studies.

(5) The use of Type 4 PM devices in attended or unattended settings is not recommended.

General Recommendations: Type 3 and 4 PM devices cannot score sleep and, therefore, do not meet some current Medicare guidelines. The use of PM devices is not recommended for general-population screening or in the absence of a pretest probability of the patient having a diagnosis of OSA, for complaints other than those associated with OSA, without review of raw data during interpretation, by physicians without familiarity with their use and limitations, and without trained personnel to perform technical scoring. Future research should address the use of PM devices in patients with comorbid conditions; non-White patients and women; larger, better-controlled studies; studies focused on the use of Type 2 and 3 devices; studies focusing on decision making and outcomes rather than simple classification using arbitrary cutoffs; and studies that seek to elucidate cost-effectiveness data on the use of PM devices.

Key Words: sleep apnea, obstructive; sleep disorders, diagnosis; polysomnography; practice guidelines; standards; consensus; quality assurance; sleep apnea syndromes; sleep-disordered breathing

Citation: Practice parameters for the use of portable monitoring 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):907-13.

INTRODUCTION

OBSTRUCTIVE SLEEP APNEA (OSA) IS A COMMON DISORDER THAT AFFECTS BOTH CHILDREN AND ADULTS. It is characterized by periods of breathing cessation (apnea) and periods of reduced breathing (hypopnea). Both types of events have similar pathophysiology and are generally considered equal with respect to their impact on patients. Accurately counting these events and assessing their impact on sleep, oxygen desaturation, and disruption of normal physiology form the basis of diagnostic polysomnography.

The standard approach to diagnosing OSA is in-laboratory, technician-attended, polysomnography. Portable monitoring (PM) has been proposed as a substitute for polysomnography in the diagnostic assessment of patients with suspected OSA. The proponents suggest that PM requires less technical expertise, is less labor intensive and time consuming, and is easier for patients to access. The term *portable monitoring* encompasses a wide range of devices that can record as many signals as does attended polysomnography or only 1 signal, such as oximetry. The use of PM to establish the diagnosis of OSA has been the subject of previous reviews of the literature.

In addition to these reviews, previous guidelines on the use of PM were issued between 1994 and 1999 by a number of authors, including the American Academy of Sleep Medicine, (AASM, formerly the American Sleep Disorders Association),[1-3] The Agency for Health Care Research and Quality (AHRQ—formerly the Agency for Health Care Policy and Research),[4] and ECRI (formerly the Emergency Care Research Institute).[5] Although differences in analysis techniques and classification of PM devices exists among these studies, a uniformity of recommendations resulted. Succinctly summarized, these reports indicate that at the present time there is insufficient evidence to recommend the widespread use of PM devices compared to traditional, technician-attended, laboratory-based polysomnography (Table 1). Nevertheless, PM devices are widely used in locations where patient access to attended laboratory polysomnography is limited or non-existent. There has also been a continuing development of new technology. Because policies guiding the development of AASM practice parameters indicate that all practice parameters are to be reviewed at least every 5 years, most of the AASM guidelines on the use of PM devices were approaching sunset review provisions. When the AASM was in the process of conduct-

ing a review of the literature that had been published since the 1994[1] and 1997 practice parameters[2,3] were developed, the American Thoracic Society (ATS) and the American College of Chest Physicians (ACCP) were also considering undertaking similar projects on this complex issue. After discussion at an ACCP-hosted conference on PM in September 2002, the 3 groups joined forces in this process. Additional groups that expressed a willingness to assist with input were the National Association for the Medical Directors of Respiratory Care and the Australasian Sleep Association.

The ATS, the AASM, and the ACCP identified members of a Steering Committee, Evidence Review Committee, and Guideline-Writing Committee. The final products are 3 coordinated publications: a review paper,[6] this practice-parameters paper, and an executive summary.[7] The procedures and methods used in this project are outlined briefly in this paper but are provided in much greater detail for the interested reader in the companion review paper. The detailed conflict of interest policy adopted is discussed in the review paper. [1.0] It is noted that all three members of the Guideline Writing Committee are directors of academic sleep disorders centers and are experienced in the use of both polysomnography and various portable monitoring devices in their clinical and/or research work, although none participate in industry sponsored research trials on PM devices for the diagnosis of apnea , or have financial interests outlined in the review paper in the conflict of interest exclusions.

This practice parameters paper is based entirely on the evidence presented in the review paper and is neither a consensus paper nor a statement of acceptable clinical practice based on expert opinion. The limitations on the strength of the recommendations are outlined in detail below.

METHODS

The compiling of evidence in the review paper[6] was collected by the Research Triangle Institute (University of North Carolina) under contract for this project and focused primarily on articles published since the 1997 AASM review.[2,3] A meta-analysis of results was not used because too much heterogeneity existed between studies with respect to types of signals measured, criteria used to define a breathing event, scoring of signals from PM devices, and study quality. Once collected, the articles were rated using the method of Sackett et al[8] to establish their levels of evidence. This method for rating the evidence of published studies regarding diagnostic tests was used because it closely aligns with accepted methods used for rating the quality of articles regarding therapeutics and prognosis. In addition this method focuses on the key aspects of the design of studies that are used to evaluate diagnostic tests: avoiding selection bias (by using a consecutively referred sample of patients), blinding interpreters, and avoiding verification bias (by performing the reference standard on all subjects). The Evidence Review Committee then compiled and analyzed these data and issued the companion report referred to as the *review paper*,[6] which will be frequently cited in this document through the use of numbers in square brackets, referring to a specific section or sections of the review paper.

Table 1—Portable Monitoring Devices

Type of Portable Monitoring Device	Parameters Measured
Type 2 Comprehensive Portable	Polysomnography Minimum of 7 channels, including electroencephalogram, electrooculogram, chin electromyogram, electrocardiogram or heart rate, airflow, respiratory effort, and oxygen saturation
Type 3 Modified Portable Sleep ApneaTesting	Minimum of 4 channels monitored, including ventilation or airflow (at least 2 channels of respiratory movement, or respiratory movement and airflow), heart rate or electrocardiogram, and oxygen saturation
Type 4 Continuous Single or Dual Bioparameters	One or 2 channels, typically including oxygen saturation or airflow

Based on data from the review paper, this paper identifies recommended practice parameters for using PM to study adult patients with suspected OSA. They define principles of practice that should meet the needs of most patients in most situations. These practice parameters should not, however, be considered inclusive of all proper methods of care or exclusive of other methods of care reasonably directed to obtaining the same results nor of those that consider the particular needs of the patient and available resources. The ultimate judgment, regarding the propriety of any specific care, must be made by the physician in light of the individual circumstances presented by the patient and the available diagnostic and treatment options and resources. The AASM, the ATS, and the ACCP expect these practice parameters to have a positive impact on professional behavior, patient outcomes, and possibly healthcare costs. These practice parameters reflect the state of knowledge at publication and will be reviewed, updated, and revised as new information becomes available. It is hoped that these practice parameters and the future research section will stimulate better studies to evaluate the role of PM devices in the evaluation of OSA patients.

BACKGROUND

The authors of the review paper[6] selected 3 endpoints to be used in their detailed review and analysis of published data. They evaluated the ability of PM devices to *reduce* the probability that a patient has an abnormal apnea-hypopnea index (AHI) (to rule out the disorder), *increase* the probability that a patient has an abnormal AHI (to rule in the disorder), and both *reduce and increase* the probability that a patient has an abnormal AHI (to both rule out and rule in the disorder).

The authors also reviewed secondary endpoints, including the reproducibility of PM results, the costs and benefits of using of PM devices, the failure rates of PM devices, patient populations studied, and the generalizability of findings.

Four types of sleep-study monitoring devices are referenced in the review paper and were defined as Type 1—standard, in-laboratory, technician-attended, overnight polysomnography—and 3 types of PM devices: Type 2—comprehensive portable polysomnography; Type 3—modified portable sleep-apnea testing; and Type 4—continuous single or dual bioparameter recording (Table 1). Using the review-paper data analysis (types of monitors, sensitivity, specificity, likelihood ratios, pretest and posttest probabilities, study biases, patients' comorbid conditions, nondiagnostic results, etc.), the authors of these practice parameters determined the utility of the devices to provide reliable diagnoses for patients with OSA. Making this determination was a much more complex task than simply evaluating a single endpoint; it required that the data be compiled in a comprehensive manner to provide answers to practical diagnostic and treatment questions that are generated when a patient is referred to a sleep laboratory. The authors developed the practice parameters after identifying the strengths, deficiencies, and reliability or reproducibility of the devices, as provided in the review paper.[6]

LIMITATIONS

In order to correctly apply these practice parameters in the appropriate clinical setting, the physician must be cognizant of both the limitations of the data and of applications related to patient care.

The assessment of the utility of PM devices is based on the AHI

The main method of comparison between PM devices and the gold standard (polysomnography) was based on the agreement in the AHIs and/or using thresholds of severity defining sleep apnea to assess the agreement of PMs with polysomnography in identifying patients with or without OSA. Other methods of comparison such as a decision to treat or observe may be more meaningful but was not generally possible from the evidence. The current approach has limitations since only minor dif-

ferences between the AHI from a PM device and polysomnography can degrade sensitivity and specificity if the difference crosses an arbitrary threshold. For example, an AHI of 12 on one test and 17 on another will lead to apparent disagreement if a threshold value of AHI of 15 episodes/hour is used even though the difference is not clinically meaningful. Patient outcomes may be a more meaningful endpoint but would need to be assessed in studies of complete pathways. Such studies would likely compare both the efficacy of diagnostic and treatment algorithms based on information from PM devices with similar algorithms based on polysomnography. The outcomes would likely depend on both the accuracy of information obtained from the PM devices and the utility of the associated algorithms.

The use of in laboratory polysomnography as the gold standard has limitations

The evidence-based analysis used the AHI determined in the laboratory by polysomnography as the gold standard. However, it is possible that some patients slept more poorly in the laboratory than at home (the polysomnography AHI could underestimate the typical severity) or spent more time in the supine position in the laboratory (the polysomnography AHI could overestimate the typical severity).

These recommendations are based on the premise that polysomnography is available for patients. Previous AASM guidelines addressed some examples of when portable monitoring might be an acceptable alternative in the absence of available polysomnography [1]. These included: (1) for patients with severe clinical symptoms that are indicative of OSA, and when initiation of treatment is urgent and standard polysomnography is not readily available; (2) for patients unable to be studied in the sleep laboratory; (3) for follow-up studies where diagnosis has been established by standard polysomnography and therapy has been initiated, and the intent is a comparison to evaluate response to therapy. Nothing in the current review paper has provided evidence-based assessment to formally change such recommendations. Clinical judgment made by the physician in light of individual circumstances has to be applied to individual patients.

The use of PM devices is limited to the evaluation of OSA

The review and the data address only the evaluation of OSA; therefore, the compiled data are insufficient to recommend the use of PM devices in evaluating patients with any disorders other than suspected OSA.

The use of PM devices does not meet some Medicare qualification criteria

The review and the data were primarily related to patients with an AHI of at least 15 because the studies that were analyzed often did not include patients with an AHI of less than 15, and the results may not be able to be extrapolated to lower AHI levels. This limitation may become progressively more relevant with the new Medicare guidelines, which suggest that an indication for treatment may be an AHI of greater than 5 plus symptoms. Because Type 3 and Type 4 PM devices do not include electroencephalography and, therefore, cannot reliably record or evaluate sleep, the use of these devices does not meet the Medicare guidelines that require at least 2 hours of documented sleep time.

Table 2—Levels of Recommendations

Term	Definition
Standard	This is a generally accepted patient-care strategy that reflects a high degree of clinical certainty. The term *standard* generally implies the use of Level I evidence, which directly addresses the clinical issue, or overwhelming Level II evidence.
Guideline	This is a patient-care strategy that reflects a moderate degree of clinical certainty. The term *guideline* implies the use of Level II evidence or a consensus of Level III evidence.
Option	This is a patient-care strategy that reflects uncertain clinical use. The term *option* implies either inconclusive or conflicting evidence or conflicting expert opinion.

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Aspects of PM use may have limitations based on practical applications to clinical use

The usual clinical application of polysomnography in the sleep laboratory is to both rule in and rule out a diagnosis of OSA (by reporting the AHI). The authors of the review paper performed separate analyses of the PM devices with respect to their ability to rule out (low likelihood ratio) [Table 2], rule in (high likelihood ratio) [Table 3], and then to both rule out and rule in (both low and high likelihood ratio) [Table 4] a diagnosis of OSA. These practice parameters were developed using this process (rule out, rule in, or both) in order to follow the data analysis in the review paper. However, few sleep disorders centers would (or could under insurance parameters) use a test to rule out a diagnosis of OSA, and if the results of the first study did not provide an answer, subsequently perform another test on the same patient to rule in a diagnosis of OSA, or vice versa. In addition, the literature review and analysis identified an appreciable number of patients with neither a positive nor a negative result [Table 4], and inconsistencies were found in the results of data from various PM devices in the same class.

Research studies that have evaluated the diagnostic accuracy of PM devices have used multiple thresholds for defining positive and negative results and assessing sensitivity and specificity. Although these results, which supplied the data for the review-paper analysis, used a variety of definitions of OSA, they were "standardized" to an AHI of 15 in order to allow a between-studies comparison of the data. Unfortunately many studies have not suggested that the evaluated devices have a single cut-off with both high sensitivity and specificity, which is a practical limitation of significance when moving that research data to laboratory use. Analysis by best-reported sensitivity gives the benefit of the lowest false negatives and lowest likelihood ratio.

RECOMMENDATIONS

The following recommendations are categorized based on classification of evidence from the accompanying review paper as adapted from the suggestions of Sackett[8] and as outlined in greater detail in the review paper [2.3.1 –2.3.2] (Table 2). Recommendations are given as standards, guidelines, and options as adapted from Eddy (Table 2).[9]

Type 2 PM Devices: Comprehensive Portable Polysomnography

1. **The clinical use of Type 2 PM devices in the attended setting is not recommended to evaluate patients with suspected OSA. (Option)**
2. **The clinical use of Type 2 PM devices in the unattended setting is not recommended to evaluate patients with suspected OSA. (Option)**

Although Type 2 devices theoretically should most resemble in-laboratory polysomnography and be best for calculating an AHI because they

Table 3—Levels of Evidence

Level of Evidence	Study Design
I	Blinded comparison, consecutive patients, reference standard performed on all patients
II	Blinded comparison, nonconsecutive patients, reference standard performed on all patients
II	Blinded comparison, consecutive patients, reference standard not performed on all patients
IV	Reference standard not applied blindly or independently

Adapted with permission from Sackett D. Rules of evidence and clinical recommendations for the management of patients. Can J Cardiol 1993;9:487-9 and [2.3.1].

permit sleep scoring, relatively few published studies provide data and address this use. Based on the small number of published studies, the absence of sensitivity and specificity data, and the low level of evidence, inadequate data are available to recommend the clinical use of Type 2 PM devices in the attended or unattended setting. In addition, a high rate of data loss in the unattended setting is often reported. [4.1.1; 4.1.2; 4.1.3; 4.2.3; 4.3.2.1; Table 2]. The absence of support for such use and the "option" guideline are based on insufficient data.

Type 3 PM Devices: Modified Portable Sleep Apnea Testing

Recommendations concerning the use of Type 3 PM devices to reduce the probability that a patient has an AHI less than 15 (ie, rule out a diagnosis of OSA at a level selected by the review-paper authors for their statistical cutoff; this is also one of the levels set by Medicare to reflect a level of significance)

3. **The use of some Type 3 PM devices in an attended setting can decrease the probability that the patient has an AHI greater than 15. (Standard)**

Type 3 PM devices have potential utility and reasonable reliability in the attended setting among patients who have a low pretest probability of having OSA and in whom the study is being conducted to confirm that impression. Use in this setting requires careful patient selection by history and examination findings to first identify a reasonably low pretest probability that OSA is present. [4.3.2.2; 4.1.1]

4. **The use of Type 3 PM devices in an unattended setting is not recommended to decrease the probability that the patient has an AHI greater than 15. (Guideline)**

The clinical use of Type 3 PM devices is not recommended in the evaluation of OSA in the unattended setting. Although some higher-level evidence (up to a Level II) is beginning to accumulate, a relatively high percentage of false negative results makes the reliability of these devices for making patient-care decisions below accepted standards. [4.1.1; 4.3.2.2]

Recommendations concerning the use of Type 3 PM devices to increase the probability that a patient has an AHI greater than 15 (ie, rule in a diagnosis of OSA at a level selected by the review-paper authors for their statistical cutoff; this is also one of the levels set by Medicare to reflect a level of significance)

5. **Some Type 3 PM devices can be used in an attended setting to increase the probability that a patient has an AHI greater than 15. (Standard)**

Available studies were of a higher quality and high likelihood ratios. Some had a lower percentage of false positive results. [4.1.2; 4.3.2.3]

6. **The use of Type 3 PM devices in an unattended setting is not recommended to increase the probability that a patient has an AHI greater than 15. (Guideline)**

The data supporting the usefulness and utility of PM devices in the unattended setting to increase the probability of the patient having a diagnosis of OSA is too limited to support clinical utility and is associated with high false-negative and false-positive rates. [4.1.2; 4.3.2.3]

Recommendations concerning the use of Type 3 PM devices to both increase and decrease the likelihood that a patient has a diagnosis of OSA with a single threshold, which is the most practical clinical use.

For practical use in a sleep center, a device should be able to reliably identify whether an AHI is less than or greater than a specific cutoff point, not simply determine one or the other. That does not appear to be the case with the use of Type 3 PM devices in unattended studies [Table 4, column 14]. In most unattended studies, multiple cutoff levels and careful screening seem to be necessary for these devices to be used. The data from unattended studies suggest that one would have to accept high rates of patients with neither a positive nor a negative (having a nondiagnostic) result, if PM devices were to be used in this setting. In addition, different AHI levels would be needed to provide a reasonable sensitivity and specificity.

7. **The use of Type 3 PM devices may be acceptable in an attended in-laboratory setting to both rule in and rule out a diagnosis of OSA. Such a use, however, would require limitations, as noted below. (Standard) [4.1.3; 4.3.2.4]**

   a) *In nearly all of the studies providing evidence that Type 3 devices could be used in an attended in-laboratory setting, the results were analyzed either manually or using a combination of automatic and manual scoring. Thus, careful review of raw data appears to be necessary.*

Scoring of results should comply with the presented evidence, which indicates the superiority of manual scoring over automatic computer-generated scoring. For most of these devices, software that is currently used clinically differs from the software used in the studies, a factor that may need additional consideration. The use of time in bed rather than accurately scored total sleep time already produces changes in sensitivity and specificity and should not be compounded by use of automated scoring at this point. [1.1.3; Table 5; Appendix 4 – Table 10]

   b) *Type 3 PM devices should be used only in a population similar to those that have been studied—patients may not have significant comorbidities such as chronic obstructive pulmonary disease, congestive heart failure, etc.—and should be used in a sleep-clinic population (not applied as generalized screening).*

Patients should be carefully screened prior to undergoing testing with a Type 3 PM device to assess the pretest probability that they do or do not have OSA. Clinically, this screening should be performed in a reliable manner by the laboratory that is doing the testing and would typically include an examination, a history, and information from a partner questionnaire. Assessment of the patient's pretest probability of having OSA is an important component of use in order to match the evidence, as reported in the review paper.[6] .

The use of PM devices has been considered here only with regard to the assessment of OSA and not to the assessment of other possible conditions in which cortical arousals, or an assessment of actual disruptions of sleep, may be an important part of clinical evaluation. The significance of this likely relates to the type of event being evaluated, the type of PM used, and has to be considered within the limitation of the outcomes being assessed. [4.3.1]

   c) *Type 3 PM devices do not measure sleep. Additionally, the AHI provided by Type 3 PM devices tends to underestimate the polysomnogram-defined AHI because monitoring time rather than total sleep time is used in the denominator. [4.1.2.2; 4.3.1]*

Under current Medicare guidelines, which require documentation of 2 hours of sleep, the use of type 3 PM devices does not fit accepted Medicare definitions, an important awareness for any physician using PM devices. Use of monitoring time rather than total sleep time may result in misclassification of patients with mild disease.[4.3] The importance of this consideration would depend on the sleep efficiency of the patient during the time studied and the severity of OSA.

   d) *Symptomatic patients with a nondiagnostic or negative Type 3 PM study should undergo a definitive evaluation to determine the cause of their symptoms. If a sleep disorder remains part of the*

clinical consideration, a full attended polysomnogram (Type 1 study) should be conducted.

e) *Patients with a diagnosis of OSA based on the results of a Type 3 PM study need a subsequent polysomnogram (Type 1 study) if continuous positive airway pressure (CPAP) titration is needed.*

Data on the use of Type 3 PM devices for reliably titrating CPAP are not available. The use of traditional polysomnography as a split study has not been compared to the use of Type 3 PM devices followed by CPAP titration with a traditional polysomnogram, and, therefore, no data are available regarding potential time or cost savings.

f) *The use of Type 3 PM devices is not recommended for split-night studies because there is little or no evidence to support such an approach. There is no data on such use of PMs.*

g) *The ability of Type 3 PM devices to perform their identified function could be device specific, and capabilities and limitations of each device must be taken into account by the interpreter of the studies. [4.3]*

8. The use of Type 3 PM devices in an unattended setting is not recommended to rule in and rule out a diagnosis of OSA. (Guideline)

Studies of limited quality using different AHI levels, and a high rate of patients with nondiagnostic studies (neither positive nor negative results) limit support for the use of Type 3 PM devices. The studies that evaluated the use of Type 3 PM devices in the unattended setting had high numbers of patients without a positive or negative result.

Type 4 PM Devices: Continuous Single Or Dual Bioparameter Recording

Type 4 PM devices generally use oximetry and a second (airflow-assessment) parameter, which varies between studies; depending upon the type of airflow evaluation, results among patients may also vary. Due to the high variability between devices and methods-related results, many of the results are device specific, and data across this group as a whole are difficult to evaluate. [4.1.1; 4.1.2; 4.1.3; 4.3.2; Tables 2, 3, and 4]

Recommendations concerning the use of Type 4 PM devices in the attended setting to increase, decrease, or both increase and decrease the probability of the patient having an AHI greater than 15.

9. The routine use of Type 4 PM devices with oximetry and at least one other airflow parameter in an attended setting is not recommended to increase the probability that a patient has an AHI greater than 15 (Option)

Some studies suggest that there is some benefit to using Type 4 PM devices in an attended setting; however, the fact that these studies show a significantly higher percentage of false-positive results is of concern, as are conflicting data, especially when coupled with issues concerning utility. These studies used a variety of methods, including oximetry alone, oximetry with airflow or nasal transducers, and other combinations such as heart rate or snoring. Among the higher-level studies, likelihood ratios are variable, as are higher numbers of false positives, resulting in conflicting data. [4.1.2; 4.3.2.3]

10. The routine use of Type 4 PM devices with oximetry and at least one other airflow parameter in an attended setting is not recommended to decrease the probability that a patient has an AHI greater than 15. (Option)

Serious limitations, as noted in the review paper, suggest that the clinical use of Type 4 PM devices may not be satisfactory for providing reliable patient care and for making treatment decisions. These limitations include a high rate of false-negative results in Level 1 and Level 2 studies, plus conflicting results from Level 1 studies. In addition, a high percentage of patients with neither positive nor negative results was seen across studies that had multiple levels of evidence [Table 4]. Other cautions are also noted: the studies that evaluated the use of Type 4 PM devices measured a variety of channels (1-3 variables), used inconsistent criteria for determining desaturations and sampling rates, and employed a variety of scoring methods (manual, computer generated, or both) [4.1.1; 4.3.2.2]

11. The routine use of Type 4 PM devices with oximetry and at least one other airflow parameter is not recommended in an attended setting to both increase and decrease the probability that a patient has an AHI greater than 15. (Option)

The studies that used Type 4 PM devices in an attempt to both reduce and increase the probability of a patient having a diagnosis of OSA used multiple cutoffs to achieve better likelihood ratios and had a high rate of patients who did not have a diagnostic result. Both of these factors defeat the purpose of a screening test and result in a lack of adequate data to establish the use of Type 4PM devices. In some studies in an attended setting, oximetry alone seems to be able to reduce, but not reasonably eliminate, the probability of the patient having an AHI of less than 15 even when the patient obtains sufficient sleep, as confirmed by other measures. If cyclic desaturation is present, clear evidence of the fact may be helpful but is not specific.

Moreover, Type 4 PM devices neither identify apnea nor measure and confirm sleep. Because oximetry identifies only saturation changes and not apneas or hypopneas and does not document sleep, the use of Type 4 PM devices does not meet Medicaid or Medicare criteria, particularly when considering an exclusion of OSA. The absence of significant desaturation does not mean the absence of upper airway resistance, hypopneas, or even apneas. [4.1.3; 4.3.2.4]

Recommendations concerning the use of Type 4 PM devices in the unattended setting to increase, decrease, or both increase and decrease the probability of a patient having an AHI greater than 15.

12. The use of Type 4 PM devices in the unattended setting with oximetry and one other airflow parameter is not recommended for diagnosing OSA or confirming that a patient has an AHI greater than or less than 15. (Guideline)

Insufficient evidence is available to suggest such use, especially in light of 1 Level 1 study in which the diagnosis of OSA was not adequately classified in 50% of patients. A substantial number of the studies used different thresholds to try to achieve their classification. In addition, most of the studies had substantial numbers of patients who were not classified as being either positive or negative with respect to an AHI greater than or less than 15. [4.1.3; 4.3.2.4]

AREAS REQUIRING SPECIAL ATTENTION

13. The use of PM devices is not recommended for general screening or clinical use without available knowledge of the patient's sleep-related history and complaints.

High and low pretest probability are important in assessing the effectiveness of the devices. Few studies were conducted in the general population. Based upon available evidence, data from the high-probability group for OSA (referrals to sleep centers) would not necessarily be generalizable for screening purposes among the general population.

14. The use of PM devices is not recommended in patients with comorbid conditions or secondary sleep complaints because there is little evidence to support the use of PM devices in evaluating these conditions or to diagnose other sleep disorders.

Most of the studies that have been evaluated in determining the evidence for the use of PM devices excluded patients with comorbid conditions, resulting in a lack of data in these conditions [4.2.4.2]. Instead, these studies focused on patients with a high pretest probability of having OSA and little or no comorbidity [5.1]. In all of the recommendations, where the possible use of PM devices is appropriate, subjects with comorbid conditions such as chronic obstructive pulmonary disease, heart failure, stroke, or severe hypertension (which are comorbidities that are frequently seen among patients in sleep clinics) should be studied with Type 1, traditional polysomnography rather than with PM devices. The review paper also raises concerns about the lack of data regarding the use of PM devices in women and ethnic groups other than Whites.

15. Even when PM devices are noted as being possibly useful, the general use of all types of devices across that category is not necessarily recommended. The laboratory should confirm that the commercial device selected in a category has specific studies documenting its performance and that it conforms to the use characteristics of that category as a whole.

All devices in a given category are not the same. Many of the results are probably device-type dependent. Any laboratory that uses a PM device should confirm that quality scientific studies have been conducted for that device and that the interpreting physician is familiar with the limitations, exclusions, and weaknesses of the particular device and interface components.

16. The review of raw data and the use of manual scoring for interpreting data from PM devices is recommended.

The interpreting physician must be able to assess and review the raw data generated by a PM device and must consider that data when interpreting the sleep study. Based on available evidence, scoring should be performed manually. The use of processed and computer-scored data has more errors and diagnostic problems.

17. Physicians with sleep training and familiarity with the devices and their limitations should interpret studies generated by PM devices and should review the raw data, as noted above. Trained and qualified technicians should perform any technical scoring.

FUTURE RESEARCH

Developing a consensus on the best way to validate the use of PM devices is urgently needed. Based on the limitations defined earlier, we need to move beyond assessing validity based on sensitivity and specificity for whether the AHI is above or below a fixed threshold, particularly given the known night-to-night variability in AHI. The urgency recognizes the fact that many OSA patients currently do not have access to in-laboratory polysomnography.

The reviewers of the evidence on the use of PM devices outlined recommendations for future research [5.0-5.3.2]. They addressed the lack of studies concerning the use of PM devices in primary-care populations, in patients with comorbid conditions such as heart failure or chronic obstructive pulmonary disease, and in ethnic populations other than Whites, and they highlighted the need for studies with sufficient numbers of women [5.1]. The reviewers also proposed key and important features of future studies to ensure that data with a high evidence level would be obtained [5.2]. The reader is referred to the review for the complete discussion.[6] A few points that the guideline-writing committee felt were particularly important are mentioned further.

As is evident throughout this report, the major problem in this area is lack of evidence. In general, studies include small sample sizes and are not particularly well designed. Other significant barriers to progress exist. First, 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 only to that device and cannot be extrapolated to other devices, even to those in the same class. Because devices have different performance characteristics, lumping together results from devices of the same class can result in misleading conclusions. Even within a given device class, (eg, oximetry) results may be affected by the data-processing method, including digital signal analysis, sampling rate, and averaging time. If the use of PM devices is to develop its full potential, consensus must be reached regarding the variables that need to be recorded for simplified, general, respiratory-only, studies.

Several specific points that were raised by the evidence review committee for future studies are as follows: Certainly patients involved in research projects that are attempting to validate PM devices should also have a reference study (usually attended polysomnography). The order of the PM study and the reference standard study should be randomly assigned. The interpreter of each study should be blind to the results of the corresponding study. Clear descriptions of how breathing events are defined and the oximeter sampling rate and averaging time should be specified. Criteria for a positive result and a negative result should be selected before the study is conducted. Ideally the same cutoff should be chosen to both diagnose and exclude a diagnosis of OSA, thereby avoiding having large numbers of patients with neither a positive nor a negative study. The review also addressed the confounding problem of night-to-night variability; obviating this problem would optimally entail conducting multiple nights of both the PM study and the reference study.

In addition to the above issues, the guideline-writing committee also felt that more data were definitely needed concerning Type 2 devices. As technology advances, the ease and practicality of using Type 2 devices should increase. Use of these devices would also assist with evaluating sleep quality as well as respiratory disturbances. Certainly the use of Type 2 PM devices should have the potential to provide equivalent data to that generated by traditional polysomnography if the problem of data handling, analysis, and loss can be solved.

As type 3 PM devices in the attended setting were the only class that could be recommended for routine use (with the limitations as listed in mind), standardization of this type of device seems particularly important. The unattended type 3 PM study is probably the most common use of these devices in clinical practice especially in locales where polysomnography is not available. Given the better evidence for use of the devices in the attended setting it is possible that different devices, different study designs, or different strategies for application of type 3 devices in the unattended setting could result in better evidence for their use in this setting. Clearly, more studies in the unattended setting are needed.

The use of PM devices to make a diagnosis of OSA will not necessarily be of benefit unless timely treatment is available. On the basis of the available evidence, type 3 PM devices could not be recommended for either attended or unattended positive pressure titration. However, auto-titrating positive pressure devices have been shown to be effective in the attended setting in some CPAP naive patients .[10, 11] As these devices usually monitor only airflow and snoring there is no obvious reason why type 3 PM devices could not be successful for attended pressure titration. More study of the use of these devices in this setting seems warranted. For patients with limited access to attended polysomnography, a method to provide adequate treatment as well as diagnosis is needed.

At present there are also no clear guidelines on the expertise physicians reading PM devices should have. Limitations on reimbursement of PM studies are undoubtedly driven in part by a reasonable concern that there may be widespread use of these devices by physicians who have little training in sleep medicine.

Finally, the utility of diagnostic testing should always be assessed in terms of treatment algorithms and final patient outcomes. For example, if a PM study is conducted that results in a positive diagnosis of OSA and is then followed by a traditional Type 1 study for the titration of positive airway pressure, the utility of PM devices will be reduced if most PM studies are positive. Cost comparisons to an alternative, split-night-study format are needed to validate the assumption, espoused by some,

that the use of PM devices will result in cost savings. However, before outcome studies are initiated, there is a need to more clearly define the goals of the studies and investigations, assessing the overall outcomes of diagnosis and therapy, and comparing results from Type 1 studies to the results from more simplified studies.

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Comment #78:
Submitter: David R. Nielsen, MD, FACS
Organization: American Academy of Otolaryngology-Head and Neck Surgery
Date: May 5, 2004
Comment:

(See next page)

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American Academy of Otolaryngology — Head and Neck Surgery

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May 5, 2004

Tiffany Sanders, MD
Centers for Medicare and Medicaid Services (CMS)
7500 Security Boulevard
Baltimore, MD 21244-1850

Dear Dr. Sanders:

I am writing in response to Dr. Terence Davidson's request for CMS to re-assess the national coverage determination (NCD) for diagnosis and treatment of obstructive sleep apnea (OSA) to include multi-channel home sleep testing as an alternative to facility-based polysomnography (PSG). The American Academy of Otolaryngology—Head and Neck Surgery (AAO-HNS/F) would support consideration of this proposal as a potential cost-effective alternative to PSG and as means of improving access to care for the large adult population at risk for sleep apnea.

At the same time, AAO-HNS/F recognizes the brief response window, and we would like to take this opportunity to raise several concerns that we request you consider as you review the available clinical evidence and formulate your final decision:

1) Is home testing equivalent to and realistically considered as a replacement for overnight PSG? If not, are there circumstances for which it should be deemed a first-line diagnostic service?

2) How will issues of inaccurate data-collection be addressed (e.g., inadequate equipment maintenance or patient instruction, loss or malposition of sensors)?

3) If an initial home sleep test is unsuccessful, will the beneficiary be allowed to have a PSG?

4) We request that CMS clearly delineate the qualifications and/or training requirements of physicians who will be offering this test to beneficiaries. We consider this to be necessary to prevent misdiagnoses, inappropriate frequency of service, or sub-optimal treatment planning.

5) We request that CMS clarify whether this test will or will not include self-titrating Continuous Positive Airway Pressure (CPAP). This may be necessary to eliminate potential confusion regarding Medicare coverage of this technology.

AAO-HNS/F welcomes the opportunity to comment further both with CMS and other stakeholders that share an interest in this potential policy change. Thank you for the opportunity to comment. If I can be of any further assistance, please call me directly at 703-519-1559.

Sincerely,

David R. Nielsen MD

David R. Nielsen, MD, FACS
Executive Vice President and CEO, AAO-HNS/F

cc: Terence Davidson, MD
Physician Payment Policy Committee (3P)
Edward Weaver, MD, Chairman, Sleep Disorders Committee
Francina Spencer, CMS

Comment #79:
Submitter: Daniel M. Steigman, MD
Organization: Fallon Clinic
Date: May 6, 2004
Comment:

(See next page)

FALLON CLINIC

May 6, 2004

Ms. Francina Spencer
CMS
7500 Security Blvd
Baltimore, MD 21244-1850

Dear Ms Spencer:

It was a pleasure talking to you recently about the issue of home sleep studies. I will not reiterate the issues that Dr. Davidson brought up in his proposal, with which I agree. I presume that he has forwarded you the studies he's referring to. I would like to share the thoughts of a clinician who has evaluated large numbers of patients for sleep apnea over the course of the past 10 years and who has transitioned his sleep practice from one based on hospital based PSGs to home sleep monitoring.

I am a pulmonary physician at the Fallon Clinic which is a 250 physician multispecialty group in Worcester MA. In our group the ordering of sleep studies is limited to pulmonary, ENT and neurology physicians. I have seen an exponential rise in the number of patients referred to me for evaluation of sleep apnea. This I believe is due to increased awareness of the disease by patients and primary care physicians along with the epidemic of obesity that is now plaguing our country. I began to think that there has to be a more efficient way of diagnosing these patients than making them go to the hospital overnight. Also in my experience the vast majority of patients I sent for PSGs confirmed my diagnosis of obstructive sleep apnea. I also found significant resistance to hospital-based studies on some patients part- single parents for example obviously couldn't leave home for a night. I then made inquiries to other similar groups concerning their practice of sleep medicine- and found that similar high quality groups to ours such as Group Health Cooperative in Seattle and Kaiser Permanente used home monitoring as well to diagnose OSA and had good results with it. Thus we transitioned our patients to home studies. We use a. level 3 system measuring pulse, oximetry, chest wall motion and airflow. It has been a stunning success. Clinically the diagnosis has been easy to make in the majority of cases showing apneas and hypopneas necessary to make the diagnosis of OSA and patients have been happy. Another advantage of this system has been that instead of doing 4-5 hours or less of CPAP titration in the lab during a split night - home study patients have the advantage of using an auto CPAP device at home which they can use for several days to a week in order to get used to the CPAP mask and to allow for a more lengthy and realistic analysis of their CPAP needs.

Now that I believe that we've validated the concept of home studies in my own practice a new (to me) technology has come along that I believe makes the home diagnosis and treatment of OSA even more compelling. This is a device called a Watch-PAT that measures peripheral arterial tone, pulse, oximetry and motion. It is worn on the wrist, has two finger probes and downloads data taken during sleep to a chip similar to

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what is found in a digital camera. The data is then downloaded to a PC and in about 30 seconds it tells us the number of obstructive respiratory events that occur during the night. Thus I can see a patient on Monday, give him this device on Tuesday, he returns it on Wednesday and if he has OSA he can go home with an Auto CPAP device. Gone is the need for subjective scoring of hours of multichannel tracings, the wait for scoring to be done etc. If this device comes into use we will finally be able to get a handle on the nearly epidemic disease of OSA. I am enclosing one recently published article and one that has been accepted for publication in SLEEP (1,2) both of which indicate that the device is very accurate in measuring obstructive events. Another advantage of this device is that it through a motion sensor can determine sleep time accurately, thus eliminating one of the objections that people have about home sleep studies that do not involve EEGs i.e. that one cannot tell for sure what the "denominator" is in determining a Respiratory Disturbance Index. (i.e. number of respiratory events/ Total Sleep Time)

I think several points have to be made:

1. I believe that there is enough data to support the use of home sleep studies multiple studies have shown adequate sensitivity and specificity I will not reiterate them as I am sure Dr Davidson has referred them to you.

2. To demand perfection compared to inpatient PSGs is unnecessary- patients sleep under different conditions at home than the lab. As patients are going to be treated with home CPAP all that is needed is a high enough RDI to institute therapy Whether the RDI is 25 in a home study and 50 during a PSG really is not relevant in this setting. If, as may happen on occasion, in a patient with a high clinical probability of OSA has a negative home study lab based polysomnography is always available as a backup

3. The paper in press from Sleep indicates to me that there is significant variability in the actual numbers of respiratory events during sleep at home vs. the sleep lab. The Watch PAT is a very simple device- there should be no difference in how it is used in the home compared to the lab. The decreased (but still excellent) R-value in home vs. lab Watch PAT indicates to me that variability is intrinsic to sleep events at home vs. lab and differences in home vs. lab RDI cannot be used to impugn the accuracy of home studies.

4. Physicians always should have a variety of tests to order for a given condition- why is OSA the only syndrome that requires the most sophisticated test possible? A physician with suitable clinical skills (for example I see over 100 patients for sleep evaluations/ year) should be able to interpret a home study result and if it does not fit with a clinical impression order a more complex test.

5. Interestingly the use of polysomnography for diagnosis of OSA is a historical artifact. William Dement's history of sleep medicine (3) tells us that the sleep studies that we now use today are a modification of a study that was used to diagnose narcolepsy. When these people decided to try to evaluate sleep apnea

they just added respiratory parameters to the diagnostic array for narcolepsy, never evaluating other ways of making this diagnosis.

6. It is my belief that specialty societies who opine that home sleep studies require more research or are not adequate to diagnose OSA have significant conflicts. The sleep labs that they are involved with are significant sources of professional and hospital revenues – home studies will significantly reduce the need for these facilities. They will also, however make them more accessible for people who really do need them- such as patients with non-OSA related sleep disorders.

7. As a practical matter we don't have enough inpatient sleep lab beds to test the 4% of men and 2% of women who have this disorder (4). The more patients we can diagnose, the more morbidity from daytime sleepiness we can ameliorate, the more potential end organ disease we may avoid.

Thank you very much for your consideration.

Yours truly,

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Evaluation of a Portable Device Based on Peripheral Arterial Tone for Unattended Home Sleep Studies*

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Background: **Diagnosis of obstructive sleep apnea syndrome (OSAS) by ambulatory systems is a growing practice in view of the large number of patients awaiting correct diagnosis. The Watch PAT100 (WP100) [Itamar Medical; Caesarea, Israel] is a portable device based on the peripheral arterial tone (PAT) signal, and is designed for unattended home sleep studies.**

Objectives: **To evaluate the efficacy, reliability, and reproducibility of the WP100 device for the diagnosis of OSAS as compared to in-laboratory, standard polysomnographic-based manual scoring.**

Design and methods: **One hundred two subjects (78 men; 69 patients with OSAS and 33 normal volunteers; mean ± SD age, 41.4 ± 15.2 years; body mass index, 26.8 ± 5.5) underwent in-laboratory full polysomnography simultaneously with WP100 recording. Fourteen subjects also underwent two additional unattended home sleep studies with the WP100 alone. The polysomnography recordings were blindly scored for apnea/hypopnea according to the American Academy of Sleep Medicine criteria (1999), and the polysomnography respiratory disturbance index (RDI) [PSG-RDI] was calculated. The WP100 data were analyzed automatically for the PAT RDI (PRDI) by a proprietary algorithm that was previously developed on an independent group of subjects.**

Results: **Across a wide range of RDI levels, the PRDI was highly correlated with the PSG-RDI ($r = 0.88$, $p < 0.0001$), with an area under the receiver operating characteristic curve of 0.82 and 0.87 for thresholds of 10 events per hour and 20 events per hour, respectively. The PRDI scores were also highly reproducible, showing high correlation between home and in-laboratory sleep studies ($r = 0.89$, $p < 0.001$).**

Conclusion: **The WP100 may offer an accurate, robust, and reliable ambulatory method for the detection of OSAS, with minimal patient discomfort.** ***(CHEST 2003; 123:695–703)***

Key words: ambulatory; automatic analysis; obstructive sleep apnea syndrome; peripheral arterial tone; respiratory disturbance index; sleep

Abbreviations: ASDA = American Sleep Disorders Association; AUC = area under the curve; BMI = body mass index; ESS = Epworth sleepiness scale; OSAS = obstructive sleep apnea syndrome; PAT = peripheral arterial tone; PRDI = peripheral arterial tone respiratory disturbance index; PSG-RDI = polysomnography respiratory disturbance index; RDI = respiratory disturbance index; ROC = receiver operating characteristic; WP100 = Watch PAT100

Obstructive sleep apnea syndrome (OSAS) is considered to be a major public health problem. The prevalence of OSAS is estimated at 2% and 4% for adult women and men, respectively, most of whom are undiagnosed and untreated.[1] The in-laboratory sleep study using full polysomnography and the manual scoring criteria set by the American Academy of Sleep Medicine is considered the "gold standard" for OSAS diagnosis.[2] The severity of the disorder is expressed as the respiratory disturbance index (RDI), which is the number of apneas/hypopnea events per hour of sleep. The high cost of in-laboratory, full-night polysomnography, together with long waiting lists for sleep studies, have led to the commonly used procedure of "split-night" for

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patients with OSAS, as well as to the development of a variety of ambulatory sleep study systems.[3]

The earliest ambulatory devices were based on overnight pulse oximetry alone, an easy and simple technology for diagnosing OSAS.[4] However, it has been shown that the pulse oximeter suffers from limited accuracy.[5,6] Portable full polysomnography and other multiple-channel ambulatory devices are frequently complex and cumbersome.[7]

The American Sleep Disorders Association (ASDA) has classified sleep study systems into four categories: level 1, in-laboratory attended standard polysomnography; level 2, unattended home sleep study with comprehensive portable devices incorporating the same channels as the in-laboratory standard polysomnography; level 3, unattended devices, which measure at least four cardiorespiratory parameters; level 4, unattended devices recording one or two parameters.[8]

The Watch PAT100 (WP100) [Itamar Medical; Caesarea, Israel] is a four-channel unattended ambulatory device (level 3) based on the peripheral arterial tone (PAT) signal with three additional channels: heart rate (derived from the PAT signal), pulse oximetry, and actigraphy (both are embedded in the device). The PAT signal measures the arterial pulsatile volume changes of the finger that are regulated by the α-adrenergic innervation of the smooth muscles of the vasculature of the finger, and thus reflects sympathetic nervous system activity.[9] The WP100 indirectly detects apnea/hypopnea events by identifying surges of sympathetic activation associated with the termination of these events. This information is further combined with heart rate and pulse oximetry data that are analyzed by the automatic algorithm of the system (which was developed on a prior group of patients). This detects respiratory events and calculates the PAT RDI (PRDI).

The primary objective of this study was to evaluate the efficacy of the device for diagnosing OSAS, by comparing its results to simultaneous polysomnography recordings. Secondary objectives were to evaluate the feasibility and reproducibility of the WP100 in an unattended home setting.

Materials and Methods

Study Population

The study group consisted of 69 consecutive subjects referred to the clinical sleep laboratory of the Technion Sleep Medicine Center (Haifa, Israel) with suspected OSAS, and 33 additional healthy adult volunteers, without complaints of snoring or daytime sleepiness. None of the subjects had previously undergone a polysomnographic study. Seventy-eight subjects were men, and 24 were women. The mean ± SD age of the group was 41.4 ± 15.2 years. The men were slightly more obese (body mass index [BMI] of 27.5 ± 5.5 vs 24.5 ± 4.8) and had higher Epworth sleepiness scale [ESS] scores (8.7 ± 5.8 vs 7.0 ± 5.7, respectively) [Table 1]. Twenty percent of the subjects had hypertension, and 4% had coronary artery disease. The exclusion criteria for the study were as follows: permanent pacemaker, nonsinus cardiac arrhythmias, peripheral vasculopathy or neuropathy, severe lung disease, status postbilateral cervical or thoracic sympathectomy, finger deformity that precludes adequate sensor application, use of α-adrenergic receptor blockers (24-h washout period required), and alcohol or drug abuse during the last 3 years. The study protocol was approved by the Ethics Committee of the Rambam Medical Center, and the subjects gave their written informed consent prior to participation.

Study Procedure

The study was a blinded study comparing the automatically scored WP100 results (PRDI) to the manually scored polysomnography RDI (PSG-RDI). The WP100 and polysomnography data were recorded simultaneously in a time-synchronization manner in the sleep laboratory. A subgroup of 14 patients from the study cohort also underwent two additional unattended home sleep studies with the WP100 device only. The subjects were selected for this subgroup based on their home location, and only included those subjects within a 30-mile range of the sleep laboratory. In the WP100 home studies, the device was delivered to the patient's home, the patient applied the device, and following the overnight recording the device was returned to the sleep center for automatic analysis. The requirements for WP100 data analysis are a personal computer and the proprietary PAT software, which can be run on Windows 98 operating system (Microsoft; Redmond, WA) or higher.

The overnight sleep studies were considered acceptable for data analysis if none of the following rejection criteria occurred: (1) polysomnography-related rejection (polysomnography actual sleep time < 1.5 h, technical failure of synchronizing the polysomnography to the WP100, and poor quality of polysomnographic recording); and (2) WP100-related rejection (WP100 valid sleep time < 1.5 h). Patient demographic and medical information, as well as the ESS questionnaire, were acquired by interview prior to the sleep study.

Equipment

WP100 Device: The WP100 used in the unattended sleep studies is comprised of a battery-powered, forearm-mounted console unit placed just above the wrist, and two finger-mounted probes: pulse oximetry and PAT probe (Fig 1).

Forearm-Mounted Console Unit: This unit provides the power supply, first-level signal processing, signal conditioning and filtering, data acquisition, and storage functions required for monitoring the pulse oximetry and PAT signals. In addition, data from an embedded actigraph and heart rate derived from the PAT

Table 1—*Study Group Mean Age, BMI, and Total ESS Score by Gender**

Variables	Male (n = 78)	Female (n = 24)	Overall (n = 102)
Age, yr	42.0 ± 15.0	39.6 ± 16.2	41.4 ± 15.2
BMI	27.5 ± 5.5	24.5 ± 4.8	26.8 ± 5.5
ESS score	8.7 ± 5.8	7.0 ± 5.7	98.3 ± 5.8

*Data are presented as mean ± SD.

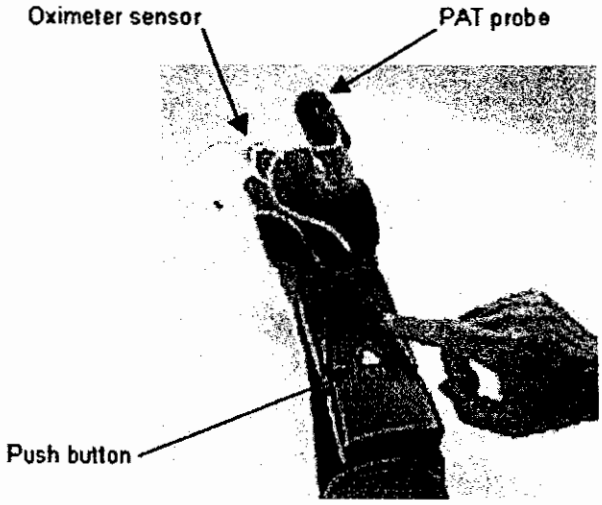

FIGURE 1. The WP100 device worn on a forearm. The PAT sensor and the built-in pulse oximetry sensor are attached to the fingers. The acquired PAT and pulse oximeter data, as well as the embedded actigraph data, are stored on a compact flash disk (not shown). The device is switched on by the indicated push button.

signal are continuously recorded. All four signals are recorded at a sample rate of 100 Hz and stored on a removable flash disk throughout the study.

Pulse Oximeter Probe: A standard-type pulse oximeter probe (Nonin OEM 2 oximetry module, 8000J; Nonin; Ellös, Sweden) is applied to a finger in a conventional manner according to the instructions of the manufacturer.

PAT Probe: The second finger probe measures the PAT of the patient's fingertip. Previous applications of this technology have been described[6–12]; however, in this study the method was specifically adapted for ambulatory unattended use.

Essentially, the WP100 finger sensor applies a uniform pressure field over the distal two thirds of the finger, including the fingertip. Previous plethysmographic devices that enveloped the fingertip, such as venous occlusion plethysmography collection cuffs tended to be pushed off the finger when pressurized. However the split-thimble design of the PAT probe allows it to actively clamp itself to the finger while applying a pressure field that facilitates the unloading of arterial wall tension without causing distal venous pooling and distension, thus avoiding the induction of venoarterial-mediated vasoconstriction.[13]

A transmission mode photoelectric plethysmograph situated at opposing lateral sides at about the middle of the distal phalanx is used to measure the optical density changes associated with pulsatile blood volume changes of the finger. The proximal two thirds of the pressure field buffers the sensing region from extraneous and artifactual signals such as perturbations in the venous system.

Isobaric, Volume-Displacement PAT Probe Design: A unique feature of the PAT finger probe is its ability to generate its own pressure field at a fixed level of pressure irrespective of the size of the finger.[14] The pressure field is created by the insertion of a finger into the probe (Fig 2, *top, A*). When the finger is inserted into the probe, a proportionate amount of air is shifted from the inner compartment of the probe to its outer compartment, causing the pretensioned outer membrane to be pushed off the wall of the inner shell and thus apply pressure to the air within the probe. The elastic properties of the balloon-like outer membrane are such that over a wide range of volumes it creates a constant pressure.

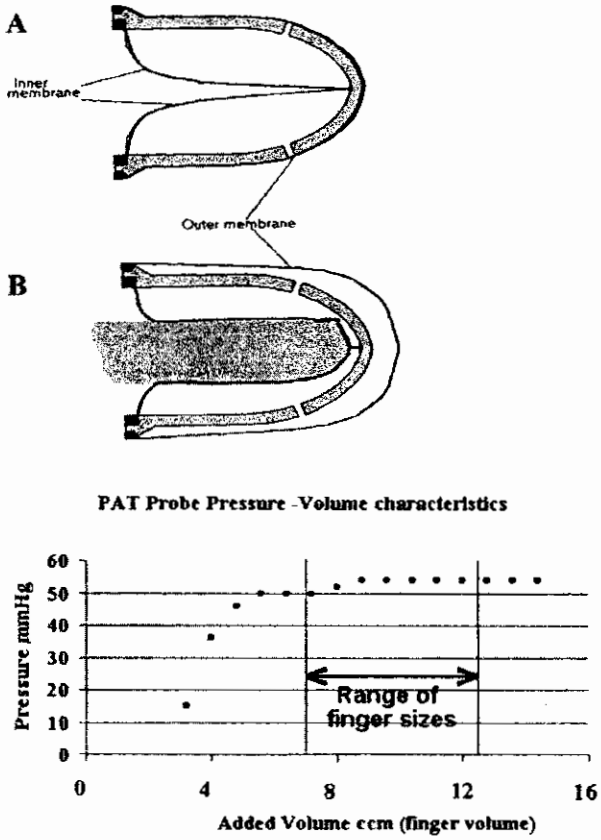

FIGURE 2. *Top, A:* The WP100 probe contains an inner and an outer membrane on either side of a rigid plastic thimble. Before insertion of the finger, approximately 10 mL of air is situated between the inner membrane and the plastic thimble. Since the inner membrane is not stretched, the air is at atmospheric pressure. The outer membrane is fitted to the external wall of the plastic thimble, and is slightly stretched from its natural size. *Top, B:* When the finger is inserted into the probe, a proportionate amount of air is shifted from the inner compartment of the probe to its outer compartment, causing the pretensioned outer membrane to be pushed off the wall of the inner shell and to thus apply pressure to the air within the probe. Insertion tabs for aiding in the insertion of the finger and an external probe cover are not shown. *Bottom:* pressure vs added finger volume graph of the PAT finger probe. It can be seen that beyond an added value of approximately 7 mL, the applied pressure remains constant. This constant pressure at variable volume behavior is characteristic of elastic balloons.

The actual pressure that the probe generates in response to differing volume displacements is shown in Figure 2, *bottom, B*. This shows that the probe applies a common and constant level of pressure over a broad range of finger sizes encountered in an adult population.

The physical basis for the ability of the probe to generate a fixed pressure is described by the law of Laplace, which relates the pressure within a distensible hollow object to the wall tension and the radius such that the pressure is proportional to wall tension divided by radius. In the case of elastic balloons in general, and in the specific case of the elastic outer membrane of the probe, wall tension varies in direct proportion to radius, and thus pressure remains constant over a large range of volumes.

Automatic Algorithm: The automatic algorithm of the WP100

is based on the PAT signal amplitude, heart rate, and oxygen saturation. The sleep/wake detection is based on data recorded by the built-in actigraph.

Polysomnography

Data Collection: Standard in-laboratory, overnight polysomnography was performed using a computerized polysomnography system (Embla; Flaga Medical; Reykjavik, Iceland), with the following channels: EEG (C3-A2 and O2-A1), electrooculogram (right and left), chin electromyogram, arterial oxygen saturation, nasal-oral airflow (thermistor), ECG, chest and abdominal wall motion (piezo electrodes), bilateral tibialis electromyogram, body position, and auxiliary channel with a synchronizing signal from the WP100 device.

Scoring: The polysomnography recordings were scored manually for sleep stages[15] and respiratory events (apnea/hypopnea) according to the American Academy of Sleep Medicine criteria, 1999.[2] An apnea/hypopnea event was defined as an airflow amplitude reduction of > 50% from the baseline lasting at least 10 s, or having a less significant reduction in the airflow amplitude, but with the presence of arousal or oxygen desaturation of at least 3%. The PSG-RDI was calculated as the number of apnea/hypopnea events per hour of sleep. The scorer had no access to the WP100 data or results while scoring the polysomnography data.

Statistical Analysis

The correlation between the PRDI and PSG-RDI was assessed using the Pearson correlation coefficient and Bland-Altman plots. Receiver operating characteristic (ROC) analysis was carried out to evaluate the WP100 diagnostic capability. A threshold of PSG-RDI > 10 was used as the cut-off point for OSAS diagnosis,[16] and PSG-RDI > 20 was defined as the commonly used cut-off point for intended CPAP treatment.[17] Based on these threshold definitions, ROC curves were derived, and areas under the curves (AUCs) were calculated.

Results

Of 102 in-laboratory studies, 3 studies were rejected: 2 polysomnography studies had synchronization failure and 1 study was rejected due to PAT valid sleep time < 1.5 h. Three of the 28 at-home PAT studies were originally rejected due to technical failure but were repeated successfully; thus, the at-home rejection rate was 3 of 31 studies. None of the participants requested to withdraw from the study due to discomfort or any other reason, and no adverse or side effects were reported. A wide range of OSAS severities were represented in the study group, with about equal number of subjects[16–19] in each of the following RDI categories: 0 to 10, 11 to 30, 31 to 50, and > 50 events per hour.

Figure 3 shows a scatter graph that demonstrates the high and statistically significant correlation coefficient between the PSG-RDI scores and the PRDI scores ($r = 0.88$, $p < 0.0001$, $n = 99$). Figure 4 shows a Bland-Altman plot of the differences between the PSG-RDI and the PRDI values vs the

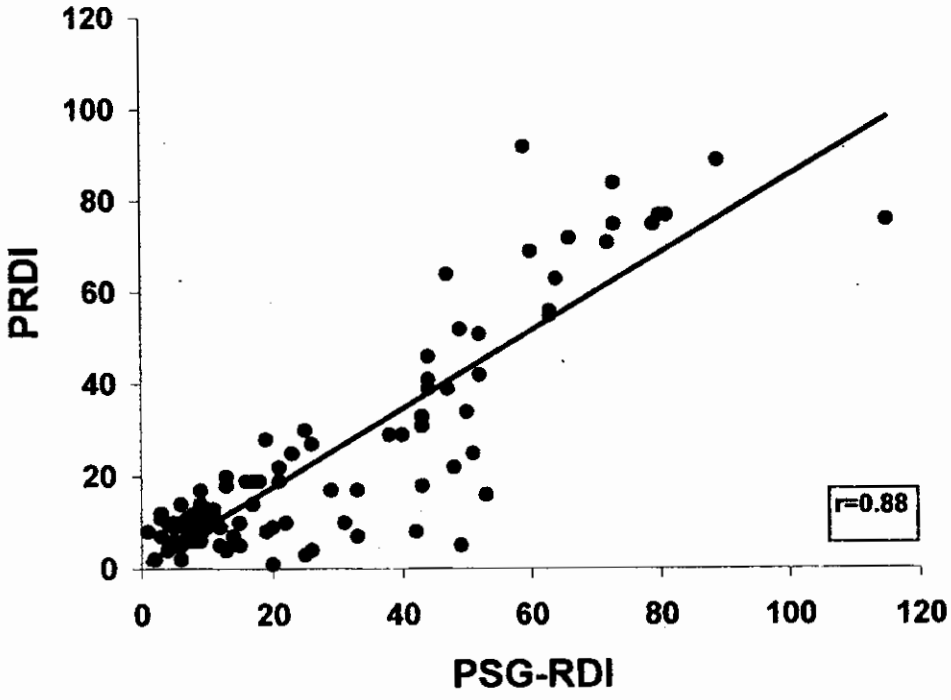

FIGURE 3. Scatter plot of PRDI (x axis) vs standard PSG-RDI (y axis). A very high and statistically significant correlation ($r = 0.88$, $p < 0.0001$, $n = 99$) was found between the PRDI (by automatic algorithm) and the PSG-RDI (manual scoring).

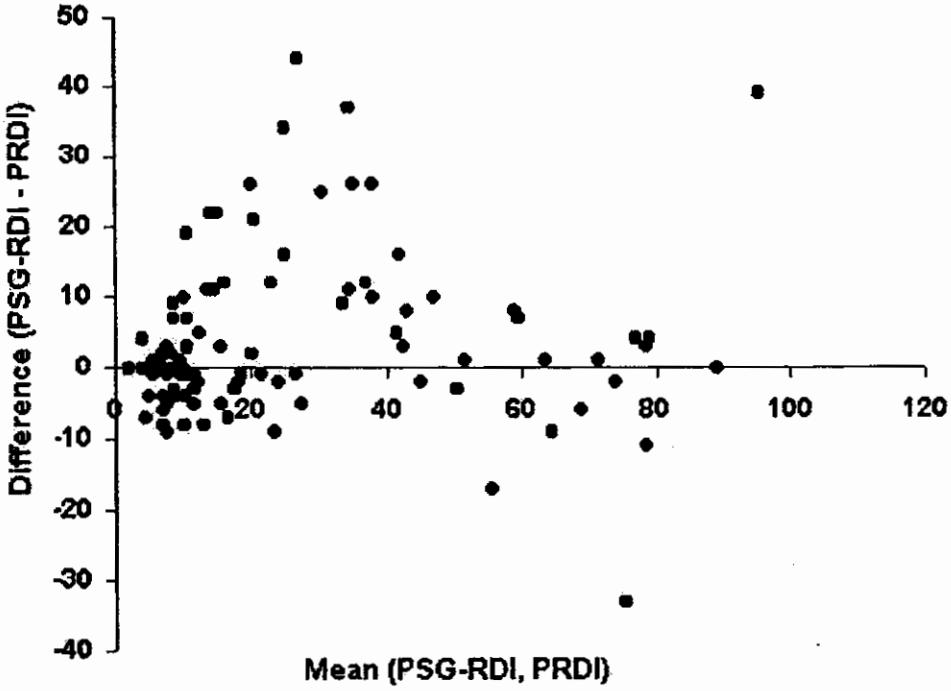

FIGURE 4. Bland-Altman plot (n = 99), showing differences between PSG-RDI and PRDI (y axis) vs the corresponding average values of the two values (x axis). Across a wide range-of-OSAS severities (RDI levels), there was a good agreement between PRDI and the PSG-RDI.

corresponding averages of the two RDI indexes. There was a slight tendency for the PAT to underscore events in the mild range of OSAS, and to overscore events in the severe range.

As can be seen in Figures 5, 6, the WP100 results in the sleep laboratory studies were highly reproducible in the home sleep studies ($r = 0.89$, $p < 0.001$, $n = 14$), with high correlation coefficient between the two home sleep studies ($r = 0.94$, $p < 0.001$, $n = 14$), indicating high internight consistency.

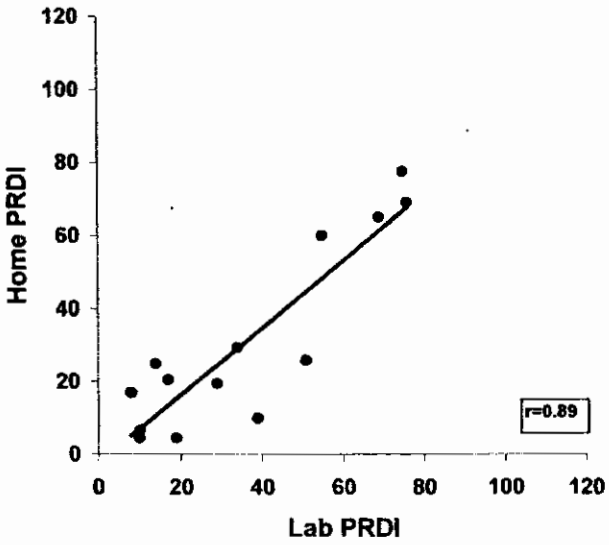

FIGURE 5. Scatter plot of home PRDI: mean of two nights (y axis) vs PRDI recorded in the sleep laboratory (Lab) (x axis). A highly significant correlation ($r = 0.89$, $p < 0.001$, $n = 14$) was found.

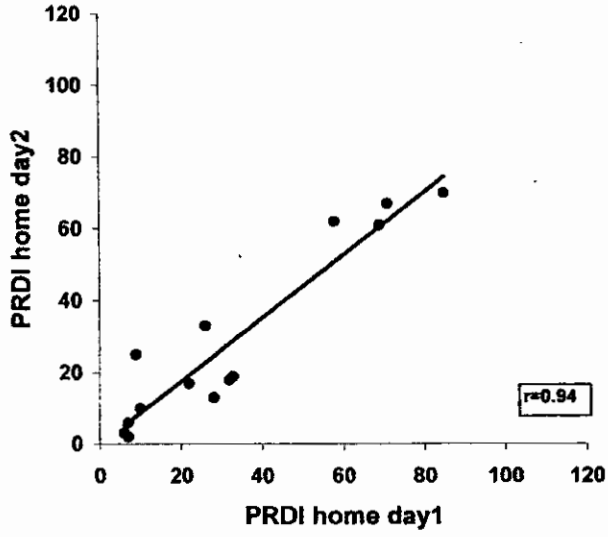

FIGURE 6. Scatter plot of repeated home PRDI values. PRDI of the second home sleep study (y axis) is plotted against PRDI recorded in the first home sleep study (x axis). A highly significant correlation ($r = 0.94$, $p < 0.001$, $n = 14$) was found between the two at-home sleep studies.

Figure 7 shows the ROC curve reflecting the diagnostic capability of PRDI when the threshold of PSG-RDI was set at 10 for OSAS diagnosis.[16] Figure 8 shows the ROC curve reflecting the diagnostic capability of PRDI when the threshold of PSG-RDI was set at a value of 20, which represents a PSG-RDI level at which continuous positive airway pressure therapy is indicated.[17] The areas under the ROC curves were 0.82 ($p < 0.0001$) for the diagnostic threshold (PSG-RDI > 10), and 0.87 ($p < 0.0001$) for the therapeutic threshold (PSG-RDI > 20).

Discussion

This study shows that the WP100 is a simple, reliable and accurate device for ambulatory diagnosis of OSAS. The in-laboratory measured PRDI results were well correlated with the in-laboratory PSG-RDI results ($r = 0.88$, $p < 0.0001$), with good efficacy for both OSAS diagnosis (RDI > 10)[16] and for CPAP therapy indication (RDI > 20)[17] [AUC of 0.82 and 0.87, respectively]. The in-laboratory PRDI results were highly reproducible in the home sleep studies, with correlation coefficients of 0.89 and 0.94, for laboratory vs home and between two home sleep studies, respectively. Given the expected inter-night variability for RDI,[18,19] the high consistency found in this study is even more significant. The device reliability is also demonstrated by the relatively low rejection rates; 1 of 102 studies in the sleep laboratory, and 10% of the home sleep studies, which were carried out as unattended self-administered studies. For comparison, data loss rate was evaluated as 4 to 33% with other unattended home sleep systems.[7,20-23]

Over 80% of patients with moderate-to-severe OSAS are undiagnosed and untreated, which can subsequently lead to the severe sequelae of the syndrome. Kapur et al[24] concluded that patients with undiagnosed OSAS had considerably higher medical costs than age and sex-matched non-OSAS subjects, and that the OSAS severity was associated with the magnitude of medical costs. The long waiting lists for in-laboratory polysomnography studies, which are expensive and time consuming, have led to an intensive search for ambulatory alternatives. According to the ASDA standards of practice (1994), sleep study devices are classified into four levels, from the attended, in-laboratory, full polysomnography (level 1) to the unattended, at-home, single/double-channel recording (ASDA level 4).[8] In general, there appears to have been a tradeoff between the amount of information and the simplicity of the device. Simple

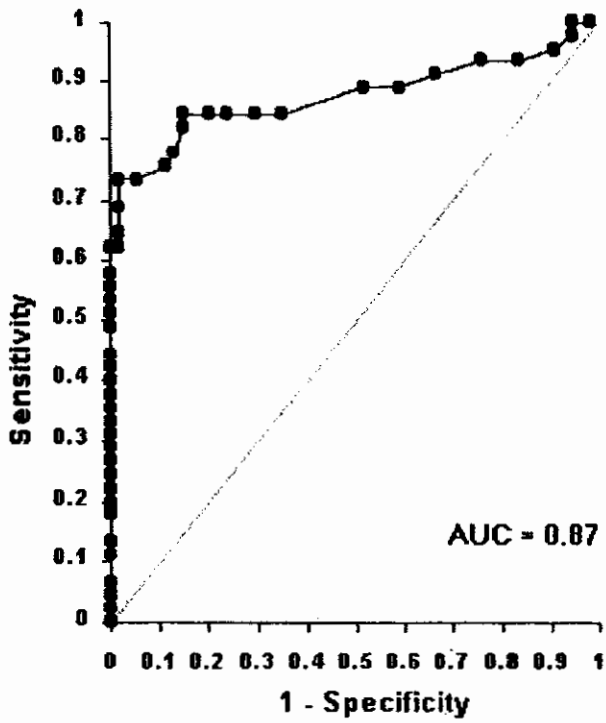

Figure 8. ROC curve for PRDI when the cutoff threshold was defined as PSG-RDI > 20. AUC for the curve is 0.87 ($p = 0.0001$), showing the potentially high sensitivity and specificity in diagnosing OSAS of a severity requiring treatment.

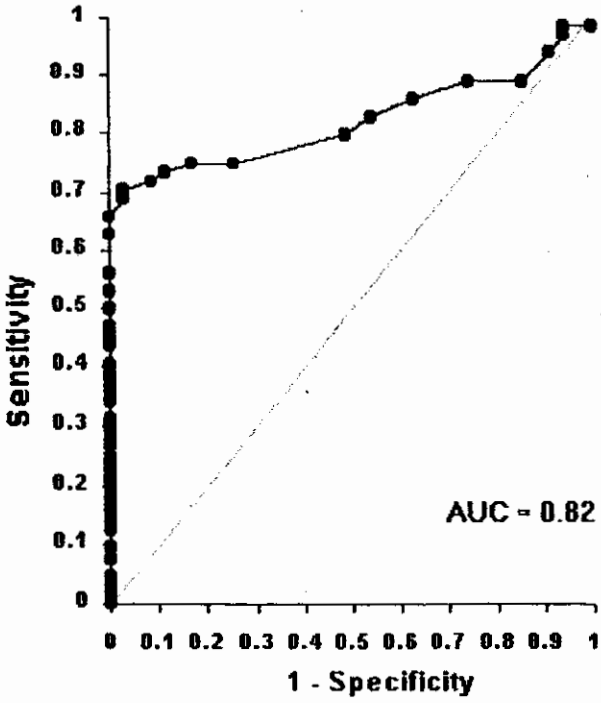

Figure 7. ROC curve for PRDI when the cutoff threshold was defined as PSG-RDI > 10. AUC for the curve is 0.82 ($p = 0.0001$), showing the potentially high sensitivity and specificity in diagnosing OSAS.

devices tend to have a high level of feasibility and saving of time and expenses, but provide less information. For example, Portier et al[7] evaluated unattended, at-home polysomnography studies (ASDA level 2) vs in-laboratory polysomnography studies, using the same recorded channels. They found that the reliability of the studies was associated with the quality of data obtained under the unattended conditions, where 33% of the recordings were not adequate for data analysis, and a further 11% of the studies had discordant results. The rejection rate of the WP100 device (10%) is in the lower-to-middle range of the ASDA grade level III devices, which were estimated to have rejection rates in the range of 4 to 24%.[20–21] Other ambulatory devices from this category could also demonstrate relative simplicity and low rejection rate, but showed unsatisfactory accuracy. Esnaola et al[25] studied 150 individuals with suspected OSAS, who underwent full polysomnography simultaneously with level III devices and reported AUC values from 0.67 to 0.76. Cirignotta et al[26] reported that the automatic scoring of such a device was unreliable in assessing patients with complicated OSAS. In contrast to these reported devices, the WP100 appears to have both the advantage of simplicity (recording only from two finger probes) and high accuracy.

The device is based on the PAT signal, a measurement of the pulsatile volume changes in the vascular bed at the fingertip, providing continuous monitoring of the pulse rate and detecting digital vasoconstriction events, both of which are affected by the sympathetic nervous system. Grote et al[9] has shown that the control of the finger arteries is almost exclusively mediated by α sympathetic receptors, so that PAT-detected episodes of vasoconstriction actually reflect sympathetic activation. Pitson and Stradling[27] reported that repeated occurrence of sleep apnea and hypopnea events causes arterial oxygen desaturation, as well as arousal from sleep with periodic episodes of increased sympathetic nervous system activation. These authors used heart rate change and the pulse transit time as indices of sympathetic activation and found that these were less well correlated with the apnea/hypopnea index ($r = 0.51$ and 0.65, respectively).

The PAT technology is a unique and relatively new concept of noninvasive measurement of sympathetic activation levels that appears to be very accurate for detecting sleep-disordered breathing events. The self-contained pressurizing mechanism of the probe allows it to be lightweight and silent, essential for a practical ambulatory device. Its ability to reliably apply a predetermined and constant level of pressure over a broad range of finger sizes is essential for the accuracy, robustness, and reproducibility of the method, and was also vital for the development of the algorithm.

The first study that demonstrated the PAT signal diagnostic capability for patients with OSAS was performed using a bedside version of the PAT system, which was automatically analyzed using PAT signal attenuation and pulse rate criteria alone. In that study, Schnall et al[10] found a high correlation between standard polysomnography scoring of total apnea-hypopnea events and PAT-vasoconstriction events with concurrent tachycardia. Later, Pillar et al[11] showed that detection of apnea and hypopnea events based on combined data from PAT and pulse oximetry was highly correlated with standard polysomnography scored results, a finding that was confirmed by Pittman et al[12] utilizing both manual and automatic analysis. O'Donnell et al[28] further explored the PAT response in patients with OSAS. They experimentally induced upper airway obstruction and have shown that airflow obstruction in patients with OSAS leads to a PAT signal attenuation in a "dose-response" manner, *ie*, greater airflow obstruction causes greater PAT attenuation.

The criteria of the automatic algorithm for respiratory disturbance event in the present study were set as either a substantial digital vasoconstriction ($> 50\%$) or substantial arterial oxygen desaturation ($> 4\%$), or a milder degree of vasoconstriction ($> 30\%$) with concurrent pulse rate acceleration ($> 10\%$) or subthreshold arterial oxygen desaturation ($> 3\%$). Based on the actigraphic data, periods of sleep and wakefulness were identified, and the automatic algorithm RDI was calculated per hour of detected sleep. Although actigraphically determined sleep time is not as accurate as polysomnography, this feature is an improvement over other modified portable devices, which provide RDI values per total recording time rather than per the actual sleep time, which may lead to a biased RDI.

It should be noted that the population we studied did not include patients with central sleep apnea. We therefore assume that, at this stage, the current algorithm would not differentiate between obstructive and central apneas. However, given the very low prevalence of central apnea among the referred population to diagnostic sleep laboratories and the fact that the treatment of choice is usually the same, we do not consider this to be a major disadvantage. It should be also noted that sympathetic activation during sleep is not exclusively associated with the resumption of respiration after disordered breathing events, but may also arise in association with a variety of other conditions that may cause sleep arousals such as gross body movements, periodic leg movements, or changes in upper airway resistance. As outlined before, in order to maximize the specificity

of the WP100 automatic algorithm to detect respiratory disturbance events, it was designed to be based not only on the presence of vasoconstriction episodes but it also takes into account their periodic nature, typical length, and combination with heart rate and oxygen desaturation changes. All these parameters were tuned in an optimizing process over a prior training set of results and were shown to give robust correlation with the polysomnography results in the validation set of the present study. Recently, we built a separate algorithm which utilizes the PAT signal to detect ASDA-defined arousals during sleep regardless of their source. This latter algorithm was based on a combination of two features of the PAT signal, amplitude attenuation and pulse rate increase. Validating the algorithm on a group of 96 patients that included normal subjects, patients with sleep apnea, and patients with periodic leg movements during sleep revealed a high correlation of 0.88 between manually scored ASDA-defined arousals and the automatically derived PAT autonomic arousal index. We believe that utilizing a combination of the features of the above-described algorithms to analyze a PAT record will allow us to distinguish between sympathetic activation due to respiratory events or due to other causes. Thus, in cases where the result of an RDI selective algorithm is consistent with or higher than that of the autonomic arousal algorithm, it can be reliably used to provide sleep apnea diagnosis. In cases where the PAT reveals a high arousal index but a low RDI, additional disorders such as periodic limb movements or upper airway resistance syndrome should be suspected and further explored. It is yet to be determined, however, if specific features of the digital response may be further analyzed to provide additional useful information about the underlying cause of the sympathetic activation.

A relatively high consistency was found between PRDI in the laboratory and at home, as well as between at-home studies, compared to previous studies that reported rather large night-to-night variability of RDI.[19,21] It is possible that the consistency found in this study results from the relatively high incidence of patients with severe apnea re-studied at home. We conclude from these results that the WP100 showed a high level of reproducibility, although this may have been related to the specific population studied.

The ability of the PAT system to detect sleep-related respiratory disturbances could be affected by peripheral vasculopathy or neuropathy, and/or autonomic nervous system dysfunction, through the disruption of the normal response of the peripheral arteries to sympathetic activations. Nevertheless, the presence of such conditions should only be applied as exclusion criteria in extremely severe cases but not for example in the common diabetic patient. Obviously, patients who are treated with α-blocker medications, those who underwent bilateral sympathectomy, and others with Raynaud disease or acrocyanosis are not candidates for the WP100 device. In patients with severe finger deformity (*eg*, rheumatoid arthritis), the adequate applying of the PAT probe could be a technical problem. In fact, none of the subjects in the current study were excluded on the basis of these conditions, and only two subjects were excluded because of treatment with α-blocking agents. Therefore, the use of the device was not in practice limited by these pathologies, and the vast majority of the subjects with suspected OSAS would be eligible to use the WP100 device.

This study has several potential limitations. First, the study population consisted of patients with snoring/sleep apnea syndrome and healthy volunteers. One could argue that the accuracy of PAT in recognizing respiratory disturbances might be different in other patient populations (such as insomniacs). However, some of our patients complained of difficulties falling and maintaining sleep along with the hypersomnolence, and we did not notice a decreased accuracy of the WP100 in recognizing events in these individuals. Nevertheless, expanding this study to other patient populations will add more information regarding its applicability. In addition, we have evaluated the PAT for apneas and hypopneas but not for increased upper airway resistance syndrome. Respiratory effort related arousals are well recognized, and indeed it would be reasonable to be able to recognize them with this device, as these are also associated with sympathetic activation. However, this was beyond the scope of this study and is currently being investigated in a separate study.

Conclusion

Despite these limitations, we believe that this study shows that the WP100 is a simple, reliable, and accurate device for diagnosing OSAS in the unattended home set-up. Using a device with sensors placed only on the fingers and forearm makes it simple to self-administer and well tolerated. Using the automated scoring algorithm allows for objectivity and is time saving.

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Using a Wrist-Worn Device Based on Peripheral Arterial Tonometry to Diagnose Obstructive Sleep Apnea: In-Laboratory and Ambulatory Validation

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Running title: Using a Wrist-Worn Device Based on PAT to Diagnose OSA

This study was performed at the Sleep HealthCenter Sleep Disorders Laboratory affiliated with Brigham and Women's Hospital.

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Abstract

Study Objectives: To assess the accuracy of a wrist-worn device (Watch_PAT 100) to diagnose obstructive sleep apnea in the home.

Design: Participants completed 2 overnight diagnostic studies with the test device, 1 night in the laboratory with concurrent polysomnography (PSG) and 1 night in the home with only the Watch_PAT. The order of the laboratory and home study nights was random. The frequency of respiratory events on the PSG was quantified using indices based on 2 definitions of hypopnea, the respiratory disturbance index using American Academy of Sleep Medicine Task Force criteria for clinical research, also referred to as the Chicago criteria (RDI.C) and Medicare guidelines (RDI.M). The Watch_PAT respiratory disturbance index (PAT RDI) and oxygen desaturation index (PAT ODI) were then evaluated against the PSG RDI.C and RDI.M, respectively, for both Watch_PAT diagnostic nights, yielding IN-LAB and HOME-LAB comparisons.

Setting: Sleep laboratory affiliated with a tertiary care academic medical center.

Patients: 30 patients referred with suspected OSA.

Interventions: N/A

Measurements and Results: The PSG and PAT measures were compared using the mean (2SD) of the differences and the intraclass correlation coefficient (ICC). The receiver-operator characteristic (ROC) curve was used to assess optimum sensitivity/specificity and calculate likelihood ratios. For the IN-LAB comparison, there was high concordance between RDI.C and PAT RDI (ICC = 0.88, mean difference 2.5 (18.9) events/hr), RDI.M and PAT ODI (ICC = 0.95, mean difference 1.4 (12.9) events/hr, and sleep time (ICC = 0.70, mean difference 7.0 (93.1) minutes) between the test device and PSG. For the HOME-LAB comparison, there was good

concordance between RDI.C and PAT RDI (ICC = 0.72, mean difference 1.4 (30.1) events/hr) and RDI.M and PAT ODI (ICC = 0.80, mean difference 1.6 (26.4) events/hr) for the test device and PSG. Home studies were performed with no technical failures.

Conclusions: In a population of patients suspected of having OSA, the Watch_PAT can quantify an ODI that compares very well with Medicare criteria for defining respiratory events and an RDI that compares favorably with Chicago criteria for defining respiratory events. The device can be used with a low failure rate for single use in the lab and home for self-administered testing.

INTRODUCTION

Obstructive sleep apnea (OSA) is a common disorder with important clinical consequences for affected individuals. Prevalence of the disorder is estimated to be 2-4% among a middle-aged population.[1] OSA is characterized by repetitive collapse of the pharyngeal airway during sleep yielding hypoxia, hypercapnia, and arousal to reestablish airway patency.[2] The associated consequences include daytime sleepiness,[3] decreased cognitive performance, decreased quality of life,[4] increased risk of automobile and industrial accidents,[5,6] and adverse cardiovascular sequelae.[7-10] Treatment of OSA leads to improvements in many of these adverse outcomes and may reduce health care costs.[11-13] Thus, diagnosis of this disorder is important.

A commonly used indicator of OSA severity is the respiratory disturbance index (RDI). The RDI represents the total number of apneas and hypopneas per hour of sleep. Most commonly, the RDI is derived primarily from overnight in-laboratory polysomnography (PSG) which includes the continuous recording of many physiologic variables including airflow, chest/abdominal movements, electroencephalography (EEG), electro-oculography (EOG), electromyography (EMG), electrocardiography (ECG), and oxygen saturation.[14] However, full PSG in the laboratory is expensive, cumbersome, and not readily available in many geographic areas due to a growing demand for the procedure.[15] Although unattended and telemonitored polysomnography are available, the reliability of these alternatives varies.[16-19] Gagnadoux and coworkers recently reported a failure rate of 23% for 98 unattended home PSGs even though subjects reported to the laboratory for equipment set up and then returned home for the study. Several investigations of unattended PSG have reported that the majority of subjects preferred in-laboratory PSG over ambulatory PSG.[17,20]

Calculating RDI with a portable testing device based on a reduced channel set makes diagnosing OSA more feasible in an ambulatory setting such as the home. Ideally, the system is designed for self-administered home use. We and others have previously reported on one technology that may be useful in the ambulatory diagnosis of OSA, the Peripheral Arterial Tonometer (PAT).[21-23] This technology uses a finger-mounted pneumo-optical sensor that eliminates venous pulsations and continuously measures the arterial pulse wave volume of the digit. Episodic vasoconstriction of digital vascular beds from sympathetic nervous system activation (mediated by alpha-adrenergic receptors) results in attenuation of the signal.[21] Episodes of upper airway obstruction (e.g. apneas, hypopneas) may cause arousal from sleep, sympathetic activation, and peripheral vasoconstriction and can therefore be detected on the PAT signal.[24]

In the present study, we assessed the accuracy of a wrist-worn device that combines this PAT technology with actigraphy and arterial oxygen saturation to diagnose OSA. Previous studies have assessed the accuracy of this device when compared to simultaneously obtained in-laboratory PSG and have demonstrated good results.[22, 23] This study utilized a similar approach, but extended the work of Bar and coworkers by also studying patients in the home where the device is intended to be used.[22]

MATERIALS AND METHODS

Subjects

Adult patients referred to the clinical sleep laboratory of Brigham and Women's Hospital with suspected OSA participated in this study. These participants were not consecutive patients, but a sample of patients who disclosed on a comprehensive questionnaire between June and December of 2002 that they were interested in being contacted about research studies conducted at the sleep laboratory. Exclusion criteria for the study were: history of peripheral vascular disease, peripheral neuropathy, non-sinus cardiac rhythm, permanent pacemaker, severe lung disease, S/P bilateral cervical or thoracic sympathectomy, finger deformity that precludes adequate sensor application, and use of alpha-adrenergic receptor blockers (24 hour washout period required). Informed consent was obtained from all participants after the protocol was approved by the Human Research Committee of Brigham and Women's Hospital.

Protocol

All subjects completed a comprehensive sleep and health survey that included an Epworth Sleepiness Scale.[25] Subjects underwent two separate evaluations of the home monitoring system (Watch_PAT 100, Itamar Medical Ltd., Caesarea, Israel): an in-laboratory comparison (IN-LAB) where subjects simultaneously wore the Watch_PAT during a full-night standard PSG and a home-laboratory (HOME-LAB) comparison during which Watch_PAT data acquired in the home were compared to PSG results obtained in the laboratory. The order of these 2 nights was random. The home and laboratory studies were scheduled to occur within 1 week of each other, thus avoiding the confounding influence of long time delays between studies.

HOME SLEEP EVALUATION

For the home study, subjects reported to the sleep laboratory on the day of their study to receive instruction on the use of the Watch_PAT device. Instruction addressed proper application of the device and subject demonstration of correct use. This process required about 5-10 minutes. The Watch_PAT device was then provided to the subject for transport to their home.

The Watch_PAT system has been described elsewhere,[22, 23] but consists of a battery-powered, wrist-mounted recording device and software for post-acquisition viewing and analysis of the recorded data. The wrist unit contains an actigraph (3-axis accelerometer for limb movement detection) to differentiate wake time from sleep time. It also includes 2 finger mounted sensors: a PAT probe (Itamar Medical Ltd., Caesarea, Israel) and a pulse oximeter sensor (Nonin 8000J, Plymouth, MN). The PAT probe applies a uniform pressure field over the distal two thirds of the finger, including the fingertip, which unloads arterial wall tension without causing distal venous pooling and distension, potential sources of veno-arterial mediated vasoconstriction. A transmission mode photo-electric plethysmograph was used to measure the optical density changes associated with pulsatile blood volume changes in the finger. The Watch_PAT device recorded 4 signals: PAT signal (arterial pulse wave volume), heart rate derived from the PAT signal, oxyhemoglobin saturation, and wrist activity (derived from the accelerometer). The device measured the oxyhemoglobin saturation at 1 sample per second from the internal pulse oximeter that used 4-beat exponential averaging of the raw pulse wave oxyhemoglobin saturation measurements (8-beat exponential averaging was used for pulse rates between 112 and 225 beats/minute). The Watch_PAT device contains a rechargeable power

supply, preliminary signal conditioning hardware, 100 Hz data acquisition, and data storage on a removable COMPACTFLASH disk.

Watch_PAT studies were uploaded for automated analysis on a personal computer using the COMPACTFLASH reader provided with the PAT software (zzz_PAT version 2.0.39.13, Itamar Medical Ltd., Caesarea, Israel). The automated analysis used wrist activity to differentiate wake from sleep to determine a PAT valid sleep time (PAT VST) using a proprietary, nonstandard algorithm. Respiratory events were detected during segments of PAT VST using a proprietary algorithm developed to match American Academy of Sleep Medicine (AASM) guidelines for measurement in clinical research (also referred to as "Chicago criteria").[26] In particular, a respiratory event was automatically scored if one of 3 criteria were met: 1) PAT amplitude reduction occurred with an acceleration in the pulse rate or an increase in wrist activity, 2) PAT amplitude reduction occurred with a 3% or greater oxyhemoglobin desaturation, or 3) a 4% or greater oxyhemoglobin desaturation. The algorithm was developed using previous Watch_PAT data collected concurrently PSG data to optimize event by event agreement. Oxyhemoglobin desaturations were quantified automatically in a similar fashion. No manual editing of the automated Watch_PAT scoring was performed. A respiratory disturbance index (PAT RDI) was then reported that represents the number of respiratory events per hour of PAT VST. In addition, an oxygen desaturation index (ODI) was reported that represented the number of oxyhemoglobin desaturations of at least 4% per hour of PAT VST.

In-Laboratory Polysomnography

All subjects underwent a standard in-laboratory overnight PSG. Signals recorded included: EEG (C4-A1, C3-A2, O2-A1 and O1-A2), EOG, submental and bilateral tibial EMG,

ECG, airflow [nasal-oral thermistor and nasal pressure (PTAF2, Pro-Tech Services, Woodinville, WA)], chest and abdominal motion (piezo bands), oxyhemoglobin saturation (Model 930 Pulse-Oximeter, Respironics, Murrysville, PA), body position, and snoring intensity. All physiological data were collected and stored using the ALICE3 digital polysomnography system (Respironics, Murrysville, PA). The oxyhemoglobin saturation was sampled once per second on the PSG and the Model 930 Pulse Oximeter used the same 4-beat exponential averaging of the raw pulse wave oxyhemoglobin saturation measurements as the Watch_PAT device (8-beat exponential averaging was used for pulse rates between 112 and 225 beats/minute). The Watch_PAT signals described above were acquired concurrently with the PSG.

PSGs were all scored manually by one technologist (SDP) who was blinded to the Watch_PAT signals. A second technologist (MMM) who was also blinded to the Watch_PAT signals manually scored the PSG records to help validate the manual PSG scoring of sleep and respiratory events. Sleep was staged according to standard criteria.[27] Arousals were defined according to the ASDA guidelines.[28] Respiratory events were first scored according to the AASM guidelines for measurement in clinical research (Chicago criteria).[26] In particular, an apnea was scored if airflow was absent for 10 seconds, and a hypopnea if airflow was reduced by 50% or a lesser extent (noticeable change) in association with a desaturation of at least 3% or an arousal. A respiratory disturbance index (RDI.C) was then calculated based on the number of apneas + hypopneas per hour of sleep. Records were then rescored for respiratory events using an alternate definition of hypopnea (Medicare criteria).[29] In this case, a hypopnea was defined as 'an abnormal respiratory event lasting at least 10 seconds with at least a 30% reduction in thorocoabdominal movement or airflow as compared to baseline, and with at least a 4% oxygen

desaturation'. A respiratory disturbance index (RDI.M) was then calculated based on the number of apneas + desaturating hypopneas (per Medicare criteria) per hour of sleep.

Data Analysis

Sleep studies were considered acceptable for data analysis if none of the following rejection criteria occurred: 1) PSG total sleep time < 1.5 hours, 2) Watch_PAT valid sleep time < 1.5 hours, 3) poor quality PSG recording (defined as a substantial portion of the PSG being not interpretable to score sleep and respiratory events), or 4) all Watch_PAT channels not available for review and automatic analysis. The PSG was considered the gold standard for identifying and quantifying OSA. The Watch_PAT was compared to respiratory events detected on the PSG using both Chicago and Medicare criteria. Detection of respiratory events using Chicago criteria was assessed by comparing the PAT RDI to the PSG RDI.C. Detection of respiratory events using Medicare criteria was assessed by comparing the PAT ODI to the PSG RDI.M. The manual PSG scoring of sleep stages and respiratory events (Medicare criteria) were validated by assessing agreement between the reference scorer and a 2nd scorer. Epoch-by-epoch comparisons yielded the percentage of epochs with agreement and Cohen's Kappa statistic measured the chance-corrected level of agreement.[30]

The utility and accuracy of the Watch_PAT indices in detecting OSA was based on summary data for both nights (laboratory and home) and was evaluated in a number of ways. These included evaluations for concordance using intraclass correlation (ICC: model 2, individual ratings)[31], agreement using the method of Bland and Altman,[32] and by constructing receiver operator characteristic (ROC) curves[33] (Analyse-It Clinical Laboratory Software ver 1.67, Leeds, England) using RDI.M and RDI.C cutoffs of 15 events per hour on the PSG to

differentiate normal cases from those with moderate-severe OSA.[26, 34] To assess the detection of varying degrees of OSA severity, we also constructed ROC curves using RDI.M and RDI.C cutoffs of 5, 10, 20, and 30 events per hour. Given that there is no well-defined RDI cut-off value for defining OSA, we also assessed diagnostic agreement using a clinical approach described previously to assess the diagnostic utility of another ambulatory device to detect OSA.[35] According to this analysis, the Watch_PAT and PSG are considered in agreement if: 1) both the RDI.C and PAT-RDI were greater than 40 events per hour, or 2) the RDI.C was < 40/hr on PSG and the PAT-RDI was within 10 events/hr of the RDI.C.

All results are given as means ± 1 standard deviation except for the means of the differences for the Bland-Altman analyses which are given as means (± 2 standard deviations for limits of agreement). Statistical significance was considered to be present when $p < 0.05$.

RESULTS

We recruited a total of 30 subjects with suspected OSA who met prospective eligibility requirements for participation in this study. Of these participants, 1 subject was excluded because of significant signal artifact on the study night in the sleep laboratory that prevented analysis of the PAT signal. Thus, 29 subjects (21 male, 8 female) are included in the data analysis. The mean age of these subjects was 43.2 ± 10.8 years and mean body mass index was 33.9 ± 7.1 kg/m^2. The mean Epworth Sleepiness Scale score was 9.2 ± 4.7 (range 2-18). The mean interval between home and laboratory studies was 1.7 ± 1.0 days. The laboratory night was first in 17 (58.6%) subjects.

Validation of the PSG manual scoring of sleep stages yielded epoch-by-epoch agreement of 93.4% (discriminating wake, NREM, and REM) with a Cohen's Kappa statistic of 0.86. The

agreement was 95.1% and Cohen's Kappa statistic was 0.83 for the RDI.M calculation between the 2 manual PSG scorers using comparisons of 0, 1, or 2 respiratory events per epoch.

IN-LAB COMPARISON

Chicago Criteria

For the night in the laboratory, mean TST per PSG was 347.4 ± 64.6 minutes while the mean Lab-PAT VST was 340.3 ± 55.5 minutes (see Table 1). There was good agreement between Lab-PAT VST and PSG TST (ICC = 0.70 mean difference 7.0 (93.1) minutes). Mean RDI.C per PSG was 31.6 ± 20.6 events per hour while the mean Lab-PAT RDI was 34.2 ± 19.2 events per hour. The Lab-PAT RDI and PSG RDI.C were concordant (ICC = 0.88, Fig. 1A). A Bland Altman plot of Lab-PAT RDI and PSG RDI.C is shown in Fig. 1B; there was no obvious systematic difference between the two variables.

We constructed ROC curves to assess the sensitivity and specificity of the Watch_PAT system using a range of PSG RDI.C threshold values (5, 10, 15, 20, and 30 events per hour) to differentiate normal cases from those with OSA. The area under the ROC curves was undefined for a threshold of 5 events per hour, 0.96, 0.89, 0.93, and 0.95, respectively. Optimal combinations of sensitivity and specificity are shown in Table 2. When using the previously described clinical approach to assess agreement,[35] concordance was found in 24 out of 29 subjects (83%). There was substantial disagreement in one case (subject #9: mild OSA by Chicago criteria). The PSG RDI.C was 10.8 events per hour in this individual, but the Lab-PAT RDI was 40.6 events per hour. In this individual, the Watch_PAT device seemed to be detecting sympathetic activation associated with events that did not meet the Chicago criteria for scoring

hypopneas (see Fig. 2). The Epworth Sleepiness Score for this individual was 16 out of a possible score of 24.

Medicare Criteria

The mean RDI.M per PSG was 18.3 ± 21.9 events per hour while the mean Lab-PAT ODI was 16.9 ± 19.5 events per hour. There was excellent agreement between Lab-PAT ODI and RDI.M (ICC = 0.95) as is shown in Fig. 1C. A Bland Altman plot of Lab-PAT ODI and RDI.M is shown in Figure 1D.

We constructed ROC curves to assess the sensitivity and specificity of the Watch_PAT system using PSG RDI.M threshold values (5, 10, 15, 20, and 30 events per hour) to differentiate normal cases from those with OSA. The area under the ROC curves was 0.99, 1.0, 0.99, 1.0, and 0.99 respectively. Optimal combinations of sensitivity and specificity are shown in Table 3. There was a substantial disagreement for one case (subject #3). The PSG RDI.M was 57.6 events per hour in this individual, but the Lab-PAT ODI was 28.3 events per hour. The source of the disagreement was obstructive apneas that met Medicare criteria, but did not yield a 4% or greater oxyhemoglobin desaturation. Thus, respiratory events included in the PSG RDI.M were not included in the Lab-PAT ODI. A representative sample from the PSG is shown in Fig. 3.

HOME-LAB COMPARISON

Chicago Criteria

No technical failures occurred during the home studies, thus data were available for analysis in all 29 subjects. The mean Home-PAT VST for the home studies was 344.1 ± 73.9 minutes. There was not a significant correlation between Home-PAT VST and PSG TST (Pearson product-moment correlation coefficient = 0.28, p=0.14). The mean Home-PAT RDI

was 30.2 ± 19.5 events per hour for the home study night. There was good agreement between Home-PAT RDI and RDI.C (ICC = 0.72, Fig. 4A) even though they were recorded on different nights. A Bland Altman plot of Home-PAT RDI and RDI.C is shown in Fig. 4B. With RDI.Cs in the severe range, the Home-PAT RDI tended to underestimate OSA severity in some cases, although the mean difference between the Home-PAT RDI and RDI.C was only 1.5 events per hour. The night-to-night variability of the PAT RDI in this study (when PAT values in the home are compared to PAT values in the lab) is shown in Fig. 5A. The ICC for Home-PAT RDI and Lab-PAT RDI was 0.62.

ROC curves were constructed as stated for the laboratory night with various PSG RDI.C threshold values (5, 10, 15, 20, and 30 events per hour) to differentiate normal cases from those with OSA. The area under the ROC curves was undefined for a threshold of 5 events per hour, 0.82, 0.97, 0.92, and 0.89, respectively. Optimal combinations of sensitivity and specificity are shown in Table 2. When using the previously described clinical approach to assess agreement, concordance was found in 21 out of 29 subjects (72%).

Medicare Criteria

The mean PAT ODI was 16.7 ± 17.1 events per hour for the home study night. There was good agreement between Home-PAT ODI and PSG RDI.M (ICC = 0.80) even though they were recorded on different nights as shown if Fig. 4C. A Bland Altman plot of Home-PAT ODI and PSG RDI.M is shown in Figure 4D. The night-to-night variability of the PAT ODI in this study is shown in Fig. 5B. The agreement between Lab-PAT ODI and Home-PAT ODI was good (ICC = 0.83).

ROC curves were constructed as stated for the laboratory night with various PSG RDI.M threshold values (5, 10, 15, 20 and 30 events per hour) differentiating normal cases from those with OSA. The area under the ROC curves was 1.0, 0.99, 0.90, 0.86, and 0.87, respectively. Optimal combinations of sensitivity and specificity are shown in Table 3.

DISCUSSION

In this study, we assessed the diagnostic accuracy of a wrist-worn device to detect OSA with concurrent PSG in the laboratory and when subject-administered in the home. This device is unique in that detection of episodic vasoconstriction of the digital vascular beds contributes to the identification of episodes of upper airway obstruction, rather than conventional measures of airflow and chest movements. The results of the IN-LAB study suggest there is generally good agreement between Watch_PAT and PSG in quantifying apnea plus hypopnea frequency with acceptable sensitivity, specificity, and diagnostic agreement between systems. The Lab-PAT ODI was concordant with the PSG RDI.M (Medicare criteria). The HOME-LAB comparison results suggest that technical failures are rare with use of the Watch_PAT system in the home (0% in this study), but there was less agreement between respiratory events detected with the Watch_PAT in the home and the laboratory PSG.

Validating an ambulatory sleep diagnostic system is challenging due to the lack of a true gold standard in detecting sleep-disordered breathing events during sleep, absence of a well-accepted cutoff in apnea-hypopnea frequency to differentiate normal cases from those with obstructive sleep apnea, and night-to-night variability in measures of sleep and respiration that makes home assessment versus laboratory evaluation difficult. These issues will be addressed separately. Detecting apneas and hypopneas during sleep studies is not exact because

quantifying airflow with pneumotachometry is not practical for routine use and the transducers that are used to measure respiration are semi-quantitative at best. Furthermore, the definition of hypopnea is not consistent from laboratory to laboratory, or even in published guidelines. One definition allows scoring a hypopnea with a noticeable change in airflow terminated by an arousal or a 3% desaturation (RDI.C)[26] while another requires at least a 30% reduction in airflow or effort combined with an oxyhemoglobin desaturation of at least 4% to improve the reliability of scoring respiratory events (RDI.M).[29] Published data suggest that manual PSG scoring of hypopneas based on arousal without desaturation is subject to more inter-scorer variability.[36] We therefore chose to quantify sleep disordered breathing using both Chicago and Medicare criteria and then compared these indices to the Watch_PAT RDI and ODI, respectively.

The absence of a clear cutoff in the RDI (Chicago or Medicare criteria) by which sleep apnea can be diagnosed presents significant challenges for calculating the prevalence of OSA[37] and ROC curves that require discrimination of normal from abnormal cases using a gold standard. Thus, we used a variety of cutoffs (5, 10, 15, 20, and 30 events per hour of sleep) to assess discrimination of subjects with OSA from normal cases with the Watch_PAT. A cutoff of 5 events could not be used for the RDI.C analysis because OSA prevalence was 100% in our study population.

A recent investigation of short-term variability in respiration and sleep during unattended nonlaboratory nights reported no significant bias in RDI between study nights.[38] However, both study nights were in the same environment. Previous investigations report considerable night-to-night variability in measures of RDI.[39, 40] In our study, subjects were studied on different nights with different environments and we suspect this could be a source of variability in the HOME-LAB comparison. As illustrated in Fig. 5A, there was a mean difference of 4.0 (33.5) events per

hour when comparing the Home-PAT RDI and Lab-PAT RDI with the bias towards larger RDIs in the lab. Therefore, false positives and false negatives encountered in the home may be attributed to night-to-night or home-to-lab variability rather than diagnostic inaccuracy of the Watch_PAT system. In spite of the problems described above (no gold standard for respiration assessment, no clear RDI cutoff for apnea diagnosis, and night-to-night variability), we conclude that the Watch_PAT system is producing accurate, clinically interpretable data.

The American Sleep Disorders Association (ASDA) classified sleep diagnostic systems into 4 categories based on the testing environment, technician attendance, and number of parameters recorded.[41] Level I was reserved for in-laboratory PSG. A number of portable sleep diagnostic systems are available, but relatively few have been validated in an unattended home setting. These vary from simple oximetry (ASDA level IV) to complex systems that fully monitor sleep and respiration in the home (ASDA level II). A comprehensive evidence review of the literature on home monitoring for sleep apnea and practice parameters for the use of portable monitoring in the investigation of suspected OSA are available.[34, 42]

Unattended, portable, full PSG performed in the home is considered a level II study by ASDA criteria. Home PSGs have been used for large epidemiology studies,[16] but may not be practical for clinical practice due to the requirement of technician set up. Furthermore, there is insufficient evidence to determine the validity of level II studies.[34]

The Watch_PAT system offers several potential advantages over other portable monitoring systems. First, the Watch_PAT detects respiratory events during epochs of sleep estimated by automated analysis of actigraphy and calculates an RDI based on this sleep time. Most ambulatory devices calculate an RDI based on the recording time since they cannot differentiate wake from sleep. This method may lead to reduced sensitivity and artificially

increase specificity. Second, the Watch_PAT can detect respiratory events that meet the Chicago criteria for scoring a hypopnea, but do not cause a substantial desaturation. Since the Watch_PAT can detect sympathetic activation associated with arousal from sleep, these events are included in the PAT RDI. In addition, the Watch_PAT calculates an ODI based on desaturations of 4% or greater, a measure that is less inclusive in the detection of obstructive respiratory events, but compared very well to the Medicare criteria for scoring events. Third, the Watch_PAT was simple to use for participants in our study with a low failure rate for single use (no technical failures for the home studies). Fourth, performing Watch_PAT studies requires minimal effort from staff. Subject instruction for operating the device only required 5-10 minutes in our study and the analysis of the studies was fully automated. Uploading a study from the COMPACTFLASH disk to computer combined with automated analysis required less than 3 minutes (Dell Optiplex 1.8 GHz GX240 Pentium 4).

There are several potential disadvantages to the Watch_PAT system as well. The principal one relates to the novelty of the PAT signal and the lack of conventional measures of airflow, chest/abdominal movement, and body position on the studies. Thus, apneas that meet Medicare criteria, but do not yield at least a 4% desaturation will not be included in the PAT ODI. This was the source of the disagreement between the Lab-PAT ODI and PSG RDI.M in subject #3 in our study (see Fig. 3). Also, the Watch_PAT system reports a PAT RDI that does not differentiate the type of respiratory event (e.g. obstructive apnea, mixed apnea, central apnea, hypopnea) and cannot calculate a supine-only RDI since body position is not detected by the device. These limitations may prove unsatisfactory in determining a differential diagnosis in some patients. Furthermore, using our clinical approach to assess agreement, concordance was not achieved in 28% of the cases when the Home-PAT RDI was compared to the PSG RDI.C.

Finally, the PAT signal is also susceptible to artifact due to certain arrhythmias such as atrial fibrillation and premature atrial contractions and its response may be limited by certain medications (e.g. alpha blockers and nitrates).

There are a number of limitations to our study. The study included a small number of consenting patients with suspected OSA at only one sleep center. Thus, the prevalence of OSA and mean RDI in our study population were high. We therefore cannot assess whether these results would extend to populations with a lower probability of OSA, for example patients at primary care facilities. One important use of a home diagnostic device might be to exclude OSA in a population where the pre-test probability is relatively low, thus saving the cost of in-laboratory PSGs. A study investigating the accuracy of home studies with the Watch_PAT device in such a population would be worthwhile. Another limitation of our study is we evaluated the accuracy of the Watch_PAT device in the home by comparing measurements in that environment on one night to the gold standard PSG acquired in the laboratory on a different night. There are inherent flaws with this method as mentioned above and in previous publications.[35] We also did not perform event-by-event analysis of the Watch_PAT and PSG data to determine agreement due to technical limitations of synchronizing PSG and Watch_PAT data while maintaining blinded manual scoring of the PSG.

In conclusion, this study indicates that the Watch_PAT device is easy to use for home sleep studies with a low failure rate for single use and minimal technician time when compared with PSG. Based on the likelihood ratios for our home study results, the system yielded a very large increase in the probability of having moderate-severe OSA (Chicago criteria) for a PAT RDI $\geq$ 12.5 events/hour (abnormal cases: PSG RDI.C $\geq$ 15 events/hour) and a large reduction in the probability of having moderate-severe OSA for a PAT RDI < 12.5 events/hour.[43] Thus, the

Watch_PAT could become a useful diagnostic tool in diagnosing moderate-severe OSA in high-risk populations where the prevalence of sleep disordered breathing is high. Studies in other sleep disorder centers are needed to confirm our experience. Nonetheless, the Watch_PAT system could become an important clinical tool and may play an import role in reducing per patient cost in diagnosing and managing OSA.

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Figure Legend

Fig. 1. In-laboratory (Watch_PAT data collected concurrently with PSG data) comparisons are shown. (A) Scatter plot of PSG RDI.C vs. Lab-PAT RDI with a best fit line of Y = -0.97 + 0.95X. (B) Bland-Altman plot of PSG RDI.C vs. Lab-PAT RDI. Agreement was good except for one case, subject #9. (C) Scatter plot of PSG RDI.M vs. Lab-PAT ODI with a best fit line of Y = 0.10 + 1.1X. (D) Bland-Altman plot of PSG RDI.M vs. Lab-PAT ODI. Agreement was good except for one case, subject #3.

Fig. 2. This represents a 3-minute sample from a PSG (subject #9: mild sleep apnea by Chicago criteria). One hypopnea is shown (event indicated by the word 'Hypopnea' in box). Five respiratory events detected by the Watch_PAT software and included in the PAT RDI are indicated on the EEG channel with the text 'Resp Event Arousal'. No oxyhemoglobin desaturations of 4% were present during this segment of the study. This illustrates a period with 20% agreement when comparing the Watch_PAT RDI to the Chicago criteria for scoring respiratory events, yet there was 100% agreement when comparing the Watch_PAT ODI to the Medicare criteria for scoring respiratory events. Thus, due to the sensitivity of the Watch_PAT algorithm to detect sympathetic activation for scoring respiratory events included in the PAT RDI and the absence of an airflow signal to increase specificity, 4 respiratory events were detected by the Watch_PAT device that did not meet Chicago criteria by PSG in this individual. However, careful examination of the raw data does indicate sustained periods of snoring and flow limitation on the nasal pressure channel. EMG_{AT}, anterior tibialis electromyography; NP, nasal pressure (surrogate for airflow); Abd, abdominal movement; HR, heart rate; SaO2, arterial oxyhemoglobin saturation.

Fig. 3. This represents a 2-minute sample from a PSG (subject #3: severe sleep apnea). Four obstructive apneas are shown (events indicated by the words 'Apnea Obstructive' in boxes). Respiratory events detected by the Watch_PAT software and included in the PAT RDI are indicated on the EEG channel with the text 'Resp Event Arousal'. An oxyhemoglobin desaturation of 4% detected by the Watch_PAT software and included in the PAT ODI is indicated on the SaO2 channel with the word 'Desaturation'. This illustrates a period with 100% agreement when comparing the Watch_PAT RDI to the Chicago criteria for scoring respiratory events, but only 25% agreement when comparing the Watch_PAT ODI to the Medicare criteria for scoring respiratory events. Thus, due to the lack of Watch_PAT airflow measurement, 3 obstructive events without adequate oxyhemoglobin desaturation were missed based on these less inclusive criteria. NP, nasal pressure (surrogate for airflow); Abd, abdominal movement; HR, heart rate; SaO2, arterial oxyhemoglobin saturation.

Fig. 4. Home-Laboratory (Watch_PAT and PSG data collected on different nights) comparisons are shown. (A) Scatter plot of PSG RDI.C vs. Home-PAT RDI with a best fit line of Y = 8.6 + 0.76X. (B) Bland-Altman plot of PSG RDI.C vs. Home-PAT RDI. (C) Scatter plot of PSG RDI.M vs. Home-PAT ODI with a best fit line of Y = 2.8 + 0.93X. (D) Bland-Altman plot of PSG RDI.M vs. Home-PAT ODI.

Fig. 5. Home-Laboratory (Watch_PAT data collected on different nights) comparisons are shown. (A) Bland-Altman plot of Home-PAT RDI vs. Lab-PAT RDI. (B) Bland-Altman plot of Home-PAT ODI vs. Lab-PAT ODI.

Table 1 – Data for Each Subject Comparing Watch_PAT with Polysomnography

		LAB						HOME		
		PSG			Watch_PAT			Watch_PAT		
Subject	ESS	TST	RDI.M	RDI.C	VST	ODI	RDI	VST	ODI	RDI
1	9	287.0	2.1	35.7	317.0	9.5	54.3	345.0	4.7	29.7
2	9	353.0	3.9	11.0	378.0	2.1	19.8	400.0	1.7	11.5
3	4	383.5	57.6	80.3	337.0	28.3	69.9	377.0	19.6	34.9
4	18	347.0	14.9	26.8	361.0	11.3	22.3	383.0	24.3	44.2
5	12	327.0	8.4	23.3	319.0	7.3	21.8	404.0	5.0	21.5
6	10	410.0	8.0	19.8	375.0	8.0	14.2	277.0	15.1	22.7
7	10	272.5	27.3	47.0	285.0	31.7	42.4	187.0	11.8	15.7
8	11	343.0	78.2	82.4	339.0	72.9	74.3	266.0	71.3	73.1
9	16	440.5	1.1	10.8	442.0	5.3	40.6	460.0	0.8	4.7
10	15	372.0	0.2	7.1	336.0	2.1	14.1	324.0	0.2	11.3
11	6	344.0	1.0	10.3	321.0	0.4	15.1	388.0	0.3	11.0
12	3	323.0	12.6	37.9	276.0	17.0	47.8	334.0	38.4	38.4
13	9	404.0	1.6	12.2	412.0	2.3	15.3	384.0	1.9	12.5
14	16	373.5	3.5	12.7	327.0	3.3	12.6	398.0	2.7	10.7
15	3	140.5	29.0	40.1	312.0	18.6	35.7	189.0	22.5	54.5
16	17	446.5	12.6	20.7	410.0	13.6	25.9	267.0	10.8	24.9
17	9	413.0	14.5	28.8	459.0	17.5	45.2	424.0	24.9	54.0
18	7	311.5	4.2	26.5	257.0	7.0	20.1	342.0	1.2	9.1
19	8	303.0	4.6	22.0	304.0	1.6	17.0	356.0	4.4	36.9
20	10	340.0	65.1	69.7	341.0	62.9	75.0	335.0	30.0	44.2
21	12	354.0	21.7	36.3	378.0	17.6	27.7	448.0	22.3	31.6
22	6	243.0	36.5	45.4	243.0	35.6	51.1	408.0	21.6	41.3
23	5	381.0	19.5	37.5	288.0	14.1	25.4	240.0	46.4	59.9
24	17	445.5	62.5	62.5	418.0	62.2	60.4	234.0	65.6	67.9
25	7	352.0	1.2	21.8	349.0	1.6	33.3	312.0	1.9	15.4
26	2	303.5	27.9	38.7	309.0	23.9	48.4	354.0	24.4	51.0
27	8	316.0	0.6	16.3	297.0	1.8	20.6	324.0	3.0	19.3
28	2	404.0	4.3	20.3	405.0	3.9	26.6	451.0	4.0	16.5
29	7	340.5	4.9	13.7	275.0	5.7	14.2	367.0	2.8	7.3
Mean	**9.2**	**347.4**	**18.3**	**31.6**	**340.3**	**16.9**	**34.2**	**344.1**	**16.7**	**30.2**
SD	**4.7**	**64.6**	**21.9**	**20.6**	**55.5**	**19.5**	**19.2**	**73.9**	**19.0**	**19.5**

TST = manual total sleep time (minutes); RDI.M = manual respiratory disturbance index with Medicare criteria per hour of sleep; RDI.C = manual respiratory disturbance index with Chicago criteria per hour of sleep; VST = automated valid (estimated) sleep time; ODI = automated oxyhemoglobin desaturation (≥4%) index per hour of estimated sleep time; RDI = automated respiratory disturbance index per hour of estimated sleep time.

Table 2 & 3: See accompanying MS Word document for landscape view of these tables.

Fig. 1

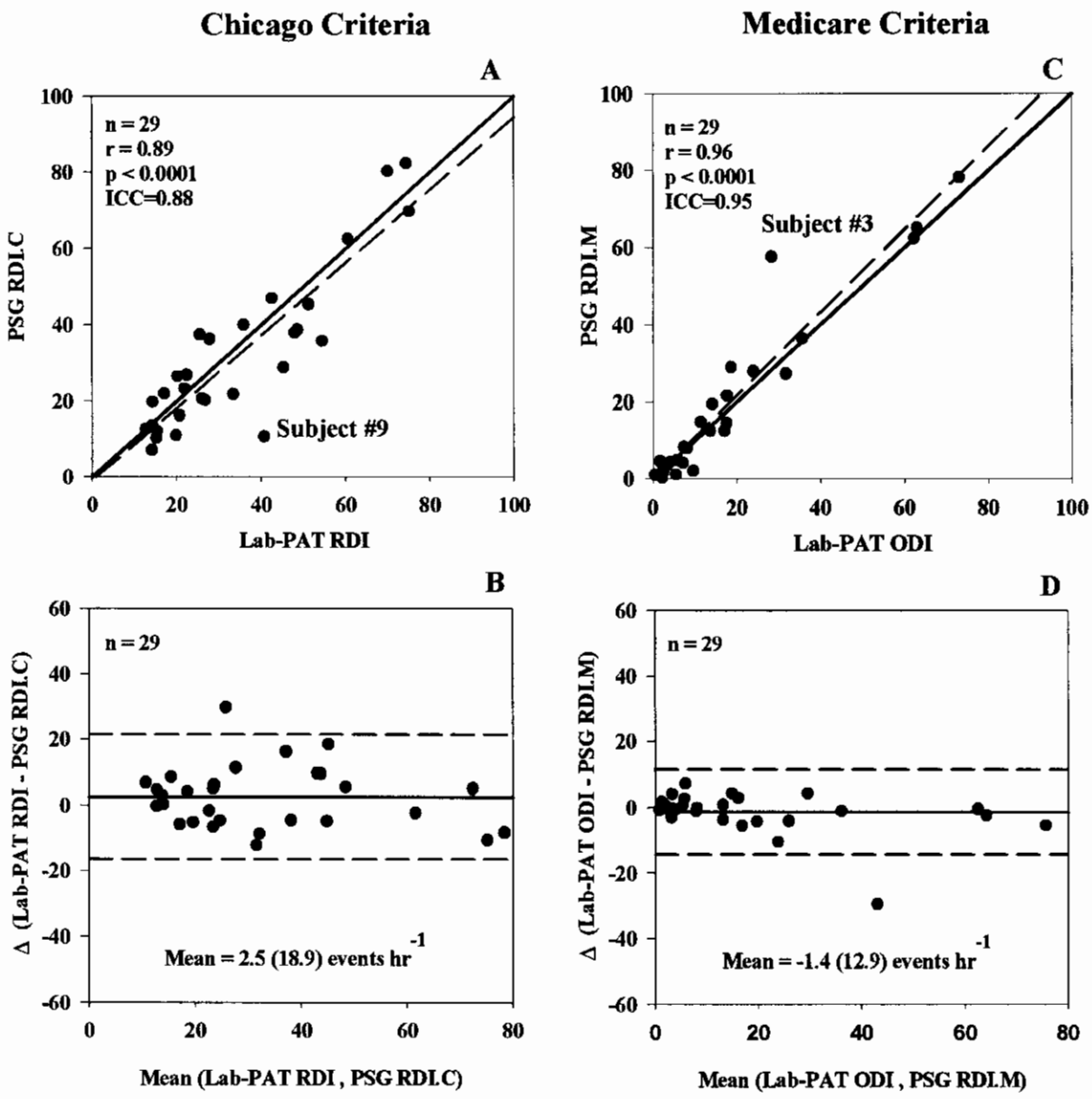
Chicago Criteria
Medicare Criteria
A
B
C
D
n = 29
r = 0.89
p < 0.0001
ICC=0.88
Subject #9
PSG RDI.C
Lab-PAT RDI
n = 29
r = 0.96
p < 0.0001
ICC=0.95
Subject #3
PSG RDI.M
Lab-PAT ODI
n = 29
Δ (Lab-PAT RDI - PSG RDI.C)
Mean = 2.5 (18.9) events hr-1
Mean (Lab-PAT RDI , PSG RDI.C)
n = 29
Δ (Lab-PAT ODI - PSG RDI.M)
Mean = -1.4 (12.9) events hr-1
Mean (Lab-PAT ODI , PSG RDI.M)

Fig. 2.

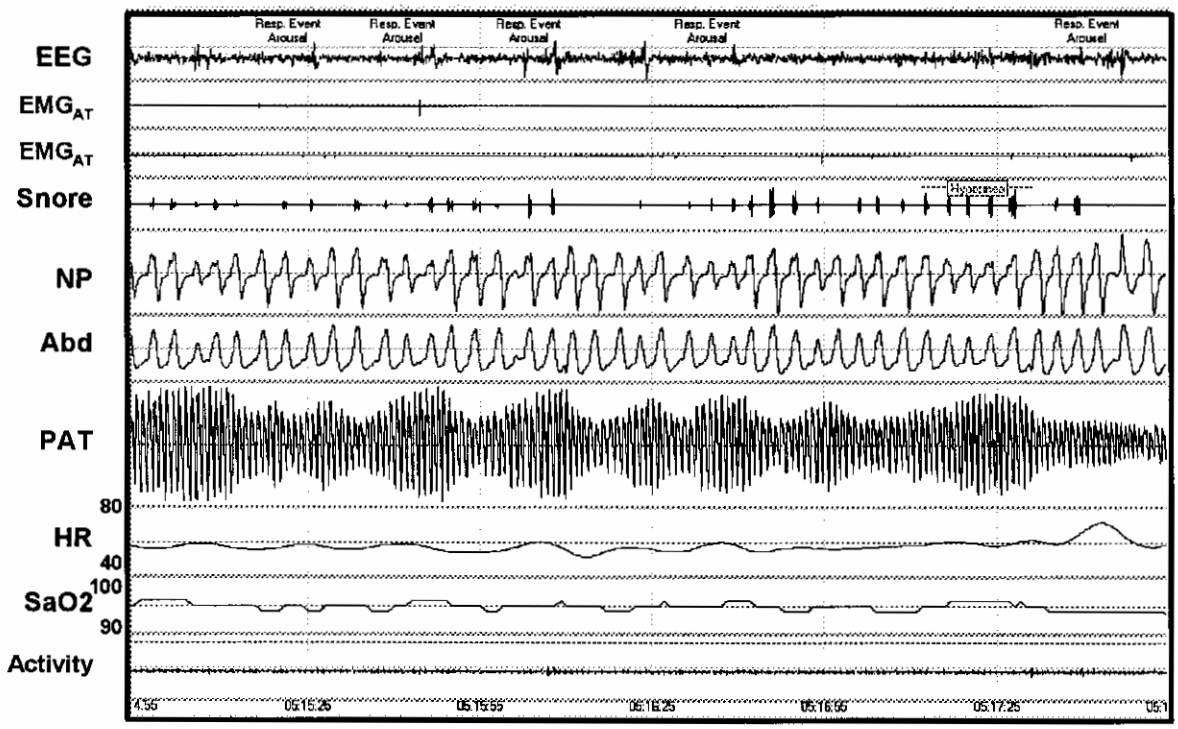
Resp. Event Arousal
Resp. Event Arousal
Resp. Event Arousal
Resp. Event Arousal
Resp. Event Arousal
EEG
EMG$_{AT}$
EMG$_{AT}$
Snore
Hypopnea
NP
Abd
PAT
80
HR
40
100
SaO2
90
Activity
4:55
05:15:25
05:15:55
05:16:25
05:16:55
05:17:25
05:1

Fig. 3.

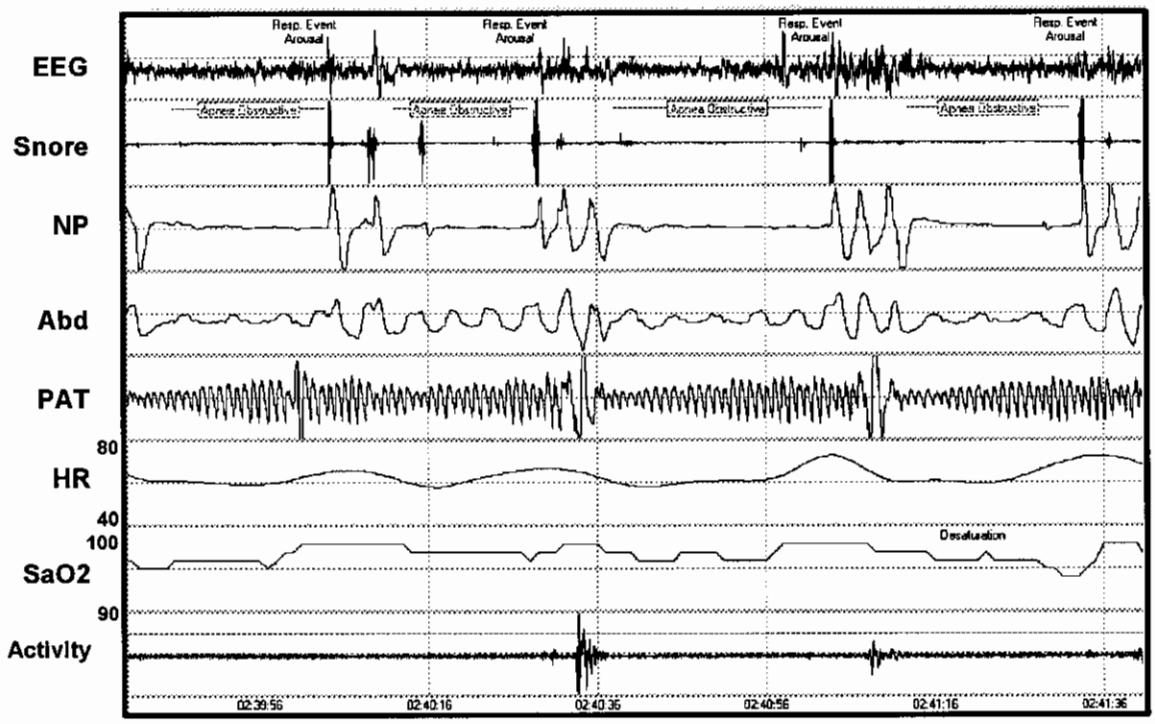
Resp. Event
Arousal
Resp. Event
Arousal
Resp. Event
Arousal
Resp. Event
Arousal
EEG
Apnea Obstructive
Apnea Obstructive
Apnea Obstructive
Apnea Obstructive
Snore
NP
Abd
PAT
80
HR
40
100
Desaturation
SaO2
90
Activity
02:39:56
02:40:16
02:40:36
02:40:56
02:41:16
02:41:36

Fig. 4.

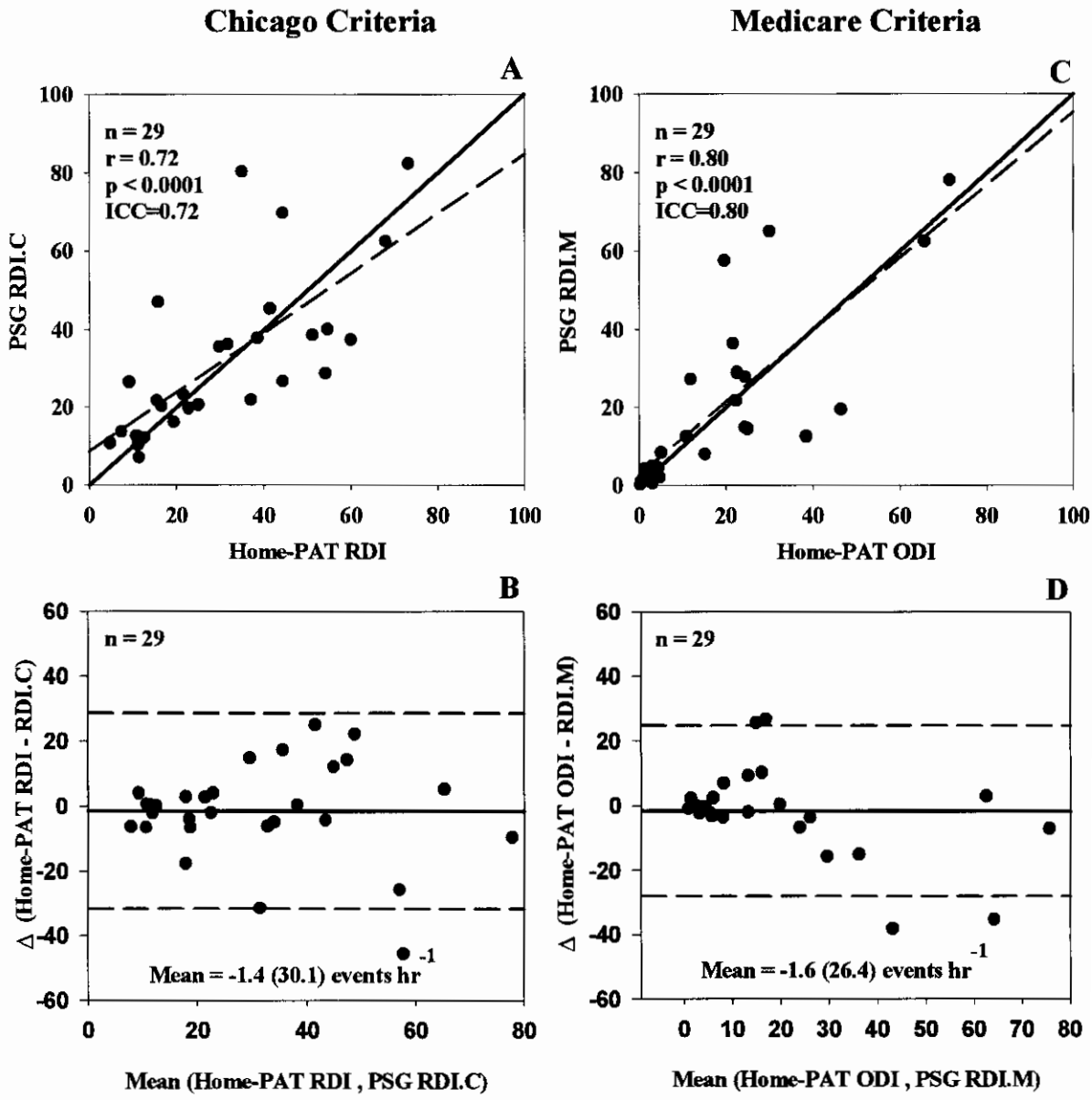
Chicago Criteria
Medicare Criteria
A
B
C
D
n = 29
r = 0.72
p < 0.0001
ICC=0.72
PSG RDI.C
Home-PAT RDI
n = 29
r = 0.80
p < 0.0001
ICC=0.80
PSG RDI.M
Home-PAT ODI
n = 29
Δ (Home-PAT RDI - RDI.C)
Mean = -1.4 (30.1) events hr
-1
Mean (Home-PAT RDI , PSG RDI.C)
n = 29
Δ (Home-PAT ODI - RDI.M)
Mean = -1.6 (26.4) events hr
-1
Mean (Home-PAT ODI , PSG RDI.M)

Fig. 5.

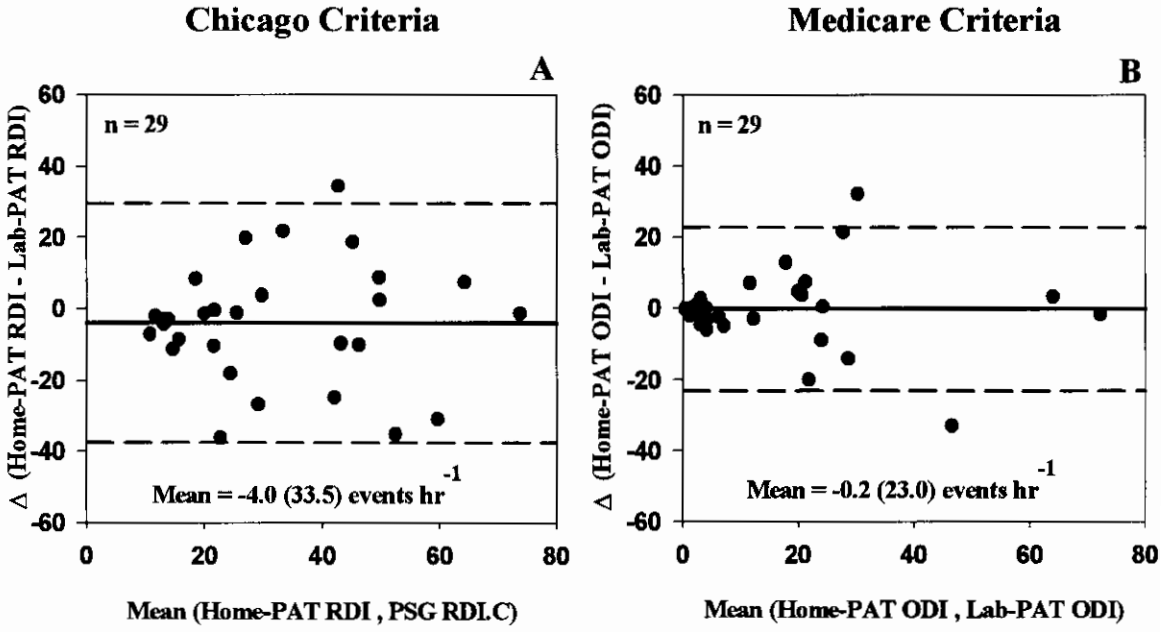
Chicago Criteria
A
n = 29
Δ (Home-PAT RDI - Lab-PAT RDI)
Mean = -4.0 (33.5) events hr-1
Mean (Home-PAT RDI , PSG RDLC)
Medicare Criteria
B
n = 29
Δ (Home-PAT ODI - Lab-PAT ODI)
Mean = -0.2 (23.0) events hr-1
Mean (Home-PAT ODI , Lab-PAT ODI)

Table 2 – Area Under the ROC Curve; Optimum Sensitivity and Specificity, Likelihood Ratios (Chicago Criteria)

		Watch_PAT in LAB										Watch_PAT in HOME									
RDI.C	OSA Prev	AUC	Sens	Spec	LR^+	Low CI	Up CI	LR^-	Low CI	Up CI	PAT RDI	AUC	Sens	Spec	LR^+	Low CI	Up CI	LR^-	Low CI	Up CI	PAT RDI
5	100	‡	‡	‡	‡	‡	‡	‡	‡	‡	‡	‡	‡	‡	‡	‡	‡	‡	‡	‡	‡
10	96.6	0.96	0.96	1.00	∞	‡	∞	0.04	0.01	0.25	14.1	0.82	0.82	1.00	∞	‡	∞	0.18	0.08	0.40	11.3
15	75.9	0.89	0.91	0.86	6.36	1.03	39.3	0.11	0.03	0.41	19.8	0.97	0.96	1.00	∞	‡	∞	0.05	0.01	0.31	12.5
20	69.0	0.93	0.90	0.89	8.10	1.27	51.7	0.11	0.03	0.43	20.6	0.92	0.80	0.89	7.20	1.12	46.30	0.23	0.09	0.56	19.3
30	41.4	0.95	0.92	0.82	5.19	1.83	14.7	0.10	0.02	0.67	26.6	0.89	0.92	0.82	5.19	1.83	14.70	0.10	0.02	0.67	24.9

RDI.C=PSG RDI (Chicago Criteria); OSA Prev = Prev of OSA; AUC=Area Under the ROC Curve; Sens = Sensitivity; Spec = Specificity; Low CI = Lower 95% Confidence Interval; Up CI = Upper 95% Confidence Interval; LR^+ = Positive Likelihood Ratio; LR^- = Negative Likelihood Ratio; PAT RDI = corresponding PAT RDI (based on Watch_PAT derived sleep time); ∞ = infinity, ‡ = cannot be calculated. Note: A ROC Curve could not be generated for a RDI.C threshold of 5 events per hour because the prevalence of OSA was 100% for that value. Thus, the AUC, optimum sensitivity/specificity, and likelihood ratios cannot be calculated.

Table 3 – Area Under the ROC Curve; Optimum Sensitivity and Specificity, Likelihood Ratios (Medicare Criteria)

		Watch_PAT in LAB										Watch_PAT in HOME									
RDI.M	OSA Prev	AUC	Sens	Spec	LR^+	Low CI	Up CI	LR^-	Low CI	Up CI	PAT ODI	AUC	Sens	Spec	LR^+	Low CI	Up CI	LR^-	Low CI	Up CI	PAT ODI
5	55.2	0.99	1.00	0.92	13.0	1.98	85.5	0.00	0.00	‡	7.0	1.00	1.00	1.00	∞	‡	∞	0.00	0.00	‡	4.7
10	48.3	1.00	1.00	1.00	∞	‡	∞	0.00	0.00	‡	9.5	0.99	0.93	0.93	13.9	2.09	93.4	0.08	0.01	0.51	10.8
15	34.5	0.99	1.00	0.90	9.50	2.56	35.2	0.00	0.00	‡	13.6	0.90	0.90	0.84	5.70	1.98	16.4	0.12	0.02	0.77	15.1
20	31.0	1.00	1.00	1.00	∞	‡	∞	0.00	0.00	‡	17.5	0.86	0.89	0.80	4.44	1.80	11.0	0.14	0.02	0.89	15.1
30	17.2	0.99	1.00	0.96	24.0	3.52	164	0.00	0.00	‡	23.9	0.87	1.00	0.71	3.43	1.84	6.40	0.00	0.00	‡	15.1

RDI.M=PSG RDI (Medicare Criteria); OSA Prev = Prevalence of OSA; AUC=Area Under the ROC Curve; Sens = Sensitivity; Spec = Specificity; Low CI = Lower 95% Confidence Interval; Up CI = Upper 95% Confidence Interval; LR^+ = Positive Likelihood Ratio; LR^- = Negative Likelihood Ratio; PAT ODI = corresponding PAT ODI (based on Watch_PAT derived sleep time); ∞ = infinity, ‡ = cannot be calculated.

Pulmonary Perspective

Access to Diagnosis and Treatment of Patients with Suspected Sleep Apnea

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BACKGROUND

Brief periods of breathing cessation (apneas) or marked reduction in VT (hypopneas) are common in adults during sleep. Prospective studies indicate that sleep apnea contributes to systemic hypertension (1), is a modifiable risk factor for motor vehicle accidents (2), and that its adverse impact on quality of life is treatable (3–6). As a result, there is substantial and growing demand by patients to access diagnostic studies and effective treatment. Wait times result when demand exceeds capacity. Demand is influenced by (*1*) prevalence and incidence of sleep apnea, (*2*) cost and patient reimbursement policies, (*3*) patient and primary physician awareness, and (*4*) wait times. Capacity is dictated by (*1*) availability of sleep laboratory beds determined by funding policies, (*2*) adherence to guidelines for diagnosing sleep apnea and continuous positive airway pressure (CPAP) titration published by the American Academy of Sleep Medicine (7) and the American Thoracic Society (8), (*3*) availability of sleep specialists, and, (*4*) policies about who can order/interpret diagnostic polysomnography and CPAP titration studies. This article represents information from five countries regarding their population, annual number of sleep studies performed, the range of wait times patients experience, and some strategies used for dealing with the mismatch between demand and capacity (Table 1). Policy issues regarding sleep laboratory funding and sleep specialist practice and training have also been addressed.

The authors have estimated data on number of sleep laboratories and studies and wait times because no country systematically tracks this.

STATUS

United Kingdom

The population of the United Kingdom is 58.8 million (www.statistics.gov.uk/census2001). It is estimated that there are 84 sleep laboratories in the United Kingdom with a total of 170 polysomnography beds (Simone De-Lacy, British Sleep Society, personal communication). The best estimate of the number of new patient sleep studies per year is 25,000 (42.5 studies per 100,000 population).

Waiting times vary widely across the country with no clear geographic trends. The average time for a nonurgent referral to be seen by a specialist is around 6 months (range, 2–24 months) and for a sleep study thereafter around 4 months (range, 0–48 months). Thereafter the delay for a CPAP titration is 4 months (range, 3–6 months). Thus, the overall wait from referral to CPAP averages approximately 14 months (range, 7–60 months).

The sleep center at the Edinburgh Royal Infirmary is university affiliated, but the funding for the clinical service is 100% from government. General practitioners refer half of the patients to this service and hospital specialists the other half. Sleep studies are ordered by one of two sleep physicians. To deal with the mismatch of demand and capacity, all referral letters are reviewed and prioritized by one of the sleep specialists. All patients living within 100 miles (160 km) are offered home-limited sleep studies, and only those with equivocal results get polysomnography. Patients living beyond 100 miles get split-night studies if their Epworth sleepiness score exceeds 11 (total score = 24) or if they report sleepiness when driving. Night nurses are cleared to start titrating CPAP if a sleepy patient's apnea–hypopnea index (AHI) exceeds 20 after 2 hours of good sleep.

These practices differ from those elsewhere in the United Kingdom. Overall, in the United Kingdom around two thirds of all "sleep studies" are oximetry alone and 20% are limited sleep studies, with only 10% being full polysomnography studies (Simone De-Lacy, British Sleep Society, personal communication). Over 50% of all such sleep studies are performed unattended at home. Oximetry alone studies are especially prevalent in England. Some general practitioners refer patients to otolaryngologists, who have no specific training in sleep, because of the long waiting times.

Reimbursement for diagnosis and treatment is provided completely from government. Almost all physicians who review patients with sleep apnea are respirologists. Training in sleep is unregulated, but at least 3 months in a sleep center is recommended for all trainee respiratory physicians.

Belgium

Belgium has a population of 10.0 million and approximately 50 sleep laboratories. In 2001, about 17,700 adult polysomnographies were reimbursed by the social security system (177 studies per 100,000 population). More than 90% of polysomnographies were performed in hospital-based sleep laboratories.

A general practitioner may request a sleep study directly but most usually through referral to a sleep specialist of the particular hospital, usually a respirologist, neurologist, or adult psychiatrist. A standard, nonurgent referral will be seen within 1 to 3 weeks. Thereafter, the waiting time for diagnostic polysomnography varies from 2 weeks to 2 months, and the waiting time for a CPAP

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TABLE 1. SLEEP STUDY RATES PER 100,000 POPULATION AND WAITING TIME FOR DIAGNOSIS AND TREATMENT WITH CONTINUOUS POSITIVE AIRWAY PRESSURE IN FIVE COUNTRIES

Country	Population	No. of Sleep Labs	No. of Sleep Beds	No. of Beds/ 100,000	No. of Studies/yr	No. of Studies/ yr/100,000	Waiting Time (mo)
United Kingdom	58,800,000	84	170	0.3	25,000	42.5	7–60
Belgium	10,000,000	50	150	1.5	17,716	177.2	2
Australia	18,970,000	65	244	1.3	53,500	282.0	3–16
United States	280,000,000	1,292			1,170,000	427.0	2–10
Canada	31,400,000	100	440	1.4	116,000	370.4	4–36

trial under polysomnography is generally 1 to 4 weeks. Thus, a patient who is nonurgent waits 1 to 3 months from referral to the start of therapy. Some laboratories add ambulatory equipment to standard hospital sleep beds to keep waiting lists within this range.

The sleep laboratory of the Cliniques Universitaires Saint-Luc, a 950-bed, private university hospital, receives referrals from general practitioners and specialists; after an outpatient assessment by a member of the medical team, a 24-hour hospital admission is ordered for testing that includes both afternoon and night polysomnography. To cope with increasing demand, we have increased the number days per week of operation from 4 nights to 7 nights (2 beds per night); we have not had to use portable monitoring or split-night studies. Clinical prediction rules are used to establish "*a priori*" probabilities but not to select patients.

Polysomnography in Belgium is reimbursed by a mandatory social security program if overseen by a specialist in neurology, psychiatry, respirology, or pediatrics, and it records standard signals. CPAP is covered if the AHI and the movement arousal index are at least 20 and 30, respectively, and the therapeutic polysomnography CPAP trial shows a clear improvement. Hospitals providing CPAP therapy have to be approved by a specific contract with the social security, thereby limiting the number of centers able to treat these patients.

Belgium has not defined the minimal requirements to read and interpret polysomnography; however, it is expected that physicians performing this task will be specialists with appropriate training.

Australia

Australia had a population of 18.97 million in 2001 (www.abs.gov.au/Ausstats). An informal listing by Sleep Disorders Australia, a patient support group, has identified a total of 65 adult sleep laboratories across the country, with the number increasing each year. In a brief survey of these laboratories (60% response rate), 52% were in the private sector, 28% were in the public sector, and the remaining 20% had a mixture of public and private beds. There are a similar number of beds ($\sim$ 122) in both the public and private sectors. The combined sectors are performing an estimated 53,500 polysomnograms per year (282 studies per 100,000 population). The real percentage of the population studied each year is likely to be only half of this figure as many studies represent treatment or follow-up studies.

Patients wait an average of 9 (range, 1–32) weeks for initial consultation after being referred. Sleep specialists request diagnostic polysomnography resulting in an additional wait of 21 (4–68) weeks in the public sector and 4 (1–12) weeks in the private sector. After completion of the diagnostic study, the time lapse until therapy is started is highly variable with some centers starting patients immediately and others waiting up to 40 weeks for a CPAP titration study. Most laboratories will prioritize studies on the basis of clinical urgency that is decided by the referring physician and some will also use clinical prediction rules. Some laboratories use split-night studies and some use oximetry studies to monitor moderate to severe cases who are started on CPAP. There are very few alternate diagnostic services (such as portable monitoring) provided by any of the sleep centers in Australia because of inadequate reimbursement. Some patients approach equipment companies directly for a trial of treatment, but little information is available about their outcomes.

Australians are provided with a federal government–funded Medicare system and state government–funded public hospitals. Sleep centers that operate in state government hospitals do not charge a polysomnography fee to the patient. Private sleep laboratories are reimbursed Australian $450 for polysomnography by Medicare; an additional Australian $350 to 500 is paid by the private health insurance fund and the patient in varying combinations. To access Medicare funding a "qualified sleep medicine practitioner" must be a Fellow of the Royal Australasian College of Physicians, necessitating postmedical degree training for 7 or more years, including a period of 1 to 3 years in full-time sleep medicine training. The Royal Australasian College of Physicians has recognized Sleep Medicine as a subspeciality of internal medicine and offers postgraduate training.

United States

The United States has an estimated population of 280 million (Central Intelligence Agency—The World Factbook 2002). A nationwide survey in June 2001 estimated that there were 1,292 sleep laboratories in the United States and that 1.17 million polysomnograms were performed in the preceding year (427 polysomnograms/100,000 population) (9). By contacting all known sleep laboratories in Massachusetts (34), Oregon (20), and Louisiana (29), this survey found polysomnography rates (studies per year per 100,000 population) of 529, 448, and 406, respectively. Estimates of rates in other states ranged from 121 (Colorado) to 1,161 (Maryland).

The Veterans Health Administration (VHA) provides additional insights concerning patient access to the diagnosis and treatment of sleep apnea in the United States. The VHA cares for approximately 3.75 million veterans (95% men, 5% women), and in 2001 there were 55 sleep laboratories in the VHA system (148 beds; 6,000 patients—160 studies per 100,000).

The average time from patient referral to sleep clinic evaluation and laboratory testing in the United States is quite variable ranging from a few weeks to more than a year. In general, wait times are longer in laboratories located in university, state, and federal government (VHA) facilities.

The Penn Sleep Center (University of Pennsylvania) receives patient referrals primarily from primary care providers within the medical center and throughout the greater Philadelphia area. Patients are scheduled for in-laboratory testing (12 beds) after clinic evaluation by sleep center specialists. The wait time from

TABLE 2. SLEEP STUDY RATES PER 100,000 POPULATION ACROSS CANADA

Region/Province	Population	No. of Sleep Labs	No. of Sleep Beds	No. of Beds/ 100,000	No. of Studies/yr	No. Studies/yr/ 100,000
Western Canada	9,417,514	15	44	0.5	11,450	122
British Columbia	4,141,272	5	18	0.4	6,000	145
Alberta	3,113,586	5	14	0.4	3,000	96
Saskatchewan	1,011,808	2	6	0.6	1,150	114
Manitoba	1,150,848	2	4	0.3	1,300	113
Central Canada	19,523,509	81	384*	2.0*	103,600*	531*
Ontario	12,068,301	69	340*	2.8*	93,700*	776*
Quebec	7,455,208	12	44	0.6	9,900	133
Eastern Canada	2,372,925	4	11	0.5	1,300	55
Nova Scotia	944,765	2	6	0.6	700	74
New Brunswick	756,652	1	3	0.4	450	60
Prince Edward Island	139,913	0	0	0.0	0	0
Newfoundland	531,595	1	2	0.4	150	28
Territories	100,042	0	0	0.0	0	0
Yukon	29,924	0	0	0.0	0	0
Northwest Territories	41,403	0	0	0.0	0	0
Nunavut	28,715	0	0	0.0	0	0

* Data from all provinces obtained from questionnaires/telephone survey. Sleep laboratory contact list from personal communications and the Canadian Sleep Society (http://www.css.to/). All sleep laboratories were surveyed except Ontario, where numbers are based on projections generated from data provided by 38 of 69 known sleep laboratories.

referral to initial clinic visit varies (2–12 weeks); the average time from clinic visit to polysomnogram is 2 to 3 weeks, although it was 4 to 5 months when the sleep laboratory capacity was four beds. Split-night studies are performed, but portable monitors are rarely used.

In contrast, the four-bed sleep center at the Philadelphia Veterans Affairs Medical Center, the only VHA sleep laboratory in the region, receives referrals from VHA providers in the states of Delaware, southern New Jersey, and eastern Pennsylvania. Funding for technology staff is only available to operate two beds, 4 nights per week. The average wait time from referral to initial clinic visit is 2 to 3 months and from clinic visit to polysomnogram an additional 2 to 3 months. Other VHA sleep programs report that patients wait on average approximately 8 to 9 months from laboratory referral to sleep evaluation. Using VHA guidelines, the Philadelphia Veterans Affairs Medical Center performs unattended home studies with validated portable monitors for diagnosis and to initiate treatment with CPAP in about 40% of patients with clinical suspected sleep apnea. When sleep apnea is diagnosed with a home study, a 1-week home auto-CPAP titration is performed before initiating CPAP treatment.

The majority of sleep evaluations are split-night polysomnograms, a practice driven by limited resources and reimbursement policies. Effective March 2, 2003, the Centers for Medicare and Medicaid Services accepts charges of US $807.69 for a split-night polysomnogram and US $223.62 for a Level II unattended sleep study (no sleep staging). Sleep laboratories such as those in the VHA and health maintenance organizations are more likely to perform sleep evaluations with portable monitors in addition to polysomnograms. The majority of sleep laboratories in the United States are directed by respirologists, and about one-third of them are accredited by the American Academy of Sleep Medicine. Certification of the sleep specialist and the sleep laboratory are increasingly being required for reimbursement by states and insurance carriers.

Canada

Canada has a population of 31.4 million (Statistics Canada: http://www.statcan.ca) residents living in 10 provinces and 3 territories. The number of sleep studies per 100,000 varies greatly across the country (0–776 per 100,000, Table 2) as do waiting times. In eastern and western Canada the wait for sleep specialist consultation averages 4 to 6 months (in some places it exceeds 12 months), and completion of a polysomnogram varies from 8 to 30 months, resulting in a total wait of approximately 24 months (range, 8–36 months). Patients in Quebec experience similar wait times as the Western and Eastern regions. With greater sleep studies per capita in Ontario, wait times are much shorter for consultation and polysomnography, averaging 2.4 and 2 months, respectively, and there is generally little time required to start CPAP.

The sleep laboratory at the Foothills Medical Centre is affiliated with the University of Calgary, has four beds, and performs approximately 1,000 polysomnograms per year. Funding, including interpretation fees, is provided by the Calgary Health Region from its global operating funds provided by the provincial government. Physician consultation fees originate from a separate, fee-for-service budget. Patients are referred mostly by primary care physicians, some otolaryngologists, and some internists/subspecialists. Polysomnography ordering is limited to eight sleep consultants who review all referred patients. Split-night polysomnograms and home monitors (oximetry, body position, snoring, and airflow) (10) are used to increase capacity. Patients are triaged on the basis of medical history, a validated clinical prediction rule (11), and reported daytime sleepiness. Treatment is often initiated at home using auto-CPAP machines. Because of extensive wait times, primary care physicians have started to order home oximetry for their patients and will not necessarily refer these patients to the sleep center. This testing is not covered by provincial Medicare.

Provinces and territories have the responsibility of providing comprehensive medical coverage to their citizens. In most provinces funding is only available to hospitals for performing polysomnography, limiting the number of laboratories; however, in Ontario funding is available based on a fee for service contract that allows for nonhospital laboratories. CPAP funding varies across the country; in some provinces it is completely covered by provincial Medicare, although in the majority, patients are responsible for paying unless they have private insurance. The Royal College of Physicians and Surgeons of Canada has not recognized sleep medicine as a specialty. An increasing number of physicians who interpret polysomnography have been certified

by the American Board of Sleep Medicine; however, this is not a stipulation of provincial licensing authorities for providing consultation and polysomnography interpretation services.

DISCUSSION

In many locations around the world patients suspected of having sleep apnea face challenges accessing diagnostic services and treatment because of the discrepancy between demand and capacity. Demand is difficult to quantify. The prevalence of sleep apnea, based on an AHI (number of apneas plus hypopneas per hour of sleep) of 5 or higher, is 24% in males (15.5%of whom self-report hypersomnolence; 4% have both) and 9% in females (22.3% of whom self-report hypersomnolence; 2% have both) aged 30 to 60 years (12). The prevalence of moderate sleep apnea (AHI ≥ 15) is 9 and 4% in males and females, respectively. Sleep apnea is suspected in patients who are obese, hypertensive, habitual snorers, and hypersomnolent (13). All of these conditions are highly prevalent; thus a conservative estimate of the "at-risk" population who might be expected to be referred for assessment is at least twice the prevalence (13%) of moderate sleep apnea. Predictions of at-risk populations in this report have not been adjusted for age less than 30 and greater than 60 because the data is preliminary; it is estimated that about 2% of children have sleep apnea (14), but there is a high at-risk population of children who habitually snore (15) that is difficult to quantify. Sleep apnea prevalence is increased in older adults (15), which would offset possible lower rates in children.

Estimation of sleep apnea incidence is problematic because of using AHI cut points to identify who is at risk for incident sleep apnea at baseline. It is recommended to estimate incidence on the basis of the difference in prevalence between baseline and follow-up (T. B. Young, personal communication). Using this approach the incidence of moderate to severe sleep apnea (AHI ≥ 15) is estimated at 0.6% (increase in prevalence of 5.1% over 8 years) (16).

The capacity for performing polysomnography is limited. The American Academy of Sleep Medicine recommends polysomnography for determining the severity of, and evaluating patients' response to treatment for, sleep apnea (7). The American Thoracic Society recommends polysomnography for CPAP titration (8). If these guidelines are followed, on the basis of incidence estimates alone, 600 polysomnograms per 100,000 population per year would be required; however, the Wisconsin sleep cohort study has found that 82% of men and 93% of women with moderate to severe sleep apnea have not been diagnosed (17). The capacity required to deal with these undiagnosed cases, spread over a 10-year period (82% of 9% of the male population and 93% of 4% of the female population), would be an additional 555 polysomnograms per 100,000 population per year. This assumes that each patient would only require a single polysomnogram and does not take into account at-risk patients who should be offered polysomnography but who ultimately are not diagnosed with sleep apnea. Using a conservative estimate that 50% of polysomnograms would be positive for sleep apnea, approximately 2,310 polysomnograms per 100,000 people per year would be required to adequately address the demand for diagnosis and treatment of patients with suspected sleep apnea of at least moderate severity. This exceeds by a factor of 10 in most countries and a factor of 50 in the United Kingdom, the actual capacity for polysomnography. In sleep centers where specialists control access to polysomnography, their availability is likely to be more limiting than polysomnography. If a full-time specialist reviewed 1,500 new patients with suspected sleep apnea per year (6 patients per day), a community would require 1.4 full-time sleep specialists per 100,000 population. For the Calgary population (~ 1,000,000), this would translate into 14 full-time sleep specialists. At the Foothills Medical Centre, eight part-time sleep specialists equate to about one full-time position. Hence, we service approximately 7% of the potential sleep apnea referral population.

Funding models clearly dictate availability of polysomnography as evidenced by the marked variation in the rate of sleep studies per year across Canada (Table 2). In most locales in Canada and many across the world, polysomnography availability is capped by administrative funding. Waiting times for consultation, diagnosis, and treatment in this type of system are excessive; the exception is Belgium, which, although has a similar ratio of sleep studies to population as other countries, does not have similar waiting times. This would suggest that the demand there is limited, perhaps because of underrecognition by primary care physicians. Excessive waits lead to polysomnography alternatives for diagnosis and CPAP titration, in some circumstances by practitioners with little or no training in sleep or respiratory medicine. There is a lack of evidence indicating that these alternative strategies offer comparable outcomes for patients.

Patient access to appropriate investigation and treatment for sleep apnea is clearly restricted. Resources in the five countries that are included in this report, including the estimated resources in the United States (9), are inadequate to deal with conservative estimates of demand based on known prevalence and incidence data. Because treatment of sleep apnea provides many benefits to patients and society, it is imperative that strategies be developed, and research evidence gathered to support them, that address the current demand–capacity chasm.

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Comment #80:
Submitter: Andrew Behar
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Date: May 7, 2004
Comment:

(See next page)

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May 7, 2004

Tiffany Sanders, M.D.
Francina C. Spencer
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Dear Dr. Sanders,

VivoMetrics® is writing in support of Dr. Mendelson, Dr. Davidson and others regarding the request to include and recognize in Medicare coverage policy the use of portable multi-channel home sleep testing devices as an alternative to facility-based polysomnography in the evaluation of Obstructive Sleep Apnea (OSA).

Enclosed is a compilation of scientific papers, articles, abstracts and marketing materials for the LifeShirt® System, a continuous monitoring system that captures PSG equivalent data in multiple environments. The LifeShirt System received FDA clearance in 2002.

The LifeShirt System consists of core and peripheral physiologic sensors and data analysis software. The core data streams are respiratory inductance plethysmography (RIP), electrocardiography (ECG) and accelerometry. Peripheral inputs include electroencephalography (EEG), arterial oxygen saturation (SpO_2), skin temperature, limb movement, blood pressure and throat sound. An electronic patient diary allows the collection of subject-reported information such as symptoms, emotions, activities, medications taken and programmed survey data. Data collected by the LifeShirt System are encrypted and stored on a data card, processed by certified sleep technicians in the VivoMetrics 21 CFR part 11 compliant data center, reviewed by a physician, and securely stored and transmitted to clinical trial sponsors or research sites as appropriate.

LifeShirt System Technology:

- Based on a miniaturized, ambulatory version of RIP
- Contains embedded RIP sensors in a comfortable garment that keeps respiratory inductance bands properly positioned
- Collects high quality, robust data from patients sleeping naturalistically in a variety of settings from the controlled laboratory environment to the home
- RIP cited in the July 17, 2002 FDA Apnea Guidance Document as capable of differentiating between obstructive and central sleep apnea

LifeShirt System Components

- Lightweight (8oz, 260g), machine washable, comfortable shirt with embedded sensors
- Integrated recorder captures continuous measures on more than 30 physiologic parameters during daily activities. Data is encrypted and stored on flash memory card.
- Electronic Patient Diary records time/date stamped symptom, mood and activity information
- VivoLogic® analysis and reporting software
    - decrypts recorded data
    - synchronizes objective physiologic data with subjective patient report
    - data is processed by certified sleep technicians and reviewed by a physician

- data securely stored and transmitted to research sites or clinical trial sponsors by VivoMetrics' 21 CFR part 11 compliant data center
- researchers can examine high-resolution waveforms and look at trends over time.

LifeShirt System technology is currently being used by physicians at academic medical institutions including Johns Hopkins University, Yale University and Stanford University; health care institutions including the Mayo Clinic, Walter Reed Army Hospital and the Rehabilitation Hospital of Indiana; and pharmaceutical companies including GlaxoSmithKline, Pfizer and Eli Lilly.

Please review the enclosed information and call me on (805) 275-5834 if you have any questions. We anticipate sending supplemental information prior to meeting with you in the late May, early June timeframe.

Thank you for your consideration

Very truly yours,

Andrew Behar
Chief Operating Officer & Founder
VivoMetrics, Inc.

Enclosures:

Selected Annotated Bibliography for the LifeShirt System
LifeShirt System Validations
Abstract Proof, Prevalence of Obstructive Sleep Apnea in Patients Surviving Ischemic Stroke, Zaneteas, Philip; Coyle, Michael; Derchak, Alexander; Mendelson, Wallace, accepted for presentation at the Associated Professional Sleep Societies, June 2004
The LifeShirt: A Multi-function Ambulatory System that Monitors Health, Disease, and Medical Intervention in the Real World; Paul Grossman, PhD, University of Freiburg
Accuracy of Respiratory Inductive Plethysmography during Wakefulness and Sleep in Patients with Obstructive Sleep Apnea, Jean Paul Cantineau, MD; Pierre Escourrou, M.D., Ph.D.; Richard Sartene, M.D.; Claude Gaultier, M.D., Ph.D., Michael Goldman, M.D., "CHEST", October 1992
Accuracy of Respiratory Inductive Plethysmography for the Diagnosis of Upper Airway Resistance Syndrome, Daniel I. Loube, M.D., FCCP; Teotimo Andrada, M.S.; Robin S. Howard, M.A., "Chest", May 1999
Summary Document for LifeShirt System for the Assessment of Sleep Disordered Breathing and Assessment of Sleep Structure Via Electroencephalography, VivoMetrics, April 2004.
VivoMetrics product materials

Abstract Proof

CONTROL ID: 77652

CONTACT (NAME ONLY): Michael Coyle

PRESENTER: Michael Coyle

Abstract Details

ABSTRACT_STATUS:

PRESENTATION TYPE: Oral Presentation

CATEGORY: J. Sleep Disorders – Breathing

KEYWORDS: sleep disordered breathing, stroke, monitoring.

AWARDS:

Abstract

TITLE:

Prevalence Of Obstructive Sleep Apnea In Patients Surviving Ischemic Stroke

AUTHORS (ALL): Zaneteas, Philip D.[1]; Coyle, Michael A.[2]; Derchak, P. Alexander[2]; Mendelson, Wallace B.[3].

INSTITUTIONS (ALL): 1. Rehabilitation Hospital of Indiana, Indianapolis, IN, USA.
2. Clinical Research, VivoMetrics, Princeton, NJ, USA.
3. Psychiatry and Clinical Pharmacology, University of Chicago, Galveston, TX, USA.

ABSTRACT BODY:

Introduction: Sleep disordered breathing (SDB) has been observed to be a pre-event characteristic of many patients who experience stroke (CVA). Also, surviving a CVA has been reported to increase the likelihood of SDB. SDB has been associated with comorbidities in the general population and may potentially have a negative impact on the recovery trajectory of CVA survivors. Therefore, a cost-effective and accessible tool for identifying SDB would have clinical value. To assess the prevalence and severity of SDB in patients who had recently survived the acute CVA trauma phase and were deemed stable, we employed a portable system to quantify apneas (obstructive (OA), central (CA), mixed (MA)) and blood oxygen saturation (S_pO2).

Methods: Recent survivors of ischemic CVA participated in the study (N = 18; n = 12 females; age = 63 ±14 years; n = 14 right hemisphere lesions). Patients were evaluated for SDB within 72 hours of the stroke diagnosis or when they were considered to be stable. CVA foci were determined and severity was quantified with the Functional Independence Measure (FIM). All relevant respiratory variables and finger tip pulse oximetry were recorded with a previously validated portable monitoring system (LifeShirt®, VivoMetrics, Inc.; Ventura, CA). Presence of SDB was defined as an apnea hypopnea index (AHI) > 10. SDB events associated with a drop in S_pO_2 of 3% or greater were classified as desaturation events. Sleep time was estimated from technician recorded Lights-off to Lights-on for the calculation of AHI ([apneas + hypopneas]/sleep time) and oxygen desaturation index (ODI; desaturation events/hour).

Results: Fifteen patients (87%) exhibited an AHI > 10. For this sub-group, FIM score at the time of admission was (mean ± SD) 65 ± 15. AHI was 34 ± 14 events per hour. Total SDB events were: OA = 148 ±11; MA = 57 ± 67 and CA = 5 ±14. Blood oxygen desaturations were common (mean nadir S_pO_2 = 79 ± 0.1%), as was the frequency of desaturations events (ODI = 45 ± 15).

Conclusion: Theses data enrich previous observations of the prevalence of SDB in patients who have recently survived stroke, as well as suggest that SDB can be efficiently identified by this portable system in this population.

Support (optional): This study was supported by VivoMetrics.

THE LIFESHIRT: A MULTI-FUNCTION AMBULATORY SYSTEM THAT MONITORS HEALTH, DISEASE, AND MEDICAL INTERVENTION IN THE REAL WORLD

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The LifeShirt: A multi-function ambulatory system that monitors health, disease, and medical intervention in the real world

Medical monitoring of health, disease, therapy and management has almost solely relied upon measurements made in the physician practice, clinic or hospital setting. Inferences about symptom improvement and quality of life have also been based exclusively upon occasional self-reports of patients during medical visits. Because the ecological validity of this approach seriously limits our potential to adequately diagnose and treat patients, there has been increasing interest in ambulatory monitoring for a variety of conditions. Despite advances made in health-related ambulatory monitoring, medical practitioners and researchers have remained seriously constrained in their ability to acquire concurrent assessments of multiple physiological systems, as well as patient reports of symptoms and well being in daily life: Almost all past and current applications have been limited to the registration of a single variable (e.g. the electrocardiogram or blood pressure), and this has resulted in incomplete information about other relevant physiological and environmental factors likely to contribute to disease or its amelioration. Monitoring of multiple physiological functions has been too complicated to achieve and has required special measurement devices that have been unavailable, too expensive, or too cumbersome to effectively employ. Concurrent assessment of pertinent information about patient activities during monitoring has remained difficult to accomplish, although such information is likely to be crucial for the interpretation of physiological findings and patients' perceptions of improvement.

The LifeShirt™ (Vivometrics, Inc., Ventura, CA, U.S.A.) is a multi-function ambulatory device capable of simultaneously monitoring several physiological signals and patient reports of symptoms and well being. The LifeShirt system is an extensible data acquisition and processing platform consisting of 3 parts: a garment, a data recorder, and PC-based analysis software. Sensors in the LifeShirt garment continuously monitor respiration (via inductive plethysmography), the electrocardiogram, activity and posture. Other functions can easily be plugged into the system, including pulse oximetry, EEG/ EOG measurement, blood pressure, temperature, capnometry and acoustic monitoring. Subjective patient data can also be entered into the LifeShirt recorder, and all data are encrypted and written to a flash memory card. Vivologic™ analysis software provides full-disclosure analysis and display of high-resolution waveforms and over 30 derived parameters;. the software also produces summary reports for clinical diagnostic purposes.

The LifeShirt has been rigorously tested for more than 38,000 hours in 90 studies with 1,750 subjects. The device has received all necessary regulatory approvals and is currently used in leading research institutions throughout the United States, Canada and Europe. Clinical applications include sleep diagnostics, heart disease, pulmonary disorders, cardiopulmonary rehabilitation, early hospital discharge and pre- and post-operative monitoring, human-factors in ergonomics (e.g. work-related concerns, aviation and the military) and behavioral medicine (e.g. fatigue and quality of life in cancer and chronic fatigue syndrome).

Key words (title): Ambulatory system, Disease, Health, LifeShirt, Medical intervention, Multi-function, Meal world

Key words (text): Ambulatory monitoring, Clinical and research applications, Physiology, Multi-signal, Respiration, Electrocardiogram, Accelerometry, Oximetry, Heart-rate variability, Electronic diary of patient symptoms

Introduction

Medical monitoring of health, disease, therapy and management has almost solely relied upon measurements made in the physician practice, clinic or hospital setting. Inferences about symptom improvement and quality of life have also been based exclusively upon occasional self-reports of patients during medical visits. Because the ecological validity of this approach seriously limits our potential to adequately diagnose and treat patients, there has been increasing interest in ambulatory monitoring for a variety of conditions. Despite advances made in health-related ambulatory monitoring, medical practitioners and researchers have remained seriously constrained in their ability to acquire concurrent assessments of multiple physiological systems, as well as patient reports of symptoms and well being in daily life: Almost all past and current applications have been limited to the registration of a single variable (e.g. the electrocardiogram or blood pressure), and this has resulted in incomplete information about other relevant physiological and environmental factors likely to contribute to disease or its amelioration. Monitoring of multiple physiological functions has been too complicated to achieve and has required special measurement devices that have been unavailable, too expensive, or too cumbersome to effectively employ. Concurrent assessment of pertinent information about patient activities during monitoring has remained difficult to accomplish, although such information is likely to be crucial for the interpretation of physiological findings and patients' perceptions of improvement.

The LifeShirt™: A multi-function ambulatory monitoring device

The LifeShirt™ (Vivometrics, Inc., Ventura, CA, U.S.A.) is a multi-function ambulatory device capable of simultaneously monitoring several physiological signals and patient reports of symptoms and well being. The system is characterized by an extensible data acquisition and processing platform consisting of 3 parts: a garment, a data recorder, and PC-based analysis software (see Figure 1).

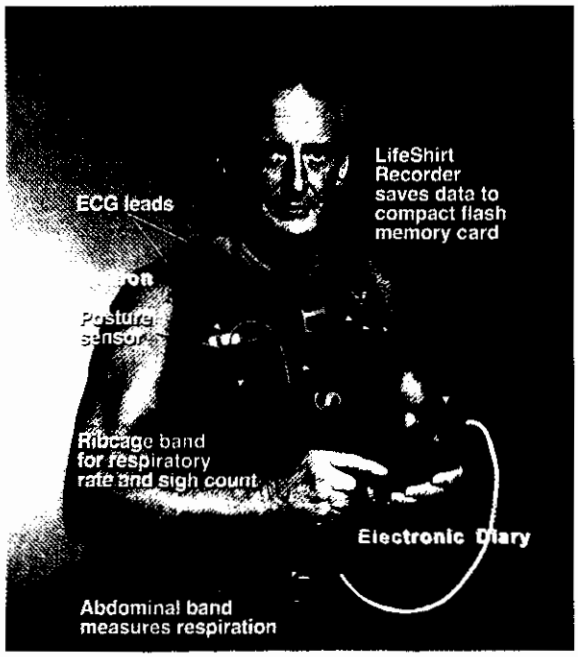

Figure 1. The LifeShirt system: the monitoring vest and data acquisition and electronic diary unit.

Sensors in or attached to the LifeShirt garment continuously monitor respiration, the electrocardiogram, activity and posture. Respiratory measures are derived from thoracic and abdominal inductive plethysmography bands sewn into the Lycra vest. Inductive plethysmography provides the gold standard for non-invasive assessment of respiratory pattern. The U.S. National Institutes of Health recognize respiratory inductance plethysmography as the best non-invasive method to assess sleep disordered breathing in infants (Ramanathan et al., 2001). The International Task Force of the

European Respiratory Society, the Australasian Sleep Association and the American Thoracic Society also concluded that RIP was the best noninvasive method of monitoring sleep disordered breathing in adults (Flemons and Buysse, 1999).

Respiratory parameters derived from the LifeShirt include volumetric (e.g. minute ventilation volume), timing (e.g. respiration rate) and flow (peak-expiratory flow) measures. These measures are relevant for a number of diverse disorders, such as pulmonary disease, heart failure, and anxiety disorders. Minute ventilation volume can also ordinarily be used as an index of metabolic activity. This variable, together with the accelerometer activity and posture signal, yields valuable information regarding activity pattern that aid in interpretation of other signals. The ECG signal is employed to detect arrhythmic activity and to quantify heart rate variability. Other functions can additionally be easily plugged into the LifeShirt system via an available port and concurrently registered, including pulse oximetry, the EEG and EOG, blood pressure, temperature, capnometry and acoustic monitoring. Subjective patient data (e.g. momentary reports of symptom and well being) are also easily entered into the LifeShirt recorder PDA by means of a programmable diary/questionnaire inventory that is easliy adapted to any disorder or health-related issue.

All data are encrypted and written to a flash memory card. Vivologic™ analysis software provides full-disclosure analysis and display of high-resolution waveforms and over 30 derived parameters (see Figure 2). Physiological data may be flexibly exported to spreadsheet programs for statistical analysis based on minute-to-minute averages, breath-byby breath analysis, or the digitized raw waveform. Moreover, newly developed software is capable of automatically analyzing segments of data synchronized to patient diary entries (see pink tab in Fig. 2); for example, physiological signal patterns immediately preceding a symptom entry can be simply analyzed to examine whether discrete physiological changes triggered symptoms. Vivologic software also produces summary reports for clinical diagnostic purposes. Figure 3 provides an example of a sleep diagnostic report automatically generated after visual editing.

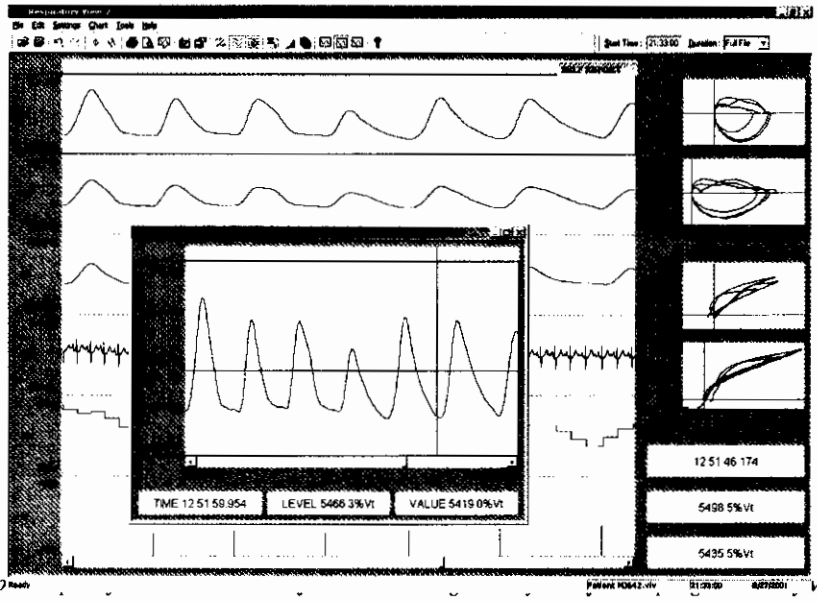

Figure 2. Samp ve panels to the left (top to bottom) are the tidal volume respiratory signal, the ribcage respiratory signal, the ECG, derived heart rate, and total respiratory cycle time. Note the full-disclosure of the respiratory and ECG waveforms. The center pop-up is a close-up of the ventilatory waveform, and the panels to the right are different respiratory flow-volume graphic relationships. Upper pink tab indicates diary entry.

The LifeShirt system has received all necessary regulatory approvals: ISO 9001 certification – October 2001
European CE mark – November 2001
FDA market clearance – April 2002
Canadian market clearance – July 2002
Compliance with 21 CFR Pt 11 – August 2002

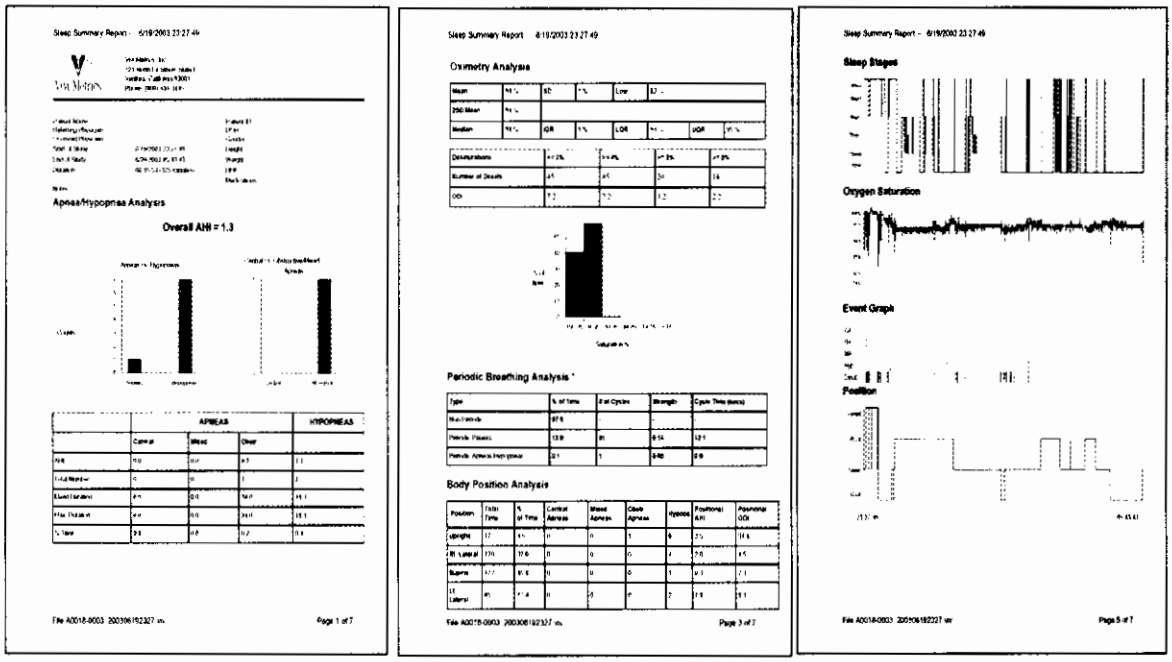

Figure 3. Example of a sleep report. Left panel, hypopnea/apnea analysis; middle panel, oximetry, periodic breathing and body position analyses; right panel, examples of specific parameters.

Real World Applications

The LifeShirt has been rigorously tested for more than 38,000 hours in 90 studies with 1,750 subjects. The units have also functioned reliably under a variety of extreme conditions, including U.S. Air Force plane testing at 7.5G, mountaineering at 4,500 m, Indianapolis 500 automobile racing, and long-haul trailer trucking driving. Not only is the system robust, but it is extremely comfortable, and user-friendly in terms of patient experience, instrumentation, data analysis and clinical interpretation.

The clinical applications of the Lifeshirt technology are equally wide-ranging. The LifeShirt makes possible ambulatory inductive plethymographic measurement of numerous respiratory parameters. Respiration has long been recognized as a critical indicator of many disease states but has not been previously reliably measurable in settings outside the hospital. Additionally, diagnosis and management of the whole range of pulmonary diseases from asthma to chronic obstructive pulmonary disorders is certain to benefit from ambulatory assessment of ventilatory activity during everyday life, since all current assessment procedures rely on clinical respiratory maneuvers and not the spontaneous breathing behavior abnormalities that are the source of patient complaints.

Clinical applications of the LifeShirt are, however, not limited to respiratory disorders. Concurrent measurement of respiration, activity and other physiological signals are important for a host of clinical syndromes and applications. Active research or clinical investigations using the LifeShirt are now taking place in the areas of sleep disorders, heart disease, anxiety disorders, diabetes, cancer, neurological conditions and functional somatic disorders, such as fibromyalgia, chronic fatigue syndrome and irritable bowel syndrome. Moreover, substantial evidence is available that measurement of heart-rate variability (HRV)–an important predictor of cardiovascular mortality and morbidity--would be greatly improved by taking into account respiratory and activity measures that confound HRV assessment (Bernardi et al., 1996; Grossman et al., 1991), which has not been previously possible. Simultaneous physiological monitoring and patient diary assessment of complaints and reported activity can lead to new insights into the relation between

Accuracy of Respiratory Inductive Plethysmography during Wakefulness and Sleep in Patients with Obstructive Sleep Apnea*

Jean Paul Cantineau, M.D.; Pierre Escourrou, M.D., Ph.D.; Richard Sartene, M.D.; Claude Gaultier, M.D., Ph.D.; and Michael Goldman, M.D.

To assess the accuracy of the respiratory inductive plethysmograph (RIP) during sleep in obese patients with obstructive sleep apnea (OSA), we monitored 13 patients with OSA during wakefulness and nocturnal sleep with simultaneous measurements of tidal volume from RIP and integrated airflow. Patients wore a tightly fitting face mask with pneumotachograph during wakefulness and sleep. Calibrations were performed during wakefulness prior to sleep and compared with subsequent wakeful calibrations at the end of the study. Patients maintained the same posture during sleep (supine, 11; lateral, two) as during calibrations. There were no significant differences in calibrations before sleep and after awakening. The mean error in 13 patients undergoing RIP measurements of tidal volume during wakefulness was -0.7 ± 3.4 percent while that during sleep was 2.1 ± 14.9 percent ($p<0.001$). The standard deviation (SD) of the differences between individual breaths measured by RIP and integrated airflow was 9.8 ± 5.5 percent during wakefulness and 25.5 ± 18.6 percent during sleep ($p<0.001$). During both wakefulness and sleep, errors in RIP tidal volume were not significantly correlated with body mass index. In 12 patients with at least 10 percent time in each of stages 1 and 2 sleep, SD was greater in stage 2 sleep compared with wakefulness and stage 1 ($p<0.001$). In three patients who manifested all stages of sleep, SD was greater in REM sleep than in wakefulness and all stages of non-REM sleep ($p<0.001$). In three patients who manifested all stages of sleep, SD was greater in REM sleep than in wakefulness and all stages of non REM sleep ($p<0.001$). This was associated with paradoxic motion of the rib cage in two patients during REM. We conclude that, despite increased errors in individual breath measurements during sleep, more marked during stages 2 and REM sleep, RIP is clinically useful to measure ventilation quantitatively in obese patients with sleep apnea. The criterion of a decrease of 50 percent in tidal volume assessed by RIP is appropriate to define hypopneas in such patients.

(Chest 1992; 102:1145-51)

ALG DIFF = algebraic difference; CI = confidence interval; CPAP = continuous positive airway pressure; OSA = obstructive sleep apnea; PSG = polysomnographic; REL DIFF = relative difference; RIP = respiratory inductive plethysmograph; SAS = sleep apnea syndrome; V_{PN} = tidal volume measured from integrated pneumotachograph tracing; V_{RIP} = RIP-derived tidal volume

Many investigations have demonstrated the accuracy of the respiratory inductive plethysmograph (RIP) in normal subjects and patients with COPD during wakefulness[1-6] using a two-compartment model of the thoracoabdominal wall proposed by Konno and Mead.[7] Several different calibration techniques are in use, including the isovolume method, the two posture method, least squares regression analysis, and a "qualitative diagnostic calibration." Acceptable results have been obtained during resting breathing in different body postures, during voluntary efforts to change the thoracic and abdominal volume displacements, and during exercise.[8] Additional reports have assessed breathing during sleep,[9-17] showing that calibrations during wakefulness before sleep and after awakening are closely similar. The criterion for acceptability of "before" and "after" calibrations has been either similarity to within 10 percent or absence of a significant change in calibration slope. When these criteria are satisfied, measurements of respiration from thoracoabdominal movements during intervening sleep have been assumed to be reliable.

Recently, it has been shown that 50 percent reductions in thoracoabdominal movements during sleep correlate better with both desaturation and arousal frequencies than 50 percent reductions in airflow measured by oronasal thermocouples.[13] However, calibrations of thoracic and abdominal movements change between wakefulness and sleep induced by ketamine anesthesia,[18] and one report[10] has concluded that RIP is unreliable for quantitative measurement of ventilation in sleeping asthmatic patients. A recent report on unrestrained normal subjects concluded that RIP is unreliable for quantitative measurements in normal subjects who are allowed to change body position during sleep, but RIP-derived tidal volume in these subjects showed considerable bias and scatter even during wakefulness.[19]

Because assessment of hypopnea is essential to the diagnosis of sleep apnea/hypopnea, the present investigation was undertaken in patients referred for evaluation of possible obstructive sleep apnea (OSA). We

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sought to evaluate the reliability of RIP calibration during wakefulness for assessing tidal volume *during* sleep. We used simultaneous measurements of tidal volume from the RIP and an integrated pneumotachograph during wakefulness and sleep to evaluate RIP accuracy when calibrations before sleep and after awakening were not significantly different.

Methods

Patients

Twenty consecutive patients presenting to the sleep laboratory of the Antoine Beclere Hospital with a history suggestive of sleep apnea syndrome were requested to participate in the study. After informed written consent was obtained, all patients underwent overnight polysomnographic (PSG) studies. Neither sedatives nor hypnoptics were used; and six patients were unable to sleep without substantial disruption due to intolerance of the face mask. An additional patient tolerated the study well, but the thoracic belt of the RIP failed intermittently during the course of the study. These seven patients are not included in the present results. The characteristics of the remaining 13 patients included in the present report (ten male) are listed in Table 1. Mean age was 55 years (range, 33 to 69 years), body mass was 99 kg (70 to 129 kg), and apnea index was 28 (15 to 53).

Patients reported to the sleep laboratory at 9 PM after eating a light meal, excluding caffeinated beverage and alcohol. Electroencephalographic (EEC), submental electromyographic (EMG), and electro-oculographic (EOC) tracings were obtained continuously by standard means. Arterial oxygen saturation was measured continuously with a pulse oximeter (Ohmeda 3740) attached to the finger. Respiratory airflow was measured by a pneumotachograph attached to a face mask that had a low pressure air-filled cushion, held in position with an elastic harness over the head and neck to ensure constant contact with the face. Tidal volume was obtained by integration of the airflow signal. Chest and abdominal RIP bands were secured with strips of adhesive tape over the thorax at the nipple level and abdomen at the level of the umbilicus, below the costal margin, and above the iliac crest. All signals were recorded on an oscillographic paper recorder.

After familiarization with the laboratory, patients were instructed in the performance of voluntary changes of thoracic and abdominal efforts during tidal volumes of different size.[18,20] During these efforts, calibration consisted of recording thoracic, abdominal, and volume signals while one investigator monitored the patients to ensure that they did not change body position and another monitored the RIP signals to ensure that they changed sufficiently and remained on scale. Calibration coefficients were calculated by the method of linear regression. All patients were instructed in the performance of isovolume maneuvers[7] to determine the ratio of the calibration coefficients. This ratio was then compared with that obtained algebraically from the method of linear regression. We calibrated all patients' thoracic and abdominal RIP signals during breathing in the posture chosen by the patient for sleeping (supine for 11 patients, lateral decubitus for two patients). Patients maintained this same posture throughout the entire study.

Calibrations were performed approximately 15 min prior to lights out. Following calibration, continuous recordings of EEG, EOG, EMG, SaO_2, thorax, abdomen, and tidal volume were obtained during wakefulness and sleep, including the transition as the patient went to sleep. Measurements were continued during sleep for 2 to 4 h, until the diagnosis of OSA was established. The patient was then awakened and a second calibration was obtained, after which patients underwent therapeutic continuous positive airway pressure (CPAP) titration. Tidal volumes from the pneumotachograph were discontinued during CPAP titration, because of the difficulty of obtaining unambiguous respiratory airflow tracings in the presence of applied nasal airway pressure.

Tracings of thoracic and abdominal displacements were measured in each stage of sleep when a series of at least 25 consecutive respiratory cycles were available for analysis. Calibration coefficients obtained during the initial (prior to sleep onset) calibration were applied to individual thoracic and abdominal tracings during wakefulness and sleep. The separate thoracic and abdominal volume contributions were added, cycle by cycle, to obtain the RIP-derived tidal volume (V_{RIP}), according to the following formula:

$$V_{RIP} = Vthoracic + Vabdominal = Kth \times Dth + Kab \times Dab \quad . \quad . \quad . \quad (1)$$

where:

V_{RIP} = tidal volume measured from abdominothoracic signals
Vthoracic = volume displaced by thoracic movements
Vabdominal = volume displaced by abdominal movements
Kth = volume-displacement calibration coefficient of thorax
Kab = volume-displacement calibration coefficient of abdomen
Dth = displacement measured from thoracic RIP tracing
Dab = displacement measured from abdominal RIP tracing.

Tidal volume measured from the integrated pneumotachograph tracing (V_{PN}) was compared for each respiratory cycle with V_{RIP}. The onset and end of inspiration were defined by the integrated airflow measurement of tidal volume; and care was taken to measure the

Table 1—*Patient Characteristics

Patient/Sex/Age, yr	WT	BMI	LAT	AW	AI	MIN	<90%
1/M/43	95	31	5	2	15	75	17
2/M/47	74	23	44	6	20	88	1
3/M/69	90	30	83	7	38	80	22
4/M/68	125	45	50	2	26	74	7
5/F/61	115	42	1	7	36	82	3
6/F/59	129	54	3	5	30	75	38
7/M/56	108	34	1	7	25	74	15
8/M/52	90	27	8	9	17	90	0
9/F/60	81	30	118	4	25	80	26
10/M/49	89	31	62	1	53	76	19
11/M/55	96	33	50	2	30	71	12
12/M/68	125	43	8	2	27	85	65
13/M/33	70	21	36	5	16	75	1
Mean 55	99	34	36	5	28	79	17
SD 10	19	9	35	2	10	6	17

*WT = body weight in kg; BMI = body mass index in kg/m²; LAT = sleep latency, in minutes; AW = number of awakenings after sleep onset; AI = apnea index (number of apneas/hour); MIN = minimum SaO_2 during sleep; <90% = total sleep time (percent) spent at SaO_2 <90 percent.

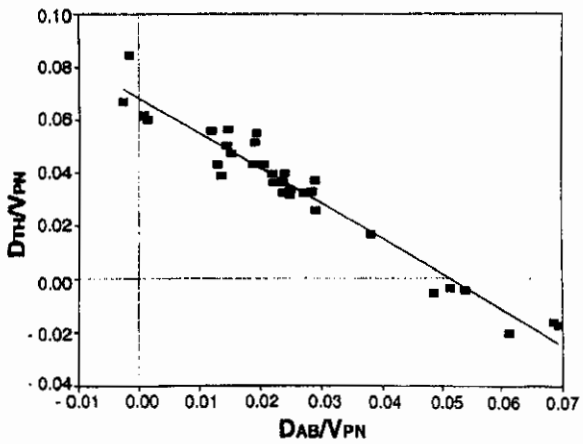

FIGURE 1. Thoracic (D_{TH}) and abdominal (D_{AB}) displacements divided by directly measured tidal volume (V_{PN}) during calibration. Points at the extreme upper left (to left of 0 abscissa) represent slight abdominal paradox during the calibration breaths and those at the extreme lower right (below 0 ordinate) represent thoracic paradox. Solid line is regression line ($r = 0.95$).

volumes displaced by thoracic and abdominal movements only between the times of onset and end inspiration. This avoids errors due to asynchronous movements of thorax and abdomen, when maximal compartmental amplitudes may be greater than independently measured tidal volume.[21] The algebraic difference (ALG DIFF) was calculated between V_{RIP} and V_{PN}, and the relative difference (REL DIFF) was calculated as ALG DIFF × 100/V_{PN}.

Validity of V_{RIP} was evaluated in terms of accuracy relative to V_{PN} and precision.[29] Accuracy was quantified by the mean algebraic or relative differences between the two methods of measuring tidal volume. Precision was quantified by the standard deviation of the differences (independent of algebraic sign) between the two methods.

RESULTS

Calibrations before sleep and after awakening were acceptably accurate in all patients. Prior to sleep onset, RIP-derived volumes were within 5 percent of integrated airflow in 11 of 13 patients and within 9.1 percent in 2 of 13. Calibrations performed prior to sleep onset and after awakening were within 5 percent of each other in 6 of 13 patients and within 9.6 percent in 7 of 13. Figure 1 shows a representative series of calibration breaths in one patient. Thoracic displacement divided by tidal volume is plotted on the y axis, and abdominal displacement divided by tidal volume is plotted on the x axis. The y- and x-intercepts of the line of regression yield the thoracic and abdominal calibration coefficients, respectively. The mean correlation coefficient (r) between pneumotachograph- and RIP-derived tidal volumes was 0.95. In ten patients, r was greater than 0.95, in two patients it was between 0.9 and 0.95, and in the remaining one patient, $r = 0.88$. There was no significant difference in the slope of the regression line, mean thoracic or abdominal calibration coefficients, or the ratio of these coefficients before sleep and after awakening; and there was no significant difference between this ratio and that obtained by the isovolume efforts performed prior to sleep.

Only three patients achieved REM sleep with the face mask in place. These three and one additional patient also manifested stage 3/4 sleep. In the remaining nine patients, we have respiratory data only during wakefulness and stages 1 and 2 sleep. In total, 1,009 respiratory cycles were measured during wakefulness, and 2,973 cycles were measured during sleep in 13 subjects. We measured 899 cycles in 12 subjects during stage 1 (75 ± 42 per patient), 1,618 cycles in 13 subjects during stage 2 (124 ± 113), 260 cycles in four subjects during stage 3/4 (65 ± 35), and 196 cycles in three subjects during stage REM (67 ± 25). Average moni-

Table 2—*Accuracy (ALG DIFF, REL DIFF),* and Precision (SD) of RIP-Derived Tidal Volume*

	Awake				Asleep			
Patient	ALG DIFF, ml	SD, ml	REL DIFF, %	SD, %	ALG DIFF, ml	SD, ml	REL DIFF, %	SD, %
1	−1.6	34.1	0.3	8.7	−156	324	−14.9	31.7
2	44.5	56.6	4.3	6.4	36.6	105	5.2	15.8
3	−40.0	41.3	−9.0	12.7	−56.0	57.7	−12.0	18.9
4	−14.0	32.6	−2.5	5.7	42.6	166	29.8	79.2
5	27.0	179	2.8	22.5	−5.4	144	1.4	22.5
6	−19.1	168	−0.4	18.6	−94.4	223	5.6	38.2
7	33.9	53.2	2.1	3.5	37.1	55.7	3.0	4.4
8	7.9	20.9	−1.3	3.6	19.2	134	13.9	33.3
9	−3.5	40.7	0.2	8.3	−34.9	54.0	−5.7	9.9
10	14.1	34.7	2.2	5.0	73.1	55.0	15.2	20.2
11	2.0	53.1	0.7	13.8	39.5	82.5	17.2	35.0
12	−26.7	56.9	−4.9	10.0	−138	66.1	−28.1	13.4
13	−7.6	69.9	−3.1	8.3	71.5	96.3	8.4	9.5
Mean	0.08	64.7	−0.7	9.8	−12.7	120	2.1	25.5
SD	23.3	48.1	3.4	5.5	74.2	76.8	14.9	18.6

*ALG DIFF = algebraic difference between mean V_{RIP} and V_{PN}, in milliliters; REL DIFF = difference between mean V_{RIP} and V_{PN}, in percent tidal volume.

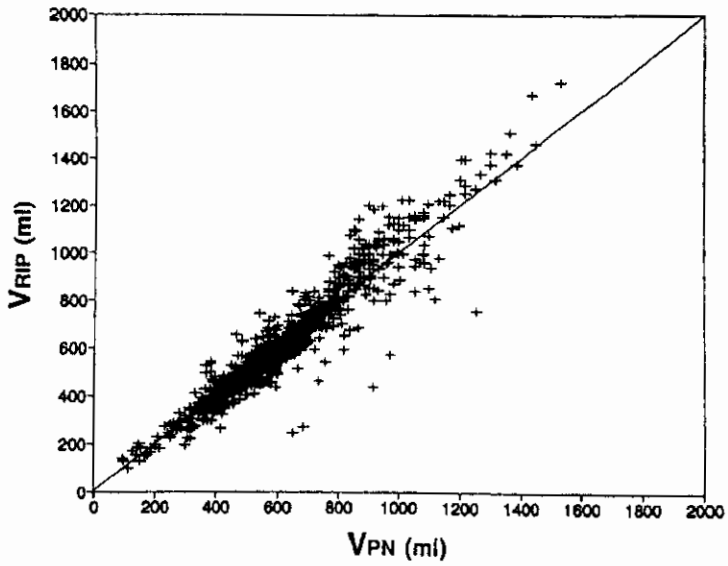

FIGURE 2. RIP-derived tidal volume (V_{RIP}) plotted as a function of tidal volume from integrated airflow (V_{PN}) during wakefulness (n = 1,009). The line of identity is shown.

toring time was 180 ± 48 min, with an average of 44 ± 23 percent in wakefulness, 14 ± 5 percent in stage 1, 33 ± 18 percent in stage 2, 7 ± 11 percent in stage 3/4, and 2 ± 4 percent in stage REM.

Table 2 shows for each patient the accuracy and precision of RIP-derived tidal volume and means for all patients during wakefulness and sleep. Accuracy is given by the algebraic or relative differences (ALG DIFF and REL DIFF, respectively) in tidal volume between the RIP and integrated airflow. During wakefulness, estimated mean tidal volume from the RIP provided a useful assessment of minute ventilation. The algebraic difference between RIP and integrated flow was less than 45 ml in all patients. In no patient did RIP-derived mean tidal volume differ by more than 5 percent from integrated airflow during wakefulness. The number of cycles was not identical for each patient (awake mean = 77 ± 21; sleep mean = 229 ± 152). For all respiratory cycles during wakefulness (n = 1,009), the mean algebraic difference was 2.89 ml, (relative difference = 0.04 percent). These differences were not significantly different from 0. Precision of the RIP (SD of difference between V_{RIP} and V_{PN}) was within 10 percent in nine of 13 patients. SD ranged from 21 ml (4 percent) to 179 ml (22.5 percent). For all cycles during wakefulness, the SD was 73 ml (10.5 percent). The 95 percent confidence interval (CI) for RIP-derived tidal volume during wakefulness was −21 to +21 percent relative to integrated airflow. Figure 2 shows the relation between RIP- and pneumotachograph-derived tidal volume for all cycles measured during wakefulness in all patients. The large majority of cycles fall relatively close to the line of identity, with somewhat more dispersion at tidal volumes greater than 600 ml.

During sleep (all stages considered together), the RIP was not as accurate (Table 2). Five patients showed algebraic differences greater than 60 ml. RIP-derived mean tidal volume was within 10 percent of integrated flow in six patients, between 10 and 20 percent in five patients, and between 20 and 30 percent in two patients. For all cycles during sleep (n = 2,973), the mean algebraic difference was 7.6 ml (relative difference, −5.2 percent). These differences were significantly different from 0. Precision was less during sleep than wakefulness in all patients except one; it was within the limits observed during wakefulness (22.5 percent) in only eight patients. In 7 of 13 patients, SD of the difference between V_{RIP} and V_{PN} was less than 100 ml; in 3 of 13 patients it was between 100 and 150 ml; and in 3 of 13, it was between 165 and 325 ml. In the latter six patients, two showed larger percentage errors in large tidal volumes, two in small tidal volumes, and two had relatively uniformly distributed percentage errors. For all respiratory cycles during sleep, SD of the difference between V_{RIP} and V_{PN} was 130 ml (33 percent). The 95 percent CI for RIP-derived tidal volume was −61 percent to +71 percent relative to integrated airflow. Precision of RIP-derived tidal volume was significantly less during sleep than wakefulness ($t = 7.43$; $p < 0.001$). Errors in all subjects' respiratory cycles during sleep showed no correlation with body mass index (BMI). Figure 3 shows the relation between RIP- and pneumotachograph-derived tidal volume for all cycles measured during sleep in all patients. The majority of cycles fall relatively close to the line of identity, with a clear tendency for greater dispersion at volumes above 800 ml.

With regard to sleep stage, there was no statistically significant difference between wakefulness and stages 1 and 2 in accuracy in patients with at least 10 percent time in each of stages 1 and 2 sleep (n = 12). However, the precision of RIP was significantly less in stage 2 (SD = 122 ml) than awake (SD = 74 ml) or stage 1 sleep

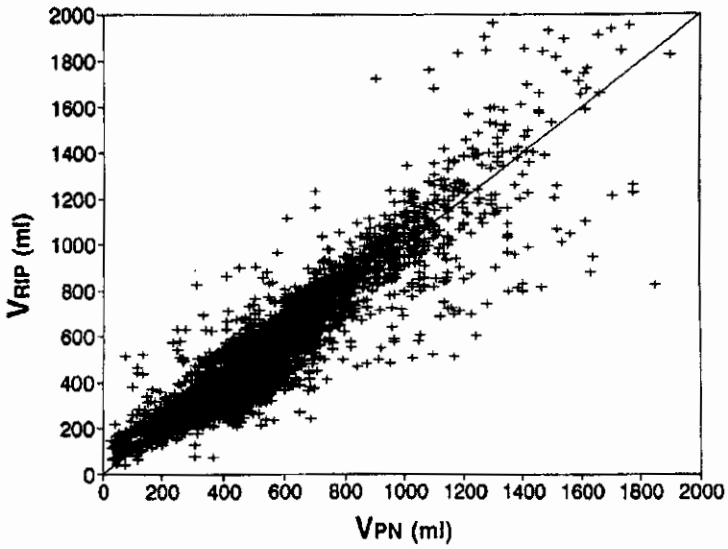

FIGURE 3. RIP-derived tidal volume (V_{RIP}) plotted as a function of tidal volume from integrated airflow (V_{PN}) during sleep (n = 2,973). The line of identity is shown.

(SD = 101 ml) ($p<0.001$). In patients manifesting all sleep stages (n = 3), there were again no differences in accuracy, but precision was less in stage 2 sleep (SD = 148 ml) than awake (SD = 41 ml) ($p<0.05$); and significantly less in stage REM (SD = 276 ml) than stages 1 (SD = 55 ml), 2, or 3/4 sleep (SD = 83 ml) ($p<0.001$).

DISCUSSION

The present study shows that use of the RIP in obese patients with sleep apnea syndrome (SAS) is acceptably accurate for estimating minute ventilation during wakefulness. Accuracy of our measurements using the method of linear calibration is comparable to that previously reported for nonobese subjects.[3,6,10,15] A recent study in young normal subjects showed a bias (algebraic difference between RIP- and pneumotachygraph-derived volumes) two to eight times larger than in the present study, with a mean of −14 percent.[19] The precision of the present method permits determination of quantitative changes in tidal volume on a breath-by-breath basis to within 10 percent in two thirds of the patients, and to within 13 to 23 percent in the remainder. We measured respiratory cycles during wakefulness at the beginning of the night just after calibration, in the middle of the night, and at the end of the study, 2 to 4 h later. Thus, the present results include a time factor comparable to that encountered during measurements of respiration during sleep. Absence of a significant difference between calibrations at the beginning and end of the study suggests that this time factor was not of major importance in reducing precision.

RIP accuracy and precision were significantly reduced during sleep. The accuracy of the RIP for estimating minute ventilation appears to be acceptable even during sleep in these obese patients, with an overall mean of relative differences from integrated airflow of 5.2 percent. This is comparable to that observed in asthmatic subjects during sleep in the absence of lower rib cage paradox[10] and somewhat better than recently reported results in normal unrestrained subjects.[19]

Precision of the RIP during sleep in these obese patients shows a clear limitation. The SD of all differences between RIP and integrated airflow during wakefulness was 10.5 percent while that during sleep was three times as large (33 percent). Thus, minute ventilation averaged over a number of cycles may be accurately estimated during sleep in obese patients with SAS, but local transients such as hypopneas of a few breaths may be estimated less accurately. The current definition of a hypopnea as a fall in ventilation of 50 percent or more[11,13] appears to be a useful guide for obese patients with SAS, since it is between the SD and 95 percent CI in the present study. In unrestrained subjects, use of continually updated amplitude criteria (50 percent fall in abdominothoracic movements relative to immediately preceding minute ventilation) as recommended[13,19] provides an appropriate reference for assessing hypopnea.

A number of factors may contribute to errors in RIP tidal volume during sleep. Some asynchrony between thoracic and abdominal movements was observed in the patients in the present study. We measured the compartmental contribution to tidal volume using the onset and end of inspiration determined by the pneumotachograph to avoid any errors due to asynchrony.[15,21] Movement of thoracic or abdominal RIP bands could cause errors during sleep, but we fixed the bands at several sites with small adhesive strips, and verified their positions at the end of the study. Furthermore, if movement of the bands contributed to greater measurement errors during sleep relative to wakefulness, we would expect different calibration factors after the period of sleep measurements. This

was not observed. Change in position of the patient is similarly not likely to be a major factor in explaining the decrease in accuracy and precision of the RIP during sleep. Our patients maintained a fixed posture throughout the study, verified by direct visual observation. Those who slept in the lateral decubitus posture might be expected to show larger errors due to undetected position change if this were a major cause of error. This was not the case in the two patients who maintained the lateral decubitus posture.

The majority of our sleeping measurements were made during stages 1 and 2 sleep, similar to those of Ballard et al.[10] We included respiratory cycles over a wide range of tidal volume, excluding the first respiratory cycle during the hyperpneic "breakthrough" respiration following obstructive apneas in order to avoid artifacts of body movement. Nevertheless, a higher percentage of respiratory cycles during stage 2 sleep were large tidal volumes, which were associated with larger errors during both wakefulness and sleep.

Relatively few respiratory cycles were available during REM sleep in the present study. In those patients exhibiting REM sleep, there was a significant decrement in RIP precision compared with wakefulness and non-REM sleep. This is in accord with results reported in animals.[23] Estimates of tidal volume based on a two-compartment model may be in error if the model is not appropriate to the behavior of the thoracoabdominal wall. During REM sleep, there is markedly decreased tone in intercostal muscles leading to a change in thoracoabdominal mechanics[24,25] and distortion of the thoracoabdominal wall, commonly with paradoxic inward motion of the thorax during inspiration. Such paradoxic inward motion of the thorax was observed in two of the three patients in the present study who manifested REM sleep. Similar thoracic paradox has been observed in asthmatic subjects,[10,14] tetraplegics,[26] during halothane anesthesia,[27] and in newborn humans.[28] Under these conditions, the two-compartment model of thoracoabdominal motions may not be valid in infants and in adult asthmatic subjects.[10,28] In effect, the thorax does not behave with a single degree of freedom, but rather the upper and lower portions move asynchronously. The decreased precision in REM in the present study was not related to BMI, since the subjects who manifested REM (1, 8, 13) were among those with the lowest BMI.

In summary, we have shown that least squares calibration of the RIP during wakefulness provides a useful quantitative estimate of tidal volume in obese patients with SAS during wakefulness. During sleep, accuracy and precision of the RIP are significantly decreased in obese patients with SAS, but errors are not correlated with BMI. Minute ventilation was estimated with a mean error of 5.2 percent during sleep in patients in the present study. REM sleep was associated with larger errors in RIP estimation of tidal volume than quiet sleep, which may be explained by thoracoabdominal distortion during REM sleep. The criterion for hypopnea of a decrement of 50 percent in ventilation as measured by the RIP has been closely associated with desaturations and arousals.[13] These authors suggested that although ventilation can only be measured semiquantitatively[19] in unrestrained sleeping subjects, inductive plethysmography appeared clinically useful. Although errors may be greater than observed in the present study during all-night recordings with a larger percentage of time asleep and especially in REM sleep, the present results support the clinical use of RIP in obese patients with SAS.

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Accuracy of Respiratory Inductive Plethysmography for the Diagnosis of Upper Airway Resistance Syndrome*

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Objective: **To determine the sensitivity and specificity of quantitative respiratory inductive plethysmography (RIP) compared with the "gold standard," nocturnal esophageal pressure (Pes) measurement, in the diagnosis of upper airway resistance syndrome (UARS) in adults.**
Methods: **Fourteen consecutive patients without obstructive sleep apnea and suspected of having UARS underwent simultaneous measurement of Pes with a catheter and standard nocturnal polysomnography along with RIP. UARS events (RERAs, respiratory effort-related arousals) were identified by observing crescendo changes in Pes with a Pes nadir ≤ −12 cm H_2O, followed by an arousal or microarousal. UARS was defined as ≥ 10 RERAs per hour. For each patient, the ratio of peak inspiratory flow to mean inspiratory flow (PIFMF) measured by RIP was performed during quiet wakefulness and with 40 randomly selected breaths in the supine position for two conditions: stage 2 sleep, immediately prior to arousals in any sleep stage. The mean PIFMF (wake-sleep) was calculated for each condition.**
Results: **The sensitivities and specificities, respectively, of RIP to distinguish UARS patients from non-UARS patients are from stage 2 sleep (67%, 80%), immediately prior to arousals (100%, 100%). For breaths occurring immediately prior to arousals, the mean PIFMF (wake-sleep) is ≥ 0.13 for UARS patients and < 0.13 for non-UARS patients.**
Conclusion: **The PIFMF measured by RIP allows for the most accurate identification of UARS patients when breaths are selected for analysis immediately prior to arousals.**
(CHEST 1999; 115:1333–1337)

Key words: obstructive sleep apnea; polysomnography; respiratory inductive plethysmography; upper airway resistance syndrome

Abbreviations: AHI = apnea-hypopnea index; BMI = body mass index; NPSG = nocturnal polysomnography; OSA = obstructive sleep apnea; Pes = esophageal pressure; PIFMF = peak inspiratory flow to mean flow ratio; RERA = respiratory effort-related arousal; RIP = respiratory inductive plethysmography; UARS = upper airway resistance syndrome

Upper airway resistance syndrome (UARS) patients present with complaints of excessive daytime sleepiness and do not have obstructive sleep apnea (OSA) on evaluation by standard nocturnal polysomnography (NPSG).[1] The diagnosis of UARS is made when nocturnal esophageal pressure (Pes) monitoring demonstrates crescendo changes in intrathoracic pressures followed by frequent arousals or microarousals.[2] Alternative methods to Pes monitoring that have been studied for use in the diagnosis of UARS include semiquantitative analysis of transduced nasal pressure waveform[3] and measurement of pharyngeal closing pressure.[4] None of these alternative methods to Pes monitoring are considered to be sufficiently validated as to be recommended for widespread application by a recent consensus group assessing the diagnostic accuracy of techniques for the measurement of sleep-disordered breathing.[5]

Few clinical sleep disorders centers in the United States routinely utilize Pes monitoring to diagnose UARS.[6] Factors preventing the widespread use of this technique include patient refusal or intolerance[7] and the requirement of additional technical expertise and expense. Thus, many patients are diagnosed as having UARS presumptively, without Pes monitoring, on the basis of the qualitative perception of possible respiratory-related arousals from standard

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NPSG. To date and to our knowledge, no studies validate the use of standard NPSG alone as an accurate method for the diagnosis of UARS.

Quantitative respiratory inductive plethysmography (RIP) measurements are based on the detection of changes in volume of the chest and abdomen over the breathing cycle. The sum of these measurements has been demonstrated to provide an estimate of tidal volume if calibration is maintained.[8] Assessment of the degree of asynchrony between chest and abdominal measurements during sleep allows detection of hypopneas, which correlates closely to events detected by pneumotachometer.[9] Based on the obvious need to diagnose UARS without Pes monitoring, the current study seeks to determine if RIP is accurate for this purpose.

Materials and Methods

Patients

Approval for this study was obtained by the Institutional Review Board and Human Use Committee of the Department of Clinical Investigation at Walter Reed Army Medical Center. Patients with symptoms suggestive of narcolepsy or other likely nonrespiratory sleep disorders were excluded from study participation. Over a 3-month period, 64 adult patients, with a median age of 34 years (range, 18 to 48 years) and median body mass index (BMI) of 27 kg/m^2 (range, 25 to 29 kg/m^2), received NPSG for the evaluation of complaints of witnessed apnea, snoring, and excessive daytime sleepiness.

Polysomnography

All patients received an initial 12-channel NPSG (Somnostar 4100 system; SensorMedics Corp; Yorba Linda, CA) that included the following standard parameters: central and occipital EEG, right and left electro-oculogram, digastric and tibialis electromyogram, continuous airflow by oronasal temperature thermistor, chest wall excursions by thoracic and abdominal inductive plethysmography, heart rate and rhythm by ECG, oxyhemoglobin saturation by pulse oximetry, and acoustic monitoring of snoring sounds. The NPSGs were scored using 30-s epochs following the Rechtschaffen and Kales[10] criteria for sleep/wake determination and sleep-staging. Arousals were defined as >3 s of a shift to alpha or theta EEG activity from a slower background frequency.[11] Microarousals were defined as >1 s but <3 s of a shift to alpha or theta EEG activity from a slower background frequency. Respiratory tracings were evaluated for the presence of apnea, which was defined as complete absence of oronasal thermistor airflow for at least 10 s. Obstructive hypopnea was defined as $\geq 50\%$ decrement in oronasal airflow for at least 10 s associated with evidence of increasing respiratory effort as measured by qualitative inductive plethysmography. The requirement of $>4\%$ decrease in oxyhemoglobin saturation from baseline was not used because the present study evaluated patients who were less likely to desaturate than typical OSA patients who have decreased lung oxygen stores due to obesity and advanced age.[12] Patients were considered to have OSA if NPSG demonstrated an apnea-hypopnea index (AHI, apneas and hypopneas per hour) ≥ 10.

For patients who did not have OSA, the following night a second NPSG was performed, which included the standard 12-channel recording montage along with the additional measurement of Pes with a 2.7-mm-diameter electronic pressure catheter (Gaeltec; Hackensack, NJ) with the tip positioned in the midesophagus by radiograph. Once correctly positioned, the catheter was secured at the nose with adhesive tape. The catheter tip transducer was referenced to atmospheric pressure and calibrated with a water manometer to -50 cm and $+50$ cm H_2O. UARS events (RERAs, respiratory effort-related arousals) were identified by observing crescendo changes in Pes followed by an EEG arousal. Events were scored only if the most negative Pes exceeded the baseline wake minimum negative Pes by 50% and was ≤ -12 cm H_2O.[5] The UARS index was defined as the mean number of RERAs per hour over the course of the night. Patients were considered to have UARS if the UARS index was ≥ 10 events per hour.

Quantitative RIP

Along with Pes monitoring and standard NPSG, RIP was recorded simultaneously (SomnoStar PT; SensorMedics Corp). The input leads for RIP consist of two cloth belts that cover curved wires that encircle the chest and abdomen. Initial calibration of the ribcage and abdominal signals were performed during the first 5 min of operation using the qualitative diagnostic calibration procedure.[13]

A software program (RespiEvents; SensorMedics Corp) allows for the breath-by-breath calculation of the peak inspiratory flow to mean inspiratory flow ratio (PIFMF). The PIFMF value is 1.57 ($\pi/2 \times$ radius) when the RIP-derived flow waveform is completely rounded, indicating normal pharyngeal resistance. As the flow waveform flattens, indicating increased pharyngeal resistance, the PIFMF value approaches 1.0. Figure 1 is a diagrammatic representation of these various waveforms and values. For each patient, PIFMF measurements were performed during quiet wakefulness and with 40 randomly selected breaths in the supine position for two conditions: stage 2 sleep, immediately prior to arousals.

Statistical Analysis

For supine, stage 2 sleep, portions of the study with >3 min of this condition were identified. Starting with the second consecutive 30-s epoch of this condition, a random number generator was used (with a range of 5 to 20) to count subsequent breaths and identify these for analysis. For supine breaths prior to an arousal, a random number generator was used to identify 30-s epochs. If the epoch contained an arousal, the breath prior to the arousal was analyzed.

Data are expressed as the mean ($\pm$ SD) unless otherwise stated. The association of the change in PIFMF (wake-sleep) with the change in Pes for each condition was evaluated using Pearson's correlation coefficient. Correlation coefficients between the PIFMF (wake-sleep) and Pes were performed using the mean of the Pes nadirs for all 40 breaths for each patient

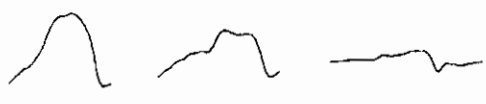

FIGURE 1. RIP-derived flow waveform contours for varying degrees of airflow obstruction with corresponding PIFMF ratio values.

under both conditions. The change in PIFMF (wake-sleep) was compared between the UARS and non-UARS groups using the Wilcoxon rank sum test. Receiver operating characteristic analysis was used to determine the sensitivity and specificity at different values for the change in PIFMF (wake-sleep). Statistical significance was accepted for $p \leq 0.05$.

Results

Polysomnographic Characteristics of Patient Groups

Standard NPSG was diagnostic for OSA in 50 of the 64 patients. The median AHI of the OSA group was 24 (range, 14 to 51). The 14 non-OSA patients had a median AHI of 3 (range, 0 to 6). These 14 patients received a second NPSG with Pes measurement and RIP. Nine of the 14 non-OSA patients met the diagnostic criteria for UARS. Figure 2 illustrates the distribution of the Pes nadir (most negative pressure for the entire study) for the UARS vs non-UARS patients (respective means, -32 ± 12 cm H_2O vs -6 ± 3 cm H_2O.). Figure 3 illustrates the distribution of UARS indexes for the UARS vs non-UARS patients (respective means, 31 ± 9 events per hour vs 2 ± 2 events per hour). The five non-UARS patients exhibited the least negative Pes nadirs and the lowest UARS indexes, with no evidence of overlap with the UARS patients. The total arousal index was increased in the UARS compared with the non-UARS group (23 ± 8 events per hour vs 12 ± 5 events per hour; $p = 0.03$). Sleep stage distributions for the UARS group and non-UARS group are compared in Table 1. The UARS and non-UARS groups were similar with respect to the

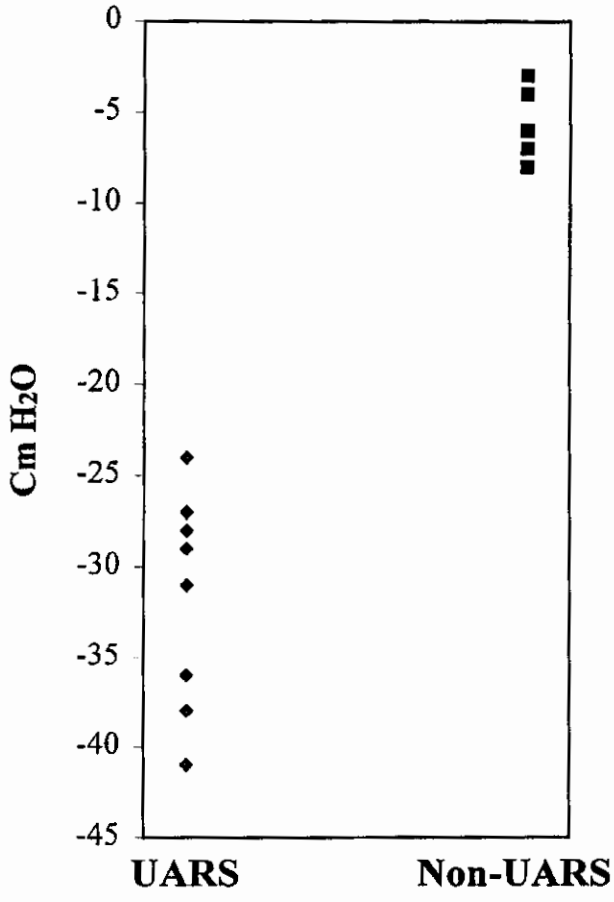

FIGURE 2. Pes nadir over the course of an entire night for UARS and non-UARS patients.

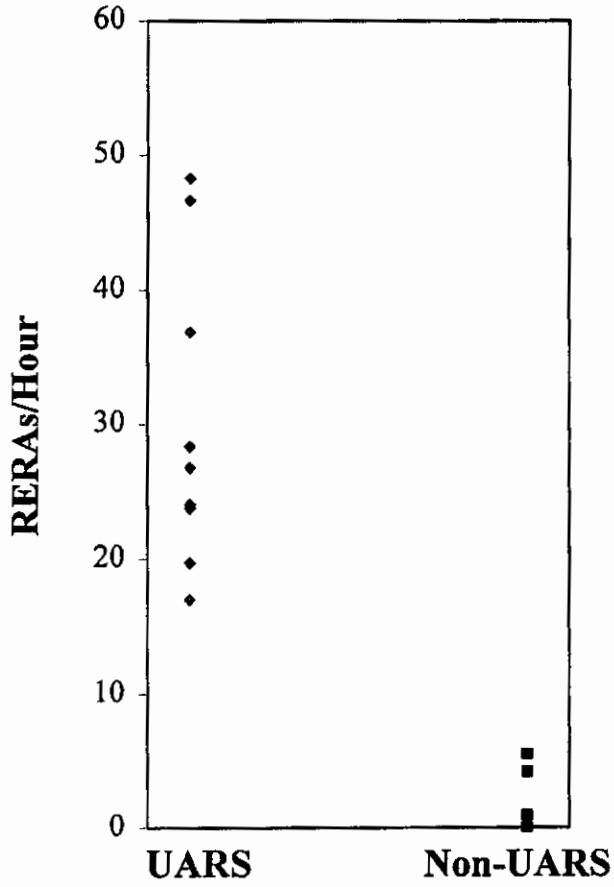

FIGURE 3. Number of RERAs for UARS and non-UARS patients.

Table 1—*Comparison of Demographics for the UARS and Non-UARS Groups

Group	Age, yr	BMI, kg/m^2	Epworth Sleepiness Scale Score
UARS	38 ± 6	27.3 ± 1.7	14 ± 4
Non-UARS	35 ± 10	27.1 ± 3.1	11 ± 3

*Values expressed as mean ± SD. p Values were not significant for comparisons between groups.

duration of the various sleep stages with the exception of stage 3 or 4 sleep, which was decreased in the UARS group.

Demographic Characteristics of Patient Groups

Table 2 demonstrates that the mean age, BMI, and Epworth Sleepiness Scale scores were similar for the UARS and non-UARS groups. The age and BMI were typical for UARS patients, as these patients tend to be younger and less obese than OSA patients.[14] The Epworth Sleepiness Scale scores suggest both groups perceived excessive daytime sleepiness, as scores in this range are typical for patients with untreated sleep disorders.[15]

Evaluation of RIP for Diagnosis of UARS

The correlations of PIFMF (wake-sleep) and Pes were significant for the combined UARS and non-UARS patient groups during stage 2 sleep ($r = -0.70$, $p = 0.035$) and for breaths occurring immediately prior to arousals ($r = -0.82$, $p = 0.016$). These correlations were performed using the mean of the Pes nadir for all 40 selected breaths for each individual patient under both conditions.

For stage 2 sleep, there was no significant difference between the PIFMF (wake-sleep) for the UARS and non-UARS groups (0.161 ± 0.122 vs 0.099 ± 0.022; $p = 0.36$). For breaths occurring immediately prior to arousals, the PIFMF (wake-sleep) was increased for the UARS group compared with the non-UARS group (0.228 ± 0.098 vs 0.099 ± 0.022; $p = 0.001$). The evaluation of PIFMF (wake-sleep) to detect changes in Pes for either stage 3 or 4 sleep was precluded by the short duration (< 5 min) of these sleep stages in four of the nine UARS patients. Breaths in stage REM sleep were not evaluated because it was expected that tidal breathing would vary appreciably from breath to breath, resulting in decreased utility to distinguish the patient groups.

The sensitivity and specificity of RIP to distinguish UARS from non-UARS patients using the PIFMF (wake-sleep) for stage 2 sleep is presented in Figure 4. The greatest diagnostic accuracy for stage 2 sleep occurs at a cutoff of 0.1 PIFMF (wake-sleep) with a sensitivity of 67% and specificity of 80%. For breaths occurring immediately prior to arousals, PIFMF (wake-sleep) had a greater diagnostic accuracy, with a sensitivity and specificity of 100%. All UARS patients demonstrated a PIFMF (wake-sleep) ≥ 0.13 for breaths occurring immediately prior to arousals and all the non-UARS patients demonstrated a PIFMF (wake-sleep) < 0.13.

Table 2—*Percentages of Total Time in Bed for the Various Sleep Stages and Wakefulness in the UARS Group Compared With the Non-UARS Group**

	Wake, %	Stage 1, %	Stage 2, %	Stage 3–4, %	Stage REM, %
UARS	8 ± 5	10 ± 6	56 ± 12	8 ± 5†	18 ± 7
Non-UARS	5 ± 3	7 ± 3	50 ± 10	17 ± 5†	22 ± 8

*Values expressed as mean ± SD. REM = rapid eye movement.
†$p = 0.039$.

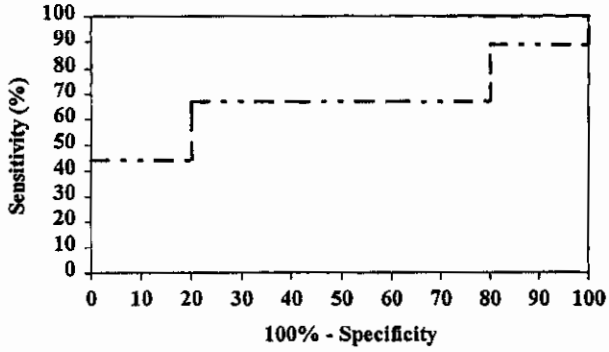

FIGURE 4. Receiver operator characteristics curve for stage 2 sleep in the supine position, plotting sensitivity and specificity simultaneously across a range of thresholds for the difference of the peak inspiratory flow to mean flow ratio during wakefulness and sleep.

DISCUSSION

This study demonstrates that RIP can accurately distinguish UARS from non-UARS patients using the analysis of PIFMF (wake-sleep). However, the most accurate application of this technique requires analysis of breaths prior to an arousal in the supine position. This application requires that the RIP signal be integrated with EEG signals. It is logical that the PIFMF (wake-sleep) is most useful prior to arousals in UARS patients, because these arousals are typically preceded by RERAs. RERAs are characterized by a crescendo pattern in intrathoracic pressure with a nadir occurring for the breaths immediately preceding an arousal or microarousal.[5] The nadir in intrathoracic pressure is a consequence of increased upper airway resistance, which accentuates the asynchrony between the chest and abdominal components of RIP and results in a RIP-derived flow waveform that suggests flow limitation.[16] Only breaths occurring prior to an arousal, rather than prior to a microarousal, were analyzed because of the potential difficulty in the reproducibility between individual scorers in the detection of microarousals.[17]

Whyte et al[18] demonstrated that there is difficulty in maintaining the calibration of RIP when it is used as a measure of tidal volume over the course of a night of sleep in normal subjects. The current study did not seek to reproduce these findings in UARS patients, hence a pneumotachometer was not used to calibrate the RIP or to document initial wake concordance between specific RIP-derived measures and tidal volume. Berg et al[19] found that RIP, nasal pressure transduction, and the widely used oronasal thermistor are not adequate in comparison to the direct measurement of minute ventilation when these are utilized to detect hypopneas. However, the current study was designed to determine if a RIP-derived measurement can distinguish UARS from non-UARS patients, although the moderate degree of correlation between individual Pes measurements and PIFMF (wake-sleep) for breaths selected from stage 2 sleep are consistent with prior studies.

Hosselet et al[20] recently demonstrated in a study of 14 patients that the semiquantitative analysis of nasal pressure waveform contour allowed for nine OSA patients to be distinguished from five non-OSA patients. Nasal pressure waveform contours were qualitatively graded as normal, intermediate, or flattened (flow limited). This study included only one patient who may have had UARS, but Pes was not monitored. The current study uses PIFMF to quantify the degree of waveform contour flattening, although the requirement to select breaths prior to an arousal to obtain optimal accuracy suggests RIP is also a semiquantitative method for identifying the increases in upper airway resistance that occur in UARS patients.

In conclusion, measurement of PIFMF (wake-sleep) for breaths randomly selected immediately prior to an arousal in the supine position allowed for the accurate identification of UARS patients from non-UARS patients. Randomly selected breaths from stage 2 sleep were not as accurate for the identification of UARS patients. Integration of RIP with standard NPSG should allow for the diagnosis of UARS without measurement of Pes.

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ENCLOSURES
TOO BULKY TO SCAN

ENCLOSURE TYPE: Publications on LifeShirt System

Comment #81:
Submitter: Rebecca Olivares and Randy Lazar
Organization: Aircare Home Medical
Date: May 13, 2004
Comment:

(See next page)

5/13/04
Presentation
Consider w/
comments

Public Comment (CAG-0093R)

By: Rebecca Olivares, VP of Ops & Finance
With Randy Lazar, CEO/President
Representing Aircare Home Medical
Van Nuys, California

Issue: Modification of current NCG (national coverage guideline) specifying that only a polysomnography done in a facility-based sleep laboratory may be used to identify and diagnose patients with OSA requiring CPAP.

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Overview

- We submit this additional information supporting a request submitted by Dr. Terrance Davidson on April 8, 2004, requesting consideration of the use of portable multi-channel home sleep testing as an alternative to laboratory testing, to diagnose and identify patient with OSA (Obstructive Sleep Apnea) in need of a CPAP device for therapy.

- We have additional supporting information, both clinical and financial.

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Our Expertise

- We are respiratory experts. Our CEO and Corporate Compliance Officer are both RRTs (Registered Respiratory Therapists).

- This report was prepared by Rebecca Olivares, VP of Ops & Finance who holds a degree in Finance. She also possesses over twelve years of DME/HME Medicare & Medicaid reimbursement experience.

- Our Director of Respiratory Therapy was our primary clinical consultant for this report.

- He possesses over 5 years of clinical experience working with CPAP patients, their physicians, and sleep apnea equipment. He is an OSA patient and uses CPAP therapy as well.

Obesity – A Contributor

- SDB (sleep disordered breathing) is associated with hypertension, heart attack, stroke, heart failure & diabetes—all of these conditions are proven to be either secondary to or exacerbated by obesity. In addition, approximately 80% of people with heart failure have sleep apnea. Recent health reports state heart failure is still the No. 1 cause of death in the U.S. How many Medicare patients have heart failure?

- Recent CDC study shows that 65% of Americans are obese (reference noted in report). As baby boomers continue to age, this statistic will have a significant effect on Medicare and Medicaid spending.

The Future (Cont'd)

- Study at RTI International and the CDC estimate that U.S. medical expenses attributed to obesity reached $75 billion in 2003. This study further notes that taxpayers financed half of that amount through Medicare and Medicaid programs.

- Another article estimates up to 25 million people in the U.S. currently suffer from OSA & many of these cases remain undiagnosed (reference noted in report).

- Over the past five years, the number of diagnosed OSA/SDB cases has grown dramatically.

A Method Already in Use

- Kaiser Permanente, one of the nation's largest managed care health plans, uses home sleep study testing as the primary clinical pathway for diagnosing OSA/SDB for all of their patients.

- Home sleep studies are also employed by the Department of Veteran Affairs in Salt Lake City, Utah as the primary method of diagnosing OSA/SDB.

- University of California Medical Centers also use this diagnostic method.

Clinical Findings

- Numerous studies have been conducted over the past 10 years to prove the accuracy of multi-channel home sleep testing used to diagnose routine sleep apnea and SDB cases. In reviewing Dr. Davidson's information, numerous studies were submitted with his original letter. Some of the studies are summarized in the following slides.

- A list was also submitted via e-mail to Ms. Spencer containing 86 references titled, "Home Diagnosis of Sleep Apnea: A systematic Review of the Literature"
[CHEST 124(4): 1543-1579, © 2003 American College of Chest Physicians].

AHI Comparison

- Dr. Davidson was courteous enough to allow us a 20-minute phone interview. This allowed us to clarify several questions we had regarding the studies and findings.

- The AHI listed in the clinical research studies comparing HSS to PSG is constantly listed at > 15 or > 30 because for many years, only an AHI of 15 or 30 was considered *clinically significant* in diagnosing OSA. Dr. Davidson referred to this AHI marker as an imaginary "magic number" that is mostly outdated.

The "Gold Standard"

- The PSG has long been considered the "gold standard" in sleep medicine and all HSS are compared to PSG, with PSG being considered *completely accurate.*

- However, an AHI is not an absolutely accurate number, such as Hematocrit. There is significant night to night variability. Although clinically, we presume we must measure up to PSG and mathematically attempt to do this, neither test is completely accurate.

- An AHI is an estimation of a respiratory event. It is not a perfect number and cannot be evaluated as such.

Sample Studies (Cont'd)

- 79 patients were tested simultaneously with PSG and home sleep study. AHI correlated with r = .90. Sensitivity was 97% and specificity was 93%. (G. Alymow et. al. (Essen, Germany) Poster 659—International Sleep Meeting – Sydney, Australia, *Circa 1999*). Embletta, Flaga unit was used.

- 116 patients underwent the same type of simultaneous study. At an AHI>10, sensitivity was 95% & specificity 92%. For an AHI of 30, sensitivity was 100% & specificity was 97% (E. Ballester et al. (Barcelona, Spain), *Eu Respir J* 2000; 16:123-127). Sibel Home-300 unit was used.

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Some Patients Require PSG

- Based on the clinical experience and expertise of our Director of Respiratory, approximately 90% of all SDB cases can be appropriately diagnosed using a home sleep study.

- Of the remaining 10%, approx. 2% of cases can automatically be referred to lab-based testing—patients with neuromuscular conditions such as ALS, MS and Muscular Dystrophy.

- The remaining 8% may need a home study to rule-out sleep apnea & may require a subsequent in-lab sleep study to diagnose other conditions such as PLM (periodic leg movement) disorder and obesity related hypoventilation.

- These patients represent a very small percent (in fact, a smaller percent than the conservative figures we noted above).

- The Embletta unit picks up PLM's - NO in lab needed

Drawbacks of HSS

- HSS measures bed time vs. sleep time. If this NCD is approved, a change would have to be made to the current NCG used to determine CPAP/BIPAP medical need. Current guidelines state a patient must have 120 minutes of "recorded sleep." HSS do not record sleep time, only total bed time.

- HSS do not incorporate EEG and most do not record PLMs. Some patients (a small population) may require a subsequent PSG if indicated.

Two Negative Studies on HSS

- A clinical study was conducted by SNAP (a sleep diagnostic device manufacturer), which correlated poorly with HSS. However, the studies were performed 3-4 months apart and are therefore considered invalid and inconclusive. 12.7.

- College debate, big "position paper" released by the American Academy of Sleep Medicine, found every possible negative on HSS and decided to put it together in one paper stating why HSS is 'bad' and inferior. Keep in mind that the academy has a significant financial interest in protecting the 'old way' and with it, its members—the PSG community.

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Need to Control Costs

- Given the current state of our Medicare & Medicaid programs, and the future estimated expenses our 65 + population will require, **the need to control costs, while preserving the quality of care, is paramount.**

- We all agree that our Medicare and Medicaid programs need restructuring and modernization to allow efficiencies to be realized through new and innovative processes, new payment methodologies and the use of new technologies.

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Facts & Figures

- The current (national) approximate reimbursement for an in-lab PSG, needed to diagnose SDB patients, is $783.05 (diagnostic study only) plus $807.69 for a titration study.

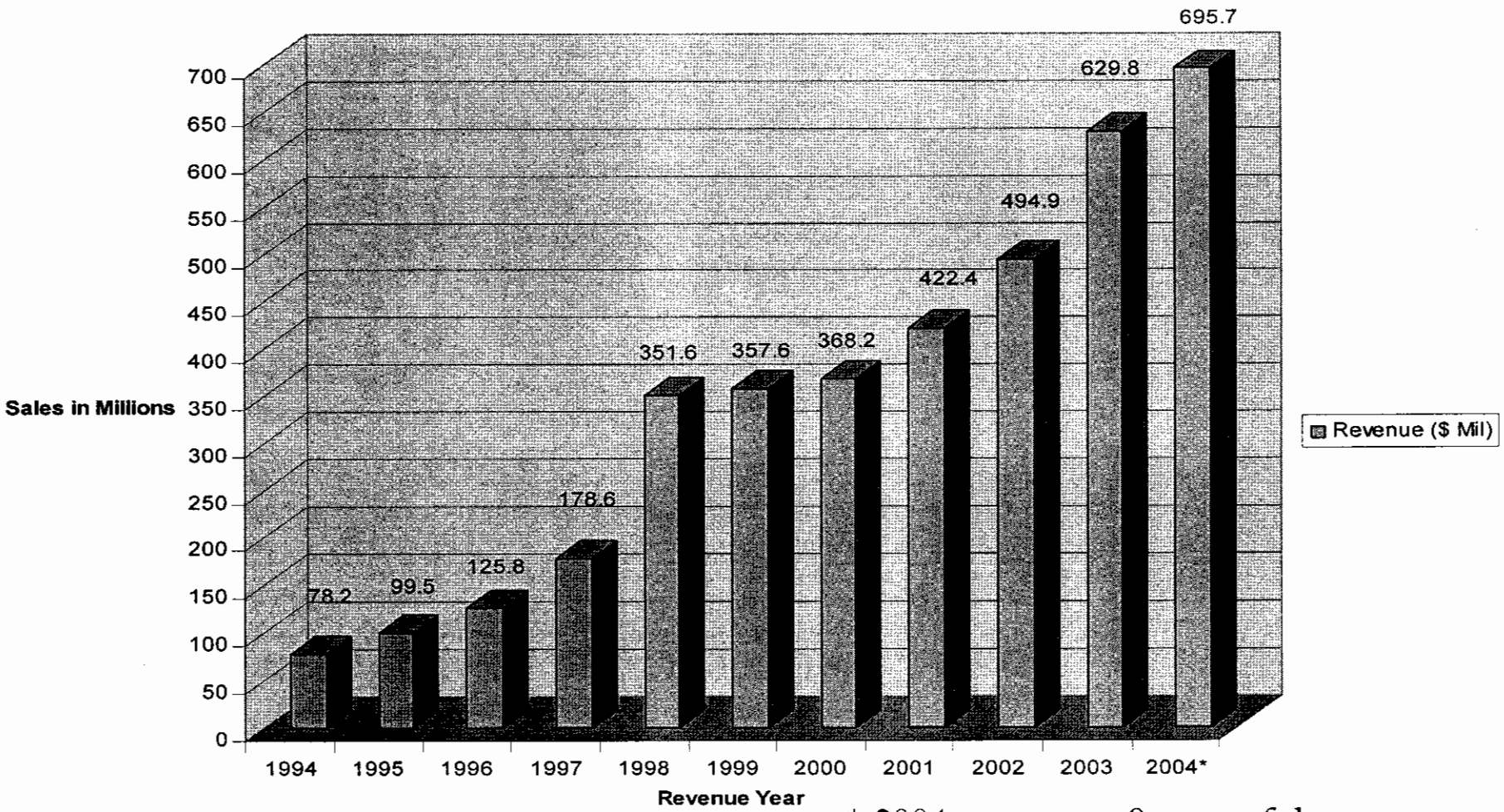
- Overall, Medicare (CMS) is paying approximately $1,000 to $1,400 per study (diagnostic and titration) per patient.

- In reviewing the annual report of a well-known sleep product manufacturer, sales have grown "dramatically." One company's sales increased by 37% (or $192 million) compared to the same quarter the previous year. The same company's sales were $368 million in 2000. For year end 2003, the company's sales are now $629 million– and growing.

- This represents growth of 71% in only three years.

Sleep Product Mfr – Revenue Chart

Sleep Product Manufacturer A - Revenue ($ Mil)



* 2004 represents 9 mos. of data

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Facts & Figures

- This 71% growth in only three years represents a common trend in the sleep product industry. OSA/SDB is a fast-growing epidemic. The large number of new diagnosed cases stem from many more physicians being aware of the condition and more people seeking treatment for it.

Given this incredible growth, the number of undiagnosed cases and and future anticipated growth, CMS must devise a cost effective method for treating this condition for its Medicare and Medicaid recipients.

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Recent Financial Reports

- We receive "Homecare Monday," a weekly trade e-mail update for HME providers. Just last week, 5/10/04, they released financial results of several companies for the quarter ending March 31, 2004.

- The results were for several companies in the home medical equipment industry.

- American Home Patient—2.8% increase in revenue.
- Apria Healthcare—5% growth in revenues.
- Invacare—16% growth.
- Option Care—11% growth.

- We can get an overall feel for the growth in the home medical equipment sector with these figures. Average growth for all of these companies is 8.7%.

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Sleep Product Manufacturers

- ResMed, an Australian co., headquartered in San Diego reported record results for the quarter and nine months ended 3/31/04. Net revenue for the quarter increased by **32%.** According to the CEO/Chairman, "much of the company's growth [is attributed] to strong domestic demand for its sleep disorder products." The U.S. market accounts for 50% of the company's sales.

- Respironics, a domestic sleep product manufacturer, reported a **22%** increase in revenue for the same quarter. The CEO added that this 20 percent year-over-year growth was led by a 23% growth in sleep therapy products.

- **Total average growth for these companies was 27%.**
- A significant difference from a mean growth of 8.7%.

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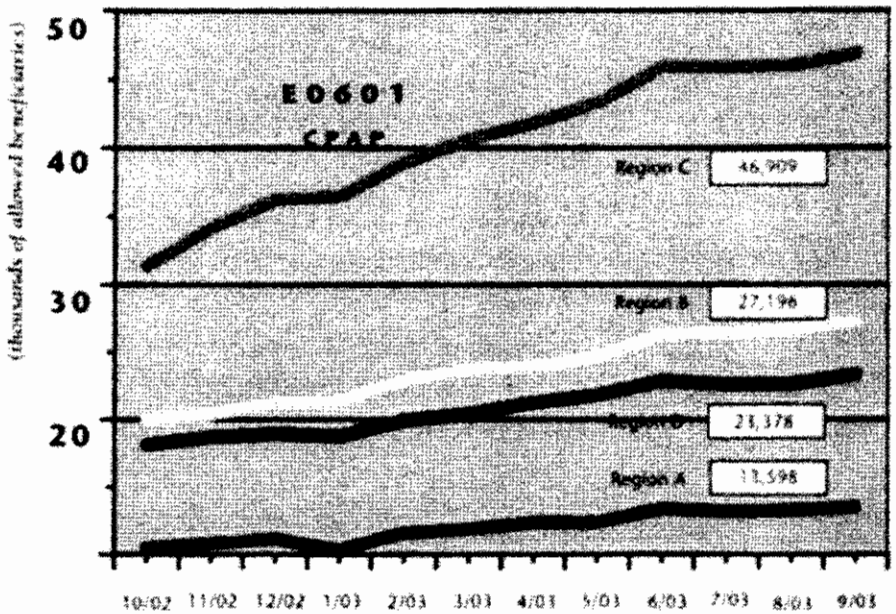
* One Projection

This graph, taken from HME News, 3/04 issue, Vol. 10, No. 3, shows CMS (Medicare) allowed a total of 111,081 CPAP claims for a 4 mo. period. This totals an avg. of 27,770 claims per month. If 40% of these claims represent new patients and we then add 20% for patients who underwent



the study but were not treated with CPAP, we estimate Medicare paid for approx. 160,000 PSG tests in 2003. If HSS had been used in 90% of these cases—saving approx. $1,000 per study per patient—Medicare would've saved $144 mil in 2003. Had this savings been invested over 20 yrs. (to prepare for further growth & health insurance payments), at a conservative 6% return, the program could save $461 mil. (based on 1 year savings).

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Facts & Figures

- Approx. cost of a home sleep study (reimbursement allowance required) is $400 based on a California Fee Schedule vs. current payment for an in-lab study of $1,000 - $1,400. Please note, however, the $400 fee represents the **diagnostic portion** of the study **only.**

- One issue that must be addressed in considering home sleep studies is **CPAP titration after diagnosis**.

- The patient normally undergoes a second study (or split-night) while using a CPAP device at various pressures until the appropriate pressure is found.

- Home sleep study patients do not need to have an in-lab titration study and instead should be allowed an auto-titrating CPAP. This provides additional cost savings while preserving the integrity of clinical treatment.

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Auto-Titrating CPAP

- Having a patient undergo a HSS for the diagnostic portion & then an in-lab titration study, defeats part of the purpose of providing an in-home study.
- Titrating the patient in the home using a portable HSS device is not possible, since a clinician would have to adjust CPAP pressures through the night.
- The solution to titrating home sleep study patients is the auto CPAP. The VA employs this method.
- It is slightly more expensive than a regular CPAP device. We estimate a 20% increase of payment based on the current CPAP allowed amount would be required.

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Auto-Titrating CPAP

- In calculating the cost of the auto-titrating CPAP device vs. an in-lab titration study, we find that CMS/Medicare will save over $500 per patient per study per equipment rental.

- CMS would have to create a special code and/or modifier and a new allowable amount, but this is simply a procedural change.

- The auto titrating CPAP also provides some significant long-term cost savings for CMS/Medicare program.

- This device's technology allows it to adjust to the patient's airway obstruction, providing the exact pressure needed. If the patient were to lose or gain weight or require pressure change to accommodate sleeping position changes, the patient would **not** have to undergo another in-lab sleep study to have pressures changed (which, is currently the case at a cost of $807.69 for each subsequent re-titration study). The auto CPAP automatically adjusts to the pressure needs of the patient as long as they use the device (up to a pressure of 20 cm).

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Summary

- Approving the use of in-home sleep study testing is one of the smartest changes CMS can currently make to prepare for the significant growth of this condition & provide innovative high-quality healthcare at a significant cost savings. CMS must consider <u>all</u> necessary changes needed to make this decision a successful one—such as approving the use of auto-titrating CPAP.

- HSS testing is as clinically effective & accurate as in-lab testing for the majority of SDB/OSA sufferers. Many studies have been performed to validate the clinical comparability of home studies to PSG.

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Summary

- Kaiser Permanente, the VA, and University of CA hospitals have already adopted this method for diagnosing OSA/SDB. They were innovative enough to take advantage of new and existing technology to deliver higher quality in-home healthcare while achieving significant cost savings for an already overburdened healthcare system. They were further able to accomplish this being careful to protect clinical and treatment integrity.

- CMS must further consider how the future & rapid growth of this condition will affect access to care. With the difficulty & labor intensity of in-lab studies, a multitude of patients cannot be quickly accommodated for testing & subsequently may remain undiagnosed. This will have significant long-term health consequences & high associated costs.

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Conclusion

Thank you for your time and careful and thorough consideration of this policy change request. We urge CMS to look at this policy as one of the few innovative changes CMS/Medicare must incorporate, not only to modernize our healthcare system, but to take full advantage of new and existing technologies to provide better and higher quality care, in the most cost-effective manner.

We can no longer be reactive. This approach has created one of the biggest challenges our healthcare system has ever had to face. We must be proactive and forward-looking in our approach & be willing to take the appropriate risks necessary to achieve innovative change & great results. If great scientists never took risks & did not believe there were better solutions to the health problems of their time, medicine would have never progressed to where it is today. Thank you. **This concludes our presentation.**

Public Comment (CAG-0093R)
By: Rebecca Olivares
Vice President of Operations & Finance
On behalf of Aircare Home Medical
Van Nuys, California

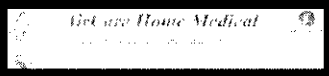
Issue: Modification of current NCG specifying that only a polysomnography done in a facility-based sleep laboratory may be used to identify and diagnose patients with OSA requiring CPAP.

AirCare Home Medical

Overview

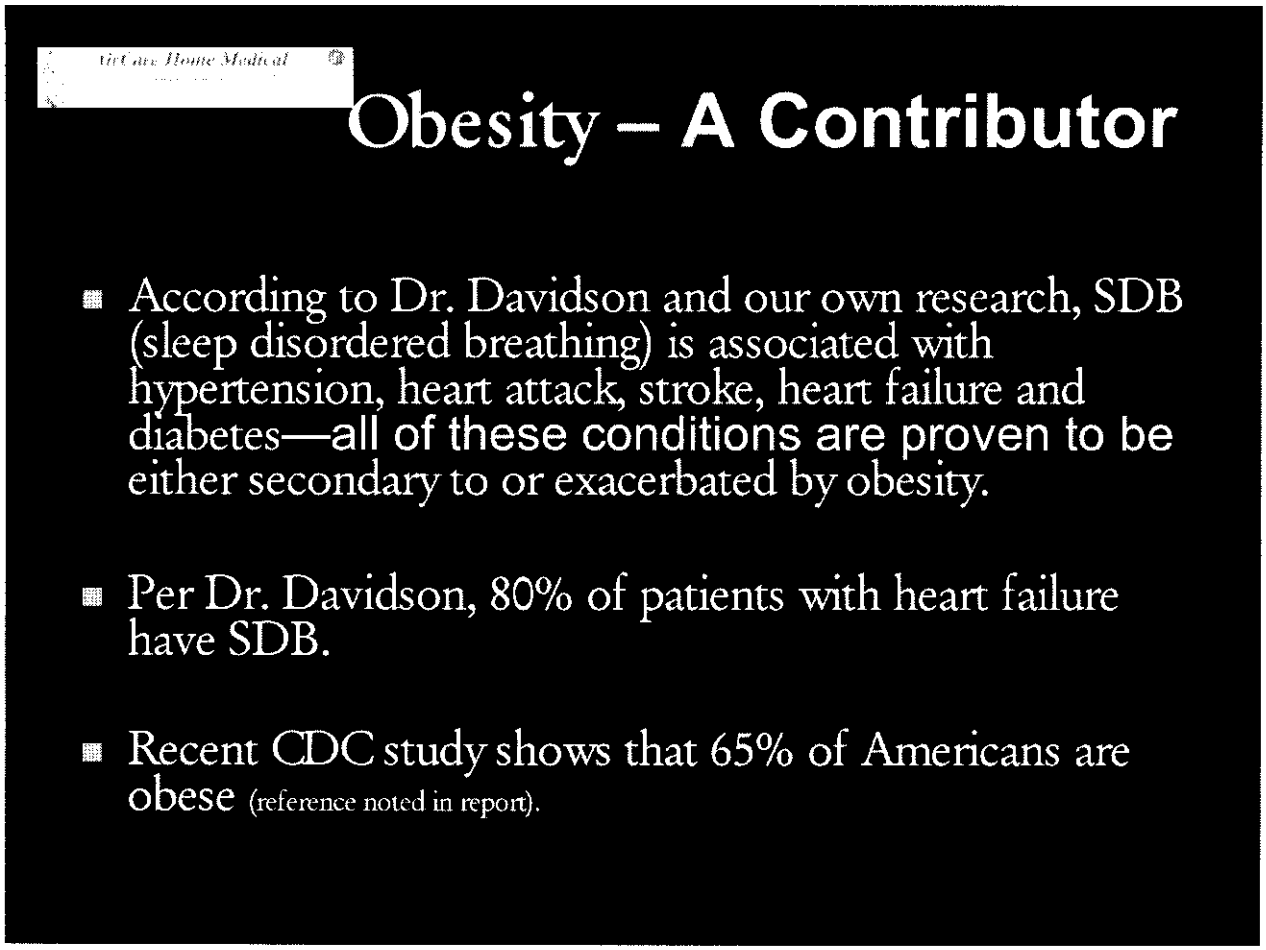
- We submit this additional information supporting a request submitted by Dr. Terrance Davidson on April 8, 2004, requesting consideration of the use of portable multi-channel home sleep testing as an alternative to laboratory testing, to diagnose and identify patient with OSA (Obstructive Sleep Apnea) in need of a CPAP device for therapy.

- This overview highlights important and crucial facts needed to fully consider coverage. A detailed report is submitted with this presentation.



Our Expertise

- We are respiratory experts. Our CEO is an RRT (Registered Respiratory Therapist) as is our Corporate Compliance Officer and our Director of Respiratory Therapy. Our company has been serving the respiratory needs of our patients for over 10 years.
- This report was prepared by Rebecca Olivares, Vice President of Operations who holds a degree in Finance/Business Management and our RRTs.
- Our Director of Respiratory Therapy was our main clinical consultant for this report. He possesses over 5 years of clinical experience working with CPAP patients, their physicians, and sleep apnea equipment. In addition, he is an OSA patient and uses CPAP therapy as well. Our Vice President of Operations was our financial and reimbursement consultant. She possesses over twelve years of DME/HME Medicare and Medicaid reimbursement experience.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Obesity – A Contributor
According to Dr. Davidson and our own research, SDB (sleep disordered breathing) is associated with hypertension, heart attack, stroke, heart failure and diabetes—all of these conditions are proven to be either secondary to or exacerbated by obesity.
Per Dr. Davidson, 80% of patients with heart failure have SDB.
Recent CDC study shows that 65% of Americans are obese (reference noted in report).

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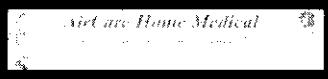
The Future (Cont'd)

- Another article estimates 20 to 25 million people in the U.S. currently suffer from SDB (OSA) and that many of these cases are currently undiagnosed (reference noted in report).
- Study at RTI International and the CDC estimate that U.S. medical expenses attributed to obesity reached $75 billion in 2003. This study further notes that taxpayers financed half of that amount through Medicare and Medicaid programs.



Need to Control Costs

- Given the current state of our Medicare & Medicaid programs, and the future estimated expenses for medical services our growing over 65 population will require, **the need to control costs, while preserving the quality of care, is paramount.**

- We all agree that our Medicare and Medicaid programs need restructuring and modernization to allow efficiencies to be realized through new and innovative processes, new payment methodologies and the use of new technologies.

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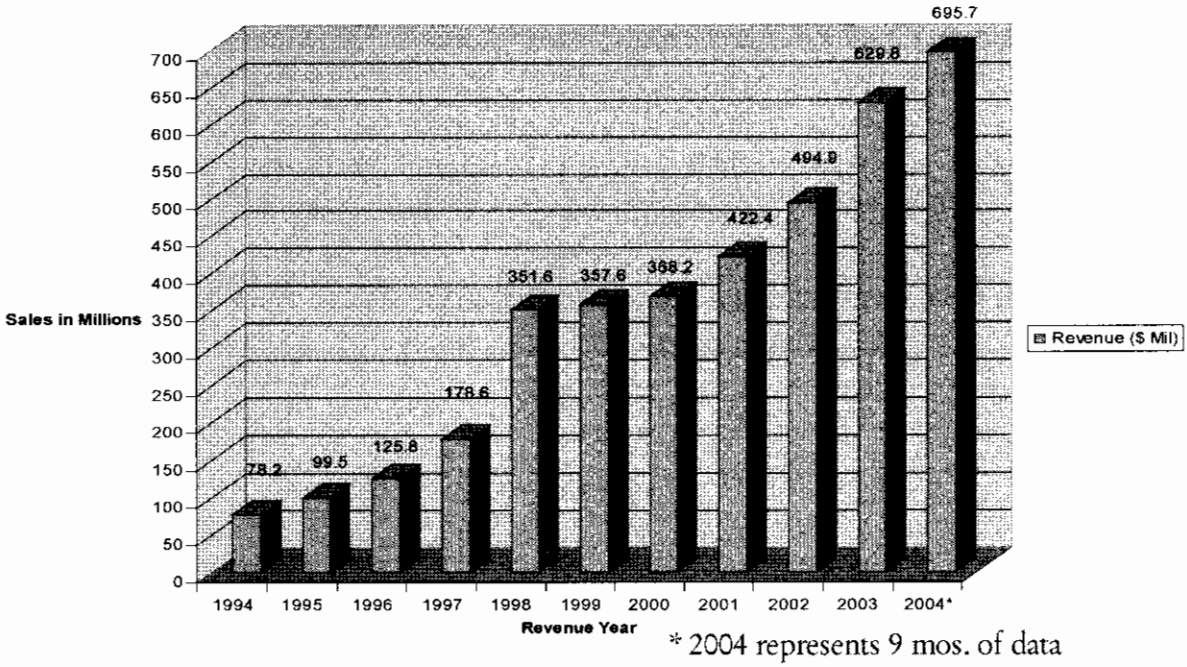
Facts & Figures

- The current (national) approximate reimbursement for a PSG (polysomnography)—sleep study performed in a lab, needed to diagnose SDB patients, is $783.05 (diagnostic study only) plus $807.69 for a titration study.
- Overall, Medicare (CMS) is paying approximately $1,000 to $1,400 per study (diagnostic and titration) per patient.
- In reviewing the annual report of a well-known sleep product manufacturer, we see that sales have grown "dramatically." One company's sales increased by 37% (or $192 million) compared to the same quarter the previous year. The same company had sales of $368 million in 2000. For year end 2003, the company's sales are now $629 million! – and growing.
- This represents growth of 71% in only three years.

Sleep Product Mfr – Revenue Chart



* 2004 represents 9 mos. of data

Facts & Figures

- This 71% growth in only three years represents a common trend in the sleep product industry. OSA/SDB is a fast-growing epidemic. The large number of new diagnosed cases stem from many more physicians being aware of the condition and more people seeking treatment for it.

Given this incredible growth, the number of undiagnosed cases and and future anticipated growth, CMS must devise a cost effective method for treating this condition

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Facts & Figures

- Approximately 90% of all SDB cases can be appropriately diagnosed using a home sleep study.
- Of the remaining 10%, approx. 2% of cases can automatically be referred to lab-based testing—patients with neuromuscular conditions such as ALS, MS and Muscular Dystrophy. These patients require lab testing for a more detailed analysis of their condition and equipment needs.
- The remaining 8% of patients may need a home study to rule-out sleep apnea and a subsequent in-lab sleep study to diagnose other conditions such as PLM (periodic leg movement) disorder.
- However, these patients represent a very small percent (in fact, a smaller percent than the conservative figures we noted above).

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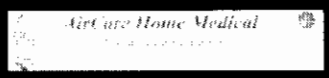
Facts & Figures

- Approximate cost of a home sleep study (reimbursement allowance required) is $400 (California Fee Schedule) vs. current payment for an in-lab study of $1,000 - $1,400. Please note, however, the $400 fee represents the **diagnostic portion** of the study **only.**
- One issue that must be addressed in considering home sleep studies is **CPAP titration after diagnosis.**
- The patient normally undergoes a second study (or split-night) while using a CPAP device at various pressures until the appropriate pressure is found.
- Home sleep study patients do not need to have an in-lab titration study and instead should be allowed an auto-titrating CPAP. This provides additional cost savings while preserving the integrity of clinical treatment.

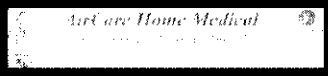
Auto-Titrating CPAP

- Having a patient undergo a home sleep study for the diagnostic portion and then have to be sent to a lab for the titration portion of the study, defeats the purpose of providing an in-home study.
- Titrating the patient at home using a portable home sleep study device is not possible, since someone would have to monitor the patient and adjust CPAP pressures through the night.
- The solution to titrating home sleep study patients is the auto-titrating CPAP.
- It is slightly more expensive than a regular CPAP device. We estimate that an additional 20% increase of payment based on the current CPAP allowed amount for this unit would be sufficient for providers to be able to provide this equipment to all home sleep study patients.



Auto-Titrating CPAP

- In calculating the cost of the auto-titrating CPAP device versus an in-lab titration study, we find that CMS/Medicare will save over $500 per patient per study per equipment rental.
- CMS would have to create a special code and/or modifier and a new allowable amount, but this is simply a procedural change.
- The auto titrating CPAP also provides some significant long-term cost savings for CMS/Medicare program.
- Since this device's technology allows it to adjust to the patient's breathing, providing the exact pressure needed at any given time, if the patient were to lose weight, gain weight, or experience any other need that would require a pressure change, the patient would **not** have to have "another" in-lab sleep study performed to adjust the pressure (which, is currently the case at a cost of $807.69 for each subsequent re-titration study). The auto-titrating CPAP automatically adjusts to the pressure needs of the patient as long as they use the device. No re-study needed!



Summary

- Approving the use of in-home sleep study testing devices used to diagnose OSA is one of the smartest changes CMS can currently make to prepare for the significant growth of this condition.
- The in-home sleep study testing device is just as clinically effective as is an in-lab study.
- Creating a code and higher allowance for an auto-titrating CPAP device, to be used to titrate patients tested using a home sleep study device is another measure that will provide significant long-term cost savings.
- We would like to note that Kaiser Permanente, one of the largest and oldest managed care organizations in the nation, adopted this method for diagnosing OSA/SDB long ago. They were quick to take advantage of technology to achieve cost savings while protecting clinical and treatment integrity.

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Conclusion

Thank you for your time and careful and thorough consideration of this policy change request.

We urge CMS to look at this policy as one of the few innovative changes CMS/Medicare must incorporate, not only to modernize our healthcare system, but to take full advantage of new and existing technologies to provide better and higher quality care, in the most cost-effective manner.

This concludes our presentation.

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Comment #82
Submitter: Randy Gorres, MS, RRT, RCP
Organization: Blank Children's Hospital
Date: May 3, 2004
Comment:

(See next page)

METHODIST & LUTHERAN
IOWA HEALTH SYSTEM

BLANK CHILDREN'S HOSPITAL
IOWA HEALTH SYSTEM

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515-241-6212

Date: May 3, 2004:

To: Steve Phurrough, M.D., MPA
Director, Coverage and Analysis Group
Office of Clinical Standards and Quality
Centers for Medicare and Medicaid Services

From: Randy Gorres, MS, RRT, RCP
Manager, Respiratory Care Services

RE: Obstructive Sleep Apnea National Coverage Determination

I would like to offer some comments on the national coverage determination for obstructive sleep apnea. I have read the letter from Dr. Davidson from San Diego regarding his views on how to allow multi-channel home testing as an alternative to polysomnography. I fully agree with Dr. Davidson's medical review of the impact that sleep disordered breathing has on patients especially as it relates to untreated sleep disordered breathing and it's impact upon the cardio-pulmonary system.

I somewhat disagree with Dr. Davidson's comment that it is grossly under diagnosed in large part due to a limited number of sleep diagnostic facilities. My view is that it is under diagnosed in large part due to many primary care personnel not being adequately trained to be able to detect sleep apnea. In addition, there is the difficulty sometimes faced by sleep labs in getting third party payers to either pay for a diagnostic polysomnogram, or if a polysomnogram is completed and the patient needs therapy vs a CPAP device, the reluctance of the third party payer to pay for the CPAP device, even when clinically indicated. There are also some problems with patients, after having been diagnosed and appropriately treated with the CPAP device, do not fully comply with using the CPAP device for a variety of reasons.

My major point of contention with Dr. Davidson's idea of using multi-channel home sleep tests is this:

> Even though they may be safely and accurately hooked up, if a qualified person is either not visually watching the patient or remotely monitoring the patient and diagnostic device via some electronic means such as a modem, there is a complete lack of ability to take action when one of the leads of the diagnostic device becomes disconnected or if there is a patient problem. If there is an equipment malfunction you can't be assured of getting a diagnostic study and thus, not be able to accurately diagnose the patient. For example, if the EEG is not being monitored because of an equipment failure so you don't know what stage of sleep the patient is in when you analyze the data, how can you properly diagnose the disease? Unattended home studies have never proven to be as accurate as monitored studies.

Being able to accurately tell the stage (s) of sleep, position of patient, what, if any hypoxemia occurs, how frequent the apneas are is etc., is essential to a complete and accurate sleep study. Even if costs less cost, having to repeat a multi-channel study that is incomplete or worse, inaccurate, even once is going to drive up the cost considerably. An inaccurate study, no matter where it is done, could lead to improper or no treatment.

I would think Dr. Davidson or someone would list the 14 studies cited using these 8 different multi-channel home sleep tests to verify the accuracy of his claims. For example, have they been published in a peer review professional journal i.e.: *Chest, American Review of Respiratory Disease, Sleep*? Have they been peer reviewed by the professionals in the world of sleep medicine such as APT Society or the American Academy of Sleep Medicine? Until that data has been peer reviewed and the case for allowing multi-channel home sleep tests being accepted as accurate as the "gold standard" that he alludes to, I found it somewhat disconcerting that CMS would consider allowing this without being able to insure accuracy of the testing and the results obtained.

I am also very concerned that Dr. Davidson seems to think that the home sleep diagnostic dispensing and titration can be performed by a large number of practitioners such as ENT surgeons, cardiologists, primary care physicians and others. I think that this is the wrong approach and this is opening up a very important diagnostic tool to anyone being able to put up the money to buy the diagnostic testing regardless of his or her qualification, training and/or background. I put this akin to opening up cardiac caths to podiatrists, chiropractors and physical therapists. Perhaps I am wrong, but I am concerned about the technical skills, training and competency of anyone performing sleep testing, no matter where they are done or who owns the devices.

Therefore, I **strongly** recommend that until the research has been done proving these devices are as accurate as the "gold" standard of polysomnography, that this has been independently verified (i.e.: the study has not been supported by one of the manufacturers of these multi-channel home sleep diagnostic tools) etc, that this not be allowed. I would encourage a large scale scientific study be done that reviews this issue to see if it is accurate and as safe as polysomnography studies done in either freestanding lab or hospital-based sleep labs.

I appreciate the opportunity to provide this input. I can be reached at 515-241-5096.

Sincerely,

Randy Gorres, M.S., RRT. RCP.
Manager, Pulmonary Services
Iowa Health – Des Moines