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CONTINUING MEDICAL EDUCATION OFFERINGS

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Statement of Educational Purpose/Overall Education Objectives
JCSM is a peer-reviewed clinical journal addressing sleep, circadian rhythms, and the diagnosis and treatment of the broad spectrum of sleep disorders. Its mission and educational purpose is to promote the science and art of sleep medicine and sleep research. Sleep disorders medicine draws clinical and scientific applications from a wide variety of primary disciplines, including pulmonology, neurology, psychiatry, psychology, otolaryngology, and dentistry. Readers of JCSM should be able to: 1) appraise sleep research in basic science and clinical investigation; 2) interpret new information and updates on clinical diagnosis/treatment and apply those strategies to their practice; 3) analyze articles for the use of sound scientific and medical problems; and 4) recognize the inter-relatedness/dependence of sleep medicine with primary disciplines.

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Employer purchasing of health benefits is undergoing a transformation. Benefits personnel are becoming more savvy healthcare consumers, broadening their long-standing focus on cost management to embrace a value-based approach that also incorporates quality and outcomes. This commentary provides insight into current employer healthcare purchasing practices from the perspective of a former sleep center co-director who is now a corporate medical director who supports employer health benefits purchasing strategy development. Sleep medicine physicians and sleep center management will benefit from a better understanding as to how employers are making decisions, and some potential future employer purchasing scenarios.

Current State of Sleep Disorders in Working Populations and Implications for Employers

Recent estimates of the prevalence of obstructive sleep apnea (OSA) have ranged from 3% to nearly 20% in adult populations.1,2 Despite a general recognition that sleep disorders are common and are associated with significant health and productivity costs, the prevalence of undiagnosed OSA cases is substantial. Between 80% and 85% of individuals with OSA are estimated to be undiagnosed.2 A range of national organizations have instituted awareness campaigns among employers as well as the population at large in an effort to overcome this barrier to effective management.

The cost to employers of OSA is considerable. OSA-associated healthcare costs include both the direct expenses of OSA diagnosis and treatment, as well as those from associated conditions, including diabetes, obesity, depression, and hypertension. Individuals with sleep problems are also less likely to be productive at work, averaging 7.9 more absence days and 7.5 more presenteeism days (lost productivity while at work due to fatigue or other health-related concerns) than those without sleeping problems.3 Additionally, an increased incidence of occupational injuries among individuals with sleep apnea further compounds the employer cost of this condition.3

Implications of Effective Treatment: Sleep Disorders Management as a Strategic Business Investment

Research has demonstrated reductions in employer healthcare and disability costs following effective sleep apnea treatment.4 This finding may, in part, be due to improved management of OSA-associated chronic conditions, including hypertension, diabetes, depression, and obesity. With the favorable impact of OSA treatment on these comorbid conditions, employer interest in effective OSA diagnosis and treatment is only likely to increase.

Further enhancing employer interest in sleep disorders management is the expanded recognition of the workplace safety risks of OSA. While initially a focus of regulatory compliance among drivers, increasing awareness of the general safety and lost productivity issues associated with sleep disorders is growing. Accordingly, employers are increasingly recognizing the substantial value potential for program offerings to identify and manage OSA.

Employer Costs of Diagnosis and Treatment as a Barrier to Promoting Diagnosis and Treatment

However, employers face a sizeable cost burden associated with diagnosis and treatment of OSA. With a near-term healthcare cost-containment focus, employer interest in expanded diagnosis and management of this condition is tempered by current up-front diagnosis costs, in addition to suboptimal adherence to therapy. Current employer interest appears most focused on health promotion and incentive strategies, where smaller investments may ultimately yield a potentially more substantial healthcare cost impact. Chronic condition management also remains an important focus, with recognition that improved disease control can result in lower healthcare costs.

Health System and Employer Health Benefits Innovations

Technological advances have yielded out-of-center polysomnography testing devices that appear comparable to traditional sleep center services for the diagnosis of sleep apnea for most patients.5 While these home-use services are not yet widely disseminated, they have the potential to improve both access and convenience for selected patient populations. With increased awareness of this technology among high-deductible health plan enrollees and risk-bearing accountable care organizations, interest and demand for out-of-center testing is certain to rise.

At the same time, employers are becoming more knowledgeable healthcare purchasers, and are increasingly engaged in identification and incorporation of high-value healthcare services as part of comprehensive health benefits. Application of business supply chain management principles to healthcare
purchasing has employers more effectively aligning their efforts with the Triple Aim goals of quality, efficiency, and cost. Examples of this include employer direct contracting for worksite clinics, Centers of Excellence for high-cost surgical procedures, and patient-centered medical homes, as well as narrow network development for high quality healthcare services. As an innovative payment strategy, bundled pricing is increasingly being used by employers to establish a fixed cost for the identified services. This payment approach has the effect of more closely aligning employer and healthcare provider interests, eliminating incentives for fee-for-service, as well as creating an incentive to optimize care delivery efficiency and minimize errors.

Complementing employer supply chain management are innovative employer benefit design strategies that incentivize health plan beneficiaries to direct individuals toward the use of these high-value services. For example, employers may implement a reduced or waived co-pay for selected high-value services, such as the Wal-Mart Centers of Excellence program, where eligible beneficiaries have no out of pocket costs for their surgical care.\(^7\)

Alternatively, some employers are incorporating a so-called reference-based pricing strategy, where a financial coverage maximum is established for a series of specific procedures, typically ones that can reasonably be commoditized, such as CT and MRI scans. Health plan enrollees can choose any provider for these services, but if the negotiated cost with the health plan exceeds the employer-established maximum, the patient is then responsible for the difference in cost. This strategy is intended to help individuals recognize variability in cost among different local service providers, using a financial incentive to steer individuals toward comparable quality, lower cost options.

These employer considerations highlight the fact that employers are becoming more discerning purchasers of healthcare services. The days when health plans dictated utilization and purchasing decisions are waning, as employers appreciate that they alone are best positioned to manage their investments in health and productivity. Not surprisingly, employers face a steep learning curve to understand the comparative value of the healthcare offerings included in their benefits offering. This scenario therefore represents an excellent opportunity for sleep center experts to articulate the value of sleep disorders diagnosis and management to interested benefits personnel.

### Implications for Sleep Disorders Diagnostic Testing

Employers are facing a growing confluence of awareness of the health and productivity costs of sleep disorders (the problem), together with growing involvement in healthcare supply chain management and innovative benefit design as a means to identify and promote use of cost-effective, high-value services (the solution). The demonstration that out-of-center polysomnography can serve as a reasonable and cost-effective substitute for traditional sleep center-based testing\(^5\) is likely to garnerincreasing employer interest.

As employers assume a more active role in their healthcare purchasing, how might this scenario play out? One possibility is that employers create a tiered benefit design where sleep studies for eligible individuals are performed by out-of-center testing services as a lower patient cost alternative to traditional sleep center evaluation. This is particularly important for employers with substantial benefits enrollment in high-deductible and consumer-based health plans, where individuals have greater responsibility for managing their costs. Another possibility is that employers contract directly with portable testing companies for both diagnosis and management, using a “carved-out” bundled pricing approach. A third scenario is that employers may choose to incorporate a reference-based pricing approach to steer patients toward lower cost, comparable value services such as home polysomnography. It is also possible that in the near future, employers may choose to contract with an accountable care organization (ACO), with the expectation that the ACO will assume responsibility for maximizing the use of out-of-center polysomnography testing as a means to maximize shared savings potential.

Sleep center directors need to understand that transformation in both healthcare supply chain management and benefit design is occurring rapidly. No longer are health plans the sole decision-makers regarding specific coverage and benefit design recommendations. Employers are rapidly becoming knowledgeable purchasers of healthcare. With the prevalence and total costs of sleep disorders in the workforce, it is likely only a matter of time before employers begin to implement innovative and aggressive cost management strategies. Once the value of these innovative models becomes more widely known (as with the previously described Centers of Excellence program), implementation can be expected to accelerate rapidly. The direct contracting precedent has already been established for diagnostic sleep studies in the transportation industry.

Looking ahead, employers will continue to expand their value-based approach to healthcare purchasing. Employers can be expected to demand more from healthcare providers, with progressively greater focus on efficiency, outcomes, and cost. Benefits strategies will be used by employers to create a financial incentive to direct individuals to use those services yielding the greatest demonstrable value. Sleep center personnel that fail to respond to these market changes may well be in for a rude awakening.

### CITATION


### REFERENCES


8. Atwood C. “The times they are a changin:” home diagnosis of sleep apnea has arrived. Sleep 2012;35:735-6.

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DISCLOSURE STATEMENT
Dr. Sherman has indicated no financial conflicts of interest.
Obstructive Sleep Apnea During Rapid Eye Movement Sleep, Daytime Sleepiness, and Quality of Life in Older Men in Osteoporotic Fractures in Men (MrOS) Sleep Study


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Study Objectives: Assess the association between REM predominant obstructive sleep apnea (OSA), sleepiness, and quality of life in a community-based cohort of men ≥ 65 years-old.

Design, Intervention and Measurements: A cross-sectional analysis of 2,765 subjects from the Outcomes of Sleep Disorders in Older Men (MrOS Sleep) Study was performed to identify subjects with an apnea hypopnea index (AHI) < 15 (n = 2,044). Subjects were divided into groups based on the AHI in REM sleep (< 5 [referent group], 5 to < 15, 15 to < 30, and ≥ 30). Daytime somnolence, sleep-related quality of life, sleep disturbance, general quality of life, depressive symptoms, and health status were quantified using Epworth Sleepiness Scale (ESS), Functional Outcomes of Sleep Questionnaire (FOSQ), Pittsburgh Sleep Quality Index (PSQI), Short Form-12 (SF-12), Geriatric Depression Scale-15 (GDS), and self-perceived health status, respectively.

Results: Prevalence of REM-predominant OSA (AHI-REM ≥ 5) was 42.8% if OSA was defined as AHI ≥ 15 and 14.4% if OSA was defined as AHI ≥ 5. Higher AHI-REM was associated with polysomnographic indices of poorer sleep architecture (reduced total sleep time, sleep efficiency, REM sleep duration and proportion). Adjusting for age, BMI, and study site, higher AHI-REM was not associated with subjective sleep measures (ESS, FOSQ, PSQI), lower quality of life (SF-12), or greater depressive symptoms (GDS).

Conclusions: In a community-based sample of older adult men ≥ 65 years-old, REM-predominant OSA was highly prevalent and was associated with objective indices of poorer sleep quality on polysomnography but not with subjective measures of daytime sleepiness or quality of life.

Keywords: Sleep apnea syndromes, sleep apnea, obstructive; sleep, rapid eye movement, disorders of excessive somnolence, epidemiology, older adults, quality of life

Citation: Khan A; Harrison SL; Kezirian EJ; Ancoli-Israel S; Orwell D; Ensrud K; Stone KL. Obstructive sleep apnea during rapid eye movement sleep, daytime sleepiness, and quality of life in older men in osteoporotic fractures in men (MrOS) sleep study. J Clin Sleep Med 2013;9(3):191-198.

Obstructive sleep apnea (OSA), as defined by an apnea hypopnea index (AHI) ≥ 5, is present in 24% to 62% of community dwelling elderly (age ≥ 65 years), and moderate to severe OSA with an AHI ≥ 15 has been noted in 19% to 44%. OSA has been associated with excessive daytime sleepiness, decreased quality of life, impaired cognition, hypertension, stroke, diastolic dysfunction, left atrial enlargement, and insulin resistance. Little is known about OSA confined only to REM sleep (REM-predominant OSA). This is of particular interest, given that disordered breathing events in REM sleep are often of longer duration and associated with a greater degree of oxygen desaturation than NREM sleep.

REM-predominant OSA also poses a difficult dilemma for the practicing clinician. There is lack of data regarding the association between REM-predominant OSA and quality of life as well as cardiovascular and metabolic outcomes. It is not clear if isolated REM-only OSA needs to be treated or if during continuous positive airway pressure (CPAP) titration, pressure should be increased for REM events if the overall AHI is in the normal range. The prevalence and impact of REM-predominant OSA is not clear due to differences in sample size and patient populations of various studies and the adjustments used in various studies to compensate for the effect of AHI in NREM (AHI-NREM) on AHI in REM (AHI-REM) sleep. This is further confounded by REM-predominant OSA being more prominent in women and relatively younger population and less common in individuals with severe OSA.
The prevalence and impact of REM-predominant OSA in individuals older than 65 years is not known. The average age of the subjects in most studies of OSA has been between 49-65 years, and individuals older than 65 have been excluded in most studies. In some studies REM related OSA was more common in the younger population, while in other studies such as the Sleep Heart Health Study, subjects with more severe REM-predominant OSA were older. Our primary objective was to define the prevalence of REM-predominant OSA in the Osteoporotic Fractures in Men Sleep Study (MrOS Sleep Study) cohort and determine whether REM-predominant OSA was associated with sleepiness and quality of life in older male adults. Our secondary objective was to describe the demographic and polysomnography (PSG) characteristics of older men with REM-predominant OSA.

**METHODS**

**Population**

From March 2000 through April 2002, 5,994 men aged 65 years and older were recruited for participation in the prospective Osteoporotic Fractures in Men (MrOS) Study from population-based listings in 6 areas of the United States: Birmingham, Alabama; Minneapolis, Minnesota; Palo Alto, California; Pittsburgh, Philadelphia; Portland, Oregon and San Diego, California. To be eligible for the study, men had to be able to walk without assistance, not have had bilateral hip replacement or a medical condition that (in the judgment of the investigator) would result in imminent death at the time of enrollment, and were willing to give informed consent and undergo the study procedures. There were no other exclusion criteria.

In an ancillary study, from December 2003 through March 2005, subjects were invited to have in-home polysomnography (PSG) and actigraphy as part of Outcomes of Sleep Disorders in Older Men (MrOS) Study. Of the 5,994 men enrolled in the MrOS Study, 3,135 (52.3%) were enrolled in the MrOS Sleep Study. All participants provided written informed consent, and the study protocols were approved by the institutional review boards at each respective study site and at the data coordinating center in San Francisco, California. The MrOS sleep visit was completed between December 2003 and March 2005. A total of 3,135 participants attended the sleep visit. Men were screened for use of mechanical devices during sleep including continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BPAP), mouthpiece for snoring or sleep apnea, or oxygen therapy. In general, those who reported nightly use of any of these devices were excluded from the MrOS Sleep Study; however, the study sample does include 11 men who reported use of one of these devices < 2 times per week. In the present analysis, data were analyzed from 2,765 subjects who took part in the MrOS Sleep Study and had adequate PSG signal quality available for ≥ 4 h, as well as adequate REM staging data (Figure 1).

**Polysomnography**

In-home sleep studies were performed using unattended PSG (Safiro, Compumedics, Inc., Melbourne, Australia). The recording montage consisted of 2 central (C3/A2 and C4/A1) electroencephalographic leads, bilateral electrocorticograms, a bipolar submental electromyogram, thoracic and abdominal respiratory inductance plethysmography, airflow (using nasal-oral thermocouple and nasal pressure cannula), finger pulse oximetry, electrocardiogram, body position (mercury switch sensor), and bilateral leg movements (piezoelectric sensors). Trained certified staff members performed home visits for setup of the sleep study units. After sensors were placed and calibrated, signal quality and impedance were checked, and sensors were repositioned as needed to improve signal quality, replacing electrodes if impedences were greater than 5 kΩ, using approaches similar to those used in the Sleep Heart Health Study. Staff returned the next morning to collect the equipment and download the data to the Central Sleep Reading Center (Cleveland, OH) for centralized scoring by trained technicians using standard criteria.

Subjects included in the present analysis included MrOS Sleep Study participants who had PSG with adequate scoring of REM sleep based on availability of reliable staging data. Less than 1% of the subjects had ≤ 10 min of REM sleep; all subjects with any REM sleep were included in the analysis. Sleep stages (REM, stages 1-4 NREM) were scored using standard criteria. The reliability of indices of sleep architecture, determined by rescoring studies over time, indicates that the inter-scorer reliability (ICC) for the percent of sleep time spent in sleep stages 1, 2, slow wave sleep, and REM were 0.60, 0.91, 0.96, and 0.94, respectively. AHI was calculated as the total number of apneas and hypopneas per hour of sleep. The inter-scorer reliability for AHI was high (ICC = 0.99).

Apneas were identified if the amplitude of the airflow signal was flat or nearly flat for > 10 seconds. Obstructive apneas were scored if persistence of effort on abdominal or thoracic inductance plethysmography was noted, and central apneas were scored if there was no evident effort on either the abdominal and thoracic plethysmography bands. Hypopneas were scored using Sleep Heart Health Study criteria (requiring a “discernible” (> 30%) reduction in amplitude of respiratory effort or airflow) and, in secondary analyses, using the American Academy of Sleep Medicine (AASM) criteria (> 50% reduction in amplitude of signals), considered according to the following hierarchy: summed inductance plethysmography channel, abdominal or thoracic inductance plethysmography, nasal pressure, or thermistor. For the current study, apneas and hypopneas associated with ≥ 4% oxygen desaturation were included, and the Sleep Heart Health Study definition was used for primary analyses. The total AHI, as well as AHI-REM and AHI-NREM were computed as the number of apneas plus hypopneas per hour of total, REM, and NREM sleep, respectively.

**Selection and Classification of Subjects**

OSA was defined as AHI ≥ 15 during the entire sleep period. REM-predominant OSA was defined as AHI < 15, but AHI-REM ≥ 5 (Figure 1). From the entire population of MrOS study participants, men were first classified on the basis of OSA: AHI < 15 (absence of moderate to severe OSA group) and AHI ≥ 15 (OSA group). The 2.015 men with AHI < 15 (analysical cohort) were further subdivided based upon the AHI-REM sleep: AHI-REM < 5 (referent group) and AHI-REM 5 to < 15, AHI-REM > 15 (cases).
Sleepiness and Functional Outcome Measures

Subjective sleepiness was measured using the Epworth Sleepiness Score (ESS), a self-administered questionnaire which provides a measurement of the subject’s general level of daytime sleepiness. Individuals rate the chances that they would doze off or fall asleep when in 8 different situations commonly encountered in daily life on a 0- to 3-point scale. Possible scores range from 0 to 24. An ESS score > 10 is considered sleepy and correlates with sleep latency measured during the multiple sleep latency test and during overnight PSG.

Sleep-related quality of life was measured using the Functional Outcomes of Sleep Questionnaire (FOSQ). FOSQ is a 30-item disease specific self-reported measure designed to assess the impact of disorders of excessive sleepiness on multiple activities of everyday living. Mean-weighted item scores are used to generate 5 subscales (activity level, vigilance, intimacy and sexuality, general productivity, and social outcome) that together produce a composite score. The total score ranges from 5 to 20, and lower scores indicate greater dysfunction. FOSQ can successfully discriminate between normal subjects and those who should seek medical attention for a sleep problem.

Subjective sleep symptoms, disturbance, and patterns were assessed using the Pittsburgh Sleep Quality Index (PSQI). PSQI is a self-reported questionnaire that assesses sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction), the sum of which yields a global score. The total global score ranges from 0 to 21; greater scores indicate higher levels of sleep symptoms. A global PSQI score > 5 yielded a diagnostic sensitivity of 89.6% and specificity of 86.5% in distinguishing good and poor sleepers.

General quality of life was measured using Short Form 12 (SF-12), a generic 12-question survey which is weighted and summed to provide interpretable scales for physical and mental health. The physical and mental health composite summary

Table 1—Baseline subject characteristics based on AHI and AHI-REM sleep of subjects in MrOS Sleep Study

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<th>Subject Characteristic</th>
<th>AHI-REM ≤ 5 (n = 858)</th>
<th>AHI-REM 5 to &lt; 15 (n = 644)</th>
<th>AHI-REM 15 to &lt; 30 (n = 409)</th>
<th>AHI-REM ≥ 30 (n = 133)</th>
<th>AHI ≥ 15 (n = 721)</th>
<th>p-value</th>
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<td>Age, mean (SD)</td>
<td>76.4 (5.6)</td>
<td>76.0 (5.6)</td>
<td>76.1 (5.4)</td>
<td>76.3 (5.3)</td>
<td>76.9 (5.5)</td>
<td>0.03</td>
</tr>
<tr>
<td>Caucasian, n (%)</td>
<td>801 (93.4)</td>
<td>586 (91.0)</td>
<td>375 (91.7)</td>
<td>128 (96.2)</td>
<td>654 (90.7)</td>
<td>0.09</td>
</tr>
<tr>
<td>BMI (kg/m²), mean (SD)</td>
<td>25.8 (3.1)</td>
<td>26.7 (3.4)</td>
<td>27.9 (3.8)</td>
<td>29.0 (4.0)</td>
<td>28.4 (4.2)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Neck circumference (cm), mean (SD)</td>
<td>147.9 (70.5)</td>
<td>149.9 (72.2)</td>
<td>145.3 (70.7)</td>
<td>150.2 (71.1)</td>
<td>140.4 (71.1)</td>
<td>0.11</td>
</tr>
<tr>
<td>Waist circumference (cm), mean (SD)</td>
<td>38.5 (2.6)</td>
<td>39.3 (3.3)</td>
<td>39.9 (2.8)</td>
<td>40.0 (3.0)</td>
<td>40.2 (2.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>PASE score, mean (SD)</td>
<td>96.1 (9.6)</td>
<td>98.4 (10.0)</td>
<td>101.5 (12.3)</td>
<td>104.1 (12.0)</td>
<td>102.7 (11.4)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Benzodiazepine use, n (%)</td>
<td>42 (4.9)</td>
<td>26 (4.0)</td>
<td>17 (4.2)</td>
<td>8 (6.0)</td>
<td>25 (3.5)</td>
<td>0.55</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>88 (10.3)</td>
<td>78 (12.1)</td>
<td>59 (14.4)</td>
<td>20 (15.0)</td>
<td>119 (16.5)</td>
<td>0.005</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>394 (45.9)</td>
<td>310 (48.1)</td>
<td>196 (47.9)</td>
<td>71 (53.4)</td>
<td>414 (57.4)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CVD, n (%)</td>
<td>342 (39.9)</td>
<td>264 (41.0)</td>
<td>169 (41.3)</td>
<td>43 (32.3)</td>
<td>340 (47.4)</td>
<td>0.004</td>
</tr>
<tr>
<td>Heart attack, n (%)</td>
<td>146 (17.0)</td>
<td>106 (16.5)</td>
<td>81 (19.8)</td>
<td>15 (11.3)</td>
<td>131 (18.2)</td>
<td>0.21</td>
</tr>
<tr>
<td>Stroke, n (%)</td>
<td>41 (4.8)</td>
<td>24 (3.7)</td>
<td>10 (2.4)</td>
<td>4 (3.0)</td>
<td>25 (3.5)</td>
<td>0.31</td>
</tr>
<tr>
<td>Respiratory Illness, n (%)</td>
<td>40 (4.7)</td>
<td>30 (4.7)</td>
<td>27 (6.6)</td>
<td>14 (10.5)</td>
<td>32 (4.4)</td>
<td>0.03</td>
</tr>
<tr>
<td>Alcohol (drinks/wk), mean (SD)</td>
<td>3.6 (4.2)</td>
<td>3.4 (4.2)</td>
<td>3.4 (4.4)</td>
<td>2.8 (4.1)</td>
<td>3.2 (4.0)</td>
<td>0.09</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>22 (2.6)</td>
<td>15 (2.3)</td>
<td>5 (1.2)</td>
<td>2 (1.5)</td>
<td>9 (1.3)</td>
<td>0.25</td>
</tr>
<tr>
<td>Ever snored, n (%)</td>
<td>637 (83.6)</td>
<td>506 (88.3)</td>
<td>319 (87.9)</td>
<td>104 (88.9)</td>
<td>606 (90.7)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

AHI, apnea hypopnea index; AHI-REM, apnea hypopnea index REM sleep; BMI, body mass index; CVD, cardiovascular disease; PASE, Physical Activity Scale for the Elderly; SD, standard deviation.
scores are computed using the scores of the 12 questions and range from 0 to 100, where a 0 score indicates the lowest level of health measured by the scales and 100 indicates the highest level of health. SF-12 does not target a specific age or disease group and the physical and mental summary scores tend to vary over the life span and for different age groups.

Depressive symptoms were assessed using the Geriatric Depression Scale (GDS). GDS is a brief questionnaire in which participants are asked to respond to either 15 or 30 questions by answering yes or no in reference to how they felt on the day of administration. GDS-15 was used in this study, and scores ≥ 6 on this scale indicates depression.

Self-reported health status was scaled as excellent, good, fair, poor, or very poor; the responses were collapsed into 2 categories excellent/good health and fair/poor/very poor health.

**Other Measurements**

Study participants completed an anthropometric evaluation and questionnaire assessment of medical history including self-reported provider–diagnosed disease which included hypertension, diabetes mellitus, cardiovascular disease (CVD), heart attack, respiratory illness, and stroke. All prescription and over-the-counter medications taken 30 days prior to the last visit were recorded by the clinics and stored in an electronic medications inventory database (San Francisco Coordinating Center, San Francisco, CA). Each medication was matched to its ingredient(s) based on the Iowa Drug Information Service (IDIS) Drug Vocabulary (College of Pharmacy, University of Iowa, Iowa City, IA). Clinic visit examination and questionnaire measurements included age (years), body mass index (BMI = kg/m²), race, neck and waist circumference (cm), tobacco smoking, and alcohol use status. Physical activity was assessed using Physical Activity Scale for the Elderly (PASE), a research instrument that measures the level of physical activity in individuals aged 65 years or older.

**Statistical Analysis**

Participant characteristics were examined across AHI-REM categories. For categorical data, chi-squared test was used. Analysis of variance (ANOVA) was used for normally distributed continuous data and Kruskal-Wallis test for continuous data that were skewed. Similarly, sleep related variables were also explored across AHI-REM categories where p-value for trend was calculated.

Least square means linear regression was used to examine the relationship between continuous outcomes, such as sleepiness and quality of life, and AHI-REM categories. Logistic regression was used to assess the relationship between AHI-REM categories and similar dichotomized outcomes. All models were initially adjusted for age and study site. Since OSA has been associated with obesity and weight loss has been associated with improvement in BMI, anthropometric measures, and OSA, further adjustment was done for either BMI or waist and neck circumference. All analyses were performed using SAS software, version 9.1 (SAS Institute, Cary, NC).

**RESULTS**

Polysomnography data quality were excellent, with a failure rate < 4% and more than 70% of studies graded as being of excellent or outstanding quality using standardized criteria. Of the 2,765 men with technically adequate PSG data (Figure 1), 2,044 subjects had AHI < 15 (analytical cohort), while 721 subjects had AHI ≥ 15. Three hundred seventy subjects were excluded due to inadequate unreliable REM/NREM data or no PSG data. There were 858 subjects with AHI-REM < 5 who served as the referent group; there were 644 subjects with AHI-REM 5 to < 15, 409 subjects with AHI-REM 15 to < 30, 133 subjects with AHI-REM ≥ 30, and 721 subjects with AHI > 15. The average time spent in REM sleep time was 70.3 ± 28.2 min and in NREM 286.3 ± 55.5 min. The prevalence of REM-predominant OSA was 42.8% if OSA was defined as AHI ≥ 15 and 14.4% if OSA was defined as AHI ≥ 5.

Among our cohort of 2,041 older men without moderate or severe OSA (AHI < 15), there were no significant differences by age or race across AHI-REM categories. A higher AHI-REM was associated with higher BMI, neck circumference, and waist circumference (p value < 0.001) (Table 1). Subject-reported histories of respiratory illness and snoring were also associated with a higher AHI-REM (p < 0.05). There were no significant associations between PASE score, benzodiazepine use, smoking status, alcohol use, physician diagnosed and self-reported diabetes, stroke, cardiovascular disease, and heart attack across categories of REM-predominant OSA (Table 1). Results were similar when AHI ≥ 5 was used to define the presence of OSA (supplemental material Table S1).

There was a significant trend in decreasing total sleep time, sleep efficiency, and minutes and percentage of time in REM sleep across AHI-REM categories (Table 2). A higher AHI-REM was associated with a higher total and NREM AHI as well as a higher AHI-REM-to-AHI-NREM ratio and arousal index (Table 2). The trend was similar when AHI ≥ 5 was used as definition of OSA (supplemental material Table S2).

Adjusted for age, study site, and anthropometric measures, AHI-REM ≥ 30 was associated with worse self-perceived health status than AHI-REM ≤ 5 (Tables 3 and 4). After adjustment for age and site, there was no evidence that level of sleepiness or vitality (as measured by ESS, PSQI, and FOSQ) or quality of life (as assessed by SF-12 physical, mental summary scale, and GDS) varied across categories of REM-predominant OSA (Tables 3 and 4). Adjusting for BMI or neck or waist circumference did not change the results (data not shown). Results were not altered in analyses when OSA was defined as AHI ≥ 5 during the entire sleep period and REM-predominant OSA was defined as AHI < 5 with AHI-REM ≥ 5 (supplemental material Table S3 and S4).

**DISCUSSION**

In a large, community-based sample of adults > 65 years old, we assessed the association between REM-predominant OSA, sleepiness and quality of life in subjects without OSA (using either AHI ≥ 15 or AHI ≥ 5 to define OSA). Our findings show that in this population of older men, an elevated AHI-REM sleep was highly prevalent even when the AHI was either low (< 5) or modest (< 15). Similar to what is known regarding total AHI levels, a higher AHI-REM was associated with a higher BMI, neck circumference, and waist circumference. Of note, even among those without an elevated AHI (overall AHI < 5
or < 15), a higher AHI-REM was associated with reduced total sleep time, sleep efficiency, and REM time and percentage. This suggests that even when the predominant number of respiratory disturbances occur in REM sleep, sleep architecture is disturbed. However, increasing REM-specific AHI levels were not linearly associated with increased sleepiness as determined

Table 2—Polysomnography characteristics of subjects in MrOS Sleep Study

<table>
<thead>
<tr>
<th>Subject Characteristics</th>
<th>AHI-REM &lt; 5 (n = 858)</th>
<th>AHI-REM 5 to &lt; 15 (n = 644)</th>
<th>AHI-REM 15 to &lt; 30 (n = 409)</th>
<th>AHI-REM ≥ 30 (n = 133)</th>
<th>AHI ≥ 15 (n = 721)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total sleep time (min), mean (SD)</td>
<td>359.9 (67.0)</td>
<td>361.6 (65.7)</td>
<td>356.1 (68.0)</td>
<td>338.2 (75.6)</td>
<td>351.9 (67.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Sleep efficiency %, mean (SD)</td>
<td>75.5 (11.9)</td>
<td>75.5 (11.6)</td>
<td>74.1 (11.3)</td>
<td>72.8 (11.9)</td>
<td>71.4 (12.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>REM time (min), mean (SD)</td>
<td>74.5 (28.4)</td>
<td>74.9 (27.9)</td>
<td>70.9 (28.2)</td>
<td>59.8 (28.3)</td>
<td>62.7 (26.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>REM sleep (% TST), mean (SD)</td>
<td>20.4 (6.4)</td>
<td>20.5 (6.4)</td>
<td>19.6 (6.4)</td>
<td>17.0 (6.6)</td>
<td>17.5 (6.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Arousal index, mean (SD)</td>
<td>19.8 (9.3)</td>
<td>20.4 (9.5)</td>
<td>22.4 (10.1)</td>
<td>24.1 (11.3)</td>
<td>31.3 (12.5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Total AHI (NREM+REM) events/h, mean (SD)</td>
<td>2.9 (3.3)</td>
<td>5.3 (3.5)</td>
<td>8.8 (3.3)</td>
<td>10.8 (3.5)</td>
<td>29.1 (12.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>AHI REM events/h, median (25-75 IQR)</td>
<td>1.5 (0.0-3.1)</td>
<td>8.8 (6.6-11.6)</td>
<td>20.4 (17.3-24.2)</td>
<td>34.6 (31.6-40.0)</td>
<td>31.1 (18.1-42.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>AHI NREM events/h, median (25-75 IQR)</td>
<td>1.5 (0.3-4.5)</td>
<td>3.5 (1.3-6.7)</td>
<td>5.4 (2.7-8.9)</td>
<td>5.6 (3.3-7.6)</td>
<td>24.4 (18.2-35.6)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

AHI, apnea hypopnea index; AHI REM, apnea hypopnea index REM sleep; 25-75 IQR, 25th-75th percentile of interquartile range; min, minutes; SD, standard deviation; TST, total sleep time.

Table 3—Self-reported perceived health status, quality of life measures and sleepiness in subjects in MrOS Sleep Study

<table>
<thead>
<tr>
<th>Subject Characteristics</th>
<th>AHI-REM &lt; 5 (n = 858)</th>
<th>AHI-REM 5 to &lt; 15 (n = 644)</th>
<th>AHI-REM 15 to &lt; 30 (n = 409)</th>
<th>AHI-REM ≥ 30 (n = 133)</th>
<th>AHI ≥ 15 (n = 721)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOSQ score (5-20), mean (SD)</td>
<td>18.7 (1.4)</td>
<td>18.7 (1.4)</td>
<td>18.8 (1.5)</td>
<td>18.8 (1.7)</td>
<td>18.5 (1.7)</td>
<td>0.003</td>
</tr>
<tr>
<td>PSQI score (0-21), mean (SD)</td>
<td>5.5 (3.2)</td>
<td>5.3 (2.9)</td>
<td>5.8 (3.3)</td>
<td>5.9 (3.6)</td>
<td>5.9 (3.4)</td>
<td>0.002</td>
</tr>
<tr>
<td>SF12 mental summary scale, mean (SD)</td>
<td>55.2 (7.3)</td>
<td>55.6 (6.8)</td>
<td>55.3 (7.4)</td>
<td>55.2 (7.5)</td>
<td>54.6 (8.2)</td>
<td>0.18</td>
</tr>
<tr>
<td>SF12 physical summary scale, mean (SD)</td>
<td>49.7 (9.7)</td>
<td>49.5 (9.5)</td>
<td>49.1 (10.3)</td>
<td>47.1 (10.4)</td>
<td>47.0 (10.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ESS score, mean (SD)</td>
<td>5.9 (3.5)</td>
<td>6.2 (3.6)</td>
<td>5.9 (3.4)</td>
<td>6.2 (3.5)</td>
<td>6.6 (4.0)</td>
<td>0.02</td>
</tr>
<tr>
<td>ESS score &gt; 10, n (%)</td>
<td>100 (11.7)</td>
<td>82.1 (12.7)</td>
<td>45.1 (11.0)</td>
<td>11.8 (8.3)</td>
<td>121 (16.8)</td>
<td>0.006</td>
</tr>
<tr>
<td>Geriatric Depression Scale ≥ 6 n (%)</td>
<td>46 (5.4)</td>
<td>31 (4.8)</td>
<td>26 (6.9)</td>
<td>9 (6.8)</td>
<td>75 (10.7)</td>
<td>0.12</td>
</tr>
<tr>
<td>Self-perceived health (excellent/good), n (%)</td>
<td>773 (90.1)</td>
<td>568 (88.3)</td>
<td>354 (86.6)</td>
<td>107 (80.5)</td>
<td>612 (84.9)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

AHI, apnea hypopnea index; AHI-REM, apnea hypopnea index REM sleep; BMI, body mass index; ESS, Epworth Sleepiness Scale; FOSQ, Functional Outcomes of Sleep Questionnaire; GDS, Geriatric Depression Scale-15; PSQI, Pittsburg Sleep Quality Index; SD, standard deviation; SF-12, Short Form 12.

Table 4—Adjusted* means (A) and odds ratios (B) (95%CI) of functional outcome measures by AHI categories

<table>
<thead>
<tr>
<th>AHI-REM</th>
<th>AHI &lt; 5 (n = 858)</th>
<th>AHI-REM 5 to &lt; 15 (n = 644)</th>
<th>AHI-REM 15 to &lt; 30 (n = 409)</th>
<th>AHI-REM ≥ 30 (n = 133)</th>
<th>AHI ≥ 15 (n = 721)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESS</td>
<td>5.84 (6.60, 6.09)</td>
<td>6.16 (6.68, 6.44)</td>
<td>5.87 (6.52, 6.22)</td>
<td>6.33 (5.71, 6.95)</td>
<td>6.66 (6.39, 6.92)**</td>
<td></td>
</tr>
<tr>
<td>PSQI</td>
<td>5.49 (6.57, 5.71)</td>
<td>5.28 (6.03, 5.92)</td>
<td>5.75 (5.44, 6.06)</td>
<td>6.86 (6.32, 7.41)</td>
<td>5.88 (6.55, 6.12)**</td>
<td></td>
</tr>
<tr>
<td>FOSQ</td>
<td>18.8 (18.6, 18.9)</td>
<td>18.7 (18.6, 18.9)</td>
<td>18.6 (18.6, 18.9)</td>
<td>18.7 (18.5, 19.0)</td>
<td>18.5 (18.4, 18.6)**</td>
<td></td>
</tr>
<tr>
<td>Physical summary scale (SF-12)</td>
<td>49.6 (48.9, 50.2)</td>
<td>49.4 (48.6, 50.1)</td>
<td>49.2 (48.2, 50.1)</td>
<td>47.9 (46.2, 49.6)</td>
<td>47.4 (46.7, 48.1)**</td>
<td></td>
</tr>
<tr>
<td>Mental summary scale (SF-12)</td>
<td>55.1 (54.6, 55.6)</td>
<td>55.5 (54.9, 56.1)</td>
<td>55.3 (54.6, 56.0)</td>
<td>55.4 (54.2, 56.7)</td>
<td>54.7 (54.1, 55.2)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B</th>
<th>AHI &gt; 10 (n = 200)</th>
<th>AHI ≥ 15 (n = 721)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESS &gt; 10</td>
<td>1.0 (reference)</td>
<td>1.0 (reference)</td>
<td></td>
</tr>
<tr>
<td>Self-perceived health (good/excellent)</td>
<td>1.0 (reference)</td>
<td>1.0 (reference)</td>
<td></td>
</tr>
<tr>
<td>Geriatric Depression Scale ≥ 6</td>
<td>1.0 (reference)</td>
<td>1.0 (reference)</td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted for age and study site, **different from REM AHI < 5 at p < 0.05 (adjustment of BMI, waist or neck circumference did not make any significant difference) in subjects with AHI < 15 in MrOS Sleep Study; AHI, apnea hypopnea index; AHI-REM, apnea hypopnea index REM sleep; BMI, body mass index; FOSQ, Functional Outcomes of Sleep Questionnaire; PSQI, Pittsburg Sleep Quality Index; SD, standard deviation; SF-12, Short Form 12.
by the ESS. In this elderly population, only adjusted AHI-REM ≥ 30 was associated with a decrease in self-perceived health status. There were no other associations between REM-predominant OSA and the behavioral measures studied.

Prior literature has provided conflicting reports regarding whether REM-predominant OSA is associated with excessive daytime sleepiness. Excessive daytime sleepiness can affect 10% to 33% of the elderly and has been associated with significant consequences, including an increased incidence of functional impairment, falls, cognitive deficits, and mortality.13,45-47 The presence of OSA has been shown to be an important risk factor for mortality from excessive daytime sleepiness in older adults.13,24 In our study, REM-predominant OSA was not associated with increased daytime sleepiness using the ESS. This is similar to two large studies which showed that OSA in NREM sleep was associated with excessive daytime sleepiness while patients with REM-predominant OSA did not have evidence of excessive daytime sleepiness.17,22

Similar to data from the Sleep Heart Health Study,22 our results show that after adjusting for age, BMI, and study site, in subjects with either AHI < 15 or < 5, REM-predominant OSA did not have a significant association with quality of life measures as measured by FOSQ, PSQI, SF-12 physical and mental summary scale, or GDS-15. Worse self-perceived health, however, was associated with REM-AHI ≥ 30 (Table 3 and 4). Similar to our results, the Sleep Heart Health Study showed that REM-predominant SDB was not independently associated with daytime sleepiness, impaired health-related quality of life, or self-reported sleep disruption.22 Self-perceived health status was not reported in the Sleep Heart Health Study.

We choose AHI ≥ 15 as the primary definition of OSA in our analysis because of the high prevalence of modestly elevated AHI levels in older adults that has no significant clinical consequences.1,24-26 Morbidity and mortality in the elderly with lower AHI levels have been shown to be similar to those without OSA.50,51 We further analyzed our data defining OSA as AHI ≥ 5 during the entire sleep period and defining REM-predominant OSA as AHI < 5 with AHI-REM ≥ 5 and the results were similar (supplemental material Tables S3 and S4).

In our cohort, the average time spent in REM sleep time was 70.3 ± 28.2 min and in NREM 286.3 ± 55.5 min. It is possible that some of the effects of REM-predominant OSA were mitigated by a decrease in time spent in REM sleep with increasing AHI-REM (Table 2). This could be due to increased events in REM sleep leading to arousals and decreasing the time in REM sleep. The total AHI in all subgroups of AHI-REM was low, with the highest being 10.8 ± 2.9 in the subgroup with AHI-REM > 30. The total AHI in subjects with AHI ≥ 15 was 29.1 ± 12.9. This significant difference may have also been responsible for the lack of any effect of AHI-REM on sleepiness and quality of life measures.

AHI levels increase with age1,48; however, it has not been clear if REM-predominant OSA increases with age. The prevalence of REM-predominant OSA in our population was 42.8%, which is higher than the 14% in men ≥ 70 years old in another published trial with a similar definition of REM-predominant OSA.16 More severe REM-predominant OSA was associated with a higher BMI, neck and waist circumference, and an increased prevalence of snoring. It has been suggested that narrowing of the upper airway in REM sleep due to REM-associated atonia may lead to changes in airway closing pressure in REM sleep.23 It is possible that an increase in BMI or neck and waist circumference lead to an increased AHI-REM before any changes were observed in AHI-NREM which may explain some of our findings. The strength of our study is that we were able to evaluate the association of REM-predominant OSA with daytime sleepiness in a large, community-based sample of older adults, a population group that has not been evaluated before for the effects of REM-predominant OSA.

Our study has several limitations. This is an observational study and with associated limitations on inferences regarding causality. Our study population consists of community-dwelling, ambulatory men aged 65 years or older with ability to walk without the assistance, who did not have either bilateral hip replacements or a medical condition that would result in imminent death at the time of enrollment.23 There were no other exclusion criteria. Another limitation is that more than 90% of our subjects were Caucasian. Our data should be taken with caution while generalizing it to other populations and racial groups. We only studied male subjects and although we used validated instruments to measure subjective indices of sleepiness, these instruments may have lower levels of discrimination in older subjects, who may also have other competing causes of sleepiness.53,54

CONCLUSION

In a cohort of community-dwelling males, 67 years or older, REM-predominant OSA was associated with small differences in objectively measured sleep quality: decreased total sleep time, sleep efficiency, minutes and percentage of time in REM sleep. However, increasing AHI-REM levels were not linearly associated with subjective measures of excessive daytime sleepiness or quality of life. Severe REM-predominant OSA was associated with worse self-perceived health status.

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A Brief Survey of Patients’ First Impression after CPAP Titration Predicts Future CPAP Adherence: A Pilot Study


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Background: CPAP adherence patterns are often established very early in the course of therapy. Our objective was to quantify patients’ perception of CPAP therapy using a 4-item questionnaire administered in the morning following CPAP titration. We hypothesized that questionnaire responses would independently predict CPAP adherence during the first 30 days of therapy.

Methods: We retrospectively reviewed the CPAP perception questionnaires of 403 CPAP-naïve adults who underwent laboratory titration and who had daily CPAP adherence data available for the first 30 days of therapy. Responses to the CPAP perception questionnaire were analyzed for their association with mean CPAP adherence and with changes in daily CPAP adherence over 30 days.

Results: Patients were aged 52 ± 14 years, 53% were women, 54% were African American, the mean body mass index (BMI) was 36.3 ± 9.1 kg/m², and most patients had moderate-severe OSA. Four of 6 items from the CPAP perception questionnaire—regarding difficulty tolerating CPAP, discomfort with CPAP pressure, likelihood of wearing CPAP, and perceived health benefit—were significantly correlated with mean 30-day CPAP adherence, and a composite score from these 4 questions was found to be internally consistent. Stepwise linear regression modeling demonstrated that 3 variables were significant and independent predictors of reduced mean CPAP adherence: worse score on the 4-item questionnaire, African American race, and non-sleep specialist ordering polysomnogram and CPAP therapy. Furthermore, a worse score on the 4-item CPAP perception questionnaire was consistently associated with decreased mean daily CPAP adherence over the first 30 days of therapy.

Conclusions: In this pilot study, responses to a 4-item CPAP perception questionnaire administered to patients immediately following CPAP titration independently predicted mean CPAP adherence during the first 30 days. Further prospective validation of this questionnaire in different patient populations is warranted.

Keywords: Sleep apnea, CPAP adherence, compliance, questionnaire, patient perception

Commentary: A commentary on this article appears in this issue on page 207.

Citation: Balachandran JS; Yu X; Wroblewski K; Mokhlesi B. A brief survey of patients’ first impression after CPAP titration predicts future CPAP adherence: a pilot study. J Clin Sleep Med 2013;9(3):199-205.
Several interventions have been shown to improve CPAP adherence, including cognitive behavioral therapy programs and bi-directional telecommunications programs. Being able to predict a patient’s “risk” for poor CPAP adherence early, ideally at the point of CPAP therapy initiation, may be useful in targeting “high-risk” patients for these interventions.

Because patient attitudes are strong early predictors of CPAP adherence, and because targeted interventions exist to improve CPAP adherence, there is a value in developing ways to assess patient attitudes in a simple way. Lewis et al. demonstrated that a single question asked on the morning following CPAP titration predicted CPAP adherence at one month in a cohort of 70 patients in the United Kingdom. However, it remains unclear how applicable and generalizable their findings are in populations of different cultural and racial backgrounds, particularly in African Americans. Along these lines, our sleep laboratory had developed a 6-question quality-improvement tool to assess patients’ perception of CPAP therapy on the morning following an in-laboratory CPAP titration. Our goal in developing this tool was to have a short questionnaire which could be completed by patients and which could aid in quality improvement in our sleep laboratory. After using this tool for several years, we designed a retrospective pilot study to quantify patients’ perception of CPAP therapy based on the responses to the 6-item questionnaire. We hypothesized that responses to these questions would independently predict mean CPAP adherence during the first 30 days of therapy.

METHODS

Patients

We retrospectively evaluated the medical records of 1,126 consecutive, CPAP-naïve adults who were referred to the University of Chicago Sleep Laboratory for their first in-laboratory PSG because of clinical suspicion for OSA between July 2007 and June 2008, and who completed our 6-item questionnaire on the morning following their PSG. Exclusion criteria for these analyses included previous CPAP use, requirement for bilevel positive airway pressure or adaptive servoventilation, central sleep apnea, or lack of adherence data because of a lack of a wireless modem transmission device or faulty wireless modem transmission. The institutional review board of the University of Chicago approved the study, and ethical standards were observed during the investigation. Given the retrospective chart-review nature of the study, the need for informed consent was waived.

Baseline PSG and CPAP Titrations

Patients underwent either an in-laboratory full-night PSG followed by a full-night CPAP titration or a single split-night PSG. Split-night PSGs were performed on patients who had 2-3 h of baseline sleep with an apnea-hypopnea index (AHI) ≥ 30 events/h, if there were at least 3-4 h of titration time remaining. Patients diagnosed with OSA and referred for CPAP therapy had CPAP set up in their homes by a durable medical equipment (DME) provider. PSGs were scored according to the standards issued by the American Academy of Sleep Medicine. A hypopnea was scored if the magnitude of ventilation signal decreased by ≥ 50% of the baseline amplitude of the nasal pressure transducer for ≥ 10 sec associated with either an oxygen desaturation ≥ 3% as measured by finger pulse oximetry or a microarousal.

Covariates

On the night of the PSG, patients completed a routine questionnaire which included demographics, medical history, sleep history and self-reported habitual sleep duration, Epworth Sleepiness Scale (ESS), and the Center for Epidemiologic Studies Depression (CES-D) Scale. Self-reported race was categorized into African American and non-African American. Self-reported education level was categorized into “high school degree or less” and “more than high school degree.” Age, gender, and medical insurance type were obtained from the medical record. Medical insurance was categorized into Medicaid and non-Medicaid. We categorized patients into 2 groups based on the specialty of the physician ordering the PSG: non-sleep specialists or board-certified sleep-specialists.

CPAP Perception Questionnaire

Upon awakening in the sleep laboratory, patients were asked by the sleep laboratory technicians to complete a 6-item questionnaire to quantify overall perception of their first experience with CPAP therapy after a night of titration (Appendix). The questionnaire was developed and implemented as part of a quality improvement initiative in our sleep laboratory to assess patient experiences during their CPAP titration PSGs. These questions were answered on a Likert-type visual analog scale ranging from 1 (no difficulty/no discomfort/positive attitude toward CPAP) to 10 (significant difficulty/significant discomfort/negative attitude towards CPAP). The questions included: (1) How much difficulty did you have tolerating CPAP? (2) How uncomfortable was the mask? (3) How uncomfortable was the CPAP pressure? (4) What is the likelihood of you wearing the equipment at night almost every night? (5) How beneficial do you think CPAP is going to be for your health and sleep? (6) What is your attitude towards CPAP therapy?

CPAP Adherence

CPAP adherence was determined objectively via wireless modem technology that enabled remote daily downloading of data from the CPAP unit during the first 30 days of use. Only 2 DME providers performed CPAP set up in patients’ homes. During the first 30 days of treatment, only the DME providers performed education on CPAP set up and any troubleshooting. The data obtained from each CPAP unit included hours of usage per night at the prescribed pressure, residual daily AHI, and average mask leak.

Statistical Analyses

Each of the 6 questions was subjected to bivariate analyses testing the correlation between question response and 30-day CPAP adherence (mean CPAP usage in minutes over the 30 days). Only questions that were significantly correlated to CPAP adherence were pooled. To validate the internal consistency of the questionnaire, we calculated Cronbach α. Factor analysis (principal component analysis) was performed to investigate the dimensionality of the scale. The sum of the
pooled question responses was used in the analysis after the normality of the score distribution was assessed.

We performed a univariate analysis to evaluate associations between mean CPAP adherence during the first 30 days and important covariates such as the specialty of the physician ordering the PSG, age, gender, race, BMI, education level, insurance status, ESS score, CES-D score, AHI, and the CPAP perception score from the night of in-laboratory titration. We then performed a stepwise linear regression model to identify independent predictors of mean CPAP adherence during the first 30 days of therapy. We included the following variables in the stepwise regression model: specialty of the physician ordering the PSG, age, gender, race, BMI, OSA severity, education level, ESS, CES-D score, insurance status, and the CPAP perception score. The backward selection method was used, as the stepping method criteria variables with p-value ≤ 0.05 were kept in the model and variables with p-value > 0.10 were removed.

As a secondary analysis to evaluate changes in CPAP adherence over time and to confirm the findings of the primary analysis, random-effects regression was used with each patient contributing 30 days of data. Patients were categorized based on the CPAP perception score above or below the mean. Both linear (nightly CPAP usage in minutes) and logistic (nightly CPAP usage ≥ 4 h) models were fit. Lowess smooth curves were added to summary plots to aid in assessment of trends.

A p-value ≤ 0.05 was considered statistically significant. All analyses were performed using PASW Statistics (v.18.0, SPSS, Inc, Chicago IL) and Stata Version 12 (StataCorp., College Station, TX).

**RESULTS**

**Patient Demographics**

Of the 1,126 consecutive patients evaluated, 786 (70%) underwent CPAP titration. Data on CPAP adherence for the first 30 days were available for analysis in 403 of these patients (Figure 1). Demographic data are summarized in Table 1. The majority of the cohort was obese, African American, middle-aged, with “more than a high school degree” of education, and more than half were women. Medicaid was the only health insurance coverage in 21% of patients. Severe OSA (defined as AHI ≥ 30 events/h) was present in 58% of patients. Mean 30-day CPAP adherence was 236 ± 162 min per day (Table 2). Split-night PSG was performed in 41% of patients. Full-night PSG followed by full-night in-laboratory CPAP titration was performed in 59% of patients. There was no significant difference in mean 30-day CPAP adherence between patients undergoing split-night PSG vs. full-night PSG (p = 0.52). Due to a lack of a wireless modem transmission device or faulty wireless modem transmission, 383 patients were excluded from the final analysis because of lack of CPAP adherence data. These patients did not differ significantly with respect to any demographic category, sleep history, medical history, or PSG characteristic (data not shown).

**Table 1**—Demographic variables for the entire analytic cohort

<table>
<thead>
<tr>
<th>Demographics</th>
<th>All Participants (n = 403)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>52 ± 14</td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>190 (47)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>36.3 ± 9.1</td>
</tr>
<tr>
<td>African American, n (%)</td>
<td>219 (54)</td>
</tr>
<tr>
<td>Married, n (%)</td>
<td>153 (38)</td>
</tr>
<tr>
<td>Education above high school, n (%)</td>
<td>276 (68)</td>
</tr>
<tr>
<td>Medicaid insurance, n (%)</td>
<td>86 (21)</td>
</tr>
<tr>
<td>Epworth Sleepiness Scale (out of 24)</td>
<td>9 ± 5</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>235 (58)</td>
</tr>
<tr>
<td>Type 2 diabetes, n (%)</td>
<td>105 (26)</td>
</tr>
<tr>
<td>Nasal allergies, n (%)</td>
<td>104 (26)</td>
</tr>
<tr>
<td>CES-D Scale (out of 60)</td>
<td>16 ± 11</td>
</tr>
</tbody>
</table>

Where applicable, data are presented as mean ± SD. BMI, body mass index; CES-D, Center for Epidemiologic Studies Depression Scale.

**Questionnaire Responses and Validation**

In order to simplify the questionnaire and to identify the most important items, we tested the correlation between each individual question response and mean 30-day CPAP adherence. Only questions 1, 3, 4, and 5—regarding difficulty tolerating CPAP, discomfort with CPAP pressure, likelihood of wearing CPAP, and perceived health benefit—were significantly correlated with CPAP adherence (Pearson correlations and p values: Q1 = -0.122, p = 0.017; Q2 = -0.098, p = 0.057; Q3 = -0.143, p = 0.005; Q4 = -0.160, p = 0.002; Q5 = -0.122, p = 0.020; Q6 = -0.040, p = 0.444). Cronbach α for these 4 questions was 0.73, suggesting good internal consistency. Unidimensionality was confirmed with factor analysis with the first factor accounting for 55% of the total variance. Since each of the 4 question responses had a range of 1 to 10, the sum of responses to these 4 questions (referred to as the CPAP perception score) ranged from 4 to 40. A higher score represented more difficulty with...
The main finding of our pilot study is that responses to a brief CPAP perception questionnaire administered to patients immediately following an in-laboratory CPAP titration predicts CPAP adherence during the first 30 days, even after adjusting for important covariates. This suggests that a brief, clinical evaluations of patient attitudes regarding CPAP therapy can have important predictive value.

**DISCUSSION**

In our cohort, variables that were not predictive of CPAP adherence in the stepwise linear regression analysis were age, gender, BMI, OSA severity, ESS score, CES-D score, education level, and insurance status. Moreover, there was no significant interaction between race or physician specialty and the CPAP perception score. We fit additional stepwise regression models that also included self-reported habitual total sleep duration, type of PSG (split-night versus full-night), DME provider, and average leak as estimated by the CPAP devices; these did not have an impact on the 3 significant variables (CPAP perception score, race, and physician specialty; data not shown).

### Table 3—Stepwise linear regression model of mean CPAP adherence over the first 30 days of therapy

<table>
<thead>
<tr>
<th>Beta coefficient (minutes)</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPAP perception score (per each point in a scale of 4 to 40)</td>
<td>-3.3</td>
<td>-5.5, -1.0</td>
</tr>
<tr>
<td>African American race</td>
<td>-46</td>
<td>-80, -12</td>
</tr>
<tr>
<td>Non-sleep specialist ordering PSG</td>
<td>-69</td>
<td>-108, -31</td>
</tr>
</tbody>
</table>

Beta coefficient represents the expected change in CPAP adherence for each point change in CPAP perception score, for presence of African American race, or for non-sleep referring specialist. Excluded variables due to nonsignificance in the stepwise model were: age, sex, BMI, OSA severity, education level, ESS, CES-D score, and insurance status.

approximately 108 minutes less nightly CPAP use than a patient with the minimum score of 4. In addition, in the stepwise linear regression model, only 2 other variables remained significant predictors of mean 30-day CPAP adherence: specialty of the ordering physician and race (Table 3).

The main finding of our pilot study is that responses to a brief CPAP perception questionnaire administered to patients immediately following an in-laboratory CPAP titration predicts CPAP adherence during the first 30 days, even after adjusting for important covariates. This suggests that a brief, clinical evaluations of patient attitudes regarding CPAP therapy can have important predictive value.

### Table 2—Polysomnographic, CPAP titration, and CPAP adherence data

<table>
<thead>
<tr>
<th>PSG Variables</th>
<th>All Participants (n = 403)</th>
<th>Beta coefficient (minutes)</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Split night PSG, n (%)</td>
<td>166 (41.2)</td>
<td>-3.3</td>
<td>-5.5, -1.0</td>
<td>0.005</td>
</tr>
<tr>
<td>Full night PSG, n (%)</td>
<td>237 (58.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TST, min</td>
<td>324 (281-363)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep efficiency, %</td>
<td>78 (67-86)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arousal index, events/h</td>
<td>29 (19-55)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AHI, events/h</td>
<td>36 (18-67)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OSA severity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe OSA, n (%)</td>
<td>235 (58.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate OSA, n (%)</td>
<td>92 (22.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild OSA, n (%)</td>
<td>76 (18.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SpO2 nadir during sleep, %</td>
<td>80.6 ± 9.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OD1, events/h</td>
<td>23 (10-54)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tsp, %</td>
<td>3 (1-16)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Where applicable, parametric data are presented as mean ± SD, and nonparametric data are presented as median (IQR). TST, total sleep time; PSG, polysomnogram; AHI, apnea-hypopnea index; OSA, obstructive sleep apnea; OD1, oxygen desaturation index based on 3% oxygen desaturations during sleep; Tsp, percent of total sleep time spent with oxygen saturation less than 90%. Average mask leakage and average residual AHI: estimated daily by CPAP device over the initial 30-day period. All CPAP units were ResMed™ devices that reported only unintentional leak.
Prior studies have demonstrated that long-term CPAP adherence patterns are often established within the first week of therapy. Moreover, measures of the experience with and benefit perceived from CPAP therapy after just the first night of CPAP titration have been shown to be important factors in determining long-term adherence. Therefore, assessing this initial night of therapy would be helpful in determining which patients are “at risk,” particularly since effective interventions such as education and support programs exist for increasing CPAP adherence.

Tools for assessing patient perceptions and beliefs about therapy already exist and are very useful for developing a multidimensional understanding of factors related to CPAP adherence. However, most of these assessments are lengthy and may not be practical in a busy clinical setting. Notably, Lewis et al. demonstrated that even a single question on the morning following CPAP titration may predict adherence. In this study, the patients were asked a closed-ended simple question: “Have you encountered any problems during this first night of CPAP?” with two possible responses: “yes” or “no.” Their study, however, included only 70 patients with significant underrepresentation of women (n = 4) and ethnic minorities. In contrast, our pilot study included significant numbers of African Americans and women and demonstrated that a four-question assessment provides a brief and simple method of assessing CPAP therapy perception and significantly predicts mean 30-day CPAP adherence. It is important to note that there are significant similarities between the single closed-ended question asked by Lewis et al. and two of the questions included in our CPAP perception questionnaire that were answered on a Likert scale: “How much difficulty did you have tolerating CPAP?” and “How uncomfortable was the CPAP pressure?” Therefore, our results confirm the findings of Lewis et al., that reporting problems after the first night of CPAP use is an important predictor of poor CPAP adherence.

We initially evaluated responses to six brief questions; of those, two questions—“How uncomfortable was the mask?” and “What is your attitude towards CPAP therapy?”—were not significantly predictive of CPAP adherence. The lack of association between the second question—“How uncomfortable was the mask?”—and CPAP adherence was observed despite the fact that the range of responses to this question was broad. Reasons for this remain unclear, but could be related to subsequent intervention and adjustment of mask fit by DME providers during the first 30 days of therapy. The lack of predictive value with the sixth question—“What is your attitude towards CPAP therapy?”—could be related to patients’ unwillingness to voice a negative attitude towards potential therapy. Alternatively, the question may have simply been too vague.

Our group has previously reported that African American race and a non-sleep specialist ordering the PSG and home CPAP therapy were also predictive of decreased CPAP adherence, even after adjusting for relevant covariates. Lower CPAP adherence in African Americans has been reported by other groups as well. Whether this finding is related to other factors not captured by education level or insurance status, such as socioeconomic status, health literacy, or health beliefs surrounding CPAP therapy, requires further study. Although it is plausible that CPAP adherence is lower in African Americans because of shorter habitual sleep duration, the impact of race on CPAP adherence remained unchanged when we introduced self-reported habitual sleep duration into the model.
Regarding our finding that a consultation with a sleep specialist prior to undergoing a diagnostic PSG was predictive of increased 30-day CPAP use, it is possible that contact with a sleep specialist may have led to improved patient education, better awareness about OSA and its implications, and emphasis on the importance of CPAP therapy. Other investigators have reported that patients managed by accredited sleep centers have a reduced risk of discontinuing CPAP therapy. In spite of this, on the importance of CPAP therapy. Other investigators have better awareness about OSA and its implications, and emphasis increased 30-day CPAP use, it is possible that contact with a specialist prior to undergoing a diagnostic PSG was predictive of socializetion on patients’ CPAP perception.

Our study had several limitations. First, a number of patients were excluded from our analysis due to a lack of objective CPAP adherence data. In all of these cases, the adherence data were missing due to either lack of or malfunction of wireless modem devices. Although there were no significant differences in baseline characteristics of included and excluded patients (suggesting a lack of systematic bias), the mean CPAP perception score was higher in the excluded cohort (18 ± 8 vs. 16 ± 7, p = 0.013). The clinical significance of this difference remains unclear given that the CPAP perception questionnaire has a scale of 4 to 40. Second, ours was a single-center study which limits the generalizability of our findings. Importantly, however, our study did include a substantial proportion of African Americans and women, two patient populations frequently under-studied with respect to CPAP therapy adherence. The retrospective nature of our study may also limit the conclusions that can be drawn about the reported associations. Our findings will therefore need to be validated prospectively in different patient populations.

It should be noted that our questionnaire was developed out of a longstanding quality-improvement initiative to assess patient perception of CPAP therapy after CPAP titration, a practice that is employed in many sleep laboratories. Our findings demonstrate the clinical utility and predictive power of a practical and simple questionnaire for post-CPAP titration assessment of patients’ perceptions.

In summary, our pilot study demonstrates that 30-day CPAP adherence can be predicted by a brief assessment of patients’ experiences and beliefs performed on the morning following CPAP titration but also on outpatient follow-up.

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SUBMISSION & CORRESPONDENCE INFORMATION

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DISCLOSURE STATEMENT

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APPENDIX

Sleep Disorders Center CPAP Questionnaire
Please answer the following questions so we can better understand how you feel about CPAP. Please circle a number from 1 to 10 to indicate your choice for each question.

1) How much difficulty did you have tolerating CPAP?
   - no difficulty 1 2 3 4 5 6 7 8 9 10
2) How uncomfortable was the mask?
   - not uncomfortable 1 2 3 4 5 6 7 8 9 10
3) How uncomfortable was the CPAP therapy?
   - not uncomfortable 1 2 3 4 5 6 7 8 9 10
4) What is the likelihood of you wearing the equipment at night almost every night?
   - very likely 1 2 3 4 5 6 7 8 9 10
5) How beneficial do you think CPAP is going to be for your health and sleep?
   - very beneficial 1 2 3 4 5 6 7 8 9 10
6) What is your attitude towards CPAP therapy?
   - greatly like CPAP 1 2 3 4 5 6 7 8 9 10

Questionnaire

6) What is your attitude towards CPAP therapy?
   - greatly like CPAP 1 2 3 4 5 6 7 8 9 10
Continuous positive airway pressure (CPAP) is well established as the most efficacious therapy for obstructive sleep apnea (OSA), improving daytime sleepiness and quality of life, as well as reducing cardiovascular morbidity and mortality. However, CPAP effectiveness is limited by adherence to the therapy. Nearly one in five patients refuse to initiate CPAP. Of those who do try, half do not use it enough to gain the symptom and cardiovascular benefits. Studies have demonstrated that usage patterns are established early, within the first week of therapy. By one year, half no longer use CPAP at all.

The challenge to our field is to ensure that this potentially life-saving therapy is actually used by patients. Diagnosis of OSA and prescription of CPAP is easy; ensuring adherence to CPAP is the challenge. Early intervention in patients likely to fail arguably may have the highest potential for increasing success by removing barriers before they give up. Given the early establishment of usage pattern, identification of those at risk prior to or soon after initiation of home CPAP therapy is needed.

Despite extensive study, predicting which patients are at high risk for poor CPAP adherence remains challenging. Demographic factors such as race/ethnicity, marital status, socioeconomic status have been associated with adherence in some studies but not uniformly. These factors may be markers of underlying neighborhood deprivation, social support, health literacy, cultural practices, and environmental challenges. Further research is needed to identify the mechanisms responsible for these associations and to tailor effective solutions.

New investigations using psychological constructs to understand health behaviors demonstrate promise in identifying modifiable factors. Self-efficacy (the patients’ belief in their power to cause an effect or their perception of ability to use CPAP to treat their OSA), readiness to change, and decisional balance have all been shown to predict short and longer-term adherence when assessed in the first week after CPAP exposure as well as in experienced users. Health values and attitudes are also associated with CPAP use as well as perceived risk of OSA and expected outcome of CPAP prior to exposure. These cognitive behavioral factors are potentially modifiable targets for interventions to improve CPAP use. However, evaluating these factors currently requires detailed questionnaires using complex scoring which are not practical in a busy sleep clinic.

In this issue of the Journal of Sleep Medicine, the pilot study of Balachandran et al. evaluates a simple questionnaire assessing CPAP perception as a predictor of adherence behavior. This retrospective study examined 1-month adherence data for consecutive OSA patients with their first exposure to CPAP in the sleep laboratory. Eligible subjects underwent either a CPAP titration study or split-night study at the authors’ sleep center, completed a 6-item questionnaire the morning after their study, and had adherence data. The questionnaire assessed the patients’ initial experience with and impressions of CPAP. Questions addressed difficulty tolerating CPAP, much like Lewis who found that subjects reporting problems the first night wearing CPAP had lower CPAP use long-term. Other questions utilized principles of self-efficacy and decisional balance, evaluating the likelihood of using CPAP and perceived benefit of CPAP. In their cohort of 403 patients, the authors found an association of the CPAP perception score, using 4 of the 6 questionnaire items, with 1-month adherence. Of those with a poor perception of CPAP (scores > 16), less than 40% used CPAP for 4 hours or more per night vs. 55% in the group with scores < 16. Those with a negative initial perception of CPAP from the sleep lab are likely to be less enthusiastic about using the device at home and perhaps have less motivation to troubleshoot and address problems. These patients would be ideal targets for early intervention to reform their first impression and improve adherence.

Though promising, the study has important limitations. The questionnaire has not yet undergone construct or content validation, reliability testing and may not have the same performance when prospectively applied in other groups. It is unclear whether all 4 items contributing to the score equally determine CPAP outcomes and whether a subset of the items would suffice. The study only includes patients from a single center, of which many were excluded due to lack of objective adherence data, raising the possibility of sampling bias. It is also unclear if the perception score would predict CPAP use in those who do not undergo in-lab CPAP titration. Further study is needed to determine if this instrument has adequate sensitivity and specificity to identify non-adherence.

If the instrument developed by Balachandran can function as a screening tool for non-adherence risk, this is an important initial step. Identification and implementation of interventions
which improve adherence in high-risk patients is the essential follow-up. The most obvious intervention is to remedy physical factors that may have led to poor tolerance such as mask discomfort, oral leak, and pressure intolerance, although these have not been shown to substantially improve adherence.21 Other interventions focusing on psychological, social, and educational strategies have been trialed. Intensive educational programs and close follow-up have had limited success.22 Cognitive behavioral therapy (CBT) interventions have shown potential, improving CPAP adherence by 1.5 to 3 hours in 3 studies23-25—a substantial clinical impact. CBT attempts to change expectations surrounding CPAP and the decisional balance toward favoring CPAP. CBT is promising but may be too expensive to administer to all comers. The instrument developed by Balachandran may facilitate targeting these interventions to those at highest risk of failure with the initial “wrong” and possibly modifiable impression of CPAP.

Sleep medicine is fortunate to have a highly efficacious treatment for OSA; we must focus research and energy into efforts to increase CPAP adherence to transform it into a highly effective therapy. A short simple questionnaire administered after initial exposure to CPAP that can predict long-term adherence would be an extremely useful tool in improving effectiveness. Such a tool would allow for targeted interventions during the critical period to improve patient experience and perceptions and ideally change use behavior. Though prospective validation studies in diverse clinic populations are needed, the current study presents a tool that has potential.

REFERENCES


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Polysomnographic Determinants of Nocturnal Hypercapnia in Patients with Sleep Apnea

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Study Objectives: Identify polysomnographic and demographic factors associated with elevation of nocturnal end-tidal CO2 in patients with obstructive sleep apnea.

Methods: Forty-four adult patients with obstructive sleep apnea were selected such that the maximal nocturnal end-tidal CO2 was below 45 mm Hg in 15 studies, between 45 and 50 mm Hg in 14, and above 50 mm Hg in 15. Measurements included mean event (i.e., apneas or hypopneas) and mean inter-event duration, ratio of mean post- to mean pre-event amplitude, and percentage of total sleep time spent at an end-tidal CO2 < 45, 45-50, and > 50 mm Hg. An integrated nocturnal CO2 was calculated as the sum of the products of average end-tidal CO2 at each time interval by percent of total sleep time spent at the corresponding time interval.

Results: The integrated nocturnal CO2 was inversely correlated with mean post-apnea duration, with lesser contributions from mean apnea duration and age (R2 = 0.56), but did not correlate with the apnea-hypopnea index, or the body mass index. Mean post-event to mean pre-event amplitude correlated with mean post-apnea duration (r = 0.88, p < 0.001). Mean apnea duration did not correlate with mean post-apnea duration.

Conclusions: Nocturnal capnometry reflects pathophysiologic features of sleep apnea, such as the balance of apnea and post-apnea duration, which are not captured by the apnea-hypopnea index. This study expands the indications of capnometry beyond apnea detection and quantification of hypoventilation syndromes.

Keywords: Obstructive sleep apnea, hypercapnia, capnography, body mass index, obesity hypoventilation syndrome

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linked to obstructive respiratory events during sleep include post-event (subsuming apneas and hypopneas) ventilation as a function of CO\textsubscript{2} load\textsuperscript{10,11} and apnea duration in relation to post-apnea duration.\textsuperscript{12}

We therefore selected groups of obstructive sleep apnea patients with different severity of nocturnal CO\textsubscript{2} elevation and assessed the relative contributions of demographic factors, sleep apnea severity, respiratory event and respiratory inter-event duration, as well as post-event amplitude relative to pre-event amplitude, to an overall measure of nocturnal ETCO\textsubscript{2}.

**METHODS**

We reviewed polysomnograms and clinical charts of patients diagnosed with obstructive sleep apnea at our center from 2008 to 2009. Inclusion criteria were age > 18 years, total sleep time ≥ 6 h with a sleep efficiency ≥ 65%,\textsuperscript{13} and an apnea-hypopnea index ≥ 5. We excluded studies where central apneas represented > 50% of the apnea-hypopnea index, studies requiring oxygen administration, titration studies, and other conditions that could confound the nocturnal CO\textsubscript{2} or impair the accuracy of the ETCO\textsubscript{2} as a measure of arterial CO\textsubscript{2} (i.e., chronic obstructive pulmonary disease, asthma, neuromuscular diseases, use of diuretics, alcohol or narcotics, or > 20 pack-year smoking history). To ensure an adequate representation of various ranges of CO\textsubscript{2} values, we aimed for an equal number of patients in each of the following groups: maximal nocturnal ETCO\textsubscript{2} < 45 mm Hg, between 45 and 50 mm Hg, and > 50 mm Hg.

All polysomnograms were recorded on Polysmith systems (Nihon Kohden, Foothill Ranch, CA), and scored using American Academy of Sleep Medicine guidelines.\textsuperscript{2} Capnometry data were obtained from calibrated Nonin RespSense devices (Plymouth, MN) interfaced to the Polysmith system. Those devices use a sidestream technology, with sampling obtained through oral/nasal cannulas (Salter labs, Arvin, CA). The sampling flow into the sample cell was 75 mL/min, the total system response time (including delay and rise times) was 4 sec, and the sampling rate for the capnograph tracing was 4 Hz. Apnea was defined as a drop in the peak thermal sensor excursion by ≥ 90% from baseline lasting ≥ 10 seconds. For the purpose of this study, a hypopnea was scored if the event met either the recommended or alternative definitions of the American Academy of Sleep Medicine (i.e., a drop in the nasal pressure signal excursion ≥ 30% from baseline for ≥ 10 sec in association with ≥ 4% oxygen desaturation, or ≥ 50% drop with ≥ 3% desaturation or an arousal).\textsuperscript{2}

The quality of the oximetry and capnographic data was assessed by review of the pulse plethysmographic signal and capnographic waveforms, with exclusion of artifacts of oximetry due to loss of the pulse signal, and exclusion of CO\textsubscript{2} waveforms without a clearly identified plateau, including those associated with deterioration of the signal due to obstructive events.

We collected demographic and polysomnographic variables at the time of the PSG: age, sex, body mass index, Epworth Sleepiness Scale score, sleep efficiency, sleep and REM latencies, sleep stage distribution, arousal index, apnea-hypopnea index, nadir oxygen saturation, and time spent below 90% oxygen saturation (as percent of total sleep time). Capnometric data were obtained from the trend report of the Polysmith system, and included stable awake end-tidal CO\textsubscript{2} at the beginning of the study before the onset of slow-rolling eye movements (evening awake ETCO\textsubscript{2}), after completion of the sleep study just before the final calibrations (morning awake ETCO\textsubscript{2}), and sleep ETCO\textsubscript{2}. The latter included minimum and maximum sleep ETCO\textsubscript{2} and the following 3 time intervals: percents of total sleep time spent with ETCO\textsubscript{2} < 45 mm Hg (T45), between 45-50 mm Hg (T45_50), and > 50 mm Hg (T50). An integrated overnight CO\textsubscript{2} was calculated as the sum of the products of the estimated average ETCO\textsubscript{2} at each of those 3 time intervals by the percent of total sleep time spent at each corresponding time interval: [T45*(45 + minimum ETCO\textsubscript{2}) / 2] + [T50*(50 + maximum ETCO\textsubscript{2}) / 2] + [T45_50*47.5]. The result was divided by 100 to provide an estimate of nocturnal ETCO\textsubscript{2} had it remained constant through the night.

Respiratory event (subsuming apneas and hypopneas) and inter-event durations were measured in seconds. Inter-event durations were measured only if the subsequent respiratory event was within 30 sec from the termination of the preceding event. Pre-event and post-event breathing amplitudes were semi-quantitatively measured on the nasal pressure transducer signal on 60-sec epochs, as the amplitude of the last breath before the corresponding respiratory event and of the first breath after that event respectively (Figure 1). To compensate for expected variation in amplitudes as may occur with positional changes or migration of the oral/nasal cannula, the mean post-event amplitude was referenced to the mean pre-event amplitude.

The onset and offset of apneas and hypopneas were respectively placed at the nadir of the last normal breath and at the start of the first subsequent normal breath approximating the baseline (Figure 1).\textsuperscript{2} If the baseline amplitude could not be easily determined, the respiratory events were also terminated as per the American Academy of Sleep Medicine guidelines when

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Figure 1—Schema illustrating event and inter-event duration, as well as pre-and post-event amplitude (with upward deflection of flow during inspiration)

Inter-event durations were included only if the subsequent respiratory event was within 30 sec from the termination of the preceding event. ad: apnea duration, pad: post apnea duration, hd: hypopnea duration, phd: post-hypopnea duration, apre and apo: pre- and post-apnea amplitude respectively, hpre and hpo: pre- and post-hypopnea amplitude, respectively. For each patient the mean of all event and inter-event durations across the polysomnography was derived and expressed in the text or tables as AD, PAD, HD, and PHD. Similarly, the mean of all pre-event amplitude and the mean of all post-event amplitudes was derived and expressed in the text as Apre, Apo, Hpre, and Hpo.
there was a clear and sustained increase in post-event breathing amplitude, or re-saturation of ≥ 2%.

For each patient we derived: mean apnea and mean hypopnea duration (AD and HD respectively), mean post-apnea and mean post-hypopnea duration (PAD and PHD), mean post-apnea and mean post-hypopnea amplitude (Apo and Hpo) expressed relative to the mean pre-apnea and mean pre-hypopnea amplitude (Apre and Hpre).

Sample size was estimated at 30 subjects based on a minimum meaningful correlation coefficient of 0.50, a power of 0.9, and α of 0.05. Groups were compared using a \( \chi^2 \) for categorical variables, and analysis of variance for continuous variables. The correlation between integrated overnight CO\(_2\) and demographic and polysomnographic variables was determined by the Pearson correlation coefficient. Comparison of correlations within a single sample was done using the Williams \( T_2 \) statistic. Multiple linear regression analysis was performed to estimate the influence of covariates on the overnight CO\(_2\). Collinearity was measured by means of tolerance and the Variance Inflation Factor. Statistical significance was set at \( p < 0.05 \).

Analyses were performed using SPSS, version 11.5. The study was approved by our institutional review board.

## RESULTS

Forty-four consecutive studies meeting the inclusion criteria were selected such that maximal ETCO\(_2\) during sleep was \(< 45 \text{ mm Hg}\) in 15 studies, between 45 and 50 mm Hg in 14 studies, and \(\geq 50 \text{ mm Hg}\) in 15 studies. The mean age of the patients was 51 years (standard deviation 14, range 18-92), mean apnea-hypopnea index was 28 events/h (standard deviation 21, range 5.1-105), and the mean body mass index was 34 kg/m\(^2\) (standard deviation 9, range 20-57). There were 24 females and 19 males. None had a diagnosis of obesity-hypoventilation. There were no significant differences between genders in the body mass index, apnea-hypopnea index, mean apnea duration, mean post-apnea duration, and mean post-event to mean pre-event ventilation, though women tended to be older than men (54 vs. 47 years, respectively, \( p = 0.06 \)), and to have a smaller neck circumference (38.7 vs. 41.4 cm, respectively, \( p = 0.07 \)).

Demographic, polysomnographic, and laboratory data categorized by level of maximal ETCO\(_2\) reached during the sleep study are shown in Table 1. Neck circumference was higher in the combined groups with maximal ETCO\(_2\) \(\geq 45 \text{ mm Hg}\) compared to the group with maximal ETCO\(_2\) \(< 45 \text{ mm Hg}\) (Table 1). Sleep efficiency, percentages of time spent at different sleep stages, percent of time in the supine position, arousal indices, and sleep and REM latency were not significantly different between the 3 groups.

Groups with progressively higher maximal ETCO\(_2\) had progressively shorter mean post-apnea duration, increased AD/PAD, and a smaller mean post-event to mean pre-event amplitude ratio (Table 2).

There was a trend towards a positive correlation between the integrated overnight CO\(_2\) and age \((r = 0.29, p = 0.06)\), as well as body mass index \((r = 0.29, p = 0.06)\), and no significant correlation with apnea-hypopnea index, neck circumference, Epworth Sleepiness Scale score, sleep efficiency, sleep stages, percent time in the supine position, and percent time with oxygen saturation < 90%.

The REM latency correlated negatively with mean post-apnea duration \((r = -0.41, p = 0.006)\), whereas REM time as percent of total sleep time correlated positively with the mean post-apnea duration \((r = 0.34, p = 0.03)\).

The integrated overnight CO\(_2\) correlated with mean apnea duration \((r = 0.41, p = 0.005)\) (Figure 2A), and mean post-apnea duration \((r = -0.67, p < 0.001)\) (Figure 2B). The correlation of the integrated overnight CO\(_2\) with mean hypopnea duration or mean post-hypopnea duration was very poor and nonsignificant \((r = -0.10, p = 0.53\) and \( r = 0.11, p = 0.50\), respectively). There was no difference between apnea and hypopneas as far as the correlation between the integrated overnight CO\(_2\) and the post-

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### Table 1—Demographic, laboratory, and polysomnographic variables at baseline

<table>
<thead>
<tr>
<th></th>
<th>Maximal sleep end-tidal CO(_2) (mm Hg)</th>
<th>(&lt; 45)</th>
<th>45-50</th>
<th>&gt; 50</th>
<th>Mean</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td>49 (14)</td>
<td>53 (16)</td>
<td>51 (12)</td>
<td>51 (14)</td>
<td>0.74</td>
</tr>
<tr>
<td>Gender (F/M)</td>
<td></td>
<td>8/7</td>
<td>9/5</td>
<td>7/8</td>
<td>24/20</td>
<td>0.63</td>
</tr>
<tr>
<td>Body mass index (kg/m(^2))</td>
<td></td>
<td>30 (7)</td>
<td>36 (7)</td>
<td>36 (10)</td>
<td>34 (9)</td>
<td>0.12</td>
</tr>
<tr>
<td>Neck circumference (cm)</td>
<td></td>
<td>37 (5)</td>
<td>41 (5)</td>
<td>42 (5)</td>
<td>40 (5)</td>
<td>(&lt; 0.05)</td>
</tr>
<tr>
<td>Epworth</td>
<td></td>
<td>12 (6)</td>
<td>10 (4)</td>
<td>11 (4)</td>
<td>11 (5)</td>
<td>0.53</td>
</tr>
<tr>
<td>Apnea-hypopnea index (events/h)</td>
<td></td>
<td>22 (13)</td>
<td>30 (22)</td>
<td>34 (27)</td>
<td>28 (21)</td>
<td>0.36</td>
</tr>
<tr>
<td>Nadir O(_2) sat (%)</td>
<td></td>
<td>83 (8)</td>
<td>82 (6)</td>
<td>80 (9)</td>
<td>82 (8)</td>
<td>0.55</td>
</tr>
<tr>
<td>% time with SO(_2) &lt; 90%</td>
<td></td>
<td>3 (4)</td>
<td>15 (23)</td>
<td>10 (16)</td>
<td>9 (17)</td>
<td>0.12</td>
</tr>
<tr>
<td>Maximal end-tidal CO(_2) (mm Hg)</td>
<td></td>
<td>40.1 (9.2)</td>
<td>48.1 (1.6)</td>
<td>57.0 (7.2)</td>
<td>48.4 (9.8)</td>
<td>(&lt; 0.001)</td>
</tr>
<tr>
<td>Awake evening end-tidal CO(_2) (mm Hg)</td>
<td></td>
<td>34.5 (3.8)</td>
<td>40.5 (2.9)</td>
<td>46.6 (3.7)</td>
<td>40.6 (6.1)</td>
<td>(&lt; 0.001)</td>
</tr>
<tr>
<td>Arousal index (events/h)</td>
<td></td>
<td>26.6 (9.8)</td>
<td>31.5 (16.9)</td>
<td>33.2 (25.6)</td>
<td>30.5 (18.4)</td>
<td>0.61</td>
</tr>
<tr>
<td>Percent supine (%)</td>
<td></td>
<td>42.1 (23.0)</td>
<td>35.1 (26.5)</td>
<td>53.5 (36.4)</td>
<td>43.8 (29.7)</td>
<td>0.24</td>
</tr>
<tr>
<td>Stage N3 sleep (%)</td>
<td></td>
<td>9 (9)</td>
<td>13 (12)</td>
<td>10 (12)</td>
<td>11 (11)</td>
<td>0.62</td>
</tr>
<tr>
<td>Stage REM sleep (%)</td>
<td></td>
<td>17 (7)</td>
<td>17 (8)</td>
<td>12 (7)</td>
<td>15 (7)</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Values expressed as mean (standard deviation) except for gender row. *One way analysis of variance unless otherwise indicated; \( \chi^2 \) test; †By contrast analysis, neck circumference in the combined groups with Max ETCO\(_2\) \(\geq 45 \text{ mm Hg}\) was higher vs. the group with Max ETCO\(_2\) \(< 45 \text{ mm Hg}\) (\( p < 0.02\)).
event relative to pre-event amplitude, with comparable correlation coefficients (p = 0.30), slopes, and intercepts. Therefore a mean post-event to mean pre-event (combining apneas and hypopneas) amplitude ratio was calculated, with which the integrated overnight CO₂ was also correlated (r = -0.71, p < 0.001) (Figure 2C).

The evening and morning awake ETCO₂ were nearly identical and closely correlated (40.7 ± 6.2 vs. 40.5 ± 5.8 mm Hg, respectively; r = 0.81, p < 0.001). The evening awake ETCO₂ correlated positively with mean apnea duration (r = 0.42, p = 0.004), inversely with mean post-apnea duration (r = -0.81, p < 0.001), and inversely with mean post- to mean pre-event amplitude ratio (r = -0.80, p < 0.001).

Cross-correlation analysis indicated that collinearity was a concern, as the mean post-event to mean pre-event amplitude ratio was correlated with mean apnea duration (r = -0.43, p = 0.005), and particularly with mean post-apnea duration (r = 0.88, p < 0.001) (Figure 3). However, mean post-apnea duration was not correlated with mean apnea duration (r = -0.25, p = 0.10).

In a multivariable regression model, mean post-apnea duration, mean apnea duration, and age were each independently correlated with the integrated overnight CO₂: mean post-apnea duration contributing the most to the variance in integrated overnight CO₂ (45%), with mean apnea duration and age contributing an additional 6% and 5%, respectively, such that the total model explained 56% of the variance in integrated overnight CO₂ (Table 3). The body mass index and apnea-hypopnea index were not significantly correlated with the integrated overnight CO₂ in the multivariable model (p = 0.17 and 0.47, respectively).

**DISCUSSION**

Our study shows that, in patients with obstructive apnea:

1. A shorter post-apnea duration is a greater contributor to an elevated integrated overnight CO₂ than apnea duration, with older age as an additional lesser contributor;
2. Post-hypopnea amplitude is equally as important as the post-apnea amplitude with post-event relative to pre-event (combining apneas and hypopneas) amplitude contributing to the integrated overnight CO₂, but also correlating strongly with apnea duration and post-apnea duration;
3. Post-apnea duration is not correlated with apnea duration;
4. The apnea-hypopnea index, body mass index, hypopnea duration, and post-hypopnea duration are not important contributors to the overnight CO₂; and
5. The baseline awake end-tidal CO₂ also correlated positively with mean apnea duration, and inversely with mean post-apnea duration and post-event amplitude relative to pre-event amplitude.

In our study, the post-event to pre-event amplitude ratio was tightly correlated with post-apnea duration (Figure 3B), suggesting that a common pathophysiologic mechanism, possibly airway collapsibility, underlies those two measures, and may explain our finding of an association between longer post-apnea duration and a more favorable REM architecture (with both a shorter REM latency and increased REM sleep). For instance, stable breathing correlated with passive collapsibility of the airway in patients with suspected obstructive sleep apnea. Consequently, multi-collinearity was seen between post-apnea duration and post-event to pre-event amplitude. Although ventilatory measures such as breath amplitude may be as important as post-apnea duration, the individual contribution of each of those two variables to the overnight integrated CO₂ is difficult to discern in the context of collinearity. We therefore included only the apnea and post-apnea durations in the final model shown in Table 3, because durations were more sharply defined, less subject to variability in measurements (compared to amplitudes), limited to apneas (and therefore independent of the various hypopnea definitions), and independent of correc-
tion measures (such as square root modification of the nasal pressure amplitude signal\textsuperscript{17,18}) to compensate for the nonlinear nasal pressure to flow relationship.

However, once the airway has collapsed and an apnea or hypopnea begun, the duration of the obstructive events may depend on factors other than collapsibility such as the arousal threshold. For instance, since arousals terminate an obstructive event, apnea duration has been considered a surrogate of the arousal threshold.\textsuperscript{19} These proposals, with separate determinants of apnea duration and post-apnea duration, are consistent with the absence of an inverse correlation between those two variables in our study as well as other studies.\textsuperscript{12}

The integrated overnight CO\textsubscript{2} did not correlate with hypopnea and post-hypopnea durations, perhaps reflecting the shape of the relationship between CO\textsubscript{2} and ventilation (the metabolic hyperbola), such that the reduced ventilation during hypopneas, was either sufficient to prevent an increase in arterial CO\textsubscript{2}, or decreased our ability to detect such an effect within the technical constraints of our study. In that regard, the most important constraint is our removal of data associated with deterioration of the capnographic waveforms during obstructive events. This may have resulted in an underestimation of the true overall nocturnal CO\textsubscript{2}, and perhaps explain why apnea duration was not as strong a predictor of nocturnal CO\textsubscript{2} as post-apnea duration in our study (an alternative explanation may be the constraint of the conventional 10-second threshold to the apnea definition).

Note that loss of the capnographic signal during obstruction, which is considered an artifact in our study, has been used diagnostically to detect apneas,\textsuperscript{3} such that the lowered overnight end-tidal CO\textsubscript{2}, was shown to be associated with the apnea-hypopnea index severity.\textsuperscript{4} We confirm the results of other studies showing a relationship between a longer apneas or shorter post-apnea duration with a higher awake arterial CO\textsubscript{2},\textsuperscript{12,20} and between an impaired post-event ventilatory response and a higher awake arterial CO\textsubscript{2}.\textsuperscript{10,11} Our study extends those results and demonstrates that, in individuals with obstructive sleep apnea, gradations of the awake CO\textsubscript{2} even within the normal range, reflect events occurring during sleep, with elevation of nocturnal carbon dioxide as a possible intermediary step associated with shorter post-apnea duration, with lesser contributions from longer apnea duration, and increased age.

In contrast, we found that the apnea-hypopnea index was not a significant predictor of the integrated overnight CO\textsubscript{2}, and that the body mass index trended towards a poor correlation with the integrated overnight CO\textsubscript{2}, though both are important determinants of daytime hypercapnia in obese patients with obstructive sleep apnea.\textsuperscript{9} A potential explanation for those findings is that, beyond causing variations of awake CO\textsubscript{2} within the normal range, inciting events to nocturnal hypercapnia (such as lower post-event ventilation, longer apnea duration, shorter post-apnea duration) require other factors (such as the apnea-hypopnea index or body mass index) for the transition to daytime hypercapnia. For instance, obese patients, and especially those with the metabolic syndrome, have a higher resting metabolic rate compared to non-obese patients\textsuperscript{21,22} but also have a decrease in metabolic rate during sleep in direct proportion to the body mass index.\textsuperscript{21} The resting to sleep differential in the metabolic rate based on body mass index, may explain the stronger contribution of
the body mass index to the development of daytime as opposed to nocturnal hypercapnia.

Our findings do not establish whether an impairment of ventilation (as determined by apnea and post-apnea duration, or post-ventilation relative to pre-ventilation) determines ETCo2, or whether elevation in the ETCo2 impairs ventilation. However, progressive hypercapnia above a certain threshold improves upper airway stability in a linear fashion. This pharyngeal chemosensitivity parallels the control gain of central and peripheral chemoreceptors, with the net effect that increased CO2 protects and increases ventilation. Our findings are therefore more consistent with a ventilatory effect that increased CO2 protects and increases ventilation. Our findings do not establish whether an impairment of ventilation during respiratory events in obstructive sleep apnea.

Our study expands the indications of capnometry during polysomnography beyond its current contexts of apnea detection and quantification of the hypoventilation syndromes to its use as a reflection of the pathophysiology, severity, or ventilatory burden of sleep apnea, which may not be fully captured by the apnea-hypopnea index. These findings may have both diagnostic and prognostic clinical implications, as exhaled CO2 may be a physiologic marker of disease severity that is independent of the apnea-hypopnea index, reflects the balance between event and inter-event duration, and may be an intermediary stage towards the development of daytime hypercapnia in some individuals. Advances in methods of exhaled breath analysis may broaden the role of exhaled CO2 as a diagnostic tool and therapeutic target in patients with sleep apnea.

**REFERENCES**


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Concordance of Polysomnographic and Actigraphic Measurement of Sleep and Wake in Older Women with Insomnia

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For assessment of insomnia, it is useful to have objective as well as subjective sleep measures. Persons with insomnia commonly report perceptions of more severe sleep disturbance than is apparent on objective sleep measures.1 Comparison of such subjective-objective differences is important for research on the etiology and subtypes of insomnia, as well as for tailoring cognitive-behavioral treatments. Actigraphy has gained acceptance as a cost-effective alternative to polysomnography; however, evidence is needed on the validity of actigraphy devices, and on accuracy of the measure in various clinical populations.

Polysomnography (PSG) remains the gold-standard to objectively measure sleep. The major disadvantages of PSG are participant burden (sleeping in a laboratory setting, wearing numerous sensors) and cost (equipment and staff for recording and visual scoring of records). By comparison, actigraphy is an attractive measure with much lower participant burden and cost. It allows measurement of 24-hour rest-activity data with minimal intrusiveness to the participant. The set-up of an actigraph recording is simple, requiring only computerized initialization of the device and placement on the wrist; scoring of the data is also simpler than PSG. Despite these practical advantages, actigraphy is not a substitute for PSG. It provides a measure of behavior but does not provide data on traditional sleep stages, quantitative measures of EEG, or respiration and muscle activity during sleep.

Methods: Concurrent validity of actigraphy and PSG was examined through (1) comparison of sleep outcomes from each recording method; (2) calculation of sensitivity, specificity, accuracy, and predictive values from epoch-by-epoch data; and (3) statistical and graphical exploration of the relationship between sleep disturbance severity and concordance of actigraphy and PSG. Subjects were 16 community-dwelling older women (mean age 69.4 ± 8.1) with insomnia who underwent 8 nights of concurrent actigraphy and PSG.

Results: Sleep efficiency reflected much greater sleep disturbance on PSG (66.9%) than actigraphy (84.4%). Based on generalized linear models, the parameter estimates for agreement between actigraphy and PSG were statistically significant (p < 0.05) for total sleep time and sleep latency, but was not significant for sleep efficiency (p = 0.20). Epoch-by-epoch analysis showed high sensitivity (96.1%), low specificity (36.4%), and modest values on agreement (75.4%) and predictive values of sleep (74.7%) and wake (80.2%). Generalized linear models showed that overall accuracy of actigraphy declined as sleep efficiency declined (unstandardized Beta = 0.741, p < 0.001). Based on this model, sleep efficiency of 73% was the point at which accuracy declined below an acceptable accuracy value of 80%.

Conclusions: Actigraphy offers a relatively inexpensive and unobtrusive method for measuring sleep, but it appears to underestimate sleep disturbance, particularly at sleep efficiency levels below 73%, in older women with insomnia.

Keywords: Actigraphy, sleep, insomnia, aging, sleep initiation and maintenance disorders

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a behavior that could potentially lead to misclassification of inactive wake time as sleep on actigraphy. This direction of actigraphy error has been shown in younger populations.\(^9,10\) Given that women across the lifespan are more likely to experience insomnia, it is possible that older women are habituated to being awake during the night, and thus more likely to lie still when awake,\(^11\) resulting in over-identification on sleep by actigraphy.

In our randomized trial of valerian effects on sleep in older women with insomnia,\(^12\) we noted that actigraphy sleep outcomes represented better sleep quality than PSG. For example, we found mean sleep efficiency on PSG was 66.91% ± 12.89%, and on the same nights it was 89.79% ± 3.80% on actigraphy. Therefore, the objectives of this secondary analysis of actigraphy and polysomnography data in the older women from our study of valerian were: (1) to explore differences between actigraphic and PSG estimates of sleep outcomes (total sleep time, sleep efficiency, wake after sleep onset, and sleep latency); (2) to examine the concurrent validity of actigraphy and PSG based on epoch-by-epoch analysis of sensitivity, specificity, accuracy, and predictive values for sleep and wake; and (3) to statistically and graphically explore whether the severity of sleep disturbance affects the validity of actigraphy compared to PSG.

**METHODS**

**Design**

This study was a secondary analysis of data from a randomized, double-blinded crossover study of valerian for older women with insomnia.\(^12\) The original study included 2 phases with 8 nights of concurrent PSG and actigraphy. The original study and secondary analysis were approved by the University of Washington Human Subjects Institutional Review Board.

**Study Sample**

This secondary analysis includes all 16 participants from the original study sample. These women were recruited from the greater Seattle community between November 2004 and February 2006. Qualifying participants were aged 55-80, ≥ 5 years post-menopause, with scores > 5 on the Pittsburgh Sleep Quality Index (PSQI) indicating overall disturbed sleep\(^13\) and scores < 22 on the Insomnia Severity Index ([ISI] ≥ 22 indicates severe insomnia).\(^14\) Sleep disturbance was confirmed at baseline by a 2-week sleep diary (≥ 30-min sleep onset latency or wake after sleep onset for ≥ 3 nights per week and a daytime complaint), and participants underwent one night of screening PSG to exclude those with an undiagnosed sleep disorder (sleep disordered breathing or periodic limb movement disorder). Women with confounding medical and psychiatric conditions were excluded (see Taibi\(^12\) for full inclusion/exclusion criteria).

The mean age of participants was 69.4 ± 8.1 years. The participants were mostly well-educated (81% attended college or graduate school) and married (69%). All but one of the participants racially identified as white/Caucasian. Several participants had minor comorbidities (e.g., arthritis), but none had major illnesses. The sample means for self-reported sleep disturbance were 8.8 ± 2.3 on the PSQI and 11.1 ± 3.9 on the ISI.

**Polysomnography and Actigraphy Data Collection**

**Actigraphy**

Actigraphy was measured using the Actiwatch-64 (Philips Respironics, Andover, MA). These devices are piezoelectric accelerometers about the size of a watch and are worn on the wrist. The Actiwatch-64 accelerometer is omnidirectional, detecting movement on all planes. Actiwatch activity counts represent both the occurrence and magnitude of arm movements. Actiwatch-64s are programmed with a calibration coefficient that minimizes variation in activity counts between different Actiwatches, thus minimizing instrument-related error. Movement data were sampled at a rate of 32 Hz, and activity counts were recorded in 30-sec epochs, the same epoch length used in PSG recordings and scoring.

Time in bed (TIB) was the time between lights out and lights on as recorded in the sleep laboratory. These times were manually entered into Actiware 5.57 software (Philips Respironics, Andover, MA) and were identical to the PSG and analyses. Mean TIB for each night was 473 min (SD 52 min, range 347-580 minutes). Each epoch was scored as sleep or wake by applying a standard mathematical algorithm, and sleep outcomes were obtained using Actiware 5.57 software (Philips Respironics, Andover, MA). Sleep onset and offset were scored as the first/last 10 min of the sleep record scored as sleep with ≤ 1 epoch scored as wake. Sleep outcomes included total sleep time (TST), sleep efficiency (total sleep time/time in bed*100), wake after sleep onset (WASO), and sleep latency (time between going to bed and sleep onset defined as 10 min with ≤ 1 epoch of wake).

**Polysomnography Recording Procedures**

The full procedures for PSG recordings are reported in Taibi et al.\(^12\) Participants completed 9 nights of PSG recording over 4 visits to the Sleep Research Laboratory (2-3 nights per visit). Actigraphs were not worn on the first PSG night, which served as screening for sleep disordered breathing and periodic limb movement disorder. Participants with evidence of these sleep disorders were excluded from further participation. Subsequently, concurrent PSG and actigraphy were recorded for 2 consecutive nights at the beginning and end of 2 study phases, resulting in 8 total nights of concurrent actigraphy and PSG measurement from each participant. All nights of concurrent actigraphy and PSG were recorded on weeknights.

Electrodes for recording the electroencephalogram, electrooculogram, and electromyogram were placed according to standard criteria.\(^15\) Signals from these leads were digitized and recorded using the EMBLA Somnologica 3.1.2 data acquisition system (EMBLA, Denver, CO). Sleep and wake stages were scored in 30-sec epochs according to the standard criteria of Rechtschaffen and Kales.\(^16\) TIB was the time between lights out and lights on as recorded in the sleep laboratory. Sleep variables were computed with a locally developed software program and included TST, sleep efficiency (total sleep time/time in bed*100), WASO, and sleep onset latency (time from lights out to first epoch of stage 2 sleep).

**Actigraphy and Polysomnography Processing for Analysis**

Fourteen participants had concurrent actigraphy and PSG data available from all 8 study nights that were used in the analy-
s. Two participants had only 4 nights of actigraphy data available for use in the analysis because of actigraphy battery failure, resulting in a total of 120 nights of data used in the analysis.

Immediately before initializing the actigraph and PSG recordings, all computers were synchronized to the National Institute of Standards and Technology (NIST) atomic clock time to ensure alignment of actigraphy and PSG epochs. Each scored PSG record was exported from Somnologica as a text file and imported into SPSS 15.0 (SPSS Inc., Chicago, IL) for analysis. Epoch-by-epoch PSG data were dichotomized to binary form (0 = wakefulness, 1 = any stage of sleep).

Actigraphy data were exported from Actiware 5.57 to comma-separated data files and imported into SPSS for analysis. The data for each epoch were automatically scored (0 = wake, 1 = sleep) in Actiware prior to export. Designation of each epoch as sleep or wake is based on a scoring algorithm that weights activity in the immediate and adjacent 2 min of epochs (where \( E = \) epoch, \( E_{a} = \) activity within preceding epochs, and \( E_{s} = \) activity within subsequent epochs): \( E^2 + 0.23(E_{a} + E_{s} + E_{a} + E_{s}) - 0.044(E_{a} + E_{s} + E_{a} + E_{s}) \).\(^9\) Each epoch was scored as wake if the algorithm resulted in a score at or above a predetermined threshold; epochs below the threshold were designated as sleep. Actiware includes 3 threshold levels for designating wake: low threshold = 20, medium threshold = 40, and high threshold = 80. Some authors refer to thresholds as “sensitivity” levels for wake detection (low threshold = high sensitivity, high threshold = low sensitivity). We use the term threshold to avoid confusion with calculated sensitivity of actigraphy versus PSG. Given that the low wake-detection threshold would be more likely to score movement epochs as wake, this setting was hypothesized to be most useful in persons with insomnia, who tend to have long periods of wakefulness while lying in bed.\(^8\) To test this hypothesis, we compared all 3 sensitivity levels.

Statistical Analyses

The intervention (valerian) was not shown to affect either PSG or actigraphically assessed sleep in the primary study analyses.\(^12\) Additionally, no differences between non-treatment (adaptation/placebo) and treatment nights on the validity outcomes were apparent on visual (mean validity outcomes) and statistically (Wilcoxon signed-ranks test) examination. Therefore, treatment was not considered in the present analyses. All statistical analyses were done in SPSS 15.0. Mean values for the sample on all sleep and validity outcomes were calculated within-subject across the whole sample to normalize for 2 subjects having only 4 nights of data.

To explore the agreement between actigraphy and PSG estimates of sleep outcomes, means and standard deviations of the sleep outcomes (total sleep time, sleep efficiency, wake after sleep onset, and sleep latency) are reported from PSG and from actigraphy at low, medium, and high wake-detection thresholds. The relationships of actigraphy values with PSG values on the sleep outcomes were analyzed using generalized linear models for continuous outcomes with mixed effects to account for within-subject repeated measures. Log transformed values of PSG and actigraphic sleep latency were used in the analyses due to the skewed distribution of these data.

To examine concurrent validity based on epoch-by-epoch comparison of actigraphy and PSG, each 30-sec epoch was scored as agreeing (true sleep/true wake) or disagreeing (false sleep = sleep scored on actigraphy but not PSG, false wake = wake scored on actigraphy but not PSG). Sensitivity, specificity, accuracy, and predictive values of the concordance in sleep/wake scoring for PSG and actigraphy were calculated for all study nights. These formulas have been described in previous studies.\(^10,16-18\) Sensitivity represents the proportion of the PSG-identified sleep epochs that are identified as sleep by actigraphy (# sleep epochs correctly identified by actigraphy / # PSG-identified sleep epochs). Specificity represents the proportion of the PSG-identified non-sleep (i.e., wake) epochs identified as wake by actigraphy (# wake epochs correctly identified by actigraphy / # PSG-identified wake epochs). Accuracy is the total percentage of PSG epochs (sleep or wake) correctly identified by actigraphy (# sleep or wake epochs correctly identified by actigraphy/total # of epochs). Predictive values were also calculated. These represent the proportion of epochs of actigraphy that are correctly classified. Predictive value for sleep (PVS) was the percent of actigraphic sleep epochs that accorded with PSG sleep, and predictive value for wakefulness (PVW) was the percent of actigraphic wake epochs that accorded with PSG wake. Accuracy values at the 3 thresholds were compared pairwise (low vs. medium, medium vs. high, low vs. high) using generalizability linear models with mixed effects to account for within-subject repeated measures. Confidence intervals around the parameter estimate representing agreement of the thresholds were compared for overlap, which would indicate a lack of substantial difference between the thresholds.

The impact of sleep disturbance severity on validity measures was examined statistically and graphically. Generalizability linear models, also accounting for within-subject repeated measures, were used to compare PSG sleep efficiency with overall accuracy. Bland-Altman plots for each of the sleep outcomes (TST, sleep efficiency, WASO, and sleep onset latency) were used to examine whether the degree of measurement error varied over the range of measurement. The Bland-Altman approach plots the difference of the 2 measures (e.g., actigraphy sleep efficiency - PSG sleep efficiency) on the y-axis against the mean of the 2 measures (e.g., [actigraphy sleep efficiency + PSG sleep efficiency]/2) on the x-axis.\(^19\) For perfect correspondence of the 2 measures, all data points for measurement difference would fall along zero difference line. If actigraphy is biased toward overestimating the sleep outcome, points fall above the zero line; if it is biased toward underestimating the outcome, points fall below the zero line. If the distance from zero changes over the plot (i.e., the left versus the right side of the graph), this indicates that measurement error varies over the measurement scale. For example, if underestimation of sleep latency were greater for higher levels of sleep latency, the data points would be below the zero line, and increasingly farther from the line towards the right side of the graph (higher sleep latency).

RESULTS

Sleep Outcomes

Mean values of the sleep outcomes, including total sleep time, sleep efficiency, WASO, and sleep latency, are shown in Table 1. On examination of the mean values, all 3 actigraphy
that the linear relationships between actigraphy and PSG values were true not only for the entire sample, but also within the majority of individuals.

Concordance Outcomes

Sensitivity was high for all 3 actigraphy wake-detection thresholds (low = 96.1% ± 3.0%, medium = 98.1% ± 1.7%, and high = 99.2% ± 0.7%; see Figure 2). Specificity was low at all 3 actigraphy thresholds (low = 36.4% ± 14.0%, medium = 28.1% ± 11.9%, and high = 19.6% ± 9.2%). Overall accuracy was moderate: 75.4% ± 10.2, 74.3% ± 11.3%, and 72.5 ± %12.1% for low, medium, and high thresholds, respectively. Predictive values indicate the proportion of epochs on actigraphy that are correctly classified. Predictive values for sleep (PVS) were moderate at the low, medium, and high wake-detection thresholds, respectively: 74.7% ± 13.6%, 73.0% ± 13.5%; and 71.1% ± 13.4% of the epochs classified as sleep by actigraphy were correct according to PSG. Predictive values for wake (PVW) were strong at the low, medium, and high thresholds: 80.2% ± 12.8%, 86.1% ± 10.6%, 90.5% ± 8.2% of the epochs classified as wake by actigraphy were correct according to PSG.

Comparison of Validity of the Three Wake-Detection Thresholds

Accuracy values from the three wake-detection thresholds were compared using generalized linear models. Comparisons showed strong agreement between each of the 3 thresholds (low, medium, β = 1.02, 95%CI = 1.00-1.05; medium-high, β = 1.08, 95%CI = 1.05-1.10, low-high, β = 1.10, 95%CI = 1.05-1.14). Overlap of the confidence intervals indicated that that accuracy did not differ significantly between these thresholds.

Impact of Sleep Disruption on Actigraphy Validity

Accuracy Versus PSG Sleep Efficiency

We compared the accuracy of actigraphy (percentage of correctly identified epochs) with PSG sleep efficiency to examine whether it varied depending on the severity of sleep disturbance, as has been reported in other studies.20,21 The generalized linear model was highly significant (p < 0.001, 95%CI = 0.65-0.84). The unstandardized Beta coefficient was 0.74, indicating close correspondence between the reduced sleep efficiency and re-

### Table 1—Sleep outcomes from actigraphy and polysomnography

<table>
<thead>
<tr>
<th>Sleep Outcome</th>
<th>Low Threshold (20)</th>
<th>Medium Threshold (40)</th>
<th>High Threshold (80)</th>
<th>PSG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Sleep Time (min)</td>
<td>404.12 (47.91)</td>
<td>422.85 (48.13)</td>
<td>438.96 (49.26)</td>
<td>314.97 (68.06)</td>
</tr>
<tr>
<td>Difference from PSG</td>
<td>+89.15</td>
<td>+107.88</td>
<td>+123.99</td>
<td>–</td>
</tr>
<tr>
<td>Sleep Efficiency (%)</td>
<td>85.82 (4.97)</td>
<td>89.79 (3.80)</td>
<td>93.19 (2.70)</td>
<td>66.91 (12.89)</td>
</tr>
<tr>
<td>Difference from PSG</td>
<td>+18.91</td>
<td>+22.88</td>
<td>+26.28</td>
<td>–</td>
</tr>
<tr>
<td>WASOa (min)</td>
<td>56.08 (21.99)</td>
<td>39.38 (16.40)</td>
<td>25.63 (10.86)</td>
<td>131.10 (60.48)</td>
</tr>
<tr>
<td>Difference from PSG</td>
<td>-75.02</td>
<td>-91.71</td>
<td>-105.47</td>
<td>–</td>
</tr>
<tr>
<td>Sleep Latency (min)</td>
<td>4.98 (4.80)</td>
<td>4.98 (4.80)</td>
<td>4.98 (4.80)</td>
<td>18.36 (12.31)</td>
</tr>
</tbody>
</table>

aWASO, wake after sleep onset.

Because 4-8 nights of data were included from each participant, all models used mixed effects to account for the effect of within-subject repeated measures. Given that the low threshold produced results closest to PSG, we used this setting to examine the relationship between actigraphy and PSG sleep outcomes by generalized linear models (Table 2). Addition of a nonlinear term did not improve the strength or significance of the model parameters; thus only linear analyses are reported. These results showed that agreement between actigraphy and PSG values was significant (p < 0.05) for TST and sleep latency, and verged on significance for WASO (p = 0.052). Sleep efficiency was not significant (p = 0.204). Unstandardized Beta coefficients reflect how much the dependent variable (actigraphy) changes when the independent variable (PSG) changes by 1 unit (e.g., one minute for TST, WASO, and sleep latency, one percentage point for sleep efficiency). A positive Beta coefficient indicates that the variables change in the same direction—that is, as one increases or decreases, the other does the same. A value of 1 would show perfect correspondence between actigraphy and PSG. Sleep latency showed strong agreement, with a Beta coefficient of 0.668 (p < 0.001). Total sleep time and WASO showed weak agreement (β = 0.367, 95%CI = 1.05-1.10, low-high, β = 1.10, 95%CI = 1.05-1.14). Overlap of the confidence intervals indicated that that accuracy did not differ significantly between these thresholds.

### Table 2—Generalized linear models comparing sleep outcomes from actigraphy and polysomnography

<table>
<thead>
<tr>
<th>Sleep Outcome</th>
<th>Unstandardized Beta</th>
<th>95%CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Sleep Time</td>
<td>0.281</td>
<td>0.044-0.517</td>
<td>0.200</td>
</tr>
<tr>
<td>Sleep Efficiency</td>
<td>0.085</td>
<td>-0.046-0.217</td>
<td>0.204</td>
</tr>
<tr>
<td>WASOa</td>
<td>0.123</td>
<td>-0.001-0.247</td>
<td>0.052</td>
</tr>
<tr>
<td>Sleep Latencya</td>
<td>0.669</td>
<td>0.367-0.969</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

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duced accuracy of actigraphy. We used the model parameters to calculate that a sleep efficiency level of 73.2% was where accuracy dropped below the generally accepted value of 80%\textsuperscript{,18}.

A scatterplot examining the relationship between PSG sleep efficiency and accuracy within participants showed a linear relationship for all participants (Figure 3).

**Bland-Altman Plots**

Bland-Altman plots were used to examine whether the magnitude of sleep disturbance affected the levels of agreement between actigraphy and PSG on sleep outcomes (Figure 4). These graphs plot the difference between actigraphy and PSG (on the y-axis) against the mean of the 2 measures (on the x-axis). The plots showed clear trends in measurement differences across the range of the measures such that the measurement differences were greater for lower TST, higher WASO, lower sleep efficiency, and longer sleep latency. These findings show that actigraphy corresponded more poorly with PSG as sleep became more disturbed, particularly with larger amounts of time spent awake.

**DISCUSSION**

In this sample of middle-aged to older women with insomnia, validity analyses revealed statistically significant agreement between actigraphy and PSG on all sleep outcomes except for sleep efficiency. Epoch-by-epoch analysis results showed that actigraphy accurately detected the majority of PSG-identified sleep, indicated by high sensitivity ($\geq 96\%$), but did so by over-classifying PSG-identified wake epochs as actigraphic sleep (reduced PVS, $\leq 75\%$). Furthermore, actigraphy identified only a small portion of PSG wake (low specificity, $\leq 36\%$) but tended not to misclassify PSG sleep epochs as wake (high PVW, $\geq 80\%$).

Consistent with our hypothesis, specificity and overall accuracy were highest at the low wake-detection threshold. Ac-
curate identification of wake appeared to come at the expense of reduced sleep identification: the low wake-detection threshold had lower sensitivity than the other thresholds. Given that actigraphy over-classified sleep, some loss in sleep detection for improved wake detection favors the low threshold in this population. Even at this “best” threshold level, specificity was poor, accuracy was moderate, sleep was overestimated by 89 minutes, and WASO was underestimated by 75 minutes. Overall, these results suggest that actigraphy may underestimate the severity of insomnia in older women with significant sleep disturbance.

We found actigraph validity declined predictably as sleep efficiency declined. Sleep efficiency around 73% was an important cut-point below which actigraphy accuracy fell below the generally accepted value of 80%. This pattern of lower validity in more disturbed sleep was evident within-subjects as well as between-subjects. A decrement in the performance of actigraphy was also apparent on the Bland-Altman plots of the sleep outcomes, which showed greater disagreement between actigraphy and PSG as each outcome reflected poorer sleep. This pattern of poorer performance in persons with worse sleep raises questions concerning the utility of actigraphy in persons with severe insomnia. Given that persons with severe insomnia are expected to experience a degree of sleep disturbance at which actigraphy has been shown to perform poorly, actigraphy may not provide valid measures of sleep in this group.

Our findings regarding sleep and wake identification are consistent with the published literature on actigraph validity in general (see Table 3), and the Actiwatch-64 in particular, which reported underestimation of wake and overestimation of sleep. Blackwell et al. found overestimation of sleep with the SleepWatch-O actigraph (Ambulatory Monitoring Inc, Ardsley, NY) in their sample of older women, but of a lesser degree than that reported here, with a mean overestimation of 17.9 minutes total sleep time. However, their sample from the Study of Osteoporotic Fractures consisted of general community-dwelling older women, not specifically women with insomnia. In the subset of the sample with sleep efficiency levels lower than 70%, overestimation of sleep was more pronounced (mean = +68 minutes). Lichstein et al., who tested the Actiwatch-64 in older men and women with insomnia, also reported a smaller difference between actigraphy and PSG than the present study (TST difference = +14 minutes). Given that our study showed better accuracy at higher levels of sleep efficiency, the higher sleep efficiencies in the Blackwell and Lichstein studies (75.5% and 77.0% versus 66.9% in our study) may explain why those studies showed measurement error in the same direction as that found in our study, but of lesser magnitude.

Our findings were highly congruent with results from Sivertsen and colleagues’ study of older men and women with chronic insomnia. That study found a similar degree of sleep disturbance as the present study, and also similar magnitudes of differences between actigraphy and PSG on the same four sleep outcomes we tested. Our study augments Sivertsen’s findings by showing the same pattern with a different actigraph device (Actiwatch-64 versus Actiwatch Plus, Cambridge Neurotechnology, Ltd., Cambridge, UK). Additionally, Sivertsen et al. reported data for only one night in each of 34 participants for a total of 34 nights, compared to the current study’s design of 120 nights in 16 participants. Although our sample is smaller, we measured 4-8 nights and demonstrated similar validity to that found by Sivertsen not only between subjects, but within subjects as well. Finally, Sivertsen et al. found slightly higher PSG-actigraph agreement in women (84%) than in men (81%), but both groups had higher agreement than found in the present...
study. Thus, it remains unclear whether the accuracy of actigraphy differs in older women versus older men and younger persons with insomnia.

Several studies have presented correlations of actigraphy and PSG sleep outcomes as evidence of the validity of actigraphy: total sleep time $r = 0.51-0.93$, WASO $r = 0.48-0.85$, sleep efficiency $r = 0.36-0.81$, sleep onset latency $r = 0.30-0.95$.9,20,25-28 These findings indicate that, while there is substantial discrepancy between the measures, they tend to change in the same direction. The unstandardized Beta coefficients from our generalized linear models comparing sleep outcomes show similar results. Given that sleep outcomes from actigraphy tend to change in the same direction as PSG, actigraphy may be useful for measuring treatment-related changes in sleep. Studies have found actigraphy to be sensitive to treatment related changes in sleep, and this use of actigraphy is supported by the AASM practice guideline on actigraphy.2 However, the over-identification of sleep found in this study suggests that the magnitude of changes in sleep may not be fully reflected, especially given that measurement error is greater in more disturbed sleep. Another use of actigraphy beyond measuring sleep outcomes is the clinical characterization of sleep-wake patterns,2 which could be useful for such applications as checking behavioral contributions to sleep disturbance and patient compliance to sleep scheduling.

Overall, the results of this secondary analysis indicate that older women with insomnia may appear to have sleep efficiency that falls within what is considered a “normal range” on actigraphy. However, the over-identification of sleep found in this study suggests that the magnitude of changes in sleep may not be fully reflected, especially given that measurement error is greater in more disturbed sleep. Another use of actigraphy beyond measuring sleep outcomes is the clinical characterization of sleep-wake patterns,2 which could be useful for such applications as checking behavioral contributions to sleep disturbance and patient compliance to sleep scheduling.

Overall, the results of this secondary analysis indicate that older women with insomnia may appear to have sleep efficiency that falls within what is considered a “normal range” on actigraphy. However, if actigraphy were to be used as a screening tool, these individuals would be at risk for under-detection of the severity of insomnia. Further, those individuals whose actigraphic measures show disturbed sleep may actually experience greater sleep disturbance than is being detected.

**Limitations**

This study has several limitations. First, certain aspects of the sample present limitations, including the small sample size which limits the power of the statistical analyses, and the lack
of racial/ethnic and gender diversity, which limits the generalizability of the findings to other populations. Second, we tested only one actigraphy device, the Actiwatch-64. This device has been shown to perform comparably to Philips Respironics’ newer Actiwatch-2 device,25 but has substantial technical differences from other actigraphy manufacturers including the type accelerometer (piezoelectric versus solid state), mode of logging activity (count of threshold crossings, sums of activity occurrences and/or magnitude, time above threshold), and sleep/wake scoring algorithms used. Thus, applicability to other devices cannot be assumed. However, previous studies have shown various actigraphs to have similar functionality and validity,25,30 so it is reasonable to hypothesize that other devices are likely to be subject to the same performance limitations as the device tested in the present analyses.

Conclusions and Implications

It is important for researchers and clinicians to recognize that actigraphy is a useful measure, but it has limitations as a measure of sleep outcomes. Because actigraphy measures movement, confounding factors such as passive movement (e.g., movement of a bed partner), quiescent wakefulness, or periodic limb movements could substantially affect the validity of actigraphy sleep outcomes. The high sensitivity of actigraphy in this sample of women with insomnia appears largely explained by over-identification of sleep, as evidenced by poor specificity. In particular, the accuracy of actigraphy declined below an acceptable level when sleep efficiency was below 73%. The validity of actigraphy for quantifying treatment changes was not addressed by this analysis and requires further research. At present, actigraphy offers a relatively inexpensive and unobtrusive method for examining sleep patterns, but users should select appropriate wake-detection thresholds for the population being tested and should interpret data with recognition that sleep disturbance is most likely underrepresented on actigraphy.

References


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DISCLOSURE STATEMENT
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Insomnia is a chronic condition for 10% of the adult population and has been described as an international public health problem. Far from being just a nuisance, individuals with insomnia disorder are at increased risk for stroke, diabetes, obesity, alcohol abuse, depressive episodes, automobile accidents, and workplace absenteeism. Given the scope of the insomnia problem, several researchers have discussed the utility of providing stepped care to meet the massive population need. One of these papers described a proposal for a stepped care model, which will now be reviewed, following which an alternative model currently in use will be outlined.

### Espie Model

Espie proposed a 5-level, stepped care model for insomnia. The levels differed in terms of provider (e.g., graduate student, psychologist, nonspecific therapist) and cost, but not content. In Espie’s proposed model, the lowest intensity intervention was self-administered cognitive behavioral therapy (CBT), either by booklet, CD/DVD, or internet. The next step in this model was a small group manualized brief CBT delivered by a trained therapist, following which individual or small group CBT delivered by a graduate psychologist would be offered. The next step up Espie’s proposed hierarchy was the opportunity to receive individual CBT by a clinical psychologist. The final step was to receive “expert CBT” by a behavioral sleep medicine specialist. Espie proposes that there be iterative assessment and review to determine predictors of “stepping up” and “stepping down” in such a model. The model under study which has been in use since 2009 contains 4 levels (see Figure 1). It has been employed in a behavioral medicine sleep clinic, in a mid-sized urban center with a population of 700,000. Although not depicted in the figure, the first intervention for most patients with chronic insomnia is the provision of hypnotic medication, which is the standard response to an insomnia complaint when patients are in the office of a family physician. The next step up the hierarchy is a 6-week, computerized treatment (return2sleep.com) that patients access from their homes, one of the first of its kind in North America. This program employs cognitive behavioral strategies for managing insomnia, includes homework exercises, determines an appropriate bedtime for the individual through use of a sleep calculator, and provides feedback to users to maximize self-management of the condition. Upon completion of return2sleep.com, or when the individual indicates that they no longer wish to continue using it, patients have the option of an on-site single session consultation with a staff psychologist or psychological associate (graduate student in clinical psychology; step 2). If after the consultation, more intensive

### Vincent Model

The model under study which has been in use since 2009 contains 4 levels (see Figure 1). It has been employed in a behavioral medicine sleep clinic, in a mid-sized urban center with a population of 700,000. Although not depicted in the figure, the first intervention for most patients with chronic insomnia is the provision of hypnotic medication, which is the standard response to an insomnia complaint when patients are in the office of a family physician. The next step up the hierarchy is a 6-week, computerized treatment (return2sleep.com) that patients access from their homes, one of the first of its kind in North America. This program employs cognitive behavioral strategies for managing insomnia, includes homework exercises, determines an appropriate bedtime for the individual through use of a sleep calculator, and provides feedback to users to maximize self-management of the condition. Upon completion of return2sleep.com, or when the individual indicates that they no longer wish to continue using it, patients have the option of an on-site single session consultation with a staff psychologist or psychological associate (graduate student in clinical psychology; step 2). If after the consultation, more intensive

### Study Objectives

Steped care models for chronic insomnia are in their infancy. This study evaluated predictors of movement in a stepped care pathway using a sample of 50 adult outpatients with chronic insomnia.

### Methods

At assessment periods, participants completed daily sleep diaries, the Insomnia Severity Index, the Multi-Dimensional Fatigue Inventory (MFI), and the Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS-10). Following this, data were collected regarding whether the individual went on to receive more intensive services (i.e., individual consultation, group or individual therapy). Data were analyzed using multinomial logistic regression.

### Results

Results showed that age, employment status, and sleep (quality, latency) predicted use of more intensive services. Results showed that psychiatric and sleep comorbidity, sleep attitudes, and insomnia severity did not.

### Conclusions

Implications of these findings are that stepped care resulted in a 69% improvement in efficiency, and that low-intensity treatment delivered in step 1 may have been particularly sufficient for the young and employed, and for those with better sleep.

### Keywords

Stepped care, insomnia, computerized treatment

### Citation

intervention is required, patients have the option of a 6-week cognitive behavioral group treatment run by a staff psychologist or a psychological associate (step 3). The components of the group intervention are identical to that of the computerized treatment; however, patients receive more individualized feedback, the opportunity to hear about how others are coping with similar problems, and more attention. Following completion of the group, if individuals are continuing to require care, they are provided with individual treatment with a staff psychologist who specializes in behavioral sleep medicine (step 4).

A review of the stepped care literature echoes the words of Edinger and illustrates that little is known about providing more or less intensive service to those with chronic sleep problems. Past research has tended to focus on the decision to seek consultation with a healthcare provider, typically a family physician or a general practitioner. Some of this research shows that increased consultation with a general practitioner regarding sleep is associated with increased sleep onset latency, time awake at night, daytime fatigue/sleepiness, and reduced total sleep time. Other research has shown that consultations were positively associated with perceived severity of insomnia, presence of comorbid medical conditions, increasing age and unemployment, and a perception that insomnia is due to poor sleep habits.

Hypotheses

Based on a review of the literature, the following hypotheses were made: (a) those who are older and unemployed will be more likely to step up the stepped care plan; (b) Those with less favorable sleep onset latency, time awake at night, and sleep quality will be more likely to step up the stepped care plan; (c) those with comorbid psychiatric conditions or symptoms suggestive of alternative sleep disorders will be more likely to step up the stepped care plan.

METHOD

Design

These data represents a consecutive series of patients who participated in a stepped care model within an outpatient behavioral medicine sleep clinic. As such, this is a non-controlled design.

Participants

Participants were 50 adults referred by physicians to a behavioral sleep clinic. Demographic and sleep features of the sample are listed in Tables 1 and 2 and illustrate that the sample was typical of help-seeking adults with chronic insomnia with regard to disturbed sleep. Inclusion criteria for the study were access to high speed internet and a home computer, a disturbance of sleep consisting of delay in sleep onset, return to sleep, or early-morning awakening > 30 min, the report of at least one symptom of daytime impairment (e.g., fatigue, lack of concentration), and a duration ≥ 6 months, occurring ≥ 4 nights per week. There was no maximum allowable total sleep time ([TST] e.g., 6.5 h) for inclusion in the study. The inclusion criteria were consistent with the general research diagnostic criteria for insomnia disorder. If a comorbid sleep or psychiatric disorder was present, treatment of this condition was stable at the time of entry into the study based on patient self-report. We did not require that medications be stable; many of the participants had not responded successfully to sleep medication. Exclusion criteria for the study were the presence of shift work, head injury, acute suicidality, current mania, schizophrenia, current or past cognitive behavioral treat-

Table 1—Descriptive features of sample

<table>
<thead>
<tr>
<th>Sleep Diary</th>
<th>M</th>
<th>SD</th>
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<tbody>
<tr>
<td>Sleep onset latency (SOL)</td>
<td>47.86</td>
<td>47.4</td>
</tr>
<tr>
<td>Number of nocturnal awakenings (NOW)</td>
<td>2.36</td>
<td>1.5</td>
</tr>
<tr>
<td>Wake time after sleep-onset (WASO)</td>
<td>77.34</td>
<td>58.2</td>
</tr>
<tr>
<td>Total sleep time (TST)</td>
<td>340.62</td>
<td>115.2</td>
</tr>
<tr>
<td>Sleep efficiency (SE)(%)</td>
<td>68.97</td>
<td>19.9</td>
</tr>
<tr>
<td>Sleep quality (SQ)</td>
<td>1.65</td>
<td>0.78</td>
</tr>
<tr>
<td>Medication use (%)</td>
<td>47.52</td>
<td>45.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Self-Report</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Insomnia Severity Index (ISI)</td>
<td>19.28</td>
<td>5.2</td>
</tr>
<tr>
<td>Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS-10)</td>
<td>40.74</td>
<td>9.1</td>
</tr>
<tr>
<td>Multi-Dimensional Fatigue Inventory (MFI-20) (general fatigue subscale)</td>
<td>13.92</td>
<td>3.6</td>
</tr>
</tbody>
</table>
ment of insomnia, or elevated substance use. Elevated substance use was defined as consuming > 14 alcoholic beverages per week for males or and > 12 alcoholic beverages per week for females.

**Measures**

**Sleep Diary**

A standard sleep diary measured information pertaining to sleep quality (SQ), wake after sleep onset (WASO), sleep-onset latency (SOL), and medication use (both psychiatric and sleeping agents). Although sleep diaries also measure TST, number of awakenings (NOW), and sleep efficiency (SE), these variables were not explicitly studied for reasons of parsimony. Sleep diary measures were scored for each night and then averaged across the recording period. Although not perfectly correlated, sleep diary ratings have been shown to correlate significantly with results obtained using polysomnographic monitoring. Sleep diary measures were scored for each night and then averaged across the recording period. Although not perfectly correlated, sleep diary ratings have been shown to correlate significantly with results obtained using polysomnographic monitoring.

Sleep diaries tend to provide overestimates of SOL and WASO, and underestimate of TST, relative to PSG; however, they are one of the most widely used measures of insomnia.

**Insomnia Severity**

The Insomnia Severity Index (ISI) measured the degree of dissatisfaction and daytime impairment associated with insomnia. The ISI has been found to have acceptable reliability and construct validity. Scores range from 0 to 28, with higher scores indicating more impairment. Scores > 14 are thought to indicate the presence of clinical insomnia.

**Fatigue**

The general fatigue subscale of the Multi-Dimensional Fatigue Inventory (MFI) measured general levels of fatigue. The general fatigue subscale has been found to have good internal consistency (ranging from 0.83-0.90), and scores have been shown to positively and significantly correlate with other self-report measures of fatigue. Scores on the subscale can range from 4 to 20, with higher scores indicating greater fatigue.

**Beliefs and Attitudes**

The Dysfunctional Beliefs and Attitudes about Sleep Scale-revised version (DBAS-10) is a 10-item self-report measure of maladaptive beliefs about sleep (e.g., beliefs about the immediate and long-term negative consequences of insomnia, beliefs about the need for control over insomnia). Although developed as an analogue scale, it was transformed into a Likert-type scale, with responses ranging from 1 (strongly disagree) to 6 (strongly agree). Thus, total scores could range from 10 to 60, with higher scores indicating more maladaptive cognitions regarding sleep. The DBAS-10 has moderate reliability and validity.

**Demographic Features**

Age, employment status, and gender were collected in a telephone screening interview. Sleep disorder symptom comorbidity was assessed using the Insomnia Interview Schedule as well as using chart information regarding physician-diagnosed sleep disorder available at the time of screening. Participants were asked about whether they experienced any of the following: snoring, pauses in breathing at night (apnea symptoms); leg twitching or jerking during sleep, awakening with cramps in legs (periodic limb movement symptoms); crawling or aching feelings in the calves, inability to keep legs still (restless legs symptoms); and nightmares, night terrors, sleepwalking/talking, teeth grinding (parasomnia symptoms). If participants endorsed any of these problems, sleep disorder symptom self-report comorbidity was scored as 1 = present. Support for the validity of the method was previously documented. With established reliability and validity, the mini-International Neuropsychiatric Interview, a structured clinical interview for the Diagnostic and Statistical Manual for Mental Disorders axis I disorders, was administered by the study coordinator and used to assess psychiatric comorbidity. We also administered the Clinical Global Improvement Scale (CGI) at the end of Step 1 to measure perceptions of change in sleep. The Clinical Global Improvement Scale-self-report version (CGI) assessed patients’ perceived global improvement. The CGI asked patients to report the overall change in their sleep and in sleep-related effects as a result of participation in their treatment. Participants are asked to rate the change in their sleep and not in any other problem such as chronic pain, depression, or anxiety. Response choices ranged from very much improved (1) to very much worse (7). Evidence of the construct validity of the CGI-self-report version comes from the demonstration that CGI scores are significantly and positively associated with treatment-related changes in sleep parameters (e.g., TST, SE). Lastly, the Client Satisfaction Questionnaire (CSQ) was administered at the end of Step 1 and measured global satisfaction with service.

**Procedure**

Upon physician referral to a teaching hospital behavioral medicine sleep clinic, potential participants received written information describing the services in the clinic and a followup telephone call from a clinic coordinator. Potential participants...
were told that the sleep clinic has a number of services including computerized treatment, on-site single-session consultation, on-site group treatment, and on-site individual treatment. All participants were told that receiving initial computerized treatment for insomnia did not remove the individual from the in-person waitlist or prioritize placement on that waiting list in any way. Participants were next asked whether they would be interested in receiving initial computerized treatment for insomnia. If interested, individuals were phone-screened to determine whether they met inclusion and exclusion criteria for the study and whether they were interested in participating. Informed consent was obtained at this time. Next, information was collected by telephone regarding symptoms of sleep disorders, as well as medical history and current medications (for sleep and any other problem). Additionally, the Mini-International Neuropsychiatric Interview (MINI) was administered by the study coordinator. All participants completed a computerized baseline questionnaire package consisting of 7 days worth of sleep diaries, the MFI, ISI, and DBAS-10.

Once complete, participants entered Step 1. A description of the steps follows:

**Step 1 Intervention**
A 6-week computerized treatment, return2sleep.com, served as the initial step. Components were psychoeducation (week 1), relaxation training (week 2), stimulus control and sleep restriction (week 3), cognitive therapy (week 4), sleep hygiene education (week 5), and mindfulness meditation (week 6). Participants logged onto the website from their homes, completed homework, and received automated feedback about their progress.

**Step 2 Intervention**
The step 2 intervention consisted of an on-site single-session consultation with a staff psychologist or psychological associate in the clinic. During this appointment, progress was reviewed and ideas regarding further cognitive behavioral intervention were generated.

**Step 3 Intervention**
The step 3 intervention consisted of a manualized 6-week on-site cognitive behavioral group treatment program. Groups met weekly for 90-min sessions, and were led by a clinical psychologist or psychological associate. There were 5 to 6 members per group. Treatment components were identical in content and sequence to the computerized program.

**Step 4 Intervention**
The step 4 intervention consisted of individual psychotherapy conducted by a clinical psychologist, resident, or psychological associate in the clinic. Intervention was uniquely tailored to the patient.

After the beginning of step 1, a brief e-mail was sent at week 3 inquiring into whether they were having any difficulties with the site, and then again at week 6 and week 10 to prompt them to re-do the questionnaire measures and the sleep diaries. At week 6, participants completed the CGI and CSQ. After week 10, there was no further contact with participants until their name came to the top of the clinic in-person waiting list. At this time, participants were contacted by telephone by a receptionist or staff psychologist to inquire about the need for and interest in having a one-session on-site consultation (step 2). Interested individuals had appointments scheduled and disinclined individuals were asked about reasons for declining. At the end of the on-site consultation meeting, interest in and need for further treatment of insomnia were reviewed with the participant, and a description of the group treatment program (step 3) was provided. Interested individuals began group treatment. At the end of the group treatment program, interest in and need for further individual treatment of insomnia (step 4) was discussed. Interested individuals were assigned a therapist. Sleep diaries were administered at the beginning of steps 1, 2, and 3, but not step 4. The ISI, DBAS-10, and MFI were administered at the beginning of steps 1 and 2 but not the remaining steps. The lack of standardization of test administration reflected that the primary intent of the study was to assess service uptake rather than outcomes at the various steps. The study was approved by the ethics review board at the University of Manitoba.

**RESULTS**
Results were analyzed using multinomial logistic regression. The criterion variable was final step (1 = return2sleep.com, 2 = single session consultation, 3 = group treatment, 4 = individual treatment). Prior to analysis, all assumptions of the approach were evaluated. Preliminary inspection of missing data revealed that there were complete questionnaire and sleep diary data at step 1, that 20% of questionnaire data and 36.8% of sleep diary data were missing at step 2, and that 36.4% of sleep diary data were missing at step 3. As a result, missing values analysis was conducted using SPSS v. 18, and missing values were imputed.

Of the initial set of participants, results in Figure 1 illustrate that 35% (19/50) moved up to step 2, 22% (11/50) moved up to step 3, and 6% (3/50) moved up to step 4. For comparison purposes, existing volume data from this clinic showed that, in the 8 years prior to the introduction of the stepped care model, 71% of referred patients received group treatment (what we are referring to as step 3).

To conduct the logistic regression analysis, we removed 3 individuals (those in receipt of step 4) due to insufficient numbers in cells. This resulted in a final sample size of n = 47 for the regression analyses. Results from examination of hypothesis one are presented in Table 3, and illustrate that age and employment status but not gender affected movement up the care pathway. For each one unit change in age (from younger to older), the odds of receiving the step 3 intervention increased by 85.7%. For each one unit change in employment status (from employed to unemployed), the odds of receiving the step 3 intervention increased by 95%. There was no significant impact of demographic variables predicting receipt of the step 2 intervention.

Results from examination of hypothesis two are presented in Table 4 and show that SQ at step 1 (return2sleep.com) significantly predicted movement up the stepped care pathway. For each one unit improvement in SQ, the odds of receiving the step 3 intervention decreased by 91%. Alternatively put, less favorable SQ was associated with more intensive service receipt. There was no significant impact of SOL or WASO at step 1 on movement up the stepped care pathway. There was no significant impact of SQ, SOL, or WASO at step 1, or change in these.
variables predicting the odds of receiving the step 2 intervention. Thus, response to treatment did not affect receipt of more intensive services.

Results in Table 5 illustrate that SOL at step 2 significantly predicted movement up the stepped care pathway. For each one unit change in SOL, the odds of receiving the step 3 intervention increased by 22-fold. Less favorable SOL predicted receipt of the step 3 intervention. Neither SQ nor WASO at step 2 predicted movement up the steps, nor did change in these variables from step 1 to step 2. Thus, response to treatment did not affect receipt of more intensive services.

Results showed that scores on the MFI-20, DBAS-10, and ISI at step 1 (or step 2) did not significantly predict movement up the steps. Results from examination of hypothesis three showed that neither psychiatric nor sleep symptom comorbidity significantly increased the odds of moving up the stepped care pathway. Among those with psychiatric comorbidity, those who did not proceed to step 2 reported no change in the frequency of nights of medication use (M = 0); those who proceeded to step 2 had fewer nights of medication usage (M = 33.33% SD = 57.7); and those proceeding to step 3 had no change in frequency of medication use (M = 0). Thus, for those with psychiatric comorbidity, it seems unlikely that increased medication use was responsible for the lack of receipt of more intensive services. A similar pattern of findings was observed for sleep symptom comorbidity.

Of this series of patients, 3 requested access to the step 1 treatment (return2sleep.com) after the conclusion of the step 3 intervention (group therapy). When examined, we noted that none of these individuals re-accessed the online program despite receiving a new username and password. Results in Table 6 illustrate the average sleep diary scores for data that was available at steps 1 (n = 50/50), 2 (n = 12/19), and 3 (n = 7/11). Both data from completers and multiply imputed data are presented. As a group, those in receipt of the step 3 intervention have experienced improvements in sleep compared to baseline.
to baseline (prior to step 1). Next, we examined perceived improvement and satisfaction with step 1. Of those who did not proceed from step 1 to step 2, 81.8% reported improvement in sleep on the Clinical Global Improvement Scale (CGI). On the Client Satisfaction Questionnaire (CSQ), and of those who did not proceed from step 1 to step 2, 83.3% rated the quality of step 1 service as good to excellent, 75% indicated that they had received the service that they wanted (in step 1), 66.7% reported that most of their needs had been met in step 1, 83.3% reported that if a friend were in need of similar type of help, that they would recommend step 1, and 75% reported that services received in step 1 helped them to more effectively manage their problem. Of those who did not proceed from step 1 to step 2, 45.5% had sleep efficiency > 85%, and 45.0% had scores on the Insomnia Severity Index which fell below a clinical cutoff suggestive of insomnia (i.e., 13.0). These results indicate that approximately half the sample that completed step 1 had sleep in the normative range, but that a larger number were satisfied with the changes and felt themselves to be improved.

DISCUSSION

This was a case series study of 50 adults presenting for psychological treatment of chronic insomnia and proceeding through a stepped care model. As such, it represents one of the first illustrations of the use of stepped care for insomnia in a public health setting. An important finding of the study was that fewer participants accessed the more intensive steps (e.g., group and individual therapy) when provided with an initial low-intensity intervention (return2sleep.com). Although not a controlled investigation, prior to the advent of this stepped care model, 71% of referred patients were receiving more intensive services (group treatment) at this site, compared to the rate of 22% noted in this case series study. Stepped care approaches, where non-responders to a less intensive therapy receive a more intensive intervention, aim to only provide intensive assistance to those who need it, thereby allocating therapeutic resources more efficiently. From a stepped care perspective, this particular model increased service efficiency by 69%. One way of envisioning how stepped care might work to treat the thousands of people with insomnia is to provide steps 1-3 in primary care, and step 4 at a specialty sleep clinic.

A second main finding of the study was that belonging to particular demographic groups (being older, unemployed) and having poor sleep (quality and latency) predicted receipt of more intensive services for insomnia. This is consistent with results from other research examining consultation patterns for those with insomnia.1,13,14 These authors reported that increasing age, more severe insomnia, and greater unemployment predicted patient consultation for the problem of insomnia. Practical considerations such as increased time available for treatment may explain why the older and unemployed were more likely to receive on-site services. In the current study, the converse finding was that younger individuals were less likely to pursue more intensive services. Other researchers have shown that younger individuals may be more receptive to technology and may have better outcomes in self-administered treatments.25 Of course other explanations are also possible and are discussed below. Available sleep diary and perceived improvement data suggest that the number of participants who became normal sleepers in step 1 was modest but perhaps typical of CBT-I self-help interventions for insomnia. A review of the effectiveness of self-help CBT-I showed that normative sleep at the end of treatment programs is typically in the range of 18% to 50%.26 In this study, an even larger number of patients detected an improvement in their sleep and were satisfied with the step 1 intervention. After receipt of step 1, approximately 50% were sleeping optimally, but the group as a whole may have had a renewed sense of hopefulness or perhaps a greater feeling of mastery associated with having some improvement in a challenging and chronic health problem. The finding that satisfaction ratings outstrip sleep status has also been found with in-person programs.

A third main finding of the study was that neither psychiatric nor sleep disorder symptom comorbidity predicted receipt of more intensive services. This is noteworthy, given that 60% of the sample met DSM-IV criteria for an axis I disorder, and approximately 22% had symptoms suggestive of alternative sleep disorders. These results suggest that individuals with comorbidity may not perceive greater need for more intensive services, may be satisfied with brief interventions, or have received additional treatments (e.g., psychiatric medications) during the course of stepped care, may have been demoralized by a poor outcome with low-intensity treatments, and/or may feel that more intensive behavioral intervention for sleep will not address a significant part of their sleep problem. A recent investigation in our laboratory showed that return2sleep.com was largely robust to psychiatric and sleep symptom comorbidity, suggesting that these groups were not disadvantaged in terms of clinical improvements associated with a low-intensity treatment (our step 1).30 Thus, both lack of significant improvement at step 1 with consequent low morale is probably an unlikely explanation for why individuals with comorbidities did not receive more intensive services in this stepped care model. Additionally, we did not find that those with comorbidities were more likely to be receiving extra medication treatments such as antidepressants or sleeping agents. Anecdotal information provided by participants in this study suggested that there was reduced need for service after completion of a low-intensity step 1 intervention. The current investigation also found that daytime fatigue, and less/more dysfunctional beliefs about sleep did not predict movement up the stepped care pathway. Fatigue in particular may not be a sufficient impediment to receiving more intensive services for insomnia.

A fourth ancillary finding of this study is that very few patients actually “stepped down” in this pathway. At the conclusion of group treatment, only 3 patients requested renewed access to return2sleep.com, and none of the patients who received individual therapy requested to rejoin a group treatment. Examination of web usage patterns reveals that these individuals did not actually revisit the site. Instead it seems that access to the website served as a reassuring aid, much like having a bottle of sleeping medicine that is rarely used near the bedside.

This study involving the use of stepped care for insomnia in routine clinical practice had a number of limitations. Some
of these include the use of a single publicly funded site and a single model to obtain this data, lack of complete outcome data for each of the steps in the model owing to the emphasis on service receipt rather than outcomes, and small sample size. Using this model at other sites might produce differing results owing to contextual factors. Upon referral, patients access health services such as this one at no charge after providing their healthcare number. Our staff are equally comfortable with providing low- and high-intensity treatments, and there was no perceived threat associated with providing self-administered treatments. This might not be the same in other contexts where low remuneration for behavioral sleep services is the norm. Additionally, the decision to step up in this stepped care model is mutually agreed upon between staff and patients, and there is/was a lack of standardized criteria to make this decision. It is possible that bias was introduced at these points. Future studies will determine whether patient and provider decision-making is inferior or superior to numerical decision aids regarding stepping up or down in stepped care pathways. Lastly, this was an uncontrolled study, so it is possible that other factors (e.g., spontaneous remission, regression to the mean) explained movement outside of the study explained movement up the steps.

Future Research

There are a number of plausible factors that may drive movement up a care pathway, some of which pertain to individual-level variables and others to contextual level variables. Individual variables may include perceived need, convenience, belief in the importance of working with a professional to solve health problems, and degree of social support. Contextual factors may include advice from others to seek care for insomnia and policies which facilitate or impede access to care for insomnia. Although this investigation focused on individual-level variables, more examination of contextual factors would be an important future area of study. For example, a study that compared a publicly funded stepped care model with a privately funded one would provide an interesting examination of context in the use of step care. Future investigations should compare outcomes in stepped care models for insomnia and contrast this with treatment as usual. The efficiency produced by stepped care models is only as good as the outcomes that the models produce. In the absence of data showing that the outcomes are at least as good as treatment as usual, stepped care is not a viable future opportunity in this area. More qualitative study of why individuals choose to proceed to more intensive services may prove to be very fruitful in this area.

REFERENCES

Sleep is a highly complex physiological process that accounts for approximately 40% of a child’s life by the age of 18 years. Obtaining sufficient sleep is important for multiple aspects of health and well-being in children. Disturbed or insufficient sleep has been associated with obesity and the lack of data on the subjective experience of sleep quality, which requires direct input from children and parents. As of 2011, more than 180 patient-reported measures had been developed to assess pediatric sleep; while there are several adolescent self-report measures, very few measures have been validated for children ages 8-12 years.

Children as young as 8 years of age can provide reliable, valid, and meaningful reports of health when developmentally appropriate assessment methods are applied. A recent Good Research Practices Task Force Report from the International Society of Pharmacoeconomics and Outcomes Research recommended the feasibility and reliability of self-reports in children 8-12 years.

The Children’s Report of Sleep Patterns (CRSP): A Self-Report Measure of Sleep for School-Aged Children


1National Jewish Health, Denver, CO; 2University of Alabama at Birmingham, Birmingham, AL; 3Monash Institute of Medical Research, Melbourne, Australia; 4University of South Australia, Adelaide, Australia; 5St. Jude Children’s Research Hospital, Memphis, TN; 6Children’s Hospital of Philadelphia, Philadelphia, PA

Study Objectives: (1) Present preliminary psychometrics for the Children’s Report of Sleep Patterns (CRSP), a threemodule measure of Sleep Patterns, Sleep Hygiene, and Sleep Disturbance; and (2) explore whether the CRSP provides information about a child’s sleep above and beyond parental report.

Methods: A multi-method, multi-reporter approach was used to validate the CRSP with 456 children aged 8-12 years (inclusive). Participants were recruited from pediatrics’ offices, sleep clinics/laboratories, children’s hospitals, schools, and the general population. Participants completed measures of sleep habits, sleep hygiene, anxiety, and sleepiness, with actigraphy and polysomnography used to provide objective measures of child sleep.

Results: The CRSP demonstrated good reliability and validity. Differences in sleep hygiene and sleep disturbances were found for children presenting to a sleep clinic/laboratory (vs. community population); for younger children (vs. older children); and for children who slept less than 8 hours or had a sleep onset later than 22:00 on actigraphy. Further, significant associations were found between the CRSP and child-reported anxiety or sleepiness. Notably, approximately 40% of parents were not aware of child reported difficulties with sleep onset latency, night wakings, or poor sleep quality.

Conclusions: The three modules of the CRSP can be used together or independently, providing a reliable and valid self-report measure of sleep patterns, sleep hygiene, and sleep disturbances for children ages 8-12 years. Children not only provide valid information about their sleep, but may provide information that would not be otherwise captured in both clinical and research settings if relying solely on parental report.

Keywords: Children, sleep, sleep hygiene, sleep patterns, sleep disturbances, validation, measurement, self-report

Citation: Meltzer LJ; Avis KT; Biggs S; Reynolds AC; Crabtree VM; Bevans KB. The Children’s Report of Sleep Patterns (CRSP): a self-report measure of sleep for school-aged children. J Clin Sleep Med 2013;9(3):235-245.

BRIEF SUMMARY

Current Knowledge/Study Rationale: Children as young as 8 years old can report on their own health, yet few self-report sleep measures exist for 8-12 year old children. The Children’s Report of Sleep Patterns (CRSP) was developed to provide a multi-dimensional self-report questionnaire for school-aged children.

Study Impact: This study demonstrates that the CRSP is a valid and reliable self-report measure of sleep patterns, sleep hygiene, and sleep disturbances in school-aged children. This measure can provide complementary information to parental report in both clinical settings and research studies.
Vocabulary and/or disease concepts, as shown with both cognitive interviews and when using Likert scales.

While none of these studies looked at sleep constructs per se, several studies have found that child report can provide information that is useful and unique from parental report. Indeed, the inclusion of children’s perspectives about sleep may provide insight in both clinical and research settings that may be missed if relying solely on parental report. One study found that in the absence of children’s report, one-third of sleep problems may go unidentified. Despite the literature suggesting the value of child report, the need remains for a comprehensive self-report measure of children’s sleep that provides an accompanying view to parental report. Because of the need for a well-validated self-report measure of sleep in children ages 8-12 years, we developed the Children’s Report of Sleep Patterns (CRSP), a questionnaire that includes three modules (Sleep Patterns, Sleep Hygiene Index, Sleep Disturbances Scale) that can be used independently or in combination. Based on the existing literature, clinical experience, and interviews with pediatric sleep experts, these three modules were chosen due to their potential to identify sleep problems or insufficient sleep.

As children get older, sleep patterns change with later bedtimes and less parental involvement with the child’s sleep routine. Although parents may have a good sense of the child’s bedtime and wake time, they may not be aware of what happens once the child tries to fall asleep or during the night. For example, more than 60% of 5th graders in one study reported being awake at least several nights per week when parents thought they were asleep. As parents may not be aware of later bedtimes, difficulties falling asleep, or night wakings that can contribute to insufficient sleep, children’s self-report of sleep patterns should be considered.

A limited number of published studies have examined sleep hygiene (e.g., caffeine, technology in the bedroom) in children and adolescents. However, to our knowledge, no studies have examined the self-reported sleep hygiene of typically developing healthy children. Since parents may be unaware of certain aspects of children’s sleep hygiene (e.g., caffeine consumption during the day or technology usage in the bedroom), it is important to include sleep hygiene in a self-report measure for children as young as 8 years.

For sleep disturbances, such as sleep disordered breathing or partial arousal parasomnias, parental report is likely to be more accurate than child report, since the child may be unaware of snoring at night or sleepwalking on occasion. However, for disorders of initiating and maintaining sleep, sleep-wake transition, or sleep arousal, children’s reports may provide complementary information. In addition, unless asked, children may not report discomfort that they experience at bedtime or during the night, and as such parents may be unaware of it. This discomfort could be symptomatic of restless legs syndrome or another underlying cause of sleep disruptions (e.g., pain). In one study, nearly one-third of children reported significant body pains during the night that the parents were not aware of. Thus, there is a need for a measure that asks children directly about symptoms of sleep disturbances.

This report provides preliminary psychometrics for the Children’s Report of Sleep Patterns (CRSP), a multidimensional self-report measure for children that provides a complementary report for clinicians and researchers. This paper addresses two questions: (1) Is the CRSP a valid and reliable self-report measure of sleep for children? and (2) Does the inclusion of a child self-report measure such as the CRSP provide information about a child’s sleep that enhances parental report and/or would not be captured by parental report alone?

Methods

Participants

Six hundred seventy children were recruited from the following settings: (1) primary care pediatricians’ offices, (2) an outpatient pediatric sleep clinic, (3) community flyers and advertisements, (4) two independent Australian schools, (5) two different pediatric sleep laboratories, and (6) outpatient clinics or inpatient units of a children’s hospital for oncology patients (Table 1). Institutional review board approval was obtained for each individual site, and informed consent/assent was obtained from all participants.

A total of 456 children completed the Children’s Report of Sleep Patterns (CRSP), a 68% participation rate. Children who completed the CRSP were 49% male, had a mean age 10.1 years (range 8-12 years inclusive, distributed across ages: 8 years = 16.7%, 9 years = 22.6%, 10 years = 21.3%, 11 years = 16.0%, 12 years = 23.5%), and were 62.6% White, 29.0% Black, 4.1% Hispanic, 1.6% Asian, and 2.8% Other. The most common reasons for not participating were not enough time or not interested. No significant difference between participants and non-participants was found for any demographic variable, including age distribution. Complete demographic information is seen in Table 1. Information about race was not collected for the Australian sample.

Measures

While all participants completed the CRSP, other measures were not uniformly collected across sites. Table 1 shows the different measures completed by each group of participants.

Children’s Report of Sleep Patterns (CRSP)

The Children’s Report of Sleep Patterns (CRSP) is a 60-item questionnaire that has 3 modules: Sleep Patterns, Sleep Hygiene Index, and Sleep Disturbance Scale (Appendix). Sleep Patterns includes questions about bedtimes, wake times, sleep onset latency, night waking frequency and duration, naps, sleep schedule variability, and subjective sleep quality, with separate questions for last night, typical weekdays when the child is in school, typical weekends/holidays when the child is not in school, and overall sleep “most days.” The Sleep Hygiene Index included questions about caffeine use, activities in the hour before bed, sleep location (where child falls asleep and wakes up), and electronics used at the time of sleep onset. The Sleep Disturbance Scale had questions about bedtime fears/worries, restless legs syndrome symptoms, parasomnias, and insomnia. Additional indicator items were included for snoring, enuresis, and nightmares. Higher scores indicate poorer sleep hygiene or greater sleep disturbances.
The Sleep Hygiene Index and Sleep Disturbance Scale questions were asked in regards to a typical week. For most items the following Likert-type scale was used: “Never” (never happens), “Not very often” (less than once a week), “Sometimes” (once or twice a week), “Usually” (3-5 times a week), or “Always” (every day). For 5 sleep disturbance items that occur during sleep (snoring, kicking, restless sleep, sleep talking, sleepwalking/terrors), children were asked if anyone told them that they engaged in these behaviors. Answer choices were: “All the time,” “Sometimes,” or “Never.”

Items were developed based on the existing literature and clinical experience of the investigators. Once developed, a group of 15 pediatric sleep experts (physicians, nurses, and psychologists) reviewed the items and were asked to place each item into one of the 3 modules (Sleep Patterns, Sleep Hygiene Index, Sleep Disturbance Scale), and then into the specific indices/scales (e.g., Caffeine Use, Restless Legs). All items had > 53% agreement across experts, with the majority (77%) of items achieving consensus rates of 87% or above.

Children's Report of Sleep Patterns—Parent Proxy

A parent proxy version of the CRSP was also administered to a subset of parents in both community and sleep laboratory populations (n = 158). This proxy version was used to measure convergent validity. No significant differences were found between children whose parents completed the CRSP Proxy and children whose parents did not complete the CRSP Proxy.

Children's Report of Sleep Patterns—Sleepiness Scale

The Children’s Report of Sleep Patterns–Sleepiness Scale (CRSP-S) has 5 items that ask children to recall how often they felt sleepy or fell asleep in different situations (at school, during short car rides, while playing, while eating, and while talking). Higher scores indicate more sleepiness.

Multidimensional Anxiety Scale for Children–10 Item

The Multidimensional Anxiety Scale for Children–10 item (MASC-10) is a child self-report measure of anxiety. This well-validated measure has been used as a screening tool in both clinical and research settings. The 10 items are summed to provide a single score, which is then translated to a standard T-score. The MASC-10 was used as a measure of construct validity in a subset of 159 participants in pediatricians’ offices or an outpatient sleep clinic.

Children's Sleep Habits Questionnaire (CSHQ)

The Children’s Sleep Habits Questionnaire (CSHQ) is a 45-item parent-report measure of children’s sleep. Parents are asked to recall sleep behaviors during a typical recent week. The CSHQ has demonstrated adequate reliability (coefficient α 0.68 to 0.78, test-retest 0.62 to 0.79) and validity, differentiating between children with and without sleep disorders. For the current study, subscale scores and the total Sleep Disturbances score were used to examine construct validity. For the CSHQ, higher scores indicate greater sleep disturbances. The CSHQ was completed by a subset of 159 parents in pediatricians’ offices and an outpatient pediatric sleep clinic.

Children's Sleep Hygiene Scale

The Children’s Sleep Hygiene Scale (CSHS) is a 22-item parent-report measure of children’s sleep hygiene. This measure has demonstrated adequate reliability (coefficient α 0.60 to 0.86) in studies of children and adolescents. Subscale scores of the CSHS (physiological, cognitive, environmental, emotional, bedtime routines, sleep stability) were used to examine construct validity. For the CSHS, higher scores suggest better sleep hygiene. The CSHS was completed by a subset of 159 parents in the pediatricians’ offices and outpatient pediatric sleep clinic.
The Micro Motionlogger Sleep Watch (Ambulatory Monitoring Inc., Ardsley, NY) was worn by 90 children (recruited from the community through advertisements and peer-nominations) for one week on their nondominant wrist. Data were excluded for one participant due to a device failure (n = 1), resulting in usable actigraphy data for 89 children. Data were collected in 1-min epochs using the zero crossing mode and the Sadeh algorithm. Sleep onset time and sleep offset time were manually scored using the 3/5-minute rule (first min of 3 consecutive min of sleep for sleep onset, last minute of 5 consecutive min of sleep for sleep offset). Participants pressed an event marker to indicate the time they attempted to fall asleep at night and the time they woke in the morning. In addition, participants kept a concurrent daily sleep diary that was used to facilitate the scoring of sleep intervals and identify artifact. Measures derived for this study were sleep onset time, sleep offset time, and total sleep time (TST: minutes of sleep from sleep onset to sleep offset).

### Polysomnography

Overnight polysomnography (PSG) was performed on 110 clinically referred children using either the Rembrandt polysomnography system (n = 61; Embla, Broomfield, CO) or the Sandman 9.2 PSG system (n = 49; Embla, Broomfield, CO). Recorded parameters included electroencephalography (F3-M2, F4-M1, C3-M2, C4-M1, O1-M2, O2-M1); left and right electrooculogram; submental electromyogram; bilateral titial electromyogram; electrocardiogram; oronasal airflow with 3-pronged thermistor; nasal pressure with pressure transducer; rib cage and abdominal wall motion via respiratory impedance plethysmography; and end-tidal capnometry. Arterial oxygen saturation with pulse waveform was also recorded, as well as digital video and audio. Studies were scored based on American Academy of Sleep Medicine (AASM) pediatric criteria. The apnea-hypopnea index (AHI) was the primary variable of interest, with the AHI also providing severity of obstructive sleep apnea (no OSA: AHI < 1.5; mild OSA: AHI = 1.5-5, moderate/severe OSA: AHI > 5).

### Data Analyses

Composite scores were created for each of the 4 Sleep Hygiene indices and 4 Sleep Disturbances scales. Preliminary analyses were conducted to examine age differences across groups used for comparison (e.g., clinical vs. community, > or < 8 h of actigraphic recorded sleep). If significant differences were found, age was controlled for (ANCOVA) in those analyses.

### Reliability and Validity of CRSP

#### Reliability

Cronbach α coefficients were used to measure internal consistency for the individual Sleep Disturbance scales. Because there were multiple indicators for each Sleep Hygiene index score that may not be related (e.g., a child who drinks soda may not also drink tea or coffee, but together these items indicate the frequency of caffeine use), we did not evaluate the internal consistency for sleep hygiene indices. Test-retest reliability (n = 123, mean days between administration = 19.2, range 7-28 days) was examined with Pearson correlation coefficients for indices/scales and Spearman rank order correlations for the individual items; paired t-tests were used to compare time 1 and time 2 sleep hygiene indices and sleep disturbances scales.

### Validity

Primary analyses including the full sample examined construct validity with group comparisons for the index/scale scores using ANOVA or ANCOVA (n = 456). Comparisons were made for group (clinical vs. community); age (8-10 years vs. 11-12 years); typical sleep quality (great/good vs. okay/poor); and typical nap frequency (always/sometimes vs. never/only when sick). Based on clinical experience, it was expected that more sleep disturbances would be reported in the clinical sample, that poorer sleep hygiene would be reported in older children, and that more sleep disturbances and poorer sleep hygiene would be reported in children with poor sleep quality or children who nap more frequently.

Convergent and divergent validity were further evaluated with Pearson correlation examining the association between the index/scale scores and both child-reported daytime sleepiness (n = 456) and child-reported anxiety (n = 159).

Secondary analyses to examine criterion validity were conducted with subsamples of the study population. For children who wore actigraphy (n = 89), one-way ANOVA or ANCOVA was used to examine differences in sleep hygiene and sleep disturbances between (1) children getting < and > 8 h of sleep (per actigraphy) and (2) children with a sleep onset time before and after 22:00 (per actigraphy, time determined by median split). Further, differences in actigraphic sleep onset time, sleep offset time, and TST were examined with one-way ANOVA for children who napped regularly (sometimes/always) versus infrequently (never/only when sick). For children who had overnight PSG (n = 110), one-way ANOVA was used to examine differences in sleep hygiene and sleep disturbances for children without OSA (AHI < 1.5), mild OSA (AHI 1.5-5), and moderate/severe OSA (AHI > 5); and Pearson correlation was used to examine the association between child reported sleep disturbances and AHI.

Parent-completed legacy measures (CSHQ and CSHS) were also used to examine validity. Pearson correlation was used to examine the association between child-reported sleep (CRSP) and parent-reported sleep patterns and sleep disturbances (CSHQ, n = 159), as well as the association between child-reported (CRSP) and parent-reported sleep hygiene (CSHS, n = 159). In addition, one-way ANCOVA was used to examine differences in sleep hygiene and sleep disturbances for children scoring above and below the clinical cutoff of 41 on the CSHQ.

### Value Added of Child Self-Report of Sleep

The value of child report was examined 2 ways. First, using the question “Most nights do you consider yourself to be a _____ sleeper” (great/good, okay/poor), differences in parental report of sleep (CSHQ and CRSP) were examined. Second, Cohen κ was used to examine interrater reliability for sleep pattern variables (Child CRSP and parent proxy CRSP, n = 156; questions about “Last Night”: sleep onset latency [SOL], night waking frequency, and sleep quality; as well as questions about “Typical Night”: weekday bedtime, wake time, night waking
frequency, and sleep quality). The mean, standard deviation, intraclass correlations, and effect size were used to examine parent-child agreement for the Sleep Hygiene Indices and the Sleep Disturbances Scales.

**RESULTS**

Means and standard deviations for individual items, Sleep Hygiene Indices, and Sleep Disturbances Scales can be found in Table 2; a correlation matrix for the indices/scales can be found in Table 3.

**Reliability**

As seen in Table 2, with the exception of the 2-item Parasomnia Scale ($\alpha = 0.64$), the Cronbach $\alpha$ coefficients for the Sleep Disturbance scales were acceptable ($\alpha \geq 0.70$). Test-retest reliability in general was good for all subscales, with correlations $> 0.80$ for all indices/scales with the exception of the Restless Legs Scale ($r = 0.65$). Differences from time 1 to time 2 were found for the Sleep Location Index Score, with children sleeping in a location other than their own bed more often at time 1.

**Construct Validity**

**Group Differences**

Significant group differences were found (controlling for age), with children presenting to a sleep clinic, sleep laboratory, or pediatric oncology hospital reporting poorer sleep hygiene (sleeping somewhere other than their own bed, more electronics at sleep onset; Table 4) and more sleep disturbance (more symptoms of bedtime fears/worries, restless legs syndrome, parasomnias, and insomnia; Table 5). Further, children in the clinical sample reported more snoring and enuresis more often than children in the community sample.

Differences between age groups were found for sleep hygiene (Table 4), with younger children reporting less caffeine use and engaging in fewer stimulating activities in the hour before bed than older children, but sleeping somewhere other than their own bed more often than older children.

Compared to children who classified themselves as good sleepers, children who classified themselves as poor sleepers reported both poorer sleep hygiene (sleeping somewhere other than their own bed, more frequent use of electronics at sleep onset, Table 4) and more sleep disturbances (more bedtime fears/worries, and more symptoms of RLS, parasomnias, and insomnia, Table 5). Further, poor sleepers reported more frequent snoring, enuresis, and nightmares.

Finally, children who reported regular napping also reported poorer sleep hygiene, including more caffeine use, more stimulating activities in the hour before bed, sleeping somewhere other than their own bed, and more electronics use at sleep onset (Table 4).

**Convergent and Divergent Validity**

**Child-Reported Sleepiness**

Significant associations ($p \leq 0.002$) were found between child-reported daytime sleepiness and all of the CRSP Sleep Hygiene Indices and Sleep Disturbances Scales. The strongest associations suggested that children who had greater daytime sleepiness also sleep somewhere other than their own bed ($r = 0.33$), use electronics more often at sleep onset ($r = 0.27$), and have more symptoms of RLS ($r = 0.38$).

**Child Reported Anxiety**

Significant associations ($p \leq 0.007$) were found between child reported anxiety (MASC-10) and the Sleep Location Index ($r = 0.21$), the Bedtime Fears/Worries Scale ($r = 0.42$), the Insomnia Scale ($r = 0.24$), and the Parasomnia scale ($r = 0.22$), suggesting that children who report more anxiety also report sleeping somewhere other than their own bed, more bedtime fears/worries, and more symptoms of insomnia and parasomnias. A significant association was also found between self-reported anxiety and nightmares ($r = 0.35$). As expected, other indices/scales were not correlated with anxiety.

**Secondary Analyses**

**Actigraphy**

Children with shorter sleep duration and a later bedtime were older than children with longer sleep duration and an earlier bedtime; thus age was controlled for in these analyses. Of the children who underwent actigraphy, those who slept $< 8$ h/night reported more symptoms of insomnia and more frequent snoring than children obtaining $> 8$ h of sleep per night (Table 5). Children with a sleep onset later than 22:00 reported more caffeine use, more stimulating activities in the hour before bed, sleeping more often somewhere other than their own bed, and more nightmares (Table 4).

**Polysomnography**

Children who had moderate/severe OSA (AHI > 5) reported more snoring than children without OSA (AHI = 0, $F_{2,107} = 4.06$, $p = 0.02$). No other differences on the CRSP were found between children with no, mild, or moderate/severe OSA. AHI was significantly correlated with the snoring item ($r = 0.25$, $p = 0.01$), but was not correlated with any of the Sleep Hygiene Indices or Sleep Disturbances Scales.

**Parent-Reported Sleep Disturbances (CSHQ)**

When parents reported poor sleep quality (above the clinical cutoff of 41 on CSHQ, controlling for child age) children reported sleeping somewhere other than their own bed and greater use of electronics at sleep onset; more symptoms of bedtime fears/worries, parasomnias, and insomnia; and more frequent snoring and enuresis (Tables 4 and 5).

Significant associations ($p \leq 0.006$) were found between the CSHQ and the CRSP for both the Sleep Hygiene Indices and Sleep Disturbances Scales. For the Sleep Hygiene Indices, children who reported sleeping somewhere other than their bed had parents who reported more bedtime resistance ($r = 0.42$) and more sleep anxiety ($r = 0.29$). Similarly, children who reported greater use of electronics to fall asleep had parents who reported more bedtime resistance ($r = 0.23$), greater sleep onset delay ($r = 0.30$), and more sleep anxiety ($r = 0.28$). Further, children who reported more worries at bedtime had parents who reported more bedtime resistance ($r = 0.40$), greater sleep onset delay ($r = 0.24$), and more sleep anxiety ($r = 0.48$).
### Table 2—Descriptive statistics (mean, SD), internal consistency (coefficient α), correlations and paired t-tests for CRSP Sleep Hygiene Indices and Sleep Disturbances Scales for the full sample and test-retest sample

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Sleep Hygiene Indices</th>
<th>Mean (SD)</th>
<th>α</th>
<th>Time</th>
<th>Mean (SD)</th>
<th>Time</th>
<th>r</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Caffeine Index</td>
<td>6.21 (2.4)</td>
<td>–</td>
<td>5.98</td>
<td>(2.2)</td>
<td>5.84</td>
<td>0.84</td>
<td>1.25</td>
<td>0.22</td>
</tr>
<tr>
<td></td>
<td>Regular or diet soda with caffeine (Coke, Pepsi, Dr. Pepper, Mountain Dew</td>
<td>2.66 (1.2)</td>
<td></td>
<td>2.58</td>
<td>(1.2)</td>
<td>2.50</td>
<td>0.80</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Iced tea or hot tea (with caffeine)</td>
<td>2.12 (1.3)</td>
<td></td>
<td>2.00</td>
<td>(1.2)</td>
<td>1.90</td>
<td>0.81</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Coffee (with caffeine)</td>
<td>1.44 (0.8)</td>
<td></td>
<td>1.46</td>
<td>(0.8)</td>
<td>1.49</td>
<td>0.85</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Activities Hour Before Bed Index</td>
<td>16.66 (3.2)</td>
<td>–</td>
<td>16.55</td>
<td>(3.0)</td>
<td>16.71</td>
<td>0.82</td>
<td>-0.90</td>
<td>0.37</td>
</tr>
<tr>
<td></td>
<td>Have activities (sports, dance, music, other activities)</td>
<td>2.61 (1.4)</td>
<td></td>
<td>2.86</td>
<td>(1.4)</td>
<td>2.98</td>
<td>0.76</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Email or instant message with friends</td>
<td>2.05 (1.3)</td>
<td></td>
<td>2.02</td>
<td>(1.2)</td>
<td>2.01</td>
<td>0.80</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Watch television or movies</td>
<td>3.83 (1.0)</td>
<td></td>
<td>3.77</td>
<td>(1.0)</td>
<td>3.72</td>
<td>0.69</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Play video games or computer games</td>
<td>3.08 (1.2)</td>
<td></td>
<td>2.82</td>
<td>(1.3)</td>
<td>2.80</td>
<td>0.77</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Take a bath or shower</td>
<td>2.14 (1.2)</td>
<td></td>
<td>2.30</td>
<td>(1.2)</td>
<td>2.43</td>
<td>0.78</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Read books or magazines</td>
<td>2.75 (1.3)</td>
<td></td>
<td>2.67</td>
<td>(1.2)</td>
<td>2.72</td>
<td>0.72</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sleep Location</td>
<td>10.47 (4.4)</td>
<td>–</td>
<td>9.66</td>
<td>(3.7)</td>
<td>9.12</td>
<td>0.71</td>
<td>2.22</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>Fall asleep in sibling's bed</td>
<td>1.57 (1.0)</td>
<td></td>
<td>1.56</td>
<td>(1.0)</td>
<td>1.45</td>
<td>0.84</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fall asleep in parent's bed</td>
<td>1.92 (1.2)</td>
<td></td>
<td>1.75</td>
<td>(1.0)</td>
<td>1.63</td>
<td>0.82</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fall asleep on couch or other place in the house</td>
<td>1.96 (1.1)</td>
<td></td>
<td>1.78</td>
<td>(0.97)</td>
<td>1.55</td>
<td>0.80</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Wake in sibling's bed</td>
<td>1.49 (1.0)</td>
<td></td>
<td>1.39</td>
<td>(0.8)</td>
<td>1.37</td>
<td>0.78</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Wake in parent's bed</td>
<td>1.81 (1.2)</td>
<td></td>
<td>1.60</td>
<td>(1.0)</td>
<td>1.54</td>
<td>0.80</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Wake on couch or other place in the house</td>
<td>1.73 (1.1)</td>
<td></td>
<td>1.56</td>
<td>(0.9)</td>
<td>1.57</td>
<td>0.62</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Electronics Use at Sleep Onset</td>
<td>6.07 (2.9)</td>
<td>–</td>
<td>5.56</td>
<td>(2.7)</td>
<td>5.34</td>
<td>0.82</td>
<td>1.56</td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td>Is a television on in your room</td>
<td>2.18 (1.6)</td>
<td></td>
<td>1.71</td>
<td>(1.3)</td>
<td>1.67</td>
<td>0.91</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Are you listening to music</td>
<td>2.04 (1.3)</td>
<td></td>
<td>1.91</td>
<td>(1.3)</td>
<td>1.89</td>
<td>0.77</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Is there a light on in your room (other than a nightlight)?</td>
<td>1.86 (1.4)</td>
<td></td>
<td>1.96</td>
<td>(1.4)</td>
<td>1.76</td>
<td>0.73</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sleep Disturbances Scales</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bedtime Fears/Worries Scale</td>
<td>3.64 (1.9)</td>
<td>0.70</td>
<td>3.87</td>
<td>(2.1)</td>
<td>3.73</td>
<td>0.88</td>
<td>1.53</td>
<td>0.13</td>
</tr>
<tr>
<td></td>
<td>Scared at sleep onset</td>
<td>1.78 (1.1)</td>
<td></td>
<td>1.86</td>
<td>(1.2)</td>
<td>1.81</td>
<td>0.81</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Upset/worried at sleep onset</td>
<td>1.86 (1.1)</td>
<td></td>
<td>2.02</td>
<td>(1.2)</td>
<td>1.93</td>
<td>0.80</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Restless Legs Scale</td>
<td>9.70 (3.4)</td>
<td>0.72</td>
<td>10.00</td>
<td>(2.6)</td>
<td>9.88</td>
<td>0.65</td>
<td>0.51</td>
<td>0.61</td>
</tr>
<tr>
<td></td>
<td>Funny feelings in your legs</td>
<td>1.79 (1.0)</td>
<td></td>
<td>1.78</td>
<td>(1.0)</td>
<td>1.72</td>
<td>0.76</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Legs bother you at bedtime or during night</td>
<td>1.76 (1.0)</td>
<td></td>
<td>1.77</td>
<td>(1.0)</td>
<td>1.74</td>
<td>0.70</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Have to move legs at bedtime/during night</td>
<td>2.28 (1.3)</td>
<td></td>
<td>2.21</td>
<td>(1.3)</td>
<td>2.04</td>
<td>0.72</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kick your legs when sleeping</td>
<td>1.76 (0.8)</td>
<td></td>
<td>2.33</td>
<td>(0.8)</td>
<td>2.32</td>
<td>0.82</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Move a lot in sleep</td>
<td>2.08 (0.8)</td>
<td></td>
<td>1.90</td>
<td>(0.8)</td>
<td>2.12</td>
<td>0.62</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Parasomnias Scale</td>
<td>2.84 (1.1)</td>
<td>0.64</td>
<td>5.21</td>
<td>(0.9)</td>
<td>5.27</td>
<td>0.82</td>
<td>-1.34</td>
<td>0.18</td>
</tr>
<tr>
<td></td>
<td>Talk in sleep</td>
<td>1.56 (0.7)</td>
<td></td>
<td>2.50</td>
<td>(0.6)</td>
<td>2.54</td>
<td>0.83</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Walk around or cry out when asleep</td>
<td>1.28 (0.6)</td>
<td></td>
<td>2.71</td>
<td>(0.5)</td>
<td>2.74</td>
<td>0.77</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Insomnia Scale</td>
<td>11.60 (4.14)</td>
<td>0.76</td>
<td>12.65</td>
<td>(2.9)</td>
<td>12.51</td>
<td>0.88</td>
<td>1.04</td>
<td>0.30</td>
</tr>
<tr>
<td></td>
<td>Have trouble falling asleep at bedtime</td>
<td>2.50 (1.2)</td>
<td></td>
<td>2.63</td>
<td>(1.2)</td>
<td>2.52</td>
<td>0.80</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Wake up during night</td>
<td>2.56 (1.3)</td>
<td></td>
<td>2.48</td>
<td>(1.3)</td>
<td>2.54</td>
<td>0.82</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Can’t fall asleep because thinking about that day or the next day</td>
<td>2.30 (1.1)</td>
<td></td>
<td>2.39</td>
<td>(1.1)</td>
<td>2.36</td>
<td>0.60</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Night waking frequency</td>
<td>1.99 (1.1)</td>
<td></td>
<td>2.99</td>
<td>(1.1)</td>
<td>2.89</td>
<td>0.76</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Return to sleep duration after night waking</td>
<td>2.25 (1.2)</td>
<td></td>
<td>2.25</td>
<td>(1.2)</td>
<td>2.29</td>
<td>0.69</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Indicator Items</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Snoring</td>
<td>1.63 (0.7)</td>
<td></td>
<td>2.47</td>
<td>(0.66)</td>
<td>2.51</td>
<td>0.84</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Wet the bed</td>
<td>1.25 (0.8)</td>
<td></td>
<td>1.24</td>
<td>(0.75)</td>
<td>1.22</td>
<td>0.86</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Have bad dreams</td>
<td>2.28 (0.9)</td>
<td></td>
<td>2.39</td>
<td>(1.0)</td>
<td>2.22</td>
<td>0.71</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Full sample n = 456, Test-Retest sample n = 122. Higher scores indicate poorer sleep hygiene/more sleep disturbances. Unless otherwise indicated with superscript letter, response choices were: Never = 1, Not Very Often = 2, Sometimes = 3, Usually = 4, and Always = 5. *Never = 1, Sometimes = 2, Usually = 3, and Always = 4. *Never = 1, Sometimes = 2, All the Time = 3. *Almost every night (5-7 times/week) = 4, Several times a week (1-4 times/week) = 3, Every now and then (2-3 times/month) = 2, I almost never wake up during the night = 1, *I usually don’t wake up during the night = 1, No time at all, I go back to sleep very quickly = 2, A few minutes (5-10 min) = 3, A little while (10-30 min) = 4, A long time (> 30 min) = 5.*
For the Sleep Disturbances Scales, children who reported more parasomnias had parents who reported shorter sleep duration \((r = 0.23)\) and more parasomnias \((r = 0.41)\); children who reported more symptoms of insomnia had parents who reported shorter sleep duration \((r = 0.32)\) and more night wakings \((r = 0.41)\); children who reported more frequent snoring had parents who reported more sleep disordered breathing \((r = 0.59)\); finally, children who reported more frequent nightmares had parents who reported shorter sleep duration \((r = 0.31)\) and more night wakings \((r = 0.22)\).

Parent-Reported Sleep Hygiene (CSHS)

Significant associations \((p \leq 0.001)\) were found between the CRSP Sleep Hygiene Indices (higher scores indicate poorer sleep hygiene) and the CSHS Scales (lower scores indicate poorer sleep hygiene). Specifically, associations were found between the CRSP Caffeine Index and the CSHS Physiological Scale (a measure of caffeine use, food and liquids consumed before bed, and rough play before bed, \(r = -0.25\)); the CRSP Activities in the Hour Before Bed Index and the CSHS Bedtime Routine Scale (a measure of having a calming bedtime routine, \(r = -0.39\)); the CRSP Sleep Location Index and the CSHS Sleep Stability Scale (a measure of consistency of sleep schedule and location of sleeping \(r = -0.36\)); the CRSP Sleep Electronics Index, and the CSHS Cognitive Scale (a measure of electronics use before bed and in bed, \(r = -0.37\)); and the CRSP Bedtime Fears/Worries Scale and the CSHS Emotional Scale (a measure of being upset or worried at bedtime, \(r = -0.41\)).

Table 3—Correlation matrix for Sleep Hygiene Indices and Sleep Disturbances Scales

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caffeine Index</td>
<td>–</td>
<td>0.29**</td>
<td>–</td>
<td>0.32**</td>
<td>0.32**</td>
<td>0.06</td>
<td>0.16*</td>
<td>0.09</td>
</tr>
<tr>
<td>Activities Hour</td>
<td></td>
<td>–</td>
<td>0.32**</td>
<td>0.21**</td>
<td>–</td>
<td>0.27**</td>
<td>0.20**</td>
<td>0.07</td>
</tr>
<tr>
<td>Bed Location</td>
<td></td>
<td></td>
<td>–</td>
<td>–</td>
<td>0.07</td>
<td>0.27**</td>
<td>0.17*</td>
<td>0.11</td>
</tr>
<tr>
<td>Electronics Use</td>
<td></td>
<td></td>
<td></td>
<td>0.30**</td>
<td>–</td>
<td>0.24**</td>
<td>0.19**</td>
<td>0.07</td>
</tr>
<tr>
<td>Restless Legs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Parasomnias</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Insomnia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

*p \leq 0.01, **p \leq 0.001.

Table 4—Means and standard deviations for the CRSP Sleep Hygiene Index ANOVA/ANCOVA analyses

<table>
<thead>
<tr>
<th></th>
<th>Caffeine</th>
<th>Activities Hour Before Bed</th>
<th>Sleep Location</th>
<th>Electronics Use at Bedtime</th>
</tr>
</thead>
<tbody>
<tr>
<td>Groupa</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical (n = 170)</td>
<td>6.48 (2.4)</td>
<td>17.01 (3.2)</td>
<td>11.66 (4.5)**</td>
<td>6.82 (3.2)*****</td>
</tr>
<tr>
<td>Community (n = 278)</td>
<td>6.05 (2.3)</td>
<td>16.45 (3.1)</td>
<td>9.73 (4.2)</td>
<td>5.60 (2.5)</td>
</tr>
<tr>
<td>Child Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-10 years (n = 272)</td>
<td>5.89 (2.3)**</td>
<td>16.24 (3.2)*****</td>
<td>10.92 (4.7)**</td>
<td>6.08 (3.0)</td>
</tr>
<tr>
<td>11-12 years (n = 176)</td>
<td>6.69 (2.4)</td>
<td>17.32 (3.0)</td>
<td>9.80 (4.0)</td>
<td>6.06 (2.8)</td>
</tr>
<tr>
<td>Sleep Quality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good Sleeper (n = 310)</td>
<td>6.06 (2.3)*</td>
<td>16.59 (3.1)</td>
<td>10.07 (4.5)**</td>
<td>5.74 (2.8)*****</td>
</tr>
<tr>
<td>Poor Sleeper (n = 137)</td>
<td>6.54 (2.5)</td>
<td>16.80 (3.2)</td>
<td>11.36 (4.3)</td>
<td>6.76 (3.0)</td>
</tr>
<tr>
<td>Nap Frequency</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regularly (n = 153)</td>
<td>5.88 (2.3)**</td>
<td>16.30 (3.1)*****</td>
<td>9.28 (3.7)**</td>
<td>5.58 (2.7)*****</td>
</tr>
<tr>
<td>Infrequently (n = 294)</td>
<td>6.83 (2.5)</td>
<td>17.33 (3.3)</td>
<td>12.77 (4.8)</td>
<td>6.97 (3.0)</td>
</tr>
<tr>
<td>Actigraphy Sleep Durationa</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than 8 hours</td>
<td>5.82 (2.4)</td>
<td>16.48 (3.7)</td>
<td>10.22 (4.6)</td>
<td>5.01 (2.9)</td>
</tr>
<tr>
<td>More than 8 hours</td>
<td>5.16 (1.8)</td>
<td>15.50 (2.6)</td>
<td>9.03 (4.6)</td>
<td>5.08 (2.5)</td>
</tr>
<tr>
<td>Actigraphy Sleep Onset Timea</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before 10 p.m.</td>
<td>4.68 (1.3)**</td>
<td>14.75 (3.0)*****</td>
<td>8.44 (3.7)*</td>
<td>4.91 (2.3)</td>
</tr>
<tr>
<td>After 10 p.m.</td>
<td>6.13 (2.5)</td>
<td>16.99 (2.9)</td>
<td>10.54 (5.2)</td>
<td>5.16 (3.0)</td>
</tr>
<tr>
<td>CSHQ Clinical Cutoffa</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Below Cutoff</td>
<td>6.22 (2.5)</td>
<td>16.37 (3.1)</td>
<td>9.71 (3.1)*</td>
<td>5.44 (2.4)****</td>
</tr>
<tr>
<td>Above Cutoff</td>
<td>6.57 (2.3)</td>
<td>17.47 (3.3)</td>
<td>11.46 (4.8)</td>
<td>6.76 (2.8)</td>
</tr>
</tbody>
</table>

*p \leq 0.05, **p < 0.01, ***p < 0.001, *group comparison controlling for age.
Differences in parent-reported sleep habits/sleep patterns (CSHQ and CRSP) were found between children who identified themselves as good versus poor sleepers (Table 6). This suggests that children who self-identify as okay/poor sleepers have parents who report more sleep disturbances in their children.

### Previous Night Agreement

For children who reported a long SOL the previous night, 38% of parents reported the child had a short SOL (κ = 0.33). For children who reported ≥ 1 night waking the previous night, 38% of parents reported no night wakings the previous night (κ = 0.40). For children reporting an okay/poor sleep quality the previous night, 42% of parents reported a good/great sleep quality the previous night (κ = 0.42).

### Typical Sleep Patterns Agreement

Similar results were found for typical sleep patterns. Of children who reported a typical weekday bedtime later than 21:00, only 12% of parents reported a typical weekday bedtime before 21:00 (κ = 0.69). When children reported a typical weekday wake time before 07:00, only 17% of their parents reported a typical weekday wake time after 07:00 (κ = 0.49). For children who reported having ≥ 1 night waking per week, 42% of parents reported that the child had no night wakings the previous night (κ = 0.42). Finally, of children who reported a typical sleep quality of okay/poor, 39% of their parents reported the child had a typical sleep quality of good/great (κ = 0.43). All variables were also examined by age category, with no differences found in the results.

### CRSP Sleep Hygiene Indices and Sleep Disturbances Scales

Moderate agreement between parent and child report (ICC > 0.50) was found for caffeine use, sleep location, and electronics use at sleep onset; as well as symptoms of both RLS and insomnia (Table 7). Fair agreement (ICC < 0.50) was found for stimulating activities in the hour before bed, bedtime fears/worries, and parasomnias.

### DISCUSSION

In this paper we have presented the preliminary psychometrics of the Children’s Report of Sleep Patterns (CRSP), a self-report measure for children ages 8-12 years that includes three modules: Sleep Patterns, Sleep Hygiene Index, and Sleep Disturbances Scale. The CRSP demonstrated good reliability and validity, and provides support for children 8 years and older reporting information about their own sleep. Further, our findings suggest that children may provide information about sleep patterns and disturbances that may not be captured if relying solely on parental report. The strengths of this study include the use of a multi-modal (objective and subjective measures) and multi-reporter (child and parent) approach for the validation of the CRSP.

The reliability of the CRSP was demonstrated through good internal consistency for three of the four sleep disturbance scales. The exception to this was the Parasomnias Scale, which
included only two items, both of which focused on what happens while the child is asleep. Test-retest reliability showed that the CRSP items, indices, and scales were relatively stable over time. The only scale that differed from time 1 to time 2 was the Sleep Location Scale, a result that may be due to greater day-to-day variability in where the child falls asleep and wakes up.

The group differences found on the CRSP highlight the validity of this measure. As would be expected, children seen in a sleep clinic, sleep laboratory, or children’s hospital had more sleep disturbances, including bedtime fears/worries, parasomnias, insomnia, snoring, and enuresis. The higher scores on the Sleep Location Index and Electronics Use at Sleep Onset Index support the fact that behavioral sleep issues (e.g., children “migrating” to the parents bed during the night, poor sleep hygiene) are commonly seen in pediatric sleep clinics.41

National surveys have shown that caffeine use and technology in the bedroom both increase with age.25,42 Thus, it was not surprising that we found that older children reported more caffeine use and more stimulating activities in the hour before bed. With earlier school start times, it is possible that older children use more caffeine to help them stay awake and alert in the evening, which allows them to engage in more alerting activities before bed (e.g., playing video games, watching television). Consequently, older children may be obtaining less sleep which perpetuates the cycle of evening caffeine use and stimulation.

Children who were self-reported poor sleepers consistently reported more sleep disturbances, demonstrating that children are not only aware of factors that disturb their sleep (e.g., bedtime worries, difficulties initiating/maintaining sleep), but also potential underlying sleep disruptors (e.g., RLS, snoring). In terms of sleep hygiene, children who reported regular napping also reported poorer sleep hygiene, including more caffeine use, and engaging in stimulating activities in the hour before bed. Notably, children who napped regularly also reported increased symptoms of underlying sleep disruptors. Asking children about napping frequency in a clinical setting could provide valuable information about potential poor sleep hygiene and/or underlying sleep disruptors.

A key strength of the present study was inclusion of objective measures to quantify sleep duration and compare with subjective reports in the CRSP. Actigraphy provided an objective measure to demonstrate the validity of the CRSP, highlighting that children provide important information about sleep disturbances, particularly insomnia and snoring. Although not statistically significant, children who slept less than 8 hours also reported more symptoms of RLS, suggesting that their sleep may have been disturbed by their discomfort. Child report of RLS symptoms was greater than parental report, suggesting children may not be reporting their discomfort to their parents. As such, children who are at least 8 years old should be directly asked about any discomfort at bedtime or during the night.

Both the well-established CSHQ and the parent proxy CRSP showed that children are able to provide information about their own sleep habits and sleep disturbances. Children scoring

| Table 6—Comparison (means, SD, ANOVA p-values) for the Children’s Sleep Habits Questionnaire and the CRSP Parent Proxy Report for children who self-report as great/good sleepers versus okay/poor sleepers |
| Children’s Sleep Habits Questionnaire | Good sleeper (n = 109) | Poor sleeper (n = 49) | p |
| Sleep Duration | 4.05 (1.5) | 5.41 (1.7) | < 0.001 |
| Night Wakings | 4.08 (1.4) | 4.90 (1.9) | 0.003 |
| Parasomnias | 8.55 (1.8) | 9.82 (1.7) | < 0.001 |
| Sleep Disordered Breathing | 3.68 (1.4) | 4.35 (1.9) | 0.01 |
| Daytime Sleepiness | 12.92 (3.4) | 15.78 (4.4) | < 0.001 |
| Bedtime Resistance | 7.33 (2.4) | 8.82 (2.9) | 0.001 |
| Sleep Onset Delay | 1.43 (0.7) | 2.02 (0.9) | < 0.001 |
| Sleep Anxiety | 5.15 (1.7) | 5.82 (2.2) | 0.04 |
| Total Sleep Disruptions | 44.22 (9.1) | 54.02 (9.7) | < 0.001 |

| Children’s Report of Sleep Patterns (Proxy) | Good sleeper (n = 105) | Poor sleeper (n = 52) | p |
| Caffeine | 5.25 (2.0) | 5.90 (2.2) | 0.07 |
| Activities Hour Before Bed | 14.53 (3.0) | 16.29 (3.1) | 0.001 |
| Sleep Location | 9.02 (4.1) | 11.31 (4.4) | 0.002 |
| Electronics Use at Sleep Onset | 5.14 (2.2) | 6.54 (2.9) | 0.001 |
| Bedtime Fears/Worries | 3.62 (1.5) | 3.90 (1.5) | 0.28 |
| Restless Legs | 3.56 (0.4) | 3.90 (1.5) | 0.03 |
| Parasomnias | 3.19 (1.0) | 3.27 (1.1) | 0.66 |
| Insomnia | 10.69 (3.3) | 13.81 (4.1) | < 0.001 |

| Table 7—Comparison (mean, SD, ICC, effect size) of child-report and parent-report for CRSP Sleep Hygiene Indices and Sleep Disturbances Scales (n = 107) |
| Sleep Hygiene Index Scores | Child-Report Mean (SD) | Parent-Report Mean (SD) | ICC | Difference (effect size) |
| Caffeine | 5.86 (2.3) | 5.42 (2.0) | 0.63 | 0.20 |
| Activities Hour Before Bed | 16.45 (3.1) | 15.08 (3.1) | 0.42 | 0.44 |
| Sleep Location | 10.22 (4.4) | 9.83 (4.4) | 0.59 | 0.09 |
| Electronics Use at Sleep Onset | 5.84 (3.1) | 5.61 (2.6) | 0.71 | 0.08 |
| Sleep Disorders Scale Scores | Child-Report Mean (SD) | Parent-Report Mean (SD) | ICC | Difference (effect size) |
| Bedtime Fears/Worries | 3.62 (1.9) | 3.72 (1.5) | 0.39 | 0.05 |
| Restless Legs | 10.20 (4.0) | 9.23 (4.2) | 0.51 | 0.24 |
| Parasomnias | 3.01 (1.2) | 3.21 (1.0) | 0.05 | 0.18 |
| Insomnia | 11.72 (4.4) | 11.70 (3.8) | 0.56 | 0.01 |

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above the clinical cutoff for the CSHQ reported poorer sleep hygiene and more sleep disturbances. Further, children self-identified as poor sleepers had parents who also reported more sleep disturbances on the CSHQ and poorer sleep hygiene on the parent proxy CRSP.

The value that a children’s report of sleep patterns provides for a clinical interview or research study was best highlighted with the examination of parent-child agreement for sleep patterns. As would be expected, there was high agreement between parents and children for typical weekday bedtimes and wake times. Although parents become less involved with the bedtime routine as children get older, the awareness of bedtimes and wake times is likely greater in children than adolescents, with teenagers often going to sleep later than their parents. What was notable, however, was that in this study approximately 40% of parents were not aware that their child had difficulties falling asleep, night wakings, or poor sleep quality either the previous night or on a typical night. Although sleep quality is based on a subjective report, self-reported sleep quality is an important treatment outcome, especially for children with insomnia. As such, this result has important clinical implications.

Parents and children had poor agreement on report of parasomnias, with parents reporting more parasomnia symptoms than children. As expected, a behavior that occurs during sleep is better reported by the parent as an outside observer than by the child. This provides evidence for the importance of obtaining both parent and child report of sleep disorders.

Study limitations should be noted. First and foremost, while the full sample was robust in size and diversity, not all participants completed each of the different measures. In addition, some of the subsamples may have lacked variability (e.g., children who wore actigraphy were primarily healthy, good sleepers), while other samples may have been biased (e.g., children recruited from schools or primary care practices may have had undiagnosed sleep disorders), resulting in muted differences between groups. Further, while a diverse sample would suggest generalizability, race/ethnicity data were not collected from the Australian sample, and no additional SES data were obtained. Finally, although we did not find any differences in terms of completion rates or any reported difficulties for younger children in completing this measure, it is possible that the CRSP may be challenging for younger children to complete. Thus we would recommend that adult supervision be available if needed, including someone to read the questions aloud, when younger children complete the CRSP.

Despite these limitations, the CRSP is a valid and reliable measure that can provide additional and important information (beyond parental report) to clinicians and researchers. Although the CRSP was not designed to be a diagnostic clinical tool, we believe this measure has utility in a clinical setting. Many pediatric sleep providers rely solely on parent-completed questionnaires about their child’s sleep. As shown by the current results, this may lead to an incomplete or misinformed assessment of the child’s sleep. The inclusion of the CRSP may provide additional information to a clinical provider, as well as be utilized as a pre-post treatment measure. In research studies, the CRSP can provide complementary information to parental report, as well as identify sleep patterns or sleep disturbances that parents may not be aware of such as delayed sleep onset latency and multiple night wakings.

**REFERENCES**


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**DISCLOSURE STATEMENT**

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Effect of Obstructive Sleep Apnea on the Sleep Architecture in Cirrhosis


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Study Objectives: Sleep disturbances in cirrhosis are assumed to be due to hepatic encephalopathy (HE). The interaction between cirrhosis, prior HE, and obstructive sleep apnea (OSA) has not been evaluated. We aimed to evaluate the additional effect of cirrhosis with and without prior HE on the sleep architecture and perceived sleep disturbances of OSA patients.

Methods: A case-control review of OSA patients who underwent polysomnography (PSG) in a liver-transplant center was performed. OSA patients with cirrhosis (with/without prior HE) were age-matched 1:1 with OSA patients without cirrhosis. Sleep quality, daytime sleepiness, sleep quality, and sleep architecture was compared between groups.

Results: Forty-nine OSA cirrhotic patients (age 57.4 ± 8.3 years, model for end-stage liver disease [MELD] 8.3 ± 5.4, 51% HCV, 20% prior HE) were age-matched 1:1 to OSA patients without cirrhosis. Sleep quality, daytime sleepiness, sleep quality, and sleep architecture was compared between groups.

Conclusions: Sleep disturbances in cirrhosis are assumed to be due to hepatic encephalopathy (HE). The interaction between cirrhosis, prior HE, and obstructive sleep apnea (OSA) has not been evaluated. We aimed to evaluate the additional effect of cirrhosis with and without prior HE on the sleep architecture and perceived sleep disturbances of OSA patients.

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were incomplete. We then generated using a random sequence, with psychoactive medication use or those whose sleep studies der and those with no sleep disorder. We also excluded patients OSA, excluding those patients with other forms of sleep disor-

without cirrhosis. We first determined age of our patients with randomly chose age-matched control subjects with OSA but

ing daytime sleepiness, sleepiness sitting in quiet place, driving

rea index, sleep efficiency, number of apneas, hypopneas, and arousals, as well as quantification in time spent in differ

mean latency to stage N1 was 24 ± 23 minutes, to N2 30 ±

13%, with a mean apnea-hypopnea index of 22.2 ± 25.0. The

score was significant positively correlated with % sleep spent

compared to cirrhotic patients without prior HE. The MELD

tionnaire. We also separately analyzed cirrhotic patients with

prior but currently controlled HE; the same patients also had

ated ascites. Patients with prior HE had similar age (54.9

and others (11%). Twenty percent (10) of cirrhotic patients had

etiology was hepatitis C (HCV) alone (51%), followed by non-alcoholic fatty liver disease (16%), alcohol and HCV (12%), alcohol alone (10%), and others (11%). Twenty percent (10) of cirrhotic patients had prior but currently controlled HE; the same patients also had controlled ascites. Patients with prior HE had similar age (54.9 ± 7.4 vs. 58.1 ± 8.4, p = 0.28), BMI (33.3 ± 4.3 vs 33.6 ± 5.1, p = 0.85), and MELD score (8.7 ± 5.9 vs. 8.2 ± 4.9, p = 0.81) compared to cirrhotic patients without prior HE. The MELD score was significant positively correlated with % sleep spent in N1 (r = 0.4, p = 0.03) but there was no correlation between the sleep latency, apneas, hypopneas, or %time spent in other stages of sleep.

Characteristics of Sleep Stages

The mean sleep efficiency in the cirrhosis group was 75% ± 13%, with a mean apnea-hypopnea index of 22.2 ± 25.0. The mean latency to stage N1 was 24 ± 23 minutes, to N2 30 ± 24 minutes, and to REM 138 ± 34 minutes. The mean % of sleep that consisted of N1 was 11%, N2 57%, slow wave sleep (SWS) 3.4%, and REM 11%. SWS was absent in 67% of cirrhotic patients. This was similar to age-matched patients with OSA without cirrhosis (Table 2). The arousal index however was significantly higher in patients with cirrhosis than those with OSA alone.

### RESULTS

Using the VA database, the charts of patients with sleep studies were reviewed. Of these, 49 patients were found to have cirrhosis. These were age-matched to 49 patients with OSA without evidence of cirrhosis using a random generator. As shown in Table 1, there was no difference in the baseline characteristics of patients with and without cirrhosis in demographics or comorbid conditions.

#### Sleep Questionnaire Responses

There were no significant differences between patients with and without cirrhosis who were asked questions pertaining to daytime sleepiness (4 questions) and sleep quality (6 questions; Table 1).

#### Patients with Cirrhosis

The mean MELD score of patients with cirrhosis was 8.3 ± 5.4, and the majority were Child Class A at the time of the sleep study (92%). The predominant cirrhosis etiology was hepatitis C (HCV) alone (51%), followed by non-alcoholic fatty liver disease (16%), alcohol and HCV (12%), alcohol alone (10%), and others (11%). Twenty percent (10) of cirrhotic patients had prior but currently controlled HE; the same patients also had controlled ascites. Patients with prior HE had similar age (54.9 ± 7.6 vs. 58.1 ± 8.4, p = 0.28), BMI (33.3 ± 4.3 vs 33.6 ± 5.1, p = 0.85), and MELD score (8.7 ± 5.9 vs. 8.2 ± 4.9, p = 0.81) compared to cirrhotic patients without prior HE. The MELD score was significant positively correlated with % sleep spent in N1 (r = 0.4, p = 0.03) but there was no correlation between the sleep latency, apneas, hypopneas, or %time spent in other stages of sleep.

#### Table 1—Baseline assessment of the groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cirrhosis +</th>
<th>OSA only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>57.4 ± 8.3</td>
<td>58.0 ± 8.3</td>
</tr>
<tr>
<td>Gender</td>
<td>94%</td>
<td>100%</td>
</tr>
<tr>
<td>Body mass index</td>
<td>33.5 ± 4.9</td>
<td>32.3 ± 5.1</td>
</tr>
<tr>
<td>Race (Cauc/AA/Other)</td>
<td>57/37/6</td>
<td>51/43/6</td>
</tr>
<tr>
<td>Diabetes</td>
<td>43%</td>
<td>35%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>89%</td>
<td>88%</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>29%</td>
<td>27%</td>
</tr>
<tr>
<td>Pre-study questionnaire</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you snore?</td>
<td>92%</td>
<td>100%</td>
</tr>
<tr>
<td>Do you stop breathing at night?</td>
<td>62.5%</td>
<td>60.9%</td>
</tr>
<tr>
<td>Do you struggle to breathe at night?</td>
<td>71.4%</td>
<td>50%</td>
</tr>
<tr>
<td>Do you gasp for air at night?</td>
<td>58.3%</td>
<td>43.5%</td>
</tr>
<tr>
<td>Excessive daytime sleepiness?</td>
<td>79.2%</td>
<td>78.3%</td>
</tr>
<tr>
<td>Sleepy during driving?</td>
<td>65.2%</td>
<td>58.7%</td>
</tr>
<tr>
<td>Sleepy while watching TV?</td>
<td>78.3%</td>
<td>84.8%</td>
</tr>
<tr>
<td>Sleepy while sitting quietly?</td>
<td>78.3%</td>
<td>87.0%</td>
</tr>
<tr>
<td>Headache in the morning?</td>
<td>41.7%</td>
<td>34.8%</td>
</tr>
<tr>
<td>Frequent heartburn?</td>
<td>43.5%</td>
<td>39.1%</td>
</tr>
</tbody>
</table>

There was no significant difference between the groups on any criteria including the pre-study questionnaire.
that the presence of HE synergizes with OSA to worsen the quality in cirrhosis can be affected by the presence of OSA and polysomnography (PSG). We found that sleep architecture in the presence of cirrhosis. In order to do this, we utilized the gold standard diagnostic test for examining the presence of diabetes between patients with and without an alcoholic etiology. As displayed in Table 2, the only differences in the sleep study time in early stages of sleep and reached the REM stage sooner (Table 3). None of the cirrhotic patients with prior HE had demonstrable SWS sleep, compared to only 33% of non-HE cirrhotic patients (p = 0.021). Prior HE, however, did not increase the apnea index, hypopnea index, or the arousal index.

### Effect of Alcoholic Etiology

Twelve patients had an alcoholic etiology of cirrhosis, although all of them had been abstinent from alcohol for > 3 months at the time of the sleep study. There was no significant difference between alcoholic etiology with (n = 4) and without HE (n = 10, p = 0.9) or in the MELD in patients with (8.7) or without an alcoholic etiology of cirrhosis (8.9, p = 0.56). There were also no significant differences in the age, BMI, or presence of diabetes between patients with and without an alcoholic etiology. As displayed in Table 4, the only differences in the sleep study values were significantly higher latency to stages 1 and 2; rest of the architecture was similar to cirrhotic patients without alcoholic etiology.

### DISCUSSION

This study was designed to examine the effect of OSA on sleep architecture in the presence of cirrhosis. In order to do this, we utilized the gold standard diagnostic test for examination of OSA, polysomnography (PSG). We found that sleep quality in cirrhosis can be affected by the presence of OSA and that the presence of HE synergizes with OSA to worsen the sleep architecture in patients with cirrhosis. The juxtaposition of increasing age of patients with cirrhosis with an overall epidemic of obesity brings OSA into the forefront while evaluating sleep disorders. This is important because there is considerable debate as to the origin of sleep disturbances in cirrhosis. Although the “reversal of sleep-wake cycle” is not specifically...
included in the original West-Haven criteria, the use of sleep abnormalities as an initial clue to possible HE has permeated clinical teaching and practice. Therefore most sleep disturbances in patients with cirrhosis are attributed to HE unless proven otherwise. However, the study shows that symptoms of sleep disturbances inquired of our patients with OSA, especially those related to daytime sleepiness, did not differ between those with and without cirrhosis. This was also true for those cirrhotic patients who had a previously experienced an HE episode.

Daytime sleepiness questionnaires such as the Epworth Sleepiness Scale have poor specificity as a screen for OSA or other diseases that affect sleep. The nonspecific nature of the daytime sleepiness complaints therefore cannot differentiate between cirrhosis-related and OSA-related sleep disturbances if they occur concurrently in a patient with cirrhosis. This overlap can result in a false, symptom-based diagnosis of HE, resulting in initiation of HE-specific therapy. HE therapy would not improve the underlying deficit associated with OSA, which could worsen the cardiorespiratory status of the patients with cirrhosis by delaying restorative OSA treatment. Therefore prior to attributing the sleep disturbances to HE purely based on symptoms, a diagnosis of OSA should be considered.

The absence of SWS in majority of patients in the sample, which was worse in patients with prior HE, is significant because SWS is the phase associated with restfulness in sleep. SWS is adversely affected in OSA and in patients with minimal HE without OSA. Since minimal and overt HE are part of the same spectrum of cognitive dysfunction in cirrhosis, SWS abnormalities seen in the minimal stage could be extended onto the same spectrum of cognitive dysfunction in cirrhosis, SWS fragmentation in HE. Another layer of complexity occurs with the tendency to go in SWS may be reflective of the underlying sleep architecture despite abstinence in HE patients. This may explain the lack of effect of MELD on most sleep parameters and only the significant difference in the arousal index between groups. Prior studies have shown an effect of cirrhosis on sleep quality as well as some preliminary observations on sleep architecture even in compensated cirrhosis compared to healthy controls. While OSA was not systematically excluded in some of the studies, it was not considered a confounder. The results of the current study show that simply asking questions regarding daytime sleepiness in patients with cirrhosis may be misleading, and studies enrolling for sleep disorders in cirrhosis should have a baseline evaluation for OSA.

The study was carried out in the population of veterans, in whom obesity, OSA, hepatitis C, and cirrhosis are epidemic. This is a relatively uniform group whose results could be widely applicable since, apart from the male predominance, the age and etiology of cirrhosis are similar to the general US population. The study is limited by its retrospective nature and the selection bias that could have occurred while referring patients with relatively compensated cirrhosis for sleep studies. Also, the retrospective nature of this study can only offer a glimpse into identifying the clinically distinguishing features between the effect of OSA and cirrhosis on sleep. This study does however lay the foundation for a more complete, prospective study. The inclusion of advanced cirrhotic patients could have magnified the negative impact of cirrhosis on sleep studies. However, the coexistent pruritus and discomfort due to refractory ascites that is often found in these patients would have confounded the ultimate interpretation. While the interpretation of EEG tracings during an acute episode of HE is fraught with the underlying HE-related changes, none of the included patients had mental status changes when the sleep study was performed. This in and of itself is a limitation, in that the effects of HE on sleep may not be adequately observed because of issues of safety.

We conclude that OSA may be a contributor to sleep disturbance in patients with cirrhosis. We also found that patients with prior HE have worse sleep architecture, shifted toward early, non-restorative sleep. Sleep questionnaires inquiring about daytime sleepiness and sleep quality cannot differentiate between OSA and HE in cirrhotic patients. Therefore, before assuming that daytime sleepiness is an early symptom of HE and initiating HE therapy, OSA should be considered in the differential diagnosis. Prospective studies are warranted in studying the effect of OSA on sleep in patients with cirrhosis.

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DISCLOSURE STATEMENT

Portions of this paper were presented in the Digestive Disease Week in Chicago in May 2011. This was not an industry supported study. The authors have indicated no financial conflicts of interest.
The presence of excessive amounts of sustained or intermittent elevations of submental muscle electromyography (EMG) tone or excessive phasic submental muscle twitching (or upper/lower limbs) is a required polysomnographic (PSG) feature for the diagnosis of REM sleep behavior disorder (RBD). However, the general and non-quantitative nature of PSG EMG activity seems to be more stable than video-recorded behavior. The night-to-night variability of RSWA in RBD patients; these values increase only moderately when a second night recording is available. Moreover, this study also supports the idea that a single PSG recording provides high values of sensitivity and specificity for the detection of RSWA in RBD patients; on the contrary, that of the number of EMG activations is higher. However, even a single PSG recording provides high values of sensitivity and specificity when a threshold value of AI ≤ 0.9 is used to define abnormal chin EMG levels during REM sleep that increase only moderately when a second night recording is available. The scope of this study was to analyze the night-to-night variability of AI. These methods seem to show sufficient sensitivity and specificity for their application in both clinical practice and research settings and probably provide comparable results. However, one of the aspects that needs to be further clarified is that of the night-to-night variability of RSWA. The availability of the above quantification methods now allows exploration of this aspect of RBD, which was previously limited to subjective evaluation of “excessive” amounts of activity during REM sleep. The night-to-night variability of the clinical manifestations of RBD is well known; however, it has been reported that PSG EMG activity seems to be more stable than video-recorded behavioral manifestations across nights, and the combination of information obtained from one video-PSG might be sufficient for the diagnosis. Regarding EMG activity, in particular, it was higher in RBD patients (19.7%) than in the 2 groups of controls (Young 1.8% and Aged 2.8%). The values of variability of chin EMG activations were much higher than those of AI, especially in the Aged controls. Sensitivity of AI ≤ 0.9 for RBD was always higher than 82% and reached 88.9% for the combined-night analysis; specificity was also high, with a value of 92.3% for the combined-value analysis. The night-to-night variability of Al seems to be very low in normal controls and remains under 20% in RBD patients; that of the number of EMG activations is higher. However, even a single PSG recording provides high values of sensitivity and specificity when a threshold value of AI ≤ 0.9 is used to define abnormal chin EMG levels during REM sleep that increase only moderately when a second night recording is available.

**Study Objectives:** To analyze the night-to-night variability of REM sleep electromyographic (EMG) features of REM sleep behavior disorder (RBD) by using the automatic quantitative method known as atonia index (AI), and to evaluate the improvement in sensitivity and specificity of AI for the diagnosis of RBD when a second recording night is available.

**Setting:** Sleep research center.

**Methods:** A group of 17 idiopathic RBD patients was recruited for whom 2 all-night polysomnographic (PSG) recordings were available. Thirty normal controls were also recruited and sub-grouped into Young (< 45 years of age) or Aged (> 45 years). Chin EMG analysis was run on all recordings; night-to-night variability of both AI and number of chin EMG activations/h during REM sleep was additionally quantified as the absolute difference between the 2 nights standardized as the percentage of their mean.

**Measurements and Results:** Night-to-night variability of AI was higher in RBD patients (19.7%) than in the 2 groups of controls (Young 1.8% and Aged 2.8%). The values of variability of chin EMG activations were much higher than those of AI, especially in the Aged controls. Sensitivity of AI ≤ 0.9 for RBD was always higher than 82% and reached 88.9% for the combined-night analysis; specificity was also high, with a value of 92.3% for the combined-value analysis.

**Conclusion:** The night-to-night variability of AI seems to be very low in normal controls and remains under 20% in RBD patients; that of the number of EMG activations is higher. However, even a single PSG recording provides high values of sensitivity and specificity when a threshold value of AI ≤ 0.9 is used to define abnormal chin EMG levels during REM sleep that increase only moderately when a second night recording is available.

**Keywords:** REM sleep behavior disorder, RBD, REM sleep without atonia, atonia index, chin EMG analysis, night-to-night variability

**Citation:** Ferri R; Marelli S; Cosentino FL; Rundo F; Ferini-Strambi L; Zucconi M. Night-to-night variability of automatic quantitative parameters of the chin EMG amplitude (atonia index) in REM sleep behavior disorder. J Clin Sleep Med 2013;9(3):253-258.
Phasic muscle activity has been reported to be more variable than tonic muscle activity.13

All the data available in full-length articles on night-to-night variability of the EMG activity of RBD have been produced by means of visual quantification methods. Thus, the primary scope of this study was to analyze the night-to-night variability of the REM EMG features of RBD by using our automatic quantitative method also known as atonia index (AI).7,8,10,14,15

This index can vary from zero (i.e., complete absence of EMG atonia) to one (stable EMG atonia) and can be calculated for any sleep stage. In addition, in the same method sequences of consecutive mini-epochs with values > 2 µV are counted as movements. The second aim of this study was to evaluate the improvement in sensitivity and specificity of AI for the diagnosis of RBD when a second recording night was available.

### METHODS

#### Subjects

Patients with idiopathic RBD (iRBD) for whom ≥ 2 PSG recordings were available, under constant pharmacological treatment, were consecutively and retrospectively recruited for this study and gave their permission for the use of their data in this analysis. The diagnosis of iRBD was based on the International Classification of Sleep Disorders, 2nd Edition (ICSD-2) criteria for RBD, including presence of REM sleep without atonia, sleep related injurious-disruptive behaviors by history or abnormal sleep behaviors documented during PSG monitoring, absence of EEG epileptiform activity during REM sleep, and sleep disturbance not better explained by another sleep disorder, medical or neurologic disorder, mental disorder, medication use, or substance use disorder.1 Secondary forms of RBD were excluded on the basis of historical data, neurologic examination, and cerebral MRI findings. All RBD patients with at least one subtentorial vascular lesion or ≥ 2 vascular supratentorial lesions > 0.5 cm were excluded.

Normal controls were also recruited. The exclusion criteria for the control group were the same as described for iRBD patients; additionally, the presence of subjective sleep complaints (insomnia, daytime sleepiness, restless legs syndrome, RBD symptoms, snoring, or witnessed apnea) was also ruled out. None of the controls was taking hypnotics or benzodiazepines.

This study was approved by the local ethics committee and all subjects provided informed consent according to the Declaration of Helsinki.

#### Nocturnal Polysomnography

Nocturnal video-PSG was carried out in a standard sound-attenuated (noise level to a maximum of 30 dB nHL) sleep laboratory room. Subjects were not allowed caffeinated beverages the afternoon preceding the recording and were allowed to sleep until their spontaneous awakening in the morning. Lights-out time was based on individual habitual bedtime and ranged between 21:30 and 23:30. The following signals were recorded: EEG (≥ 2 channels, one central and one occipital, referred to the contralateral earlobe; however, multiple-channel EEG was available for patients at their first diagnostic assessment in order to exclude the presence of frontal lobe seizures); electrooculogram (electrodes placed 1 cm above the right outer canthus and 1 cm below the left outer canthus and referred to A1); electromyogram (EMG) of the submentalis muscle (bipolar derivations with 2 electrodes placed 3 cm apart and affixed using a collodion-soaked gauze pad); EMG of the right and left tibialis anterior muscles; and ECG (one derivation). Impedance was kept < 10 KΩ (typically < 5 KΩ). Sleep signals were sampled at 200 or 256 Hz and stored on hard disk for further analysis. The sleep respiratory pattern of each patient was monitored using oral and nasal airflow thermistors and/or nasal pressure cannula, thoracic and abdominal respiratory effort strain gauge, and by monitoring oxygen saturation (pulse oximetry). This was performed in all subjects in a previous recording (within 1 week) or during the study recording; patients with an apnea-hypopnea index > 5 were not included. Sleep stages were scored following standard criteria5 on 30-s epochs; since muscle atonia can be absent in RBD, REM sleep was scored without submental EMG atonia, using electroencephalogram and electrooculogram only. According to a method specifically developed for RBD,2,17 onset of a REM sleep period was defined as the occurrence of the first rapid eye movement in the presence of an EEG signal characteristic of REM sleep (low amplitude mixed frequencies, absence of sleep spindles and K complexes). Offset of a REM sleep period was determined by the occurrence of a specific EEG feature indicative of another stage (K complex, sleep spindle, or EEG signs of arousal) or absence of rapid eye movements during 3 consecutive minutes. Epochs containing technical artifacts or extremely elevated muscle activity causing saturation of amplifiers were carefully detected and marked for exclusion from the subsequent quantitative EMG analysis.

Two recordings were obtained from each patient, with a variable time lag between them (see results); however, drug therapy was the same in both nights. For normal controls, 2 consecutive nocturnal PSG recordings were obtained.

#### Quantification of the Submentalis Muscle EMG Amplitude

For the computer quantitative analysis of the submentalis muscle EMG activity we used our established automatic scoring algorithm.7,8,14 The submentalis muscle EMG signal was digitally band-pass filtered at 10-100 Hz, with a notch filter at 50 Hz and rectified. Subsequently, each REM sleep epoch included in the analysis was divided into 30 1-sec mini-epochs. The average amplitude of the rectified submentalis muscle EMG signal was then obtained for each mini-epoch. After a noise reduction procedure,8 the values of the submentalis muscle EMG signal amplitude in each 1-sec mini-epoch were used to compute the percentage of values in the following 20 amplitude (amp) classes (expressed in µV): amp ≤ 1, 1 < amp ≤ 2, …, 18 < amp ≤ 19, amp > 19. Muscle atonia is expected to be reflected by high values of the first class (amp ≤ 1), while phasic and tonic activations are expected to increase the value of the other classes. As proposed in previous studies, an index summarizing the night-to-night variability of the EMG activity of RBD have been produced for RBD,2,17 an index was developed for RBD,2,17 onset of a REM sleep period was defined as the occurrence of the first rapid eye movement in the presence of an EEG signal characteristic of REM sleep (low amplitude mixed frequencies, absence of sleep spindles and K complexes). Offset of a REM sleep period was determined by the occurrence of a specific EEG feature indicative of another stage (K complex, sleep spindle, or EEG signs of arousal) or absence of rapid eye movements during 3 consecutive minutes. Epochs containing technical artifacts or extremely elevated muscle activity causing saturation of amplifiers were carefully detected and marked for exclusion from the subsequent quantitative EMG analysis.

Two recordings were obtained from each patient, with a variable time lag between them (see results); however, drug therapy was the same in both nights. For normal controls, 2 consecutive nocturnal PSG recordings were obtained.

Mathematically, this index can vary from 0 (absence of mini-epochs with amp ≤ 1), i.e., complete absence of EMG atonia, to 1 (all mini-epochs with amp ≤ 1) or stable EMG atonia in the epoch.
In addition, sequences of consecutive mini-epochs with values > 2 μV were counted as movements. The algorithm was run blind to the condition of the subject, even though no manual modifications of the parameters is possible.

### Statistical Analysis

For the comparison of sleep architecture parameters, the analysis of covariance was used and age of the subjects served as a covariate; while for the comparison of AI and number of chin EMG activations/h during REM sleep obtained in the 3 groups of subjects, the Kruskal-Wallis ANOVA was first carried out, followed by the Mann-Whitney test used as a post hoc test.

The analysis of the night-to-night variability of AI and number of chin EMG activations/h during REM sleep was first carried out by means of the Kendall W coefficient of concordance, which expresses the simultaneous association (relatedness) between different sets of rankings. The range of Kendall concordance is from 0 to 1; values close to 0 represent lack of agreement in the rankings of the variables among nights in this case, while values close to 1 represent perfect agreement. Night-to-night variability of both AI and number of chin EMG activations/h during REM sleep were additionally quantified as the absolute difference between the 2 nights, standardized as the percentage of the mean of the 2 nights. These values were compared by means of the Kruskal-Wallis ANOVA, followed by the Mann-Whitney test used as a post hoc assessment.

Finally, sensitivity, specificity, positive predictive value, and negative predictive value of AI ≤ 0.9 for the diagnosis of iRBD vs. Aged controls were computed for the first and second recording nights, separately or combined (AI ≤ 0.9 in either the first or the second recording night).

### RESULTS

For this study, 17 consecutive iRBD patients were retrospectively recruited (14 men and 3 women, mean age 66.0 ± 4.93 years). Average disease duration was 9.1 ± 12.86 years at the time of the first recording. All patients were taking clonazepam (0.5-1 mg) at bedtime.

A group of 30 normal controls (15 men and 15 women) was also retrospectively recruited and then subdivided into 2 age groups, based on age below or above 45 years. The younger subgroup (Young) included 16 subjects (mean age 30.6 ± 6.86 years), while the older subgroup (Aged) was formed by the remaining 14 subjects (mean age 58.2 ± 9.63 years).

Patients and controls differed for their gender composition, but we have previously reported that our chin EMG measurement seems to be independent of gender14,15; in this new study, the number of women in the RBD group was too low to allow us to control for the influence of this factor.

Table 1 shows the descriptive statistics of sleep architecture parameters obtained from the first recording available for each subject in these 3 groups of subjects. A comparison was also run between iRBD and Aged controls by means of the analysis of covariance, to take into account the age of the subjects in the 2 groups, using age as a covariate. Time in bed and sleep period time were significantly shorter in iRBD patients.

As mentioned above, the 2 PSG recordings available for iRBD patients were not consecutive; the second PSG recording was obtained with an average time lag of 2.5 ± 1.17 years after the first. Two consecutive recordings were available for all controls.

The left panels of Figure 1 shows the comparison of the chin EMG amplitude parameters (AI and number of chin EMG activations/h during REM sleep) found during the 2 PSG recordings among subject groups. As expected, in iRBD patients, AI was significantly lower and the number of chin EMG activations/h was significantly higher than those of both groups of controls in both recordings. However, night-to-night variability (top right panel of Figure 1) of AI was higher in iRBD patients (19.7%) than in the 2 groups of controls (Young 1.8%, Aged 2.8%). The values of variability of chin EMG activations were generally much higher than those of AI, especially in the Aged controls. The Kendall W coefficient of concordance between the 2 nights (Table 2) showed high (Young) to moderate (iRBD patients) values, which reached

### Table 1—Sleep architecture parameters

<table>
<thead>
<tr>
<th></th>
<th>Young (n = 16)</th>
<th>Aged (n = 14)</th>
<th>iRBD (n = 17)</th>
<th>Aged vs. iRBD ANCOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
<td>SD</td>
<td>mean</td>
<td>SD</td>
</tr>
<tr>
<td>Time in bed, min</td>
<td>483.5</td>
<td>50.24</td>
<td>504.4</td>
<td>89.88</td>
</tr>
<tr>
<td>Sleep period time, min</td>
<td>457.7</td>
<td>42.05</td>
<td>473.6</td>
<td>90.33</td>
</tr>
<tr>
<td>Total sleep time, min</td>
<td>424.9</td>
<td>64.79</td>
<td>381.6</td>
<td>92.80</td>
</tr>
<tr>
<td>Sleep latency, min</td>
<td>16.4</td>
<td>17.37</td>
<td>21.4</td>
<td>24.97</td>
</tr>
<tr>
<td>REM latency, min</td>
<td>95.2</td>
<td>64.66</td>
<td>98.0</td>
<td>42.05</td>
</tr>
<tr>
<td>Stage shifts/hour</td>
<td>10.4</td>
<td>3.41</td>
<td>13.1</td>
<td>3.88</td>
</tr>
<tr>
<td>Awakenings/hour</td>
<td>3.8</td>
<td>2.40</td>
<td>4.2</td>
<td>2.23</td>
</tr>
<tr>
<td>Sleep efficiency, %</td>
<td>88.0</td>
<td>11.32</td>
<td>75.7</td>
<td>11.88</td>
</tr>
<tr>
<td>WASO, %</td>
<td>7.3</td>
<td>10.29</td>
<td>19.2</td>
<td>13.15</td>
</tr>
<tr>
<td>S1, %</td>
<td>3.8</td>
<td>2.47</td>
<td>6.5</td>
<td>3.87</td>
</tr>
<tr>
<td>S2, %</td>
<td>48.6</td>
<td>7.76</td>
<td>41.0</td>
<td>10.54</td>
</tr>
<tr>
<td>SWS, %</td>
<td>17.7</td>
<td>8.44</td>
<td>17.3</td>
<td>8.56</td>
</tr>
<tr>
<td>REM, %</td>
<td>22.6</td>
<td>7.00</td>
<td>16.0</td>
<td>4.95</td>
</tr>
</tbody>
</table>

WASO, wakefulness after sleep onset; S1, sleep stage 1; S2, sleep stage 2; SWS, sleep stages 3-4.
statistical significance for AI of both control groups and for the number of EMG activations of only Young controls.

Finally, an analysis of sensitivity, specificity, positive predictive value, and negative predictive value of AI ≤ 0.9 for the diagnosis of iRBD vs. Aged controls was run (Table 3). These parameters were computed for the first and second recording nights, separately or combined (AI ≤ 0.9 in either the first or the second recording night). Sensitivity was always higher than 82% and reached 88.9% for the combined-night analysis; specificity was also high, with a value of 92.3% for the combined-value analysis. Overall, the combined-night analysis gave better results, but the values obtained for the single nights were also high, and the improvement obtained by using the combined nights was relatively small.

DISCUSSION

It has been reported that, using a visual quantification of the chin EMG amplitude during REM sleep and video-analysis of behaviors, only increased tonic chin muscle activity can be considered to be a relatively stable measure for RBD diagnosis; conversely, enhanced phasic chin muscle activations and motor and vocal behaviors are more variable between nights. We have now extended this type of night-to-night variability analysis to our automated quantification method and have found that, similar to the above study, AI is a more stable feature than the number of chin muscle activations in both normal controls and iRBD patients. These results underline once more the concordance between visual and automatic analysis of the chin EMG amplitude during REM sleep in RBD, with the added value of speed and strict objectivity of the automatic analysis.

The retrospective nature of our analysis is the major limitation of this study, which allowed us to collect the second recording of iRBD patients obtained only after a long period from the first; consecutive night recordings were available for normal controls. This might mean that consecutive recordings in iRBD patients (if available) might have yielded more stable results; but this is only a speculative consideration that needs to be checked in
future studies. Another important limitation deriving from the retrospective nature of the study was the impossibility of arranging an adequately age-matched control group. This was partially controlled for by using the ANCOVA for some comparisons. However, it should also be underlined that we have already reported that in adulthood, A1 shows relatively stable values > 0.9 in normal controls15 (this was true also in the present study); thus, we believe that our analyses can still be considered as reliable.

Finally, after a technical improvement of our method to compute A1,8 we have indicated a normality threshold value of > 0.9 for this parameter, because the vast majority of normal adults provide scores above this threshold. We have also previously reported that using this A1 threshold, a sensitivity of 74.3% and a specificity of 91.4% were obtained for iRBD patients compared to controls; in the same study we found both sensitivity and specificity of 100% for multiple system atrophy.8 More recently, we have applied the same type of analysis in a group of Parkinson disease patients with or without RBD and have obtained sensitivity 93.8% and specificity 90.6%.16 In the present study, we have found that sensitivity ranged from 82.3% to 88.2% and specificity 88.2% to 92.8% in the two nights. Only a moderate improvement was obtained when either night was used to detect A1 ≤ 0.9 (sensitivity 88.9, specificity 92.3%). All these results were obtained from studies which only involved limited numbers of patients, if considered singularly; however, taken together, they involved 48 patients with iRBD, 27 with Parkinson disease, and 10 with multiple system atrophy—a nontrivial total number of patients. Thus, they show a convincing convergence toward high values of sensitivity and specificity for A1 ≤ 0.9 and seem to support the conclusion that a single recording night might be considered sufficient for the diagnostic work-up of RBD, especially if we take into account that other video-PSG and clinical parameters contribute to its definition.11-13

Table 2—Concordance of the different chin EMG amplitude parameters found during the two polysomnographic recordings in the groups of subjects

<table>
<thead>
<tr>
<th></th>
<th>Kendall W</th>
<th>Chi-square</th>
<th>p &lt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atonia Index</td>
<td>0.847</td>
<td>25.412</td>
<td>0.045</td>
</tr>
<tr>
<td>EMG activations</td>
<td>0.912</td>
<td>27.353</td>
<td>0.026</td>
</tr>
<tr>
<td>Aged</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atonia Index</td>
<td>0.745</td>
<td>22.352</td>
<td>0.05</td>
</tr>
<tr>
<td>EMG activations</td>
<td>0.585</td>
<td>17.538</td>
<td>NS</td>
</tr>
<tr>
<td>iRBD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atonia Index</td>
<td>0.605</td>
<td>19.353</td>
<td>NS</td>
</tr>
<tr>
<td>EMG activations</td>
<td>0.591</td>
<td>18.922</td>
<td>NS</td>
</tr>
</tbody>
</table>

Table 3—Analysis of sensitivity, specificity, positive predictive value, and negative predictive value of A1 ≤ 0.9 for the diagnosis of iRBD vs. aged controls

<table>
<thead>
<tr>
<th></th>
<th>AI ≤ 0.9</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>PPV, %</th>
<th>NPV, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>yes</td>
<td>no</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st night</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>iRBD</td>
<td>14</td>
<td>3</td>
<td>82.3</td>
<td>86.7</td>
<td>87.5</td>
</tr>
<tr>
<td>Aged</td>
<td>2</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2nd night</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>iRBD</td>
<td>15</td>
<td>2</td>
<td>88.2</td>
<td>92.8</td>
<td>93.7</td>
</tr>
<tr>
<td>Aged</td>
<td>1</td>
<td>13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined nights</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>iRBD</td>
<td>16</td>
<td>1</td>
<td>88.9</td>
<td>92.3</td>
<td>94.1</td>
</tr>
<tr>
<td>Aged</td>
<td>2</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PPV, positive predictive value; NPV, negative predictive value. The results are shown for the first and second recording nights, separately or combined (AI ≤ 0.9 in either the first or the second recording night).

REFERENCES


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This work was carried out at the Oasi Institute for Research on Mental Retardation and Brain Aging (IRCCS), Trienza, Italy and the Scientific Institute and University Ospedale San Raffaele, Vita-Salute University, Milan, Italy. This study was supported by the Italian Ministry of Health (“Ricerca Corrente”).
Insomnia, especially experienced as difficulty maintaining sleep, is quite common in older individuals, with epidemiologic studies indicating rates of 40% to 70%. Numerous age-related changes are thought to increase the likelihood of insomnia in senescence, including changes to the circadian timing system and sleep homeostatic mechanisms, decreased arousal threshold, increased rates of anxiety, pain, and depression, and generally poor health. While all of these factors might contribute to the decline of sleep continuity in older adults, the overwhelming reason given by older adults themselves is that their sleep is disturbed because they need to get up to urinate (nocturia). Between two-thirds and three-quarters of older individuals surveyed in epidemiological studies report that their sleep is disturbed because of nocturia. The majority report that nocturia is the only reason their sleep is disturbed. Further, survey studies have shown that the greater the number of nocturnal voids, the greater the self-described poor sleep, insomnia symptoms, and daytime sleepiness. For those individuals who report nocturia as bothersome there is even a stronger correlation with disturbed sleep.

As noted, to date, no study of the relationship between sleep and nocturia has used objective measurements of sleep, nor have previous studies examined the relationship between sleep and nocturia prospectively, on a night-to-night basis. Such data could enable the comparison of nights with or without nocturia in the same individual. To fill this gap, we here report on the relationship between objective and subjective measures of sleep and nocturia collected prospectively from a group of healthy, community-dwelling older adults over a two-week period.

METHODS

A group of community-dwelling older men (n = 55, aged 64.3 ± 7.52 years) and women (n = 92, aged 62.5 ± 6.73 years) were recruited for a research study of insomnia and aging. All subjects had a self-reported complaint of insomnia and were recruited into the study specifically on this complaint. Presence or absence of nocturia was not a consideration in recruitment. To establish a baseline sleep pattern, all subjects had 2 weeks of sleep logs, and a subset (n = 60: 44 women and 16 men) had an additional week of wrist actigraphy. Sleep logs were used to collect information concerning daily timing (i.e., bedtime, wake up time) of sleep, subjective quality of “restedness” in the morning (Likert-like scale from 1-7 with 1: “not at all rested,” 4: “moderately rested,”
and 7: “very rested”), the number of nocturnal awakenings, the time it took to fall asleep, and the number of times that subjects woke to use the bathroom. We collected 12.1 ± 3.39 days of sleep logs per subject. Not all logs were fully completed, resulting in some missing data. Of the 1,786 days of logs, 1,774 had information concerning the number of trips to the bathroom, 1,108 had information concerning morning restedness, and 1,784 had sleep timing data. Sleep efficiency [(time in bed – time awake) / time in bed] was calculated from the self-reported sleep data. Wrist actigraphy collects arm movement data by means of a wrist-worn device that contains a 3-dimensional accelerometer. From these data, sleep and, notably, the occurrence of wakefulness during sleep are inferred.17 Actigraphy data were collected with an Actiwatch-L (Minimitter, Bend OR) for 7 days in 58 subjects and 6 days in 2 subjects. Sleep was determined using the built-in algorithms in the Actiware-Sleep software (v.3.1, Mini-Mitter, Bend OR). Sleep efficiency, the number and length of nocturnal wake episodes, and the overall amount of wakefulness after sleep onset (WASO) were all calculated from actigraph data. Subjects also had one night of at-home recording of breathing parameters (EdenTrace, Mallinckrodt, Hazelwood, MO) from which the respiratory disturbance index (RDI) was calculated. Data were scored based on the Chicago Criteria18 for hypopneas and discernable apneas; RDI was calculated using self-reported sleep times. Due to technical problems, 14 of the 147 recordings were unavailable.

Data were analyzed using several different approaches. Initially, we examined all actigraphic data from individual nights for individual subjects, classifying each night by the number of logged nocturnal bathroom visits. These data were analyzed both continuously and categorically (i.e., 0/1/2/3/4 or more) using linear regression and analysis of variance (ANOVA), respectively (OriginPro8, Origin Lab, Northampton MA). Secondly, in order to examine the relationships between nocturnal bathroom trips and sleep quality on a within subject basis, we examined the data of the 19 subjects who during the one week of actigraphy data collection had ≥ 2 nights on which they went to the bathroom at least once and ≥ 2 nights on which they did not use the bathroom after going to bed. For each of these nights, we calculated percent difference from the one-week average for each sleep variable of interest. The average percent difference was calculated for toileting and non-toileting nights and pairwise comparisons made. Data throughout the manuscript are shown as mean ± SD.

Prior to the collection of any data, subjects signed a consent form approved by the Stanford University Institutional Review Board. All procedures conformed to the principles outlined in the Declaration of Helsinki.

### RESULTS

Subjects (Table 1) reported 1.4 ± 1.2 trips to the bathroom per night (range 0-9) and 2.4 ± 1.6 nocturnal awakenings per night (range 0-15). More than half (54.2% ± 39.9%) of all nocturnal awakenings were associated with using the bathroom. As these subjects were all recruited for the presence of self-reported insomnia, they had generally poor sleep efficiency with a not unexpected difference between the subjective (sleep log) and objective (actigraphy) measures of sleep efficiency (67.8% ± 16.9% and 79.2% ± 9.74%, respectively). When limiting the analysis to sleep data collected by log and actigraphy concomitantly, the subjective sleep efficiency was similarly poor (67.1% ± 16.1% by sleep log). Given their poor sleep, subjects reported being only moderately rested (3.8 ± 1.5; scale = 1-7, with 7 being the most rested). Subjects were relatively free of sleep-related breathing disruption, as the RDI was 3.44 ± 2.85 and only 2 subjects had an RDI > 10. Thus, older subjects with a primary complaint of insomnia slept poorly and getting up to use the bathroom was associated with more than half of all nocturnal awakenings.

Data for individual nights, subdivided by the number of trips to the bathroom at night, are presented in Table 2. The number of trips to the bathroom at night was negatively associated with subjective measures of restedness (r = -0.13, linear regression; F_{4,109} = 4.27, p < 0.01 ANOVA) and sleep efficiency (r = -0.22, linear regression; F_{4,109} = 24.5, p < 0.001 ANOVA). The number of trips to the bathroom at night was positively associated with objective, actigraph-derived measures of sleep disruption, including the number of nocturnal wake bouts (r = 0.23, linear regression; F_{4,109} = 5.03, p < 0.001 ANOVA), the mean length of the nocturnal wake bouts (r = 0.13, linear regression; F_{4,109} = 3.48, p < 0.01 ANOVA), and the overall WASO (r = 0.24, linear regression; F_{4,109} = 5.66, p < 0.001 ANOVA). The relationship between objective (actigraph-derived) sleep efficiency and the number of trips to the bathroom at night was mixed, with a weak linear relationship (r = -0.099, p < 0.05, linear regression), but no categorical relationship (F_{4,111} = 1.24, p = 0.29 ANOVA). Splitting the data into nights with or without a trip to the bathroom did reveal a difference in objective sleep efficiency (p < 0.05, 2-tailed t-test), with lower sleep efficiency occurring on nights with a trip to the bathroom. Since common factors (e.g., age, sex, RDI, body mass index, diabetes, use of diuretics; see Table 1) might be related to the number of trips to the bathroom, we examined each of the linear relationships

<table>
<thead>
<tr>
<th>Male</th>
<th>n</th>
<th>Age (y)</th>
<th>RDI</th>
<th>BMI</th>
<th>Diuretics/BP Meds (%)</th>
<th>Diabetes (% yes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>92</td>
<td>62.5 ± 6.73</td>
<td>3.2 ± 3.0</td>
<td>24.4 ± 4.44</td>
<td>17%</td>
<td>3%</td>
</tr>
<tr>
<td>Male</td>
<td>55</td>
<td>64.3 ± 7.52</td>
<td>3.8 ± 2.4</td>
<td>26.1 ± 3.59</td>
<td>29%</td>
<td>0%</td>
</tr>
</tbody>
</table>

**Table 1**: Demographic characteristics

Due to missing data, n = 85 (female, RDI), n = 48 (male, RDI), n = 81 (female BMI), n = 44 (male, BMI). RDI, respiratory disturbance index; BMI, body mass index; BP Meds, blood pressure medications.
Table 2—Sleep parameters and their association with using the toilet at night

<table>
<thead>
<tr>
<th>Number of Nocturnal Trips to the Bathroom</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>&gt; 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restedness (self-report) (%)</td>
<td>3.9 ± 1.5</td>
<td>3.9 ± 1.5</td>
<td>3.6 ± 1.4</td>
<td>3.5 ± 1.5</td>
<td>3.3 ± 1.5</td>
</tr>
<tr>
<td>Sleep efficiency (self-report) (%)</td>
<td>71.4 ± 16.9</td>
<td>69.8 ± 15.1</td>
<td>65.6 ± 17.2</td>
<td>58.9 ± 19.0</td>
<td>61.6 ± 17.2</td>
</tr>
<tr>
<td>Sleep efficiency (actigraph) (%)</td>
<td>80.8 ± 9.89</td>
<td>78.8 ± 9.72</td>
<td>79.0 ± 9.47</td>
<td>77.5 ± 10.7</td>
<td>77.2 ± 7.29</td>
</tr>
<tr>
<td>Wake bouts (actigraph)</td>
<td>27.5 ± 11.2</td>
<td>31.4 ± 11.9</td>
<td>34.5 ± 15.2</td>
<td>39.3 ± 19.5</td>
<td>37.5 ± 17.4</td>
</tr>
<tr>
<td>Mean wake bout length (actigraph) (min)</td>
<td>1.92 ± 0.983</td>
<td>2.07 ± 1.02</td>
<td>1.87 ± 0.750</td>
<td>2.27 ± 0.833</td>
<td>2.60 ± 1.07</td>
</tr>
<tr>
<td>WASO (actigraph) (min)</td>
<td>53.5 ± 35.8</td>
<td>64.8 ± 36.2</td>
<td>63.3 ± 32.3</td>
<td>87.8 ± 49.8</td>
<td>90.1 ± 40.7</td>
</tr>
</tbody>
</table>

detailed above using multiple regression. In an initial regression analysis, we found that age (p < 0.001), RDI (p < 0.001), body mass index (p < 0.01), and use of diuretics (p < 0.05), but not sex (p = 0.12), were related to the number of trips to the bathroom at night. These factors were, therefore, included in the multiple regression models. After adjusting for these factors, subjective (restedness, sleep efficiency) and objective (number of wake bouts, mean length of wake bouts, WASO, sleep efficiency) measures were all still significantly related to the number of trips to the bathroom at night. In toto, it appears that going to the bathroom at night is associated with significant subjective and objective disruption of nocturnal sleep.

In the subset of subjects with ≥ 2 nights of bathroom use and ≥ 2 nights of no bathroom use, pairwise comparisons of the length of wake bouts indicated that bouts were 11.5% ± 23.5% longer on nights on which there was a trip to the bathroom (p < 0.05, paired t-test). Similarly, WASO was 20.8% ± 33.0% longer on nights on which there was a trip to the bathroom (p < 0.05, paired t-test). There were no differences in total sleep time (p = 0.18), the length of sleep bouts (p = 0.52), or the number of sleep (p = 0.12) or wake (p = 0.15) bouts. Thus, nocturia appears to be associated with the length of individual nocturnal wake episodes without affecting the overall amount or structure of sleep as imputed through actigraphy.

**DISCUSSION**

Our data indicate that toileting at night is a common occurrence in older individuals with insomnia, significantly associated with the amount of wakefulness occurring during the night and decreasing subjective restedness after sleep. Previous epidemiological work relying on self-reported sleep has described the negative relationship between subjective sleep quality and nocturia, as well as the common occurrence of nocturia in older individuals. More recently, data from the Sleep Heart Health Study have indicated that more general characteristics of nocturia summarized over a one-month interval were related to poorer quality sleep on a single night of polysomnography. Our work extends this research as it provides the first objective measurement of sleep disruption and its association with nocturia on nights in which both were documented simultaneously. Nocturia appears to worsen the already poor sleep of individuals with insomnia, perhaps by providing a stimulus for waking which is then often accompanied with turning on the lights (further decreasing sleepiness) and an opportunity for a lengthy awakening. The ultimate question remains whether the urge or need for urination causes the awakening, or after awakening due to another cause, an individual then feels the urge or need to urinate. This is more than an esoteric question since the answer could help guide therapeutic intervention, as is evinced by current experimental protocols.

Our study is not without its limitations. We were unable to capture which of the awakenings were associated with the trips to the bathroom. Further, although actigraphy is useful in determining overall amounts of wakefulness during a sleep episode, it is not as accurate as polysomnography in determining the precise length of specific awakenings. Future research studies should use polysomnography and objective urination monitoring to better delineate the effects of nocturia on sleep.

**REFERENCES**


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SUBMISSION & CORRESPONDENCE INFORMATION

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DISCLOSURE STATEMENT

This was not an industry supported study. Dr. Zeitzer is a PI for a study funded by Vanda Pharmaceuticals. Dr. Bliwise has consulted for Ferring Pharmaceuticals. The other authors have indicated no financial conflicts of interest.
Nocturia is defined as waking up one or more times at night to void, and is a common affliction among elderly. The prevalence of nocturia increases across age groups to more than 50% reporting 2 or more voids per night at age of 70. Higher prevalence of nocturia in this age group is multifactorial, and possible contributing causative factors include impaired bladder voiding, reduced bladder capacity, decreased vasopressin levels at night, increased comorbid conditions, and sleep disturbances.

Nocturia has been associated with lower quality of life, cardiovascular disease, falls, mortality, and hip fractures. It has been suggested that decreased quality of life and some of the adverse health outcomes could be due to sleep disruption from nocturia. Several studies have looked at self reported sleep measures and suggest a causal association between nocturia and poor sleep after controlling for confounders such as diabetes mellitus, congestive heart failure, and diuretics. These studies used questionnaires or survey and report poor sleep and nocturia was associated with longer wake time, but there was no difference in total sleep time or sleep structure. The authors reported that nocturia in subjects with insomnia is associated with increased wake time and subjective feeling of decreased restedness.

However, the study has several limitations. Even though the regression coefficients were statistically significant, as evident in the ANOVA F p-values, the residual error levels, that is, variance in the dependent variables, are extremely high. These are such indicate very weak precision in the models. Also, the authors do not indicate whether or not the categorical groupings of the independent variable were indicator or dummy coded, since the groupings of trips were made into a categorical variable they need to be indicator coded (k-1).

Regarding the magnitude of the effect, taking just one of the six measures, mean wake bout length, if we look at the difference from zero trips in actual seconds, we can see the data demonstrate a very tiny effect. There was a 9 second difference in the wake bout length if there was 1 trip and -3 seconds if there were 2 trips.

In conclusion, the relation between nocturia and its causal effect on sleep parameters needs to be further elucidated. Further, prospective studies controlling for major confounders need to...
be conducted to better clarify this relationship. Future studies should consider polysomnogram to capture awakening and associated voids, bladder monitoring to study if sleep disturbances per se cause awakening and hence nocturia, or vice versa by looking at the effect of bladder manipulation on sleep. This would help to tailor the treatment according to patient and possibly improve sleep and related consequences.

REFERENCES


CITATION


SUBMISSION & CORRESPONDENCE INFORMATION

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DISCLOSURE STATEMENT

The author has indicated no financial conflicts of interest.
Obstructive sleep apnea is characterized by repetitive partial (i.e., hypopnea) or total (i.e., apnea) obstruction of the upper airway with subsequent increased ventilatory effort (e.g., snoring, gasping, choking), resulting in cortical arousals and/or oxygen desaturations. Body position during sleep influences the frequency of apneas and hypopneas in 50% to 60% of individuals with obstructive sleep apnea (OSA).\(^1\) In such cases, the apnea-hypopnea index (AHI) is increased in the supine posture and reduced in the lateral posture. Positional sleep apnea is said to be present when there is a 50% reduction in the AHI during non-supine sleep.\(^2\)\(^-\)\(^6\)

Central sleep apnea (CSA) is characterized by cessation of respiration due to repetitive lapses in ventilatory effort resulting in cortical arousals and/or oxygen desaturations. While positional changes commonly affect the severity of obstructive sleep apnea, the effect of positional changes on the severity of central sleep apnea is less well known.

**Keywords:** Central sleep apnea, sleep position, sleep disordered breathing

**Citation:** Zaharna M; Rama A; Chan R; Kushida C. A case of positional central sleep apnea. *J Clin Sleep Med* 2013;9(3):265-268.

The patient presented to our lab for a diagnostic polysomnogram which showed the results reported in Table 1. Electrocardiography showed sinus rhythm with one premature ventricular contraction noted. There were no periodic limb movements or unusual behaviors noted, apart from occasional somniloquy. The patient was urged to return for an overnight CPAP and bilevel titration with servoventilation on standby in the event that central apneas were not effectively treated on CPAP or bilevel therapy. A positional pillow to avoid supine sleep was also recommended until positive airway pressure was initiated. (see Figures 1-3)

The patient returned for an overnight titration study. CPAP pressures of 5 to 18 cm water were tested. Bilevel pressures of 17/12 to 20/17 cm water were tested. Central sleep apnea dramatically improved on both CPAP and bilevel therapy in the supine and lateral position. A CPAP pressure of 14 cm water was recommended. A mean oxygen saturation of 96%, minimum oxygen saturation of 94%, RDI 2.7, and supine REM was observed at this pressure setting. A positional pillow was not used during the titration study (Figure 4).

The patient returned one month later for follow-up after using CPAP. Although he still experienced fatigue, download data showed effective treatment of his sleep apnea. Compliance data showed 100% of days with device usage, with an average of 7.5 h of usage per night. Therapy data showed an average residual AHI of 4.1 on CPAP of 14 cm water. Although download information was satisfactory, the presence of residual fatigue suggests that there may be residual respiratory events that were undetectable by the CPAP device. Although further testing was not pursued, a repeat titration study may have been considered at this point.

The patient was referred back to his primary care physician to evaluate further for possible underlying conditions; however,
Table 1—Results of diagnostic polysomnogram testing of patient present to the laboratory

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
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<td>Total Recording Time</td>
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</tr>
<tr>
<td>Total Sleep Time</td>
<td>6 hours, 55 minutes</td>
</tr>
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<td>Sleep Efficiency</td>
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</tr>
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<td>0 hours, 12 minutes</td>
</tr>
<tr>
<td>REM Latency</td>
<td>2 hours, 40 minutes</td>
</tr>
<tr>
<td>REM Periods</td>
<td>2</td>
</tr>
<tr>
<td>N1</td>
<td>4.0%</td>
</tr>
<tr>
<td>N2</td>
<td>81.3%</td>
</tr>
<tr>
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<td>0%</td>
</tr>
<tr>
<td>REM</td>
<td>14.7%</td>
</tr>
<tr>
<td>Supine</td>
<td>2 hours 4 minutes</td>
</tr>
<tr>
<td>Prone</td>
<td>0 hours 0 minutes</td>
</tr>
<tr>
<td>Left</td>
<td>1 hour 35 minutes</td>
</tr>
<tr>
<td>Right</td>
<td>3 hours 15 minutes</td>
</tr>
<tr>
<td>Apnea-Hypopnea Index (AHI)</td>
<td>49.3</td>
</tr>
<tr>
<td>Central Al</td>
<td>42.7 (Supine CAI of 101.6, Left CAI 39, Right CAI 7.1)</td>
</tr>
<tr>
<td>Obstructive AHI</td>
<td>6.7</td>
</tr>
<tr>
<td>Obstructive RDI</td>
<td>14.7</td>
</tr>
<tr>
<td>Respiratory Disturbance Index (RDI)</td>
<td>57.3</td>
</tr>
<tr>
<td>Mean Sleep Oxygen Saturation</td>
<td>94.3%</td>
</tr>
<tr>
<td>Minimum Sleep Oxygen Saturation</td>
<td>82%</td>
</tr>
<tr>
<td>Transcutaneous CO₂</td>
<td>Mean wake TcCO₂ high 40s mm Hg, Maximum sleep TcCO₂ low 50s mm Hg.</td>
</tr>
</tbody>
</table>

Figure 1
Central apneas in supine sleep on diagnostic polysomnogram.

Figure 2
Central apneas in supine sleep on diagnostic polysomnogram which resolved in lateral (left sided) sleep.

Figure 3
Central apneas in supine sleep on diagnostic polysomnogram which resolved in lateral (left sided) sleep.

Figure 4
Improvement of positional sleep apnea on CPAP and Bilevel therapy in both lateral and supine sleep.
he denied any symptoms consistent with an underlying cardiac, renal, or neurologic condition. Further diagnostic testing had not been performed at the time of his sleep evaluation. An echocardiogram had not been performed, so further information on cardiac systolic and diastolic function, pulmonary artery pressure, and valvular problems was not available.

**DISCUSSION**

Positional sleep apnea is defined as greater than 50% reduction in the AHI between supine and non-supine positions. Sleeping position commonly affects the severity of obstructive sleep apnea. Specifically, sleeping in the supine position is associated with a worsening of obstructive sleep apnea and is more frequently seen in those patients with less severe OSA and smaller neck circumference. Worsening OSA in supine sleep is thought to be related to relaxation of muscles in the jaw and throat under the influence of gravity that cause narrowing of the airway.

Positional changes in central sleep apnea are less well understood and have mostly been documented in the literature in patients with Cheyne-Stokes respiration associated with congestive heart failure. There are only a few reports in the literature of positional central sleep apnea in patients with no known cardiac history or congestive heart failure. One study did show a change in sleep disordered breathing pattern from obstructive to almost all mixed and central apneas on both diagnostic and CPAP titration studies with change to supine sleeping position in 8 patients who had no cardiac history (one patients had a history of cerebral hemorrhage, and one had cerebral ischemia). Another study showed significant supine worsening of sleep apnea in patients with treatment-emergent central sleep apnea or complex sleep apnea both on CPAP therapy and adaptive servoventilation therapy (ASV).

This case report showed idiopathic central sleep apnea in an otherwise healthy young man that was significantly worse in supine sleep. While CPAP therapy is not always helpful or even the first choice treatment in CSA, significant improvement in AHI was noted in our patient with CPAP pressures as low as 6 cm water during supine sleep. Treatment of central sleep apnea is generally based on correction of the causative etiology. Central sleep apnea may be primary (idiopathic) or due to Cheyne-Stokes breathing (secondary to congestive heart failure, stroke, and possibly renal failure), positive airway pressure (i.e., complex sleep apnea), high altitude (i.e., >4,000 meters), various medical conditions (e.g., brainstem lesion, cardiac or renal disorders), or drugs (e.g., opioids). In this patient, none of these potential causes were suspected or identified. Additionally, Cheyne-Stokes respiratory pattern and periodic breathing were absent on both the diagnostic and titration studies. Additional treatment options for central sleep apnea include other forms of positive airway pressure (i.e., servoventilation, bilevel PAP), supplemental gases (i.e., oxygen, carbon dioxide), medications (i.e., theophylline, acetazolamide), and correction of the causative etiology.

Sleeping in the supine position reduces cardiac output and increases venous return. Decreased cardiac output delays the transfer of blood gas information from the pulmonary capillary bed to the chemoreceptors and can lead to sustained fluctuations in respiratory output (i.e., central sleep apnea). Atrial pacing has been shown to reduce central sleep apnea in those with low cardiac output due to bradycardia. An increase in venous return could additionally exacerbate both diastolic and systolic dysfunction. This could result in an inability to reduce ventilation with carbon dioxide levels remaining near the central apnea threshold.

In addition to reducing cardiac output and increasing venous return, sleeping in the supine position can result in a reduction of both the functional residual capacity and the metabolic rate, which consequently enhances plant gain. Enhanced plant gain, which is defined as a large change in carbon dioxide levels relative to a small change in ventilation, is another proposed mechanism in the development of central sleep apnea.

The application of positive airway pressure in this patient could conceivably increase cardiac output and reduce venous return, improving arterial circulation time and reduces plant gain, which successfully normalizes ventilation.

The question must be considered whether this could be a mistaken case of obstructive sleep apnea. Given the worsening respiratory pattern in supine sleep, the lack of underlying causative etiology for CSA, absence of esophageal pressure manometry testing, normal wake baseline TCOCO, levels of 40-43 mm Hg, and the positive response to CPAP therapy, the possibility of obstructive sleep apnea cannot be ruled out. Although idiopathic central sleep apnea is usually associated with hypcapnia and this patient’s TCOCO, levels were slightly elevated, it is not required. Eupneic patients with congestive heart failure may also have central sleep apnea. More important is the proximity of the central apnea threshold to the carbon dioxide level. Other features of central sleep apnea were evident on the patient’s sleep studies, including improvement of respiratory events in REM sleep and clear flattening of the chest and abdominal belts even with an increase in sensitivity.

The present case suggests that positional changes in severity of central sleep apnea may be an important factor to consider. Many patients have difficulty tolerating current treatment options for CSA including CPAP, bilevel PAP, and servoventilation therapy. Positional pillows are often viewed by patients as a more tolerable alternative treatment of sleep apnea. Further research on the prevalence of positional CSA and exploration of positional therapy as a viable treatment option for CSA is needed. Although a positional pillow was recommended to this patient, he did not attempt positional therapy as a treatment option.

**REFERENCES**


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DISCLOSURE STATEMENT
This was not an industry supported study. Dr. Kushida receives research support from Philips Respironics and ResMed through Stanford University. The other authors have indicated no financial conflicts of interest.
Narcolepsy-cataplexy is an uncommon sleep disorder which may present in childhood. We report a case of an 8-year-old presenting with narcolepsy-cataplexy following a streptococcal infection. Autoimmune etiology for narcolepsy has been suggested. In our patient increased anti-streptolysin O and anti-DNAse B titers were noted. As suggested by recent cases, the streptococcal infection was likely a trigger for narcolepsy onset in this genetically predisposed child. The patient was initially diagnosed as having Sydenham chorea due to motor movements. However, these transient movements may be due to the narcolepsy onset. Narcolepsy in childhood may present with atypical symptoms; it might be difficult to obtain accurate history and can be misdiagnosed as in the reported case. A high index of clinical suspicion is needed to diagnose these patients. Keywords: Narcolepsy, streptococcal infection

**Citation:** Natarajan N; Jain SV; Chaudhry H; Hallinan BE; Simakajornboon N. Narcolepsy-cataplexy: is streptococcal infection a trigger? *J Clin Sleep Med* 2013;9(3):269-270.

## DISCUSSION

Narcolepsy-cataplexy is believed to be autoimmune, given the strong genetic association with HLA DQB1*0602, and polymorphisms in the T-cell receptor alpha locus. Recent studies show antibodies against the anti-tribbles homolog 2 (TRIB2) in new onset narcolepsy-cataplexy. Recently, there are reports of narcolepsy following H1N1 influenza infection and vaccination. The risk of narcolepsy is 5.4 times higher (95% CI, 1.5-19.1) in patients with a physician-diagnosed streptococcal infection. Moreover, prior to the onset of narcolepsy, a higher prevalence of streptococcal throat infections was noted in most prepubertal and peripubertal versus postpubertal children. Furthermore, higher ASO and ADB titers were found in patients with recent diagnoses, as compared to age-matched controls and patients with long-standing disease. Similar to other post-streptococcal sequelae, there may be cross-reactivity between the antibodies against group A Streptococcus and hypocretin secreting neurons. In a genetically predisposed individual, this may trigger the onset of narcolepsy. Interestingly, this patient had complex motor movements which led to diagnosis of SC. However, these are associated with new-onset narcolepsy in children. Moreover, SC is an occasional feature of encephalitis lethargica (EL), a neurological disorder characterized by hypersomnia and posterior hypothalamic lesions, associated with elevated ASO titers.
Narcolepsy-cataplexy is a multifactorial disease. The diagnosis in prepubertal children may be difficult. Recent observations from the Pediatric group of Sleep Research Network have suggested increased new cases of childhood narcolepsy following infections. The Network is currently working on examining this issue in a systematic manner.

REFERENCES

10. www.sleepresearchnetwork.org (Pediatric sleep disorders section)
Background: Hypoxemia is an immediate consequence of obstructive sleep apnea. Oxygen (O₂) administration has been used as an alternative treatment in patients with obstructive sleep apnea (OSA) who do not adhere to continuous positive airway pressure (CPAP) in order to reduce the deleterious effects of intermittent hypoxemia during sleep. This systematic review aims to investigate the effects of O₂ therapy on patients with OSA.

Method: We conducted a systematic search of the databases Medline, Embase, Cochrane Central Register of Controlled Trials (1st Quarter 2011), Cochrane Database of Systematic Reviews (from 1950 to February 2011). Our search strategy yielded 4,793 citations. Irrelevant papers were excluded by title and abstract review, leaving 105 manuscripts. We reviewed all prospective studies that included: (1) a target population with obstructive sleep apnea, (2) O₂ therapy and/or CPAP as a study intervention, (3) the effects of O₂ on the apnea-hypopnea index (AHI), nocturnal hypoxemia, or apnea duration.

Results: We identified 14 studies including a total of 359 patients. Nine studies were of single cohort design, while 5 studies were randomized control trials with 3 groups (CPAP, oxygen, and placebo/sham CPAP). When CPAP was compared to O₂ therapy, all but one showed a significant improvement in AHI. Ten studies demonstrated that O₂ therapy improved oxygen saturation vs. placebo. However, the average duration of apnea and hypopnea episodes were longer in patients receiving O₂ therapy than those receiving placebo.

Conclusion: This review shows that O₂ therapy significantly improves oxygen saturation in patients with OSA. However, it may also increase the duration of apnea-hypopnea events.

Keywords: OSA, CPAP, oxygen therapy


Obstructive sleep apnea (OSA) is the periodic reduction (hypopnea) or cessation (apnea) of airflow due to narrowing of the upper airway during sleep, often accompanied by hypoxemia and sleep disturbance.¹ The prevalence of OSA is estimated to be between 2% and 25% in the general population. OSA is linked to hypertension, ischemic heart disease, stroke, premature death, and motor vehicle crash.²-⁷

Oxygen desaturation is an immediate consequence of obstructive sleep apnea. Intermittent hypoxemia increases sympathetic activity and norepinephrine levels and leads to hypertension.⁸,⁹ It has also been associated with an increased risk of diabetes.¹⁰ Indeed, most of the sequelae of obstructive sleep apnea are more strongly linked to the degree and duration of oxygen desaturation than to the numbers of apneas and hypopneas or disruptions in sleep architecture.¹¹ The resolution of nocturnal intermittent hypoxemia associated with sleep apnea is a major goal of the treatment of patients with obstructive sleep apnea.

Many treatment approaches have been employed for the treatment of moderate to severe OSA, but CPAP is the treatment of choice and has been widely prescribed.¹²,¹³ In placebo-controlled and uncontrolled studies, CPAP has been shown to reduce apnea-hypopnea index (AHI) and to improve hypoxemia associated with respiratory events during sleep.¹⁴,¹⁵ CPAP adherence has been reported to be as low as 50%, at least in part because it is a burdensome treatment.¹⁶

Oxygen administration has been used as an alternative treatment in patients with OSA who are not somnolent or not compliant with CPAP; the purpose of supplemental oxygen in this situation is to reduce the deleterious effects of transient hypoxemia during sleep.¹⁷ Supplemental oxygen has been shown to be effective in improving the AHI, respiratory arousal index, and nocturnal desaturation during apneic episodes.¹⁸ However, oxygen therapy may lengthen apnea duration, thus accelerating CO₂ retention.¹⁹

This systematic review aims to investigate the effects of CPAP and oxygen on patients with OSA. This review addresses the following questions: (1) Does evidence from controlled trials support the preferential use of CPAP over oxygen for improving OSA symptoms? (2) Can oxygen therapy be safely used in patients who are non-adherent with CPAP?

METHODS

For purposes of this analysis, the target population consisted of adult humans with a diagnosis of obstructive sleep apnea defined as an AHI > 5 events per hour. The diagnosis of OSA was made using polysomnography (PSG). The study intervention included
either the CPAP and oxygen therapy or oxygen therapy compared with the placebo. Outcomes of interest included the effects on AHI, nocturnal hypoxemia, apnea duration, and arousal index.

Literature Search

The literature search was performed according to the PRISMA (Preferred Reporting Items for Systematic reviews and meta-analysis) guidelines.20 The databases Medline, Embase, Cochrane Central Register of Controlled Trials (1st Quarter 2011), Cochrane Database of Systematic Reviews (from 1950 to Feb 2011) were thoroughly searched to include all available evidence for the systematic review. We developed and executed the search strategy with the help of an expert librarian familiar with the literature search protocol of the Cochrane Collaboration. The following target population keywords were used for the literature search: “obstructive sleep apnea,” “obstructive sleep apnea syndrome,” “obstructive sleep apnea-hypopnea syndrome,” “sleep disordered breathing,” “obesity hypoventilation syndrome” and “apnea-hypopnea,” “sleep apnea syndrome and apnea.” The target intervention keywords used were “oxygen”, “oxygen therapy,” “oxygen inhalational therapy,” “CPAP,” “positive airway pressure,” and “continuous positive airway pressure.” The results of the target population were combined with the target intervention results (using an “and”). Studies focusing on central sleep apnea were excluded by including “NOT central sleep apnea” in the search strategy. The search strategy was limited to English language abstracts and adult human population. Duplicate records, if any were removed from the final search result. We also reviewed the reference lists of relevant articles to retrieve potentially relevant articles.

1. Medline (Ovid SP) (1948 to Feb 2011)
2. EMBASE (1980 to Feb 2011)
3. Cochrane Database of Systematic Reviews (1st quarter 2011)
4. Cochrane Central Controlled Trials Registry (1st quarter 2011)

The databases of the Cochrane Library were used to confirm the completeness of the search. The time period searched was 1948 to 2011.

Study Selection

The search results were evaluated by two independent reviewers (VM, TSV). First, irrelevant papers were excluded by reviewing the title of the records. Next, the abstract and/or full text articles of the remaining papers were retrieved and carefully evaluated to determine if they met the eligibility criteria.

All prospective studies, including randomized and non-randomized placebo controlled trials were included if they reported the effects of CPAP treatment or oxygen therapy on AHI, oxygen saturation, apnea duration, and arousal index in patients with OSA. Studies not reporting at least one of these outcomes were excluded. All observational studies were graded for strength of evidence according to the Oxford level of evidence.21 We used the Cochrane risk of bias tool to assess the risk of bias for 6 randomized controlled trials (Table 1).22

Data Extraction

Data extraction was completed by two reviewers (VM, TSV) and validated by the senior author (FC). Various data extracted from these studies included the type of study, level of evidence, number of patients receiving the study intervention, type of study intervention, duration and effects of intervention on AHI, SpO2, arousal index, and apnea duration. We divided the studies into 2 groups: the first group included studies which used CPAP and O2 treatment; the second group included studies which used only O2 therapy as an intervention. The methodological qualities of the included studies were independently evaluated by the first author (VM), if any doubt the senior author was consulted (FC). Individual authors were contacted via emails for the details of the results

Statistical Analysis

We performed the meta-analyses by using fixed-effects model if no heterogeneity was present. In order to assess the heterogeneity between studies, we used χ2 tests and estimated the F statistic. We considered the heterogeneity to be present if the p value on the χ2 test was < 0.05. In the presence of heterogeneity, we pooled the results by using random-effects (DarSemoni-an and Laird method) model. The standardized mean difference was used to pool continuous variables that used different scales. We performed separate random-effects meta-analyses among randomized controlled studies comparing CPAP, placebo CPAP, and oxygen. We did not correct for multiple comparisons.

RESULTS

The Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) guidelines were followed for the description of the search strategy. Our search strategy yielded 4,793 citations (Figure 1). In the first session of screening, most studies were eliminated based on the predetermined eligibility criteria, leaving 105 articles. In the second session, 105 articles were evaluated and 14 articles were identified as

Table 1—Cochrane risk of bias in included studies

<table>
<thead>
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<th>Study ID</th>
<th>Adequate Sequence Generation</th>
<th>Allocation Concealment</th>
<th>Blinding</th>
<th>Incomplete Outcome Data Assessed</th>
<th>Free of Selective Outcome Reporting</th>
<th>Free of Other Biases</th>
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</tbody>
</table>

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meeting the inclusion criteria, with subsequent exclusion of 91 articles. Articles were excluded for the following reasons: Non-pertinent papers—excluded by abstract/full-text review (n = 64), O₂ therapy in pediatric OSA (n = 11), reviews papers (n = 10), correspondence (n = 4), and case reports (n = 2).

Study Characteristics

Tables 2 and 3 summarize study characteristics included in the systematic review. There were 6 studies²³⁻²⁸ that used a randomized control design with 3 groups, each group being assigned to CPAP, placebo CPAP, or O₂ to evaluate the effects of CPAP and O₂ on AHÍ, O₂ saturation, and arousal indices. Eight studies²⁹⁻³⁶ used a single cohort in which the outcome was measured in the same study population before and after the study intervention. All of these observational studies compared the effects of room air with O₂ on mean oxyhemoglobin saturation, sleep disordered breathing (SDB) events, and SDB event duration. These 8 studies were graded according to Oxford level of evidence and had a 2b level of evidence. We could not pool the results from the study by Block et al.³³ because the authors did not provide the standard deviation for the outcome of interests.

Patient Characteristics

Table 2 represents a group of patients who received CPAP and O₂ intervention versus placebo CPAP. Table 3 represents a group of patients who received O₂ intervention compared with control (air). A total of 339 patients were included in the 14 studies. All the patients had a diagnosis of OSA confirmed by in-laboratory polysomnography. The inclusion criteria of the patients differed among the studies selected for the review. Two studies²³,³³ used AHÍ > 5; 5 studies²⁴⁻²⁸ used AHÍ > 15; one study²³ used SDB event > 50/h, and one study³³ used RDI > 20 for OSA patient selection. Four studies²⁶,³¹,³⁴,³⁶ selected patients with a confirmed diagnosis of OSA following overnight PSG with no description of any specific AHÍ criteria. Most of the patients were male, accounting for 89% of the study population. All the patients in the reported studies had moderate to severe OSA with AHÍ ranging from 20.5 ± 5 to 88.2 ± 27. The duration of the study intervention across the different studies was in the range of 1 night to 3 months.

Effects on Oxygenation, Respiratory Events, and Sleepiness

Table 2 summarizes the effects of the different treatment modalities on AHÍ, SpO₂ and arousal events studied by 6 RCTs. The respiratory disturbances occurring during the nighttime in OSA patients were measured using AHÍ, respiratory disturbance index (RDI), or SDB events. When CPAP was compared with O₂, CPAP was significantly more effective in reducing AHÍ, while O₂ was shown to be more effective in elevating the mean SpO₂ and mean nadir SpO₂ during hypoxemic events. Both CPAP and O₂ improved the oxygenation as compared to placebo (sham) CPAP; this effect was statistically significant (p < 0.05). Four studies showed that CPAP versus O₂ therapy was more effective in improving the arousal events/total arousal index, but we could not pool the arousal events for the meta-analysis because of insufficient data.

The effects of CPAP and oxygen supplementation on the daytime somnolence was evaluated by 2 studies.²³,²⁴ In one study, nasal CPAP was more effective in improving objectively measured daytime sleepiness than oxygen. This effect was apparent due to the significant efficacy of CPAP in lengthening the multiple sleep latency test (MSLT) time compared to baseline.²³ Similarly, another study showed the effectiveness of CPAP in reducing Epworth Sleepiness Scale score; however, it was not statistically different from placebo-CPAP or supplemental oxygen.²⁴

Effects on Systemic Blood Pressure

Three studies showed the treatment outcome on systemic blood pressure in patients treated with CPAP, oxygen, and placebo-CPAP.²³,²⁵,²⁶ Two studies showed that CPAP effectively reduced both the systolic as well as the diastolic blood pressure as compared to oxygen (p < 0.05).²³,²⁶ In one study, CPAP and oxygen both had the effects in lowering the systolic blood pressure as compared to diastolic blood pressure; however, the changes were not statistically significant.²³

The effects of O₂ therapy on the oxygen saturation and SDB events are summarized in Table 3. Seven studies showed that oxygen therapy was effective in improving the oxygenation as compared to air (control) in OSA patients. The SDB events
showed a decreasing trend in the number of events when the patients received O₂ therapy after breathing room air. One study demonstrated an improved cardiovascular status in OSA patients following oxygen enrichment night. Similarly, another study showed an improvement in daytime somnolence in patients receiving oxygen therapy.

Meta-Analysis of Randomized Controlled Trials

Effects on Apnea Hypopnea Index (Figure 2)
A pooled analysis of 5 randomized controlled trials demonstrated that the use of therapeutic CPAP lead to a statistically significant reduction in the AHI versus nocturnal administration of oxygen (SMD -3.37, 95% CI -4.79 to -1.96). There was also a statistically significant reduction in AHI in CPAP group versus placebo (SMD -3.65, 95% CI -5.31 to -1.98). Nocturnal oxygen did not show significant reduction in AHI compared to placebo CPAP (SMD -0.32, 95% CI -0.74 to 0.08).

Effects on Mean Nocturnal Oxyhemoglobin Saturation (Figure 3)
A pooled analysis of 4 studies that reported mean oxyhemoglobin saturation showed that both therapeutic CPAP and nocturnal administration of oxygen lead to significant improvement in oxyhemoglobin saturation compared to placebo CPAP. Comparison of CPAP to nocturnal oxygen did not demonstrate

### Table 2—Study characteristics and effects of CPAP vs. oxygen therapy in OSA patients

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Design / Total Population</th>
<th>Intervention</th>
<th>Duration</th>
<th>Baseline Data</th>
<th>Variables</th>
<th>CPAP</th>
<th>Oxygen</th>
<th>P-CPAP</th>
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</thead>
<tbody>
<tr>
<td>Phillips 1990</td>
<td>Randomized crossover / 8</td>
<td>Nasal O₂, Nasal Air, Nasal CPAP</td>
<td>3 month</td>
<td>20.5 ± 4.8</td>
<td>AHI</td>
<td>3.0 ± 0.9*</td>
<td>16.8 ± 3.2</td>
<td>22.1 ± 5.7</td>
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<td>Loredo 2006</td>
<td>RCT / 63</td>
<td>CPAP, P-CPAP, Oxygen</td>
<td>2 weeks</td>
<td>65.9 ± 28.6</td>
<td>AHI</td>
<td>3.4 ± 3.0*</td>
<td>43.6 ± 3.8</td>
<td>50.1 ± 32.1</td>
</tr>
<tr>
<td>Norman 2006</td>
<td>RCT / 46</td>
<td>CPAP, P-CPAP, Oxygen</td>
<td>2 weeks</td>
<td>66.1 ± 29.1</td>
<td>Mean SpO₂</td>
<td>95.6 ± 4.0</td>
<td>96.2 ± 4.4*</td>
<td>91.1 ± 3.8</td>
</tr>
<tr>
<td>Mills 2006</td>
<td>RCT / 50</td>
<td>CPAP, P-CPAP, Oxygen</td>
<td>2 weeks</td>
<td>65.0 ± 8.3</td>
<td>Mean SpO₂ &lt; 90%</td>
<td>0.07 ± 0.08*</td>
<td>2.5 ± 0.5*</td>
<td>5.8 ± 0.8</td>
</tr>
<tr>
<td>Bardwell 2007</td>
<td>RCT / 38</td>
<td>CPAP, P-CPAP, Oxygen</td>
<td>2 weeks</td>
<td>59.4 ± 31.1</td>
<td>RDI</td>
<td>3.6 ± 3.9*</td>
<td>55.8 ± 40.9</td>
<td>51.0 ± 23.5</td>
</tr>
<tr>
<td>Lim 2007</td>
<td>RCT / 46</td>
<td>CPAP, P-CPAP, Oxygen</td>
<td>2 weeks</td>
<td>65.5 ± 7.8</td>
<td>Mean SpO₂</td>
<td>96.2 ± 2.8*</td>
<td>95.9 ± 3.5*</td>
<td>91.2 ± 4.1</td>
</tr>
</tbody>
</table>

RCT, randomized controlled trial; CPAP, continuous positive airway pressure; P-CPAP, placebo CPAP; O₂, oxygen, n, number of patients; AHI, apnea-hypopnea index; SSS, Stanford Sleepiness Score; ESS, Epworth Sleepiness Score; ODI, oxygen desaturation index; TAI, total arousal Index; RDI, respiratory disturbance index; SBP, systolic blood pressure; DBP, diastolic blood pressure. *Statistically significant change from placebo (p < 0.05). †Statistically significant change from oxygen (p < 0.05). ‡Statistically significant change from baseline (p < 0.05). §§Statistically significant change from oxygen or P-CPAP (p < 0.001).
Table 3—Study characteristics and effects of oxygen therapy in OSA patients

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Design</th>
<th>Population (n) Type / Total</th>
<th>Intervention</th>
<th>Baseline Data</th>
<th>Variables</th>
<th>Oxygen</th>
<th>Air</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kearley 1980</td>
<td>Single Cohort OSA with COPD / 11</td>
<td>1st half of night: Air(Control) ↓ 2nd half of night: O₂</td>
<td>– –</td>
<td>O₂ desaturation episodes/h</td>
<td>0.7*</td>
<td>4.5</td>
<td></td>
</tr>
<tr>
<td>Smith 1984</td>
<td>Single Cohort randomized study OSA with EDS / 12</td>
<td>1 night: Air(Control) ↓ 1 night: O₂</td>
<td>69 ± 10</td>
<td>SaO₂ (%)</td>
<td>96 ± 0.6*</td>
<td>94 ± 0.06</td>
<td></td>
</tr>
<tr>
<td>Gold 1986</td>
<td>Single Cohort nonrandomized trial OSA / 8</td>
<td>1 month: Air(Control) ↓ 1 month: O₂</td>
<td>77 ± 16</td>
<td>SaO₂ (%)</td>
<td>94 ± 2*</td>
<td>87 ± 3</td>
<td></td>
</tr>
<tr>
<td>Alford 1986</td>
<td>Single Cohort Crossover Study OSA (SDB &gt; 50/h) with COPD / 20</td>
<td>1 night: Air(Control) ↓ 1 night: O₂</td>
<td>88.2 ± 27</td>
<td>SaO₂ (%)</td>
<td>94.6 ± 3.5*</td>
<td>87.7 ± 6</td>
<td></td>
</tr>
<tr>
<td>Block 1987</td>
<td>Single Cohort nonrandomized nonblinded study OSA (AHI &gt; 5) / 20</td>
<td>1st half of night: Air(Control) ↓ 2nd half of night: O₂</td>
<td>–</td>
<td>SaO₂ (%)</td>
<td>92.0 ± 1.1*</td>
<td>89.4 ± 0.93</td>
<td></td>
</tr>
<tr>
<td>Pokorski 2000</td>
<td>Single Cohort Single blind trial Pre-surgical OSA patients / 5</td>
<td>1 night: Air(Control) ↓ 1 night: O₂</td>
<td>52.7 ± 10.4</td>
<td>SaO₂ (%)</td>
<td>36*</td>
<td>91</td>
<td></td>
</tr>
<tr>
<td>Friedman 2001</td>
<td>Single Cohort nonrandomized nonblinded study OSA / 21</td>
<td>1st half of night: O₂ ↓ 2nd half of night: Air(Control)</td>
<td>28.6 ± 15.6</td>
<td>SaO₂ (%)</td>
<td>93.3 ± 3.84*</td>
<td>82.4 ± 4.73</td>
<td></td>
</tr>
<tr>
<td>Kumagai 2008</td>
<td>Single Cohort nonrandomized nonblinded study OSA patients on PD / 11</td>
<td>1 month: O₂</td>
<td>31.1 ± 8.8</td>
<td>SaO₂ (%)</td>
<td>97.7 ± 0.9*</td>
<td>94.2 ± 1.2</td>
<td></td>
</tr>
</tbody>
</table>

ID, identification; Dx, diagnosis; OSA, obstructive sleep apnea; n, number; M, male; F, female; O₂, oxygen; PSG, polysomnography; AHI, apnea-hypopnea index; RDI, respiratory disturbance index; PD, peritoneal dialysis. All data in mean or mean ± SD. *p < 0.01, †p < 0.001, ‡p < 0.05.

Figure 2—Effect of CPAP versus oxygen on apnea hypopnea index (AHI)

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>SMD (95% CI)</th>
<th>% Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phillips</td>
<td>1990</td>
<td>-5.87 (-8.26, -3.49)</td>
<td>14.46</td>
</tr>
<tr>
<td>Loredo</td>
<td>2006</td>
<td>-2.53 (-3.33, -1.73)</td>
<td>22.69</td>
</tr>
<tr>
<td>Norman</td>
<td>2006</td>
<td>-1.69 (-2.76, -0.63)</td>
<td>22.42</td>
</tr>
<tr>
<td>Mills</td>
<td>2006</td>
<td>-6.27 (-7.95, -4.60)</td>
<td>18.22</td>
</tr>
<tr>
<td>Bandwell</td>
<td>2007</td>
<td>-1.73 (-2.64, -0.81)</td>
<td>22.21</td>
</tr>
<tr>
<td>Overall (I² = 87.4%, p = 0.000)</td>
<td>-3.37 (-4.79, -1.96)</td>
<td>100.00</td>
<td></td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis
a significant difference in the degree of improvement in oxygenation (SMD 0.07, 95% CI -0.27 to 0.41).

**Meta-Analysis of Observational Studies**

**Effects on SDB events (Figure 4)**

A pooled analysis of 6 observational studies showed significant reduction in SDB events with oxygen compared to air (SMD -0.95, 95% CI -1.69 to -0.21).

**Effects on Mean Nocturnal Oxyhemoglobin Saturation (Figure 5)**

A pooled analysis of 6 observational studies showed significant improvement in mean oxyhemoglobin saturation with oxygen compared to air (SMD 2.45, 95% CI 1.49 to 3.4).

**Effects on Sleep Disordered Breathing (SDB) Event Duration**

We identified 5 observational studies reporting the SDB event duration as an outcome. We could not pool the results of these studies for statistical analysis due to the lack of sufficient data. However, 3 of these studies reported that administration of oxygen lead to the prolongation of SDB event duration.

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**DISCUSSION**

In this systematic review, we identified and reviewed 14 studies evaluating the effects of oxygen supplementation for the treatment of intermittent nocturnal hypoxemia in patients with OSA. We performed a meta-analysis of the six randomized controlled trials that evaluated the effect of CPAP, placebo CPAP, versus oxygen on AHI and SpO2. In this analysis, patients with obstructive sleep apnea who used CPAP had significant reduction in AHI compared to those who used nocturnal oxygen. However, both nocturnal oxygen and CPAP improved oxyhemoglobin saturation equally.

Obstructive sleep apnea is a prevalent disorder with its serious health related consequences. Many patients with sleep apnea have intermittent episodes of hypoxemia at night secondary to the periods of the upper airway obstruction. These episodes have been shown to be associated with harmful se-
quelae including insulin resistance, cognitive deficit, and the development of other cardiovascular morbidity.\textsuperscript{38-40} Both nasal CPAP and nocturnal administration of oxygen improve oxyhemoglobin saturation, but nocturnal oxygen has little effect on the blood pressure surge following apneas in patients with sleep apnea.\textsuperscript{41-43} On the other hand, CPAP has been shown to lower the blood pressure variability in patients with sleep apnea.\textsuperscript{25,26} This suggests that there might be some other factors such as hypercapnia, arousals, respiratory efforts, intrathoracic pressure changes, or fragmented sleep contributing to the increase in the blood pressure seen in sleep apnea.\textsuperscript{44-47} In a study in human adults, the arousals from NREM sleep was shown to increase the sympathetic discharge with increase in the systolic blood pressure.\textsuperscript{48}

Patients with OSA frequently have cognitive dysfunction and excessive daytime sleepiness (EDS), possible secondary to the combination of hypoxemia and fragmented sleep. These symptoms worsen with increasing severity of hypoxemia and increasing frequency of arousals. Nasal CPAP improves both the arousals and hypoxemia and thereby has been shown to improve the sleepiness in contrast to the nocturnal administration of oxygen.\textsuperscript{25,49} On the other hand, both CPAP and oxygen supplementation have been shown to improve psychological symptoms, including depression.\textsuperscript{77}

CPAP is clearly the treatment of choice in patients with OSA due to its immediate efficacy. It has been shown to improve AHI, hypoxemia, and arousals, thereby improving sleepiness and hypertension in contrast to the nocturnal administration of oxygen. However, patient adherence to CPAP is less than optimum.\textsuperscript{52} In one study, adherence to CPAP was reported to be higher in patients who had consultation with the sleep physician prior to undergoing the sleep study,\textsuperscript{53} but adherence to CPAP is between 50\% and 70\%, even with excellent management.\textsuperscript{54}

Hypoxemia is a major problem for patients with OSA in the postoperative period and hypoxemic episodes have been reported to occur mostly between the postoperative nights two to five.\textsuperscript{55} Up to 40\% of patients undergoing abdominal or thoracic surgery may experience postoperative hypoxemia.\textsuperscript{56} In particular, surgical patients with OSA are at high risk of having postoperative complications.\textsuperscript{57,58} A recent cohort study showed that oxygen desaturation with $\text{SpO}_2 < 90\%$ was the most common postoperative complication in patients with OSA.\textsuperscript{59} These hypoxemic episodes have been shown to have serious consequences, including poor wound healing, cardiac arrhythmias, and delirium.\textsuperscript{60,61} The use of supplemental oxygen in the perioperative period has been shown to reduce nausea and vomiting and hospital length of stay, and to improve wound healing.\textsuperscript{62-64}

Long-term oxygen therapy (LTOT) has been shown to improve survival and quality of life in patients with COPD.\textsuperscript{65-67} However, its role in obstructive sleep apnea treatment is more controversial. The administration of nocturnal oxygen leads to the improvement of intermittent hypoxemia in patients with OSA. It may be considered in hypoxemic patients with OSA who are intolerant to the other treatment modalities for sleep apnea. However, the long-term consequences of chronic nocturnal administration of oxygen are unknown in patients with OSA. Further nocturnal oxygen has been shown to prolong apnea duration in patients with OSA, perhaps as a result of the suppression of the hypoxic respiratory drive.\textsuperscript{31,33} In an observational study, the rise in blood pressure following each apneic episode was primarily linked to apnea duration and was not linked to hypoxemia.\textsuperscript{42} Prolonged apnea duration may also increase the severity of hypercarbia and acidosis in patients with OSA.\textsuperscript{19,31,32} This potential risk mandates careful monitoring for arrhythmias and other consequences of hypercarbia, especially in those with comorbid lung disease.

In conclusion, the evidence from the controlled trials does support the preferential use of CPAP over oxygen in patients with OSA since CPAP significantly improves the oxyhemoglobin saturation and reduces AHI and systemic blood pressure with improvement in daytime sleepiness. On the other hand, oxygen therapy is a double-edged sword, which not

---

**Figure 5**—Effect of oxygen versus air on nocturnal mean oxyhemoglobin saturation ($\text{SpO}_2$)

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>SMD (95% CI)</th>
<th>% Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smith</td>
<td>1984</td>
<td>4.69 (3.09, 6.29)</td>
<td>13.88</td>
</tr>
<tr>
<td>Gold</td>
<td>1986</td>
<td>0.96 (-0.06, 2.03)</td>
<td>17.83</td>
</tr>
<tr>
<td>Alford</td>
<td>1986</td>
<td>1.40 (0.71, 2.10)</td>
<td>20.22</td>
</tr>
<tr>
<td>Pokoroski</td>
<td>2000</td>
<td>2.55 (0.79, 4.31)</td>
<td>12.83</td>
</tr>
<tr>
<td>Friedman</td>
<td>2001</td>
<td>2.53 (1.71, 3.35)</td>
<td>19.41</td>
</tr>
<tr>
<td>Kumagai</td>
<td>2008</td>
<td>3.30 (1.98, 4.62)</td>
<td>15.83</td>
</tr>
<tr>
<td>Overall (I-squared = 78.1%, $p = 0.000$)</td>
<td></td>
<td>2.45 (1.49, 3.41)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

**NOTE:** Weights are from random effects analysis.
only lengthens the apneoa duration but potentially increases the risk of hypercarbia with minimal to no effect on blood pressure and daytime sleepiness. Hence, at present it is difficult to recommend oxygen therapy for patients who are non-adherent with CPAP until the results of a multicenter clinical trial, Heart Biomarker Evaluation in Apneoa Treatment, are available.

REFERENCES


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Author Roles:
• Vanita Mehta: Conception and study design, data extraction, data analysis, and manuscript preparation
• Tajender Vasu: Data extraction, meta-analysis, and manuscript preparation
• Barbara Phillips: Manuscript preparation
• Frances Chung: Conception and study design, acquisition and interpretation of data, manuscript preparation

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SUBMISSION & CORRESPONDENCE INFORMATION

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DISCLOSURE STATEMENT

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Sleep disorders are highly prevalent across the general population, but education in their recognition and diagnosis is often lacking for health care providers, including neurologists. Trainees who are not exposed to sleep education during their residency education run the risk of failing to provide appropriate diagnoses and management interventions that could result in improvement of primary neurological conditions and quality of life. In addition we believe that sleep problems, including central nervous system hypersomnias, sleep related movement disorders, sleep disordered breathing, and complex behaviors at night, all which have underlying neurologic pathophysiology, are the responsibility of neurologists to evaluate, diagnose, and treat. As such, we suggest that neurology residencies have the responsibility of offering trainees sufficient sleep medicine knowledge necessary to assess, diagnose, and treat key sleep problems. At present, no unified curriculum or requirement exists about the scope of sleep education experience residents receive. Over the past twenty years, sleep medicine has dramatically changed from a novelty to a mainstream specialty. Sleep medicine was recognized as a unique discipline by the American Board of Medical Specialties (ABMS) and the Accreditation Council for Graduate Medical Education (ACGME), with ACGME accredited fellowship programs starting in 2005. An increasing amount of research further tightens the link of sleep medicine to over-3,101 articles whose title is related to sleep compared to 798 in 1990, a jump of 3.9 times as many articles over the course of two decades. As an example of the neurology literature, the journal *Neurology* published 168 articles on the topic of sleep in 2010 compared to only 11 in 1990, an increase of 15.3 fold. Our understanding of the effect of sleep states and sleep disorders on neurological diseases has also improved. Some sleep disorders such as REM sleep behavior disorder predict the development of neurodegenerative disease such as Parkinson disease, Lewy body dementia, and multiple system atrophy, sometimes decades later. Sleep disorders such as sleep apnea and restless legs syndrome appear to increase the risk of vascular disease including data implicating sleep apnea as an independent risk factor for stroke. Furthermore treatment of sleep disorders can improve various comorbid neurological conditions such as migraine and epilepsy. These and other key data can help neurologists understand the importance of sleep medicine in treating our patients and add insight to the critical need for including sleep disturbances in neurology residency training.

Based on a survey conducted in 1998, the average amount of teaching time devoted to sleep at medical schools was only 2.1 hours. This baseline of instruction in sleep medicine would not suffice for the educational need of the trained neurologist. Residency training may serve as a unique window of opportunity for the neurologist trainee to gain exposure to a wide variety of
diagnostic and therapeutic avenues for a spectrum of patients with neurological complaints. While disciplines such as pulmonary medicine, otolaryngology-head and neck surgery, and psychiatry have taken initiatives to generate competency-based sleep medicine curricula for their trainees, in contrast, the role of sleep medicine in neurology residencies has been somewhat neglected.2-7 In 2001, sleep issues were included in the required list of topics to be reviewed during neurology residency, demonstrating recognition of the relationship of sleep medicine to neurology. The July 2007 revision of the program requirements stipulated that faculty with special experience in sleep disorders must be available on a regular basis to neurology residents.8 Additionally, residents must be instructed in the effects of sleep deprivation and fatigue on their performance. Now, nine years after initial inclusion of sleep medicine in neurology training, we decided to analyze the adequacy of sleep medicine education in neurology residencies.

**METHODS**

In March 2010, we conducted an online survey among neurology residency training program directors regarding the resources available and the amount of sleep education offered for the neurology residents. The survey was created by a task force from the American Academy of Neurology (AAN) Sleep Section and received peer review by the section executive committee and the AAN Residency Education subcommittee. Questions focused on sleep education resources available in neurology residencies, and topics included in the survey were those determined from review of the sleep education curriculum described for other subspecialties.1,6 Our Sleep Education Survey (SES) consisted of 20 questions and was approved by the AAN Education Committee and Program Directors Committee prior to being sent out to the cohort of neurology residency program directors (Appendix). Program directors completed the survey on line using an online “Survey Monkey” questionnaire, and statistics were compiled regarding the responses. Pearson product momentum correlation was used to determined correlation (significance level p < 0.05). In addition, we obtained the ACGME data for residents entering a sleep medicine fellowship in the 2009-2010 year, including each resident’s primary residency discipline. We also reviewed the geographic locations of all 126 ACGME accredited neurology residencies and compared them to the list of accredited sleep centers maintained by the American Academy of Sleep Medicine (AASM) for location and proximity.

**RESULTS**

We obtained 58 responses from 126 neurology residency program directors (46% response rate; Table 1). The program directors reported a mean of 3.9 residents per year (range 1-10). Seventy-five percent of programs (43/57) reported that they were associated with a sleep center, and 33 of the 43 centers were accredited by the AASM. Eighty-one percent of programs offer a sleep rotation, and over 80% of these were 1 to 2 weeks in duration. Programs had a median of 2 faculty with expertise in sleep medicine and 1.3 board certified in sleep medicine (by either the American Board of Sleep Medicine or American Board of Psychiatry and Neurology). Thirty-one percent of programs reported no faculty with sleep medicine experience; 24% of the responding programs reported resident participation in sleep research.

Many programs noted incorporating sleep lectures and clinical exposure as part of the EEG or epilepsy rotation. One program that did not have faculty in sleep medicine noted they used a sleep medicine PowerPoint slide module as a teaching lecture set. Overall, lectures were the most commonly used teaching format. The mean duration of didactic lectures was 5.2 h/year, with 37% noting ≤ 3 h per year on sleep education and 7% offering no lectures. The distribution of lecture topics suggested that major neurologically based topics such as REM sleep be-

---

**Table 1—General statistics of programs and sleep education**

<table>
<thead>
<tr>
<th>Number of programs</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent programs requiring a sleep rotation</td>
<td>8.6%</td>
</tr>
<tr>
<td>Mean number of didactic hours for sleep topics</td>
<td>5.2</td>
</tr>
<tr>
<td>Percent of programs offering no sleep lectures</td>
<td>7%</td>
</tr>
<tr>
<td>Mean percentage of residents entering sleep medicine fellowships in preceding 5 years</td>
<td>5.7%</td>
</tr>
</tbody>
</table>

---
behavior disorder and restless legs syndrome were missing in up to a third of the programs surveyed, and relatively low numbers of programs offered clinical exposure or case review as formats for specific topics (Table 2). Programs have used a variety of innovative approaches to teach sleep medicine including sleep medicine electives, regular weekly sleep clinics, teaching sleep during other neurophysiology rotations, non-continuity subspecialty sleep clinics, and didactic neurophysiology and sleep lecture series.

The correlation analysis demonstrates that neurology programs that had substantial faculty investment in sleep medicine were more likely to be associated with a sleep center, offer lectures, and promote other educational formats (Tables 3A and B). The association of resources and learning opportunities is listed in Table 3A. Highest associations are between the presence of faculty in sleep medicine and hours of lectures and learning opportunities such as research. Experiential learning as indicated by presence of clinical exposure or case review was also associated with the presence of clinical faculty boarded in sleep medicine (r = 0.17) and those faculty fellowship trained in sleep medicine (r = 0.17). We identified three programs that participated in experiential learning in sleep medicine despite no sleep faculty.

Program directors reported that over the preceding 5 years, 5.7% of residents entered sleep medicine fellowship training programs. Programs that had a sleep center were more likely to report residents entering a sleep medicine training program. This was similar to the data from the ACGME, which showed

Table 2—Number of programs (%) that offer each sleep topic in particular format

<table>
<thead>
<tr>
<th>Topic</th>
<th>Lecture Form</th>
<th>Clinical Exposure</th>
<th>Case Review</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep Physiology</td>
<td>47 (81%)</td>
<td>19 (33%)</td>
<td>5 (8%)</td>
</tr>
<tr>
<td>Polysomnography and MSLT</td>
<td>36 (62%)</td>
<td>37 (64%)</td>
<td>9 (15%)</td>
</tr>
<tr>
<td>Sleep Evaluations</td>
<td>31 (53%)</td>
<td>36 (62%)</td>
<td>6 (10%)</td>
</tr>
<tr>
<td>Normal Sleep</td>
<td>43 (74%)</td>
<td>24 (41%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Hypersomnia</td>
<td>38 (65%)</td>
<td>28 (48%)</td>
<td>5 (8%)</td>
</tr>
<tr>
<td>Narcolepsy</td>
<td>41 (71%)</td>
<td>33 (57%)</td>
<td>9 (15%)</td>
</tr>
<tr>
<td>Obstructive Sleep Apnea</td>
<td>41 (71%)</td>
<td>37 (64%)</td>
<td>7 (12%)</td>
</tr>
<tr>
<td>Central Sleep Apnea</td>
<td>38 (65%)</td>
<td>30 (52%)</td>
<td>4 (6.9%)</td>
</tr>
<tr>
<td>Restless Legs Syndrome</td>
<td>41 (71%)</td>
<td>37 (64%)</td>
<td>8 (13.7%)</td>
</tr>
<tr>
<td>Parasomnia</td>
<td>40 (69%)</td>
<td>27 (46%)</td>
<td>9 (15%)</td>
</tr>
<tr>
<td>REM Sleep Behavior Disorder</td>
<td>39 (67%)</td>
<td>33 (57%)</td>
<td>12 (20.6%)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>34 (59%)</td>
<td>32 (55%)</td>
<td>4 (6.9%)</td>
</tr>
<tr>
<td>Circadian Rhythm Disorders</td>
<td>37 (64%)</td>
<td>24 (41%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Neurological Disorders and Sleep</td>
<td>40 (69%)</td>
<td>28 (48%)</td>
<td>7 (12%)</td>
</tr>
<tr>
<td>Psychiatric Disorders and Sleep</td>
<td>30 (52%)</td>
<td>24 (41%)</td>
<td>3 (5.1%)</td>
</tr>
<tr>
<td>Medications and Sleep</td>
<td>36 (62%)</td>
<td>35 (60%)</td>
<td>7 (12%)</td>
</tr>
</tbody>
</table>

Table 3A—Correlation of program attributes

<table>
<thead>
<tr>
<th>Association</th>
<th>Program with sleep center</th>
<th>Program with accredited sleep center</th>
<th>Program with sleep faculty</th>
<th>Program with board certified sleep faculty</th>
<th>Program with fellowship trained sleep faculty</th>
<th>Association of offering an elective</th>
<th>Association of hours of lectures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Offer sleep elective</td>
<td>0.27</td>
<td>0.29*</td>
<td>0.36*</td>
<td>0.39*</td>
<td>0.28</td>
<td>0.28</td>
<td>0.16</td>
</tr>
<tr>
<td>Hours of sleep lecture</td>
<td>0.10</td>
<td>0.12</td>
<td>0.37*</td>
<td>0.39*</td>
<td>0.16</td>
<td>0.16</td>
<td>0.22</td>
</tr>
<tr>
<td>Case base review and Clinical Exposure</td>
<td>0.08</td>
<td>0.14</td>
<td>0.14</td>
<td>0.17</td>
<td>0.17</td>
<td>0.17</td>
<td>0.17</td>
</tr>
<tr>
<td>Number of resident doing sleep research</td>
<td>0.33*</td>
<td>0.05</td>
<td>0.47*</td>
<td>0.72*</td>
<td>0.53*</td>
<td>0.27</td>
<td>0.22</td>
</tr>
<tr>
<td>Number of Residents pursuing sleep fellowship</td>
<td>0.32*</td>
<td>0.17</td>
<td>0.33*</td>
<td>0.32*</td>
<td>0.32*</td>
<td>0.20</td>
<td>0.21</td>
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<td>Any residents pursuing sleep fellowship</td>
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<td>0.34*</td>
<td>0.33*</td>
<td>0.29*</td>
<td>0.23</td>
<td>0.01</td>
<td>0.19</td>
</tr>
</tbody>
</table>

*p < 0.05.
6.2% of neurology residency graduates entered a sleep residency for the 2008–2009 year. Of 126 ACGME listed neurology residencies, 117 have an accredited sleep center within the same city as the program. Of the remaining programs, all have a sleep center (accredited or not accredited) within 30 miles of the teaching institution.

DISCUSSION

This is the first study of its kind assessing sleep medicine exposure among neurology residents. Despite the fact that neurologists frequently encounter patients with sleep disturbances and that sleep is a required topic by the Residency Review Committee (RRC), our data show that the exposure to sleep medicine education in neurology residents remains limited. Although the survey did not include exploratory questions to gain insight into barriers to exposure, we found that most program directors noted in the comment section similar hurdles of resources and available faculty. We also found that inclusion of sleep medicine in the training schedule correlates with available resources in sleep medicine, such as the presence of specialized faculty and sleep laboratories.

Programs that had faculty trained or experienced in sleep medicine were more likely to offer electives or rotations in sleep medicine and lectures in sleep. Furthermore, residents were more likely to do research in sleep medicine when they had access to faculty who were board certified in sleep medicine. Our results reveal that approximately three-quarters of programs have access to sleep laboratories, and a similar percentage teach many of the identified topics of sleep medicine. The programs that have access to a sleep laboratory were more likely to provide electives in sleep medicine: 36 of 43 programs with a sleep center offered a sleep elective, whereas only 7 of 14 without a sleep center did so. Offering an elective and the number of hours of sleep lectures correlated strongly with access to faculty. Overall, programs offering sleep electives and having a sleep center associated with the residency appeared to correlate with a greater number of residents pursuing sleep training.

Review of specific topics revealed that sleep physiology and normal sleep were the most commonly covered. This is most likely related to the requirement that all residencies cover duty hour limitation, sleep, and fatigue. Topics of insomnia, psychiatric disorders in sleep, and general sleep evaluation were least likely to be covered. A surprisingly high percentage of programs did not cover sleep issues in neurological disorders and classic neurologic sleep disorders, such as narcolepsy, restless legs syndrome, and REM sleep behavior disorder. The most common format for covering the topics was formal lectures, whereas case review was the least common method utilized. Advantages of lectures are that they can transmit a great deal of information in a tightly compact time frame and use fewer faculty resources. Lectures, however, have many disadvantages: they may not be easily attended by all residents, information may not be reviewed more than once, application of the information may not be readily apparent, and learners assume a more passive learning style. More recent emphasis on active experiential learning has shown improvement in retention and subsequent behavioral application of the subject. In particular, some educators believe that residents may learn more by inclusion of case-based learning with discussion, allowing the transformation of knowledge to clinical applications. We found four programs without faculty in sleep medicine that offered experiential learning, but these case review topics were very limited.

This survey was not completed by all of the program directors. We received information from approximately half of the programs, raising the possibility of type 2 bias. Our survey could have triggered responses from program directors with extreme views—those who view sleep education in neurology positively and are keenly interested in sleep medicine; and those who view sleep education curriculum in residency training negatively and are opposed to teaching sleep medicine. To validate the responses, we looked at the rate at which residents entered into sleep medicine residency. From the survey, we calculated that 5.7% of the resident pool entered into sleep training. We then reviewed the ACGME statistics for number of residents with a neurology background that were in 2009-2010 sleep medicine fellowships and divided that by number of graduates from all neurology residencies. This demonstrated a national average of 6.2% of 398 neurology resident graduates entering sleep medicine fellowship training. Thus we feel the survey provides good cross sectional data of current training practices. These data also suggest that the number of neurology residents entering into sleep medicine, assuming maintenance of the current number of graduates and those graduates on average having a 25-year career, would support approximately 450 neurologists nationally with an interest in sleep medicine at any one time.

We see key opportunities to improve training in sleep medicine in neurology residency programs. The most important requirement is improvement of access of residency programs to sleep centers where infrastructure exists to deliver sleep education, clinical experience in sleep disorders, and exposure to recording and interpreting sleep studies. We also recommend provision of resources for sleep educational modules to ensure uniform teaching material and access to faculty with sleep medicine experience. When reviewing the primary geographic location of all neurology residencies listed by the ACGME, 93% (117 of 126) of programs were located in the same vicinity as an AASM accredited sleep center, which ensures that quality education and clinical training are standardized and available. With one exception, all programs that did not have access to these accredited centers were within close geographic proximity (about 30 miles) to accredited laboratories. These sleep centers can be a valuable resource for residency programs to partner with to foster sleep education. This association could be encouraged by the residency program requirements specifically requiring such a relationship similar to that of clinical neurophysiology laboratories. Other ACGME residency committees have required residents to have exposure to a sleep medicine rotation and sleep laboratory experience. When this was mandated as part of the pulmonary fellowship requirements, the number of pulmonary medicine physicians entering the field of sleep medicine increased sharply. Greater exposure of sleep medicine in neurology residency could result in similar gains.

However, we understand that the requirement of having access to sleep trained faculty would put excessive burden on many smaller programs, and thus more creative mechanisms to include this training are needed. Advances in distance learning can provide exposure to many topics that could be available via...
e-learning modules, webinars, or packaged electronic teaching sets and case review. This would allow residency programs to access shared faculty resources, some of which may be available through centralized professional societies, at a relatively nominal cost. The advent of educational modules also fosters a change in mindset from the traditional educational metric of time spent on a clinical rotation equated to successful learning. Competency-based education focuses on the metric of attainment of knowledge and application, allowing learners the ability to learn at an individual rate and show proficiency of a specific topic. This creates the opportunity for development of self-assessment and competency-based tools to be developed for residency programs.

Knowledge of sleep medicine offers an opportunity for improvement in care for patients with neurological disorders. The inclusion of sleep education is not uniformly applied in neurology residencies, despite ACGME requirements. Although this lack of uniformity may be a result of variability of access to faculty in sleep medicine, sleep laboratories, or other valuable resources, most of these issues can be addressed by partnering and newer learning tools.

REFERENCES


SUBMISSION & CORRESPONDENCE INFORMATION

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DISCLOSURE STATEMENT

Dr. Avidan served as a consultant for Merck; has received speaker honoraria from the American Academy of Neurology, American Academy of Sleep Medicine, American College of Chest Physicians, and book royalties from Elsevier and Lippincott Williams & Wilkins. He received speaker honorarium from Takeda Pharmaceuticals, Sanovian, Somaxon, GlaxoSmithKline, Purdue, and Teva, and received support from the American Academy of Sleep Medicine. He is also serving as the editorial board of Sleep, and a special section editor of Sleep Medicine.

Dr. Vaughn is on the Editorial Boards and an Associate Editor for Sleep Multimedia, Medlink Neurobase Sleep and Epilepsy 2011 receiving Publishing Royalties, and received an honorarium for serving as guest editor for Neurologic Clinics. He has received speaker honoraria from the following organizations: American Academy of Neurology, American Academy of Sleep Medicine and Medical Education Resources (nonprofit). He serves as chair of the Sleep Examination Committee (a multidiscipline committee) administered by the American Board of Internal Medicine. He is a Professor of Neurology at University of North Carolina, which involves 50% interpreting clinical neurophysiology and sleep studies. His research Support, and Commercial Entities are through the Johns Hopkins University and Glaxo Smith Kline.

Dr. Silber is program director of the Mayo Clinic Sleep Medicine Fellowship. He is chair of the steering committee of the Sleep Medicine Program Director’s Council. He receives royalties from two books “Sleep Medicine in Clinical Practice, 2nd edition” and “Atlas of Sleep Medicine.”

Author contributions: Dr. Avidan: drafting/revising manuscript, study concept and design, Dr. Vaughn: drafting/revising manuscript, study concept and design, analysis or interpretation of data. Dr. Silber: drafting/revising manuscript, analysis or interpretation of data.
Appendix—AAN Sleep Education Survey (SES)

SURVEY OF SLEEP EDUCATION OFFERED BY NEUROLOGY TRAINING PROGRAMS

Program:
Location:
Program Director:

DEMOGRAPHICS
Number of residents per year:
Number of neurology faculty with sleep specialization:
How many are boarded in sleep?
Number of neurology faculty with sleep fellowship experience:
Is your department affiliated with a sleep laboratory?
Is the sleep laboratory/center accredited by the AASM?

NATURE OF SLEEP EDUCATION
Does your program have a sleep elective?
If yes, for how many weeks?
Does your program have a required sleep rotation?
If yes, for how many weeks?
How many hours of didactic sleep medicine teaching do you offer each year?
Do you have a formalized sleep clinic in your program for the residents?
If yes, for how many ½ day sessions per week and how many weeks?
Please describe any innovative clinical and educational opportunities your program has put together to expose your residents to clinical sleep medicine:

RESEARCH EXPERIENCE
Are any of you residents participating in sleep research?
If yes, how many
Did the research lead to any publications?

SLEEP AS A CAREER PATH
In the past 5 years, how many residents pursued sleep fellowship training?
Please check which topics are taught in your residency and how

<table>
<thead>
<tr>
<th>Topic</th>
<th>Lecture</th>
<th>Clinical Exposure</th>
<th>Case Review</th>
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<tr>
<td>Normal Sleep</td>
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<td>Hypersomnia</td>
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<td>Narcolepsy</td>
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<td>Obstructive Sleep Apnea</td>
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<tr>
<td>Central Sleep Apnea</td>
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<tr>
<td>Restless Leg Syndrome</td>
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<td></td>
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<tr>
<td>Parasomnia</td>
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<td></td>
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<tr>
<td>Insomnia</td>
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<td></td>
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<tr>
<td>Circadian Rhythm Disorders</td>
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<td>Neurological Disorders and Sleep</td>
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<tr>
<td>Psychiatric Disorders and Sleep</td>
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A 3-month-old infant girl with achondroplasia presented with a 2-month history of snoring without breathing pauses, nasal flaring, chest retraction, or cyanosis. The baby was born at 38 weeks gestation to a 33-year-old mother via elective cesarean section. Apgar score was 9. The father is achondroplastic. At 6 months gestation, fetal ultrasound was consistent with achondroplasia; prenatal and perinatal history was otherwise unremarkable.

Physical exam revealed an alert playful baby with macrocephaly, head circumference of 44 cm (50% percentile achondroplasia chart); mid-face hypoplasia; and large anterior and posterior fontanelles. Upper airway was Mallampati IV with 2+ tonsillar enlargement. No excessive palatal arching was noted. Neurologic exam revealed mild hypotonia, lumbar kyphosis, and normal deep tendon reflexes throughout. The remainder of the exam was normal.

Computerized tomography (CT) of the head with 3-dimensional reconstruction showed widening of the metopic, coronal, and sagittal sutures, with patent anterior and posterior fontanelles. Mild foramen magnum narrowing was noted without evidence of cervicomedullary junction stenosis (Figure 1). Diagnostic polysomnogram (PSG) revealed a total sleep time (TST) apnea-hypopnea index (AHI) of 4, with 15 obstructive apneas and 15 central apneas; NREM AHI of 1.8; and REM AHI of 11.6. The apneas were not associated with bradycardia; the lowest heart rate for the night was 95 bpm. The apneas were brief and met American Academy of Sleep Medicine Scoring Manual criteria for duration with 2 missed breaths. The central apneas were associated with 3% oxygen desaturation. The minimum oxygen saturation was 91%. There was no evidence of hypoventilation. The end-tidal CO₂ remained below 50 mm Hg for the entirety of the night, with an average of 35 mm Hg.

QUESTION: Which of the findings mentioned above have been commonly associated with achondroplasia?

Figure 1—Three-dimensional reconstructed computerized tomography of the head in a patient with achondroplasia

(A) Open anterior fontanelle with a transverse diameter of 80 mm and an anterior-posterior diameter of 127 mm. (B) Open posterior fontanelle with a transverse diameter of 46 mm and an anterior-posterior diameter of 19 mm. (C) Small short cranial base with mild narrowing of the foramen magnum: 16.8 mm by 18.8 mm.
Achondroplasia is an autosomal dominant mutation in the fibroblastic growth factor receptor-3 (FGFR3) gene that affects 1 in 30,000 children and leads to underdevelopment of the long bones formed by endochondral ossification. Achondroplasia is a clinical diagnosis based on history, physical examination and skeletal radiography. Prenatal diagnosis is possible through ultrasound or by DNA testing. Most cases are sporadic and associated with increased paternal age. Skeletal features include: macrocephaly with frontal bossing, short stature, proximal short limbs (rhizomelia), midface hypoplasia, and large fontanelles.

A large fontanelle diameter, rapidly increasing head circumference, or radiologic evidence of ventriculomegaly should prompt evaluation for hydrocephalus. In most cases of achondroplasia, a communicating hydrocephalus develops from venous outflow obstruction at the base of the skull and does not require shunting. Hydrocephalus has been found in 28% of achondroplastics with obstructive sleep apnea (OSA), suggesting a link between hydrocephalus and sleep disordered breathing (SDB) in patients with achondroplasia.

Midface hypoplasia and skull base deformities in achondroplasia due to abnormal ossification may predispose these children to SDB and otologic complications. Otologic complications occur in 68% of achondroplastics and include recurrent acute otitis media, chronic otitis media, tympanic membrane perforation, and hearing loss. Up to 75% of achondroplastic children have SDB consisting of obstructive apneas, central apneas, or both. Obstructive apneas are thought to be associated with mid-face hypoplasia and reduction in the nasopharyngeal space. Nocturnal hypoxemia (SpO₂ < 90%) without apnea has been found in up to 44% of children with achondroplasia and may represent restrictive lung disease, secondary to a combination of hypotonia, thoracolumbar kyphosis, and a small thoracic cavity.

Babies with achondroplasia have significantly smaller foramen magnum diameters than unaffected babies, and this difference persists across the lifespan. Both obstructive apneas and central apneas have been reported in achondroplastics with foramen magnum stenosis. Compression of the lower motor neurons innervating the respiratory muscles may result in obstructive apneas, while compression of the medullary respiratory centers may lead to central apnea. The increased apneic events, paired with a decreased arousal response may contribute to the increased risk of sudden death, reported in up to 5% of achondroplastics.

Other neurologic consequences of cervicomедullary compression (CMC) include myelopathy with mono-, hemi-, paraplegia or quadriplegia and hyperreflexia/clonus, hypotonia, and dysphagia due to unilateral or bilateral pharyngeal paresis. It is unclear whether the absolute dimension of the foramen magnum is helpful in determining which patient will benefit from decompression. The American Academy of Pediatrics recommends an initial evaluation with a thorough neurologic history, complete physical examination, neuroimaging, and polysomnography, with subsequent annual screening for hyperreflexia and sleep apnea. No specific recommendations are given regarding home apnea monitors.

Symptomatic patients with notable CMC on neuroimaging (i.e., a narrow foramen magnum and/or T2 weighted image hyperintensity on magnetic resonance imaging [MRI] of the brainstem/cervical spinal cord) should undergo cervicomедullary decompression (CMD). CMD has shown to improve the central apneas and the degree of oxygen desaturation. The most common surgical complication of CMD is CSF leak and infection. Recurrence of stenosis has also been reported.

Management of SDB with tonsillectomy/adenoidectomy or continuous positive airway pressure (CPAP) therapy has shown improvement in respiratory indices, arousal indices, oxygen saturation, and hypercapnia. Treatment of SDB may also have neurocognitive benefits in some patients. Oxygen supplementation has been used in premature babies or children with restrictive lung disease. Tracheostomy is effective in severe or emergent cases.

Respiratory stimulants such as caffeine and doxapram, commonly used for apnea of prematurity and respiratory depression after anesthesia, could be a future treatment option in babies with achondroplasia, due to the stimulation of breathing on the medullary respiratory centers and carotid bodies; however, they have not been evaluated for use in this patient population.

Our patient underwent three-dimensional computerized tomography (CT) of the cervicomедullary junction without sedation instead of MRI with sedation, because of faster image acquisition time with CT than MRI, and the risks associated with sedating an infant patient with SDB in order to acquire MRI images.

Benefits and risk of CPAP and CMD were discussed with the parents; both the parents and sleep medicine physicians preferred to wait a few months and obtain a repeat PSG. PSG performed 3 months later showed AHI of 0.4, and minimum oxygen saturation of 95%. The improvement in AHI may be attributed to maturity of the brainstem. Prior studies have demonstrated that SDB is more prevalent in infants younger than 12 weeks of age.

It is the opinion of the authors that in a neurologically asymptomatic baby with achondroplasia, evaluation of apnea with a PSG should be delayed until at least 6 months of age. Our patient is currently stable, does not show signs or symptoms of medullary compression, and continues close follow-up by a multidisciplinary medical team (neurologist, sleep medicine physician, pediatrician, and geneticist).

**DISCUSSION**

**ANSWER:**

The following findings are common in children with achondroplasia: macrocephaly; mid-face hypoplasia; persistent open fontanelles; lumbar kyphosis; hypotonia; narrow cervicomедullary junction (CMC), and both central apneas and obstructive apneas.

**CLINICAL PEARLS**

1. The American Academy of Pediatrics recommends that every infant with achondroplasia should be screened for CMC. The assessment should include a thorough neurologic history, physical, neuroimaging (CT or MRI), and polysomnography.
2. Repeating neuroimaging should be considered for evaluation of hydrocephalus or symptoms of CMC.
3. SDB in patients with achondroplasia can include central apnea, obstructive apnea, and hypoventilation.
4. Treatment options for SDB in achondroplasia include: cervicomedullary decompression, tonsillectomy and adenoidectomy, CPAP, oxygen supplementation, and tracheostomy.
5. Infants with achondroplasia will benefit from the intervention of a multidisciplinary team of pediatricians, geneticists, sleep medicine physicians, pulmonologists, neurologists, otolaryngologists, neuroradiologists, and neurosurgeons.

CITATION

REFERENCES

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DISCLOSURE STATEMENT
This was not an industry supported study. The authors have indicated no financial conflicts of interest.
Sleep in Childhood Neurological Disorders is a rare book in that it captures one’s interest on the very first page and sets a comfortable and unremitting pace until the final word of the final chapter. Each author has carefully chosen his/her subject material and succinctly summarizes the assigned topic such that the reader finds a finely tuned wealth of knowledge with something new in every chapter. Many of the commonly struggled with sleep disorders are addressed, defined, and then presented with material consistent with the latest literature on the subject. Disorders that may be common themes only to pediatric sleep specialists in tertiary care practices are also fully addressed, with key features of each disorder highlighted.

This book provides something for everyone who has an interest in pediatric sleep medicine, particularly for those whose practice includes the treatment of children with neurological pathology.

The first chapter immediately captivates the reader, beginning with the science of sleep, providing intriguing examples of the role of sleep in humans, reptiles, amphibians, birds, and other beings. The functions of sleep, sleep architecture, neuro-anatomy, and neurotransmitters are clearly explained; this sets the stage for the ensuing chapters. Subsequent chapters provide practical ways to evaluate children with sleep disorders, examples of sleep histories, and discussion of other assessment tools.

The fundamental disorders of restless legs syndrome, childhood parasomnias, narcolepsy, and circadian rhythm disorders are clearly defined along with the pathogenesis, identification, treatments, and—most importantly for the purpose of this book—how each disorder variably affects children with special needs.

Detailed attention is given to sleep in the context of epilepsy, neurodevelopmental disorders and children with brain tumors. Many readers will be surprised at the prevalence of seizures that occur primarily during sleep. In this book, information not readily offered or in a format not easily absorbed in other resources is served up like a delectable meal, ready to be tasted and savored. Topics include sleep and pediatric traumatic brain injury, craniofacial disorders, and Chiari malformations. The captivating subject of inverted melatonin secretion in disorders such as Smith-Magenis Syndrome is especially well done. Congenital central hypoventilation syndrome (CCHS), which is eponymously referred to as Ondine’s Curse, the etiologically defined gene PHOX2b, and ventilator management of these patients is expertly described.

The importance of the multidisciplinary team approach for evaluating children and psychiatric disorders is addressed, and there is a thorough explanation of how sleep problems adversely affect mood and neurobehavioral dysfunction. The authors do a nice job of discussing common psychiatric disorders and appropriate medication management.

Among our many favorite chapters was one describing the association of poor sleep and headaches, a subject that must be very familiar to all sleep specialists. Also discussed is the association of headaches and other sleep disorders, such as periodic limb movements of sleep, and treatment strategies are explored.

The chapter on pharmacology is like icing on a cake. The effects of various medications to induce sleep and the latest treatment of narcolepsy and obstructive sleep apnea are described in easy-to-understand and captivating detail.

The plethora of well-placed pictures, graphs, and summarizing paragraphs (including “pearls” and “key points”) make this an especially welcome resource.

Sleep in Childhood Neurological Disorders will bring the reader up to date with the latest medical information on this subject, providing ideas which are immediately useful, as well as presenting new ideas that many will find fascinating and challenging.

In summary: Sleep in Childhood Neurological Disorders is a unique compilation of excellent chapters that brings much insight and understanding to the pathological sleep states that affect many children, especially those with neurological disorders. This book is interesting, captivating, and provides important up-to-date information. At only $85, Sleep in Childhood Neurological Disorders is a must-read for any clinician who wishes to increase his/her understanding of sleep problems and have a positive impact in the pediatric population with neurological disorders. A book of this caliber should be considered as part of the routine curriculum of any sleep fellowship that emphasizes training in pediatric sleep medicine. This book is so well written that even the non-specialist is able to read and understand crucial information to help serve the needs of those very special patients.

CITATION

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The authors have indicated no financial conflicts of interest.
In Memoriam: Sheldon Kapen, M.D.

Dr. Sheldon Kapen, M.D., 77, of West Bloomfield, Michigan passed away on November 22, 2012. Dr. Kapen was a longtime member of the Wayne State University Department of Neurology and chief of Neurology at the John Dingell Veterans Administration Hospital in Detroit, Michigan for 25 years until his retirement in November 2011. Dr. Kapen started the first sleep lab in any VA facility in 1985 when he took over a new 2 bed unit in the old Detroit VAMC in Allen Park. When the Detroit VA Medical Center moved to Detroit and became the John D. Dingell VA Medical Center, Dr. Kapen was able to expand the clinic into a new 8 bed facility with state of the art equipment and more staff. Dr. Kapen’s sleep medicine clinic and laboratory was the first VA sleep lab to be accredited, and approximately the 20th in the nation. He also had the first VA-based accredited fellowship program in 1989 (the 4th overall in the country) and it has also been reaccredited multiple times. A plaque was dedicated to him outside the lab in November 2011 as he retired from the VA after 30 years. The plaque which honors him at the VA hospital calls Dr. Kapen “A Physician, a teacher, a scientist, a leader, and a friend.”

“Sheldon Kapen was an important contributor to the academic and clinical missions of the Department of Neurology and the Veterans Administration hospital for many years,” said Robert Lisak, M.D., professor and former chair of Neurology. “He was a pioneer in the study and treatment of disorders of sleep. For that reason the sleep laboratory at the John Dingell VA Hospital was recently named in his honor. Shelly was a dedicated physician and a person of integrity. He will be missed.”

Dr. Kapen achieved many successes over the years. Among the grants he won, Dr. Kapen received a VA Research Grant to study stroke and sleep.

Dr. Kapen is survived by his wife, Rachel, and his children and grandchildren.

The Journal of Clinical Sleep Medicine thanks Dr. Kapen’s wife, Rachel, for contributing to this obituary.
Thank You 2012 JCSM Reviewers

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Daniel O'Hearn
Arie Oksenberg
Lyle Olson
Jason Ong
Mark Opp
Kathryn Orzech
Robert Owens
Allan Pack
James Parish
Barbara Parry
Sairam Parthasarathy
Shalin Paruthi
Sanjay Patel
Yukels Peker
Rafael Pelayo
Plamen Penev
Thomas Penzel
Paul Peppard
Justin Peperell
Barbara Phillips
Daniel Picchetti
Dante Picchioni
Giora Pillar
Giuseppe Pizzari
Dalva Poyares
Naresh Punjabi
Shadab Rahman
Winfried Randerath
David Rapoport
David Rector
William Reeves
Luxana Reynaga Omelas
Thomas Rice
Renata Riha
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Beth Rodgers
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Avi Sadegh
R Bart Sangal
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Catherine Sassoon
Michael Sateia
Amy Sawyer
Michael Scharf
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Carmen Schröder
Skai Schwartz
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Denise Sharon
Laila Simpson
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Yakov Sivan
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Adam Spira
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Jeffrey Stanley
Roland Staub
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Riccardo Stochs
Kingman Strohl
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Masaya Takahashi
Asher Tal
Ariel Tarasuk
Janet Tatman
Daniel Taylor
Mihai Teodorescu
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Michael Thorpy
Pablo Tordero
Claudia Trenkwalder
Lynn Marie Trotti
Adrienne Tucker
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