IN THIS ISSUE:

Impact of Group Education on Continuous Positive Airway Pressure Adherence
Lettieri, Walter

A Pilot Study of CPAP Adherence Promotion by Peer Buddies with Sleep Apnea
Parthasarathy; Wendel; Haynes; Atwood; Kuna

Commentary on: Lettieri and Walter; Parthasarathy et al.
Don't Start Celebrating—CPAP Adherence Remains a Problem
Weaver

Sleep Habits, Insomnia, and Daytime Sleepiness in a Large and Healthy Community-Based Sample of New Zealanders
Wilsmore; Grunstein; Fransen; Woodward; Norton; Ameratunga

Sleep Duration and Reported Functional Capacity among Black and White US Adults
Brimah; Oulds; Olafiranye; Ceide; Dillon; Awoniyi; Nunes; Jean-Louis

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Authors response to Snapp and Sharma
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# Table of Contents

## Continuing Medical Education Offerings

**526**

## Analysis and Perspectives

### Editorial

**527**

**PSGs: More Than Just the AHI**

Bradley A. Edwards; Andrew Wellman; Robert L. Owens

## Scientific Investigations

### Long-Term Continuous Positive Airway Pressure Therapy Normalizes High Exhaled Nitric Oxide Levels in Obstructive Sleep Apnea

Ai-Ping Chua; Loutfi S. Aboussouan; Omar A. Minai; Kelly Paschke; Daniel Laskowski; Raed A. Dweik

**537**

### Impact of Group Education on Continuous Positive Airway Pressure Adherence

Christopher J. Lettieri; Robert J. Walter

**543**

### A Pilot Study of CPAP Adherence Promotion by Peer Buddies with Sleep Apnea

Sairam Parthasarathy; Christopher Wendel; Patricia L. Haynes; Charles Atwood; Samuel Kuna

**551**

### Commentary on: Lettieri and Walter; Parthasarathy et al.

Don’t Start Celebrating—CPAP Adherence Remains a Problem

Terri E. Weaver

**553**

### Comparison of Polysomnographic and Clinical Presentations and Predictors for Cardiovascular-Related Diseases between Non-Obese and Obese Obstructive Sleep Apnea among Asians

Naricha Chirakalwasan; Busarakam Teerapraipruk; Rosalind Simon; Prakobkiet Hirunwiwatkul; Nattapong Jamchayaratam; Tayard Desudchit; Natamon Charakom; Chaisiri Wanlapakorn

**559**

### Sleep Habits, Insomnia, and Daytime Sleepiness in a Large and Healthy Community-Based Sample of New Zealanders

Bradley R. Wilsmore; Ronald R. Grunstein; Marlene Fransen; Mark Woodward; Robyn Norton; Shanthi Ameratunga

### The Relation between Insomnia Symptoms, Mood, and Rumination about Insomnia Symptoms

Colleen E. Carney; Andrea L. Harris; Ashley Falco; Jack D. Edinger

**577**

### Perceived Insufficient Rest or Sleep among Veterans: Behavioral Risk Factor Surveillance System 2009

Paul M. Faestel; Christopher T. Littell; Michael V. Vitiello; Christopher W. Forsberg; Alyson J. Littman

**585**

### Total Sleep Time and Other Sleep Characteristics Measured by Actigraphy Do Not Predict Incident Hypertension in a Cohort of Community-Dwelling Older Men

Maple M. Fung; Katherine Peters; Sonia Ancoli-Israel; Susan Redline; Katie L. Stone; Elizabeth Barrett-Connor; for the Osteoporotic Fractures in Men (MrOS) Research Group

### Sleep Oxygen Desaturation Predicts Survival in Idiopathic Pulmonary Fibrosis

Likurgos Kolilekas; Effrosyni Manali; Katerina A. Vlami; Panagiotis Lyberopoulos; Christina Triantafillidou; Konstantinos Kagouridis; Katerina Baou; Sotiros Gyftopoulos; Konstantinos N. Vougas; Anna Karakatsani; Manos Alchanatis; Spyros Papiris

**593**

### Comment on Kolilekas et al.

Can We Predict the Survival of Idiopathic Pulmonary Fibrosis Patients? Sleep Must Be Re-appreciated

Paschalis Steiropoulos

**605**

### Sleep Duration and Reported Functional Capacity among Black and White US Adults

Perry Brimah; Franscene Oulds; Oladipupo Olafiranye; Mirnova Ceide; Shavon Dillon; Olasumbo Awoniyi; Joao Nunes; Girardin Jean-Louis

## Case Reports

### Narcolepsy with Cataplexy Mimicry: The Strange Case of Two Sisters

Fabio Pizza; Stefano Vandi; Francesca Poli; Keivan Kaveh Moghadam; Christian Franceschini; Claudia Bellucci; Carlo Cipolli; Francesca Ingravallo; Giuliana Natalini; Emmanuel Mignot; Giuseppe Plazzi

**611**

The current issue podcast and instructions to authors are available online at www.aasmnet.org/jcsm.
<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>613</td>
<td>Obstructive Sleep Apnea and Nonarteritic Anterior Ischemic Optic Neuropathy: Evidence for an Association</td>
<td>Erica L. Archer; Susan Pepin</td>
</tr>
<tr>
<td>620</td>
<td>Sleep Medicine Pearls</td>
<td></td>
</tr>
<tr>
<td>620</td>
<td>A Patient with Rhythmic Movements during REM Sleep</td>
<td>Brendan P. Lucey; Clifford J. Molin</td>
</tr>
<tr>
<td>625</td>
<td>Journal Club</td>
<td></td>
</tr>
<tr>
<td>625</td>
<td>New Feature: JCSM Journal Club summarizes new clinical evidence related to Sleep Medicine from a number of journals. It is a recurring feature of the Journal. The editorial staff regularly assesses newly published medical literature related to Sleep Medicine and features papers that are important for Sleep Medicine clinicians.</td>
<td></td>
</tr>
<tr>
<td>625</td>
<td>Primary vs. Specialist Care in Management of Sleep Apnea</td>
<td>Nancy Collop; Shirin Shafazand</td>
</tr>
<tr>
<td>629</td>
<td>Letters to the Editor</td>
<td></td>
</tr>
<tr>
<td>629</td>
<td>What Can Sleep Medicine Do?</td>
<td>Allan I. Pack</td>
</tr>
<tr>
<td>631</td>
<td>Aerophagia May Not Cause Gastroesophageal Reflux</td>
<td>Meredith Snapp; Sunil Sharma</td>
</tr>
<tr>
<td>633</td>
<td>Authors response to Snapp and Sharma</td>
<td></td>
</tr>
<tr>
<td>633</td>
<td>CPAP-induced Aerophagia May Precipitate Gastroesophageal Reflux</td>
<td>Kelly Shepherd; David Hillman; Peter Eastwood</td>
</tr>
<tr>
<td>635</td>
<td>Book Review</td>
<td></td>
</tr>
<tr>
<td>635</td>
<td>Rapid Eye Movement Sleep: Regulation and Function</td>
<td></td>
</tr>
</tbody>
</table>

The current issue podcast and instructions to authors are available online at www.aasmnet.org/jcsm.
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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.

<table>
<thead>
<tr>
<th>Articles in this issue that may be read for CME credit</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Impact of Group Education on Continuous Positive Airway Pressure Adherence</strong></td>
<td>537</td>
</tr>
<tr>
<td><em>Objective:</em> Understand the importance of novel educational approaches on CPAP adherence.</td>
<td></td>
</tr>
<tr>
<td><strong>Sleep Habits, Insomnia, and Daytime Sleepiness in a Large and Healthy Community-Based Sample of New Zealanders</strong></td>
<td>559</td>
</tr>
<tr>
<td><em>Objective:</em> Quantify the high level of sleep dissatisfaction <em>(1 in 3)</em>, insomnia <em>(1 in 5)</em>, and daytime sleepiness <em>(1 in 10)</em> on a relatively healthy population.</td>
<td></td>
</tr>
</tbody>
</table>
The in-laboratory attended polysomnogram (PSG) has been the driver of the growth in Sleep Medicine for the last 25 years. Reimbursements drove construction of more laboratory space and the training of more technicians. However, within the last two years, the in-laboratory PSG has been increasingly replaced by home sleep testing (HST). This rapid shift has had a disastrous impact on practices built around an in-laboratory model. Reasons behind the shift have been discussed both in the lay press and in academic journals. First, HST devices are marvels of biomedical engineering, which offer patients the option of accurate testing in the comfort of their own home. Second, home studies are much cheaper than in-lab studies and thus offer value to both patients and their insurers. Implicit in these arguments is the idea that all we need from a sleep study of any type is the apnea-hypopnea index (AHI), and that continuous positive airway pressure (CPAP) is the only viable treatment for obstructive sleep apnea (OSA). We believe that this singular focus on the AHI and CPAP is detrimental to both patients and to the field. We argue here that physiology is the key to revitalizing Sleep Medicine. That is, the PSG can re-vitalize Sleep Medicine if we are able to use the valuable information that each study contains.

Using a PSG for nothing more than the AHI is as absurd as using an electrocardiogram (ECG) for nothing more than the heart rate. Instead, the ECG is interpreted to provide anatomic (e.g., ventricular hypertrophy) or functional information (localizing coronary ischemia), as well as to diagnose other conditions (e.g., pericarditis, atrial fibrillation). From this simple test, there is a wealth of information gained. In contrast, an in-laboratory PSG requires more than 20 electrodes and other sensors, approximately 45 minutes of setup time, hours of sleep time, a specialized laboratory, and the continuous presence of a trained and certified technician. At the end of the study, however, for the overwhelming majority of studies, the only “take-home” value is the AHI, or perhaps also the oxygen saturation nadir. Certainly the PSG has a role in a subset of patients, but in the vast majority of cases—that is, patients with OSA—it is clear that most of the recorded data are never used. We should be able to do better.

So what could a PSG tell us (that HST cannot)? First, we and others believe that careful study of the PSG might reveal the underlying cause of OSA in individual patients. That is, two OSA patients might have the same AHI for very different reasons. Although the majority of cases will be due to poor airway anatomy, other factors such as ventilatory control, arousal threshold, and upper airway muscle responsiveness might be important in some.1 We recently described a method to determine these traits, but we hypothesize that much of the same information could also be determined from a careful study of the PSG.2 Similarly, careful study of inspiratory flow patterns (not just peak amplitude of flow, as respiratory events are currently scored) might tell us about timing (inspiratory vs. expiratory) or location (e.g., palate, tongue base, lateral walls) of upper airway collapse. These observations could lead to targeted OSA therapy. Second, EEG parameters may also yield useful information about the effect of sleep in a variety of biological processes. For example, EEG and cardiorespiratory coupling parameters signal glucose-insulin homeostasis.3 Focus on the AHI has limited recognition that different PSG-derived parameters may be more relevant for other clinical, patient-centered outcomes of interest.4 Thus, the PSG could predict individual OSA-related morbidity and mortality. Overall, sleep apnea research suggests such a personalized approach is possible in the near future, but it will require more careful diagnostic testing, not less.

In terms of treatment for patients, the era of all-night attended CPAP titration is also over, and likely unnecessary if these studies are only used to determine an effective CPAP level. Instead, we propose that an in-laboratory, technician attended study is an ideal opportunity to try the effectiveness of both CPAP and non-CPAP therapies. After a period of acclimatization to CPAP and rapid rough titration (e.g., 1 hour of sleep), other therapies such as position therapy, oral appliance or suction device, nasal insufflation, oxygen therapy, nasal valves, etc. could be tried for ~1 hour each, with the choice of attempted therapies informed by the baseline PSG. In-lab studies will only make sense if we move beyond the AHI, and are able to provide three key pieces of information to patients: (1) why they have OSA, (2) what OSA-related complications they are at risk of, and (3) what non-CPAP treatment options are likely to provide benefit.

While ambitious, we believe that this goal is attainable. Indeed, it might be essential for the success of Sleep Medicine. Our dependence on the AHI has reduced the care of OSA patients to treatment algorithms that minimize the role of the Sleep Medicine physician. Interesting physiology and multiple options for treatment could restore the physician’s role, and draw in the best and brightest residents who are interested in practicing the art of medicine in an exciting and dynamic field. Again, using the ECG analogy above, witness the growth in cardiac electrophysiology over the last 25 years. The emphasis on CPAP has also kept some patients away from the clinic;
understanding which patients might be treated without CPAP could improve their quality of life and prevent morbidity. If we can justify bringing back the in-lab attended PSG, it will be because we have better understood OSA pathophysiology, put the PSG information to good use, and are better serving our patients.

CITATION
Edwards BA; Wellman A; Owens RL. PSGs: more than just the AHI. J Clin Sleep Med 2013;9(6):527-528.

REFERENCES
Long-Term Continuous Positive Airway Pressure Therapy Normalizes High Exhaled Nitric Oxide Levels in Obstructive Sleep Apnea

Ai-Ping Chua, M.B.B.S.1,3; Loutfi S. Aboussouan, M.D., F.A.A.S.M.1,3; Omar A. Minai, M.D., F.A.A.S.M.1,3; Kelly Paschke, B.A.2; Daniel Laskowski, B.S.5; Raed A. Dweik, M.D.23
1Sleep Disorder Center, Neurology Institute, Cleveland Clinic, Cleveland, OH; 2Lerner Research Institute, Cleveland Clinic, Cleveland, OH; 3Respiratory Institute, Cleveland Clinic, Cleveland, OH

Study Objectives: Upper airway inflammation and oxidative stress have been implicated in the pathogenesis of obstructive sleep apnea (OSA) and may be linked to cardiovascular consequences. We prospectively examined fraction of exhaled nitric oxide (FENO), a surrogate marker of upper airway inflammation using a portable nitric oxide analyzer (NIOX MINO).

Design: In consecutive adult nonsmokers with suspected OSA, FENO was measured immediately before and after polysomnographic studies, and within 1-3 months following continuous positive airway pressure (CPAP) therapy.

Measurement and Results: FENO levels were increased in the 75 patients with OSA compared to the 29 controls, both before sleep (13.4 ± 6.5 ppb vs. 6.5 ± 3.5; p < 0.001) and after sleep (19.0 ± 7.7 ppb vs. 6.9 ± 3.7; p < 0.001). Furthermore, in patients with OSA, FENO levels were significantly higher post-sleep than pre-sleep (19.0 ± 7.7 ppb vs. 13.4 ± 6.5; p < 0.001), while there was no significant overnight change in patients without OSA. The rise in FENO correlated with the apnea-hypopnea index (r = 0.65, p < 0.001), nadir oxygen saturation (r = 0.54, p < 0.001), and arousal index (r = 0.52, p < 0.001). Thirty-seven of these patients underwent CPAP titration and treatment. Successful titration was associated with a lower overnight increase in FENO (7.2 ± 3.3 vs. 11.0 ± 4.3, p = 0.02). FENO levels declined after 1-3 months of CPAP therapy (11.7 ± 4.4 ppb, p < 0.001).

Conclusions: FENO levels are elevated in OSA, correlate with severity, and decrease after positive pressure therapy. This study supports the role of upper airway inflammation and oxidative stress have been implicated in the pathogenesis of OSA. In this study, we set out to demonstrate that FENO measurement and results using a portable nitric oxide analyzer (NIOX MINO) adds to the increasing knowledge on the role of upper airway inflammation in the pathophysiology and treatment of obstructive sleep apnea. It also provides further insight into the role of exhaled nitric oxide gas measurement in the diagnosis and monitoring of this common sleep condition.

Keywords: Sleep disordered breathing, endogenous nitrate vasodilator, positive pressure ventilation

Citation: Chua AP; Aboussouan LS; Minai OA; Paschke K; Laskowski D; Dweik RA. Long-term continuous positive airway pressure therapy normalizes high exhaled nitric oxide levels in obstructive sleep apnea. J Clin Sleep Med 2013;9(6):529-535.

BRIEF SUMMARY

Current Knowledge/Study Rationale: We perform this study to examine FENO levels in patients with OSA and the impact on these levels by CPAP therapy. Thus we hope to establish the role of FENO measurement in the assessment and control of sleep apnea.

Study Impact: This scientific work adds to the increasing knowledge on the role of upper airway inflammation in the pathophysiology and treatment of obstructive sleep apnea. It also provides further insight into the role of exhaled nitric oxide gas measurement in the diagnosis and monitoring of this common sleep condition.

O bstructive sleep apnea (OSA) is a sleep disorder characterized by recurrent episodes of upper airway collapse leading to significant hypoxemia and disturbed sleep with increased arousals and sleep fragmentation. The etiology of obstruction of the upper airway in OSA is postulated to be multifactorial, including anatomic narrowing due to structural changes, neurologic, vascular, and upper airway inflammation (UAWI). Mechanical stress on the mucosa caused by intermittent airway closure and reopening as well as ischemia-reperfusion injury from intermittent nocturnal hypoxemia produces oxygen free radicals which can lead to increased UAWI. However the extent to which the presence of UAWI plays a role in the pathogenesis of sleep disordered breathing is not clear. The fraction of exhaled nitric oxide (FENO) has been proposed as a marker of airway inflammation (AWI) and can be easily measured in exhaled breath.

Prior studies that have evaluated the FENO levels in OSA have shown inconsistent results. Specifically, studies have shown no difference, mild increase, or significant increases in FENO compared to controls. Post- vs. pre-sleep FENO was significantly increased in one study but unchanged in another. The FENO correlated with the apnea-hypopnea index (AHI) in one study but not in another. Finally, few studies have assessed the impact of CPAP on FENO, generally showing a decrease in FENO with CPAP.

We therefore sought to address these issues and hypothesized that patients with OSA would have elevated levels of exhaled NO at baseline and immediately after sleep, and that the levels would be reduced by nasal continuous positive airway pressure (CPAP), the current standard recommended treatment for OSA. In this study, we set out to demonstrate that FENO is elevated in OSA; to assess whether increase in FENO level correlates with body mass index (BMI) and polysomnographic
parameters such as AHI, arousal indices, pulse oximetry oxyhemoglobin saturation (SpO2), and percentage of total sleep time (TST) with recorded SpO2 < 90% (%TST SpO2 < 90); and to determine whether FENO levels are reduced after short-term (overnight) or long-term (1-3 months) CPAP treatment.

**METHODS**

This was a prospective 1-year follow up study of consecutive adults ≥ 18 years of age recruited from September 2009 to June 2010 at a single sleep disorder center in a tertiary care facility. Patients were selected during their outpatient office visit or when they came for their diagnostic overnight polysomnography in the sleep laboratory (Figure 1). Subject exclusion criteria included current smoking; history of chronic airway or lung disease, atopy, nasal allergy, or polyps; active pulmonary infections; autoimmune conditions; liver diseases or systemic infections; current use of immunosuppressive medications including corticosteroids or leukotriene modifiers; non-communicable patients; and absence of informed consent. Patients who underwent subsequent CPAP titration on the same night as diagnostic PSG, i.e., split-night studies, were also excluded. The protocol was approved by the institutional review board. All patients signed a written informed consent before participation.

Polysomnography (PSG) was performed in accordance to the methods outlined by the American Academy of Sleep Medicine (AASM). Sleep stage and arousals were scored manually in 30-sec epochs and respiratory events were identified, both according to the standard criteria of the AASM. The alternative rule in the AASM manual for scoring hypopneas was used. The Epworth Sleepiness Scale (ESS) was used to evaluate subjective daytime sleepiness, with a score ≥ 12 denoting diurnal hypersomnia.

Subjects diagnosed with OSA and planned for CPAP treatment subsequently returned for a full-night CPAP titration study in accordance to AASM recommendations. Preliminary education and habituation for CPAP was performed 30 min prior to the start of the CPAP titration. An optimal titration study was defined as one in which an optimal CPAP pressure was reached that normalizes the AHI and eliminates snoring, desaturation, and arousals, and restores a normal flow contour. Patients were prescribed CPAP treatment at the optimized titrated pressure. A face-to-face reevaluation during an office visit was performed in accordance with CPAP Medicare guidelines between 30 to 90 days after initiating therapy.

Adherence to the CPAP was assessed on the follow-up visit by reviewing the download information from the CPAP device. Adherence was defined as CPAP use for an average of 4 h on ≥ 70% of the nights.

FENO measurements were performed with the portable NIOX MINO analyzer (Aerocrine, Sweden) according to international recommendations, using the on-line standardized single-breath technique at a constant mouth flow rate of 50 mL/s. We measured FeNO levels within 1 h before (between 21:00 and 23:00) starting PSG (prePSGno) or CPAP titration (preCPAPno), and within 30 min (06:00-08:00) after completing the PSG (postPSGno) or CPAP titration study (postCPAPno). A final FENO level (Tno) was measured during a scheduled follow-up office visit. An outline of the study work flow is shown in Figures 1 and 2.

Demographic, anthropometric, and polysomnographic data were analyzed. Comparisons between groups were performed using Student t-test for normally distributed data and the Wilcoxon rank sum test for non-normally distributed data. The relationship between the continuous variables was explored using Pearson correlation coefficient for normally distributed data, or Spearman correlation test if data were not normally distributed. Potential correlations were identified using linear regression analysis. Descriptive statistics for patient clinical characteristics and polysomnographic parameters were expressed as mean ± standard deviation (SD) for normally distributed data and median (25th, 75th percentiles) if data were not normally distributed. Statistical analysis was performed using SPSS 13.0 software (SPSS Inc. Chicago, IL, USA). Significance level was set at p-value < 0.05.

The study was powered to detect a 5 ppb mean difference between the post-PSG FENO and the post-treatment FENO. We also adopted a conservatively elevated standard deviation of 15 for the difference in the response of matched pairs. Other assumptions included a type I error probability for a 2-sided test of 0.05 (α), and a power of 0.80 of correctly rejecting the null hypothesis of equal population means. These assumptions yielded a sample size of 73 with a goal to enroll 100 patients to accommodate loss to PAP follow-up and other attrition factors.

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**Figure 1**—Flow diagram summarizing study enrollment

- Clinically suspected OSA scheduled for overnight PSG (N = 750)
- Recruited subjects performed pre-sleep FENO (prePSGno) & post-sleep FENO (postPSGno) (N = 104)
- Polysomnographically confirmed OSA, i.e., AHI ≥ 5 (N = 75)
- OSA patients recalled for CPAP titration
- OSA subjects performed pre-CPAP FENO (preCPAP no) & post-CPAP FENO (postCPAP no) (N = 37)
- Patient contacted every 2 weeks to enforce compliance
- OSA subjects performed FENO at office visit (Tno) 31-90 days post-CPAP treatment (N = 37)
- Exclusion criteria
  - Tobacco use
  - Chronic pulmonary disease
  - Sinonasal symptoms
  - Systemic infections
  - Respiratory tract infections
  - Anti-inflammatory drug use
- Drop-outs (N = 38)

**Table**—Flow diagram summarizing study enrollment
RESULTS

One hundred four patients who fulfilled the inclusion criteria were recruited for the study: 75 had OSA with an overall AHI (AHI_{total}) ≥ 5, and 29 had no OSA (non-OSA group). Table 1 summarizes the characteristics of both groups. Although there was a trend for increased age, greater representation of the male gender, and increased BMI and neck circumference in the OSA compared to the non-OSA group, those differences were not statistically significant. Symptoms and polysomnographic abnormalities were significantly more prevalent in the OSA than the non-OSA group.

Table 1—Characteristics of OSA and non-OSA patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>OSA (N = 75)</th>
<th>Non-OSA (N = 29)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>46 ± 14</td>
<td>35 ± 14</td>
<td>NS</td>
</tr>
<tr>
<td>Male (%)</td>
<td>57</td>
<td>45</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>37.0 ± 10.3</td>
<td>31.7 ± 9.3</td>
<td>NS</td>
</tr>
<tr>
<td>Neck girth (cm)</td>
<td>41.3 ± 4.6</td>
<td>37.4 ± 4.0</td>
<td>NS</td>
</tr>
<tr>
<td>Snoring (%)</td>
<td>97</td>
<td>69</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Witnessed apnea (%)</td>
<td>55</td>
<td>21</td>
<td>0.002</td>
</tr>
<tr>
<td>Choking in sleep (%)</td>
<td>44</td>
<td>24</td>
<td>0.048</td>
</tr>
<tr>
<td>Morning headache (%)</td>
<td>35</td>
<td>37</td>
<td>NS</td>
</tr>
<tr>
<td>Morning dry mouth (%)</td>
<td>73</td>
<td>55</td>
<td>NS</td>
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<tr>
<td>Epworth Sleepiness Scale</td>
<td>11 ± 6</td>
<td>11 ± 5</td>
<td>NS</td>
</tr>
<tr>
<td>Sleep latency (min)</td>
<td>15 ± 22</td>
<td>13 ± 19</td>
<td>NS</td>
</tr>
<tr>
<td>TST (min)</td>
<td>327 ± 76</td>
<td>386 ± 100</td>
<td>NS</td>
</tr>
<tr>
<td>Sleep efficiency (%)</td>
<td>76 ± 14</td>
<td>84 ± 11</td>
<td>NS</td>
</tr>
<tr>
<td>% Supine time</td>
<td>52 ± 33</td>
<td>54 ± 30</td>
<td>NS</td>
</tr>
<tr>
<td>% REM time</td>
<td>16 ± 10</td>
<td>16 ± 8</td>
<td>NS</td>
</tr>
<tr>
<td>AHI_{total} (h⁻¹)*</td>
<td>40 ± 33</td>
<td>2 ± 1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>AHI_{supine} (h⁻¹)</td>
<td>47 ± 36</td>
<td>3 ± 4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>AHI_{REM} (h⁻¹)</td>
<td>47 ± 37</td>
<td>5 ± 3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Arousal index (h⁻¹)</td>
<td>38 ± 17</td>
<td>19 ± 11</td>
<td>0.029</td>
</tr>
<tr>
<td>SpO₂aseline (%)*</td>
<td>99 ± 1</td>
<td>100 ± 1</td>
<td>NS</td>
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<tr>
<td>SpO₂mean (%)</td>
<td>92 ± 3</td>
<td>96 ± 2</td>
<td>0.028</td>
</tr>
<tr>
<td>SpO₂rest (%)</td>
<td>80 ± 9</td>
<td>91 ± 5</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD. OSA, obstructive sleep apnea; CPAP, continuous positive airway pressure; NS, nonsignificant p > 0.5; BMI, body mass index; TST, total sleep time. *Average apnea-hypopnea index during TST. †Average apnea-hypopnea index during supine sleep. ‡Average apnea-hypopnea index during REM sleep. **Oxyhemoglobin saturation on pulse oximetry.
Sleep apnea patients had significantly higher pre-sleep FENO (prePSGno) than non-OSA patients (13.4 ± 6.5 ppb versus 6.5 ± 3.5 ppb, p < 0.001), who had normal FENO levels. They also had significantly higher post-sleep FENO (postPSGno) levels than non-OSA patients (19.0 ± 7.7 ppb versus 6.9 ± 3.7 ppb, p < 0.001; Figure 3). There was a significant rise in FENO levels following sleep (∆FENO pre-postPSG) in OSA, which was not seen in non-OSA patients (6.0 ± 2.9 ppb versus 0.4 ± 0.8 ppb, p < 0.001). The prePSGno was significantly correlated with AHI total on PSG (r = 0.73, p < 0.001) but was not significantly correlated with any of the demographic or anthropometric parameters, nor with the other polysomnographic data such as arousal index (AI), average SpO2 during sleep (SpO2mean), lowest SpO2 recorded during sleep (SpO2nadir), and %TST SpO2 < 90. Similarly, postPSGno was also significantly correlated with AHI total on PSG (r = 0.79, p < 0.001) but was not associated with any of the demographic or anthropometric, nor with the polysomnographic parameters. In linear regression analysis, ∆FENOpre-postPSG was positively correlated with AHI total (r = 0.65, p < 0.001; Figure 4) and AI (r = 0.52, p < 0.001), and negatively correlated to SpO2nadir (r = 0.54, p < 0.001). Incorporating these 3 variables in a multiple linear regression model, only AHI remained significantly correlated to ∆FENOpre-postPSG (p < 0.001).

Of the 75 OSA patients, 37 subsequently underwent CPAP titration with FENO levels measured before and after sleep as outlined in the methodology section. Table 2 summarizes the characteristics of these 37 study subjects. Mean TST during titration was 337.4 ± 65.0 min, and mean percentage of TST duration...
ing which AHI was < 5/h (%TST AHI < 5) was 77% ± 29%. After a night of CPAP titration, FENO levels (postCPAP\textsubscript{no}) taken immediately following sleep were higher than pre-sleep levels (preCPAP\textsubscript{no}) (22.7 ± 7.7 ppb versus 14.7 ± 6.6 ppb, p < 0.001). This trend was similar to that observed after sleep without CPAP application during diagnostic PSG. Mean rise in FENO level post-sleep following CPAP titration (ΔFENO\textsubscript{pre-postCPAP}) was 8.0 ± 3.7 ppb. Seventy-three percent (N = 27) of the subjects underwent an optimal titration study. ΔFENO\textsubscript{pre-postCPAP} was significant lower in patients who achieved an optimal titration than those who did not (7.2 ± 3.3 vs. 11.0 ± 4.3, respectively; p = 0.02). Information on whether CPAP was started prior to the CPAP titration to allow acclimatization to the device was available in 45 patients. There was no difference in postCPAP\textsubscript{no}, postPSG\textsubscript{no}, or ΔFENO\textsubscript{pre-postCPAP} between those who received and those who did not receive an acclimatization device. There was no association between postCPAP\textsubscript{no} or ΔFENO\textsubscript{pre-postCPAP} levels and any of the demographic or anthropometric parameters.

Comparing FENO levels obtained during CPAP titration night and that of diagnostic PSG, there was no significant difference between mean preCPAP\textsubscript{no} and prePSG\textsubscript{no} levels (14.7 ± 6.6 ppb versus 13.4 ± 6.5 ppb). However mean postCPAP\textsubscript{no} was slightly higher than mean postPSG\textsubscript{no} level (22.7 ± 7.7 ppb versus 19.0 ± 7.7 ppb, p < 0.001).

All 37 patients were successfully initiated on CPAP and returned for their first office visit with repeat FENO measurements between 1 to 3 months of starting CPAP therapy. The mean duration of CPAP treatment among these 37 subjects was 9.0 ± 3.2 weeks at a mean pressure level of 12 ± 6 cm H\textsubscript{2}O for an average of 6.2 ± 2.1 h per night (Table 2). All the patients were adherent to the CPAP therapy. Figure 5 shows the FENO levels at various timelines in the study in these patients (N = 37). We saw a reduction in the mean FENO level performed at the post-CPAP treatment office visit, T\textsubscript{no}, compared to their baseline mean pre-sleep FENO levels, prePSG\textsubscript{no} and preCPAP\textsubscript{no} (11.7 ± 4.6 ppb versus 13.4 ± 6.5 or 14.7 ± 6.6 ppb, respectively; both p < 0.001; Figure 5).

Of the 75 subjects with sleep apnea, 38 did not complete the study. Figure 2 summarizes the reasons for non-completion of the study. Twenty-six of them received non-CPAP forms of therapy because of the nature and severity of their sleep apnea, comorbidities (morbid obesity, retroglossina and otolaryngological pathology, e.g., enlarged tonsils, adenoids, and turbinates, deviated nasal septum), and/or as a result of patient’s treatment preference. The remaining 12 patients were advised CPAP treatment but did not undergo CPAP titration and follow-up for various reasons (Figure 2). Of these 12 patients, 5 were lost to follow-up; we were unable to ascertain the reason as they were not available via mail or phone.

## DISCUSSION

Our study conclusively demonstrates that baseline pre-sleep FENO levels are elevated in untreated OSA patients and rise further after overnight sleep. The overnight increase in FENO levels correlates with AHI, hypoxia, and sleep fragmentation. The overnight rise in FENO is not affected by a single-night CPAP application, but declines significantly to below baseline levels after long-term regular use of CPAP.

Nasal, tonsillar, and oropharyngeal tissues are potential inflammatory sites in patients with OSA.\textsuperscript{4,23-24} The results we observed in our study are consistent with the current evidence showing elevated cytokines and inflammatory markers in exhaled breath as well as upper airway tissues of OSA patients.\textsuperscript{5,9-17,23,25-28} Salerno et al. and Devouassoux et al. detected increased neutrophils and reduced macrophages in the induced sputum of OSA patients.\textsuperscript{27,28} The latter study also observed a concurrent higher interleukin-8 concentration in the induced sputum specimen of these patients.\textsuperscript{28} Petroyan et al., using samples of exhaled breath condensate demonstrated increased levels of NO, carbon monoxide (CO), 8-isoprostan, leukotriene B\textsubscript{4} (LT\textsubscript{B}4), nitrates, and hydrogen peroxide (H\textsubscript{2}O\textsubscript{2}) in OSA patients compared to control subjects; they found AHI to be positively correlated with nitrates, H\textsubscript{2}O\textsubscript{2}, LT\textsubscript{B}4, and 8-isoprostane. They also concluded that AWI and oxidative stress are present in OSA patients.\textsuperscript{17}

Previous reports on FENO measurements in OSA revealed inconsistent results.\textsuperscript{3,17} Part of the problem could have been patient selection or the use of old technology and methodology. With the latest generation portable FENO analyzer, we demonstrated a rise in FENO levels following sleep in adult OSA patients reflecting increased UAWI that were not present in healthy controls with normal airways. Airway inflammation in this patient group could indicate physical injury to the mucosal lining due to repetitive airway closure and reopening. Oxidative stress from recurrent nocturnal oxygen desaturation may be contributive. In our study, the correlation between FENO levels and markers of OSA severity such as AHI, degree of nocturnal oxygen desaturations, and arousals suggests more severe OSA patients have an increased amount of UAWI. Przybyłowski et
as study participants.

levels only after a period of compliant and effective CPAP therapy, rather quickly within minutes of any changes in flow. As such, knowledge and experience with the use of FENO, it equilibrates and thus did not consider this in our study plans. Based on our not aware of any evidence for this possibility in the literature in that regard remains to be determined, but with their increasing portability, it may be feasible to expand the role of FENO to the monitoring of AWI and follow-up on CPAP therapy in otherwise healthy OSA patient, similar to their use in the diagnosis and management of bronchial asthma.

CONCLUSIONS

Our study supports the emerging concept that UAWI is present in OSA, is directly related to its severity, responds to treatment, and likely contributes to its pathogenesis. In addition, our findings suggest that parallel to its established role in the evaluation and management of asthma, FENO may have a role in the assessment and control of sleep apnea. Measuring FENO levels with a portable analyzer may thus be a simple way to monitor AWI in OSA patients.

REFERENCES


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Impact of Group Education on Continuous Positive Airway Pressure Adherence

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Study Objectives: To compare the impact of a group educational program versus individual education on continuous positive airway pressure (CPAP) adherence.

Methods: Post hoc assessment of a performance improvement initiative designed to improve clinic efficiency, access to care, and time to initiate therapy. Consecutive patients newly diagnosed with obstructive sleep apnea (OSA) initiating CPAP therapy participated in either an individual or group educational program. The content and information was similar in both strategies.

Results: Of 2,116 included patients, 1,032 received education regarding OSA and CPAP through a group clinic, and 1,084 received individual education. Among the cohort, 76.6% were men, mean age 48.3 ± 9.2 years, mean body mass index 29.6 ± 4.6 kg/m², and mean apnea-hypopnea index was 33.3 ± 24.4 events/hour. Baseline characteristics were similar between groups. CPAP adherence was significantly greater in those participating in a group program than those receiving individual education. Specifically, CPAP was used for more nights (67.2% vs. 62.1%, p = 0.02) and more hours per night during nights used (4.3 ± 2.1 vs. 3.7 ± 2.8, p = 0.03). Further, fewer individuals discontinued therapy (10.6% vs. 14.5%, p < 0.001), more achieved regular use of CPAP (45.2% vs. 40.6%, p = 0.08), and time to initiate therapy was shorter (13.2 ± 3.1 versus 24.6 ± 7.4 days, p < 0.001). Group education resulted in a 3- to 4-fold increase in the number of patients seen per unit time.

Conclusions: A group educational program facilitated improved CPAP adherence. If confirmed by prospective randomized studies, group CPAP education may be an appropriate alternative to individual counseling, may improve acceptance of and adherence to therapy, and decrease time to treatment.

Commentary: A commentary on this article appears in this issue on page 551.

Keywords: CPAP, OSA, adherence, education


The growing recognition of obstructive sleep apnea (OSA) continues to increase demands for clinical evaluations and continuity of care. Means to improve the efficiency of sleep medicine clinics and increase access to care without adversely affecting outcomes are needed.

While the benefits of continuous positive airway pressure (CPAP) are well recognized, acceptance of treatment and adherence with therapy remain problematic. Despite advances in CPAP platforms and comfort features, both short-term and long-term compliance patterns have not significantly improved. Current estimates indicate that 29% to 83% of patients prescribed CPAP are non-adherent with therapy (≤ 4 h of use per night).1

In light of the ongoing challenge of CPAP adherence, any methods implemented to improve the efficiency of sleep centers in order to meet growing demands should not impair CPAP use. To that end, methods that could both improve clinic output and foster better adherence would be ideal. Given that the use of CPAP during the initial treatment period, even the first few days of therapy, has been consistently shown to predict long-term use,2,3 strategies aimed at improving the process of therapy initiation could enhance both clinical operations and subsequent adherence.

Patients’ lack of comprehension regarding the adverse effects of untreated OSA, benefits of therapy, and proper use of CPAP is an important contributor in the unacceptably poor observed rates of CPAP adherence.4-6 Like other disorders, comprehensive education regarding these factors is an important component of therapeutic acceptance and may improve treatment adherence by facilitating incorporation of patients into the therapeutic plan, thereby allowing them to participate in an active and informed manner in the decision-making process.7,8 Previous studies have demonstrated that intensive education and support may improve CPAP adherence.9-13 However, as the demand for sleep evaluations continues to increase, the ability for physicians to provide one-on-one, comprehensive education may diminish. Moreover, the allocation of time and resources needed to provide this education on an individual basis could limit access to care for new
The efficacy, efficiency, and cost-effectiveness of these programs compared to a group class setting.

Patient evaluations without exploring the use alternatives strategies or developing mechanisms to improve efficiency. A comprehensive intensive educational approach appears to increase patient understanding and awareness, facilitate acceptance of therapy, and improve adherence. However, the efficacy, efficiency, and cost-effectiveness of these programs remains controversial. While intensive education may benefit individual patients, the clinical improvements it generates may not outweigh the allocation of resources it requires. In contrast, group educational programs increase access to care and reduce individual resource allocation. While this has not yet been explored for CPAP initiation, group patient education has been demonstrated to improve outcomes in several other disease processes, particularly diabetes mellitus and rheumatoid arthritis. While these programs decrease overall resource allocation, they also limit individualized education and counseling, and consequently, may negatively impact adherence.

While patient education affords significant benefits, it is associated with inherent costs related to clinic efficiency, time, resources, and access to care. In contrast, improving clinic efficiency at the expense of patient education will likely adversely affect adherence. Given the growing demand for sleep clinics to diagnose and treat OSA in the context of continued difficulties with CPAP adherence, initiating CPAP therapy in a group setting offers several potential benefits, such as more comprehensive education and additional patients cared for per unit of time. We sought to determine if adherence differed between patients who initiated CPAP therapy following individual counseling compared to a group class setting.

**METHODS**

**Study Design**

We report the outcomes of a performance improvement initiative designed to improve the efficiency and patient-specific outcomes in our sleep disorders center. The initiative involved development of a multidisciplinary group education clinic for patients with newly diagnosed OSA who were initiating CPAP therapy.

We included all adult patients initiating CPAP therapy in our center between January 2009 and July 2010. All patients received their care from a single academic sleep disorders center (Walter Reed Army Medical Center, Washington DC). Patients eligible for care in our institution constitute a range of Active Duty Service members, their dependents, and those retired from Military service. Our population represents a wide range of patient demographics (age, gender, ethnicity, educational, and socioeconomic backgrounds) which, in general, are representative of the US population and populations cared for at academic civilian institutions. Patients seen at our sleep disorders center have the option of being cared for in our institution or at a local civilian center. There is no cost to their health care regardless of where they are seen.

Individuals who were unable to participate in a group counseling center due to cognitive impairments or refusal to participate in a group setting were not included in this investigation. Otherwise no records were excluded from this analysis.

OSA was diagnosed by an attended, overnight level I polysomnogram in all patients, in accordance with the American Academy of Sleep Medicine guidelines. Patients undergoing either full-night diagnostic polysomnograms followed by CPAP titrations or split-night studies were eligible for inclusion. All polysomnographic studies were manually scored and interpreted by board certified sleep physicians in accordance with published guidelines.

The protocol was approved by our institution’s Department of Clinical Investigation (Scientific Review Committee, Human Use Committee, and Institutional Review Board). No external funding was utilized to complete this study.

**Interventions**

Patients were categorized by whether they initiated CPAP therapy following an individual or group counseling session. Assignment to individual counseling or a group class was not determined by any pre-established criteria, but rather reflected our clinic’s procedure at that time. Specifically, placement of patients into one of the two educational programs was based upon the day of the week they scheduled their overnight polysomnogram was performed. Further, all polysomnographic studies at our institution are scheduled to accommodate the patient’s wishes, and there was no difference in the acuity or complexity of studies between the different weeknights. Patients were not aware of this distinction at the time they scheduled their polysomnogram. However, those who did not wish to participate in a group clinic were able to request an individual follow-up appointment.

Patients receiving individual counseling initiated CPAP during a scheduled clinic appointment after their initial sleep clinic consultation and polysomnographic studies were completed. During this appointment they received one-on-one counseling by a board-certified sleep physician regarding the results of their polysomnographic studies, basic information on OSA, its known effects on comorbid conditions, proper sleep hygiene, adjunctive/conservative methods to improve sleep, and the importance of treatment adherence. Patients were also provided specific counseling on the proper use and maintenance of CPAP and underwent personalized, formal mask fitting by a specialized respiratory therapist trained in sleep apnea and CPAP equipment. This format adhered to a standardized approach according to our clinic’s procedures. The total time for this method was 45min/patient.

Patients who participated in group classes for CPAP initiation were scheduled for a shared session, generally consisting of 15-20 patients. Consent to participating in a group class was obtained at the time of scheduling, and all personally identifying information was protected during the classes. This session consisted of a 20-min lecture given by a board-certified sleep physician involving basic information regarding OSA, its sequelae, treatment options, and the benefits therapeutic adherence, similar to the information provided during individual counseling sessions. This was followed by a 10- to 15-min lecture from the sleep clinic’s registered nurses regarding proper sleep hygiene, adjunctive/conservative methods to improve sleep, and reinforcement of the benefits of adherence. Patients were then instructed on the proper use and maintenance of the CPAP equipment and underwent formal mask fitting by a spe-

*Journal of Clinical Sleep Medicine, Vol. 9, No. 6, 2013*
pecialized respiratory therapist. To ensure privacy, no personal information was discussed during the group portion of this program. At the completion of the group session, all patients enrolled in the group sessions were seen on an individual basis by one of the board-certified sleep physicians to provide them the opportunity to discuss the details of their respective polysomnograms, to help identify any barriers to therapy they might have, and to address questions or concerns not covered in the shared lectures. The total time for the group sessions was approximately 2-2.5 hours. In comparison, the group educational program was able to initiate CPAP therapy in 15-20 patients in the same time frame as we were able to initiate therapy in 6 patients receiving individual counseling. In other words, the group class facilitated a 3- to 4-fold increase in clinic efficiency in this regard.

Other than the type of educational session, all patients treated with CPAP in our center received similar care. All patients cared for in our clinic had a comprehensive sleep evaluation by one of our sleep medicine physicians prior to undergoing any polysomnographic studies. All individuals received a telephone follow-up during the first 2 weeks of treatment to ensure proper mask fit and to identify any potential barriers to CPAP adherence; all had access to a 24-h support line for problems arising from CPAP therapy. Additionally, all patients were automatically scheduled to undergo a clinical evaluation after the first month of therapy to optimize care. All patients received the same model of CPAP (Respironics System One Auto, Phillips Respironics, Murrysville, PA).

**Measured Variables**

Age, gender, body mass index (BMI), diagnostic apnea-hypopnea index (AHI), Epworth Sleepiness Scale (ESS), and Fatigue Analog Scale were recorded for each patient. In addition, objective use of CPAP was measured in all patients during their initial follow-up evaluation after their first month of therapy (Encore Anywhere, Phillips Respironics). Specifically, we recorded the percentage of nights CPAP was used, the mean hours of CPAP use per night for all nights, and the mean hours of CPAP use per night during nights used.

**Endpoints**

The primary outcome measured was the difference in the use of CPAP during the first 4 weeks of therapy between the 2 groups. Differences in the rates of discontinuation of therapy and regular use of CPAP between groups served as secondary outcomes. We defined regular use as the use of CPAP > 4 h/night on more than 70% of nights. In the event a patient failed to return for follow-up, we assumed therapy had been discontinued, and CPAP use was recorded as zero. The time between the titration polysomnogram and initiation of CPAP therapy was also compared between the two groups.

**Statistical Analysis**

Data are presented as the mean ± one standard deviation. All tests were two-tailed, and p values < 0.05 were assumed to represent statistical significance. Differences between groups were examined using the independent-samples t-test for continuous variables and the χ2 test for categorical data. Data were analyzed using the PAWP 17.0 (SPSS Inc, Chicago, IL).

**RESULTS**

During the inclusive time period, 2,158 patients initiated CPAP therapy in our center. Forty-two individuals were excluded from the final analysis (a group setting was considered to be inappropriate by their sleep physician in 24, and 18 did not wish to participate in a group clinic). The final included cohort consisted of 2,116 patients (98.1%). Of the total cohort, 32.7% underwent a split-night study. The remainder (67.3%) participated in a full-night in-lab CPAP titration following their initial diagnostic polysomnogram.

The majority of the cohort were men (76.6%), with a mean age of 48.3 ± 9.2 years, and mean BMI of 29.6 ± 4.6 kg/m2. Most patients had moderate-severe OSA, with a mean AHI of 33.3 ± 24.4 events/h. For the entire cohort, CPAP was used on 64.7% of nights, with a mean nightly use of 3.2 ± 2.8 h on all nights and 4.1 ± 2.0 h on nights CPAP was utilized. Regular use among all patients was 42.8%, and 12.5% discontinued therapy.

Among the cohort, 1,084 (51.2%) received individual counseling and 1,032 (48.8%) participated in a group education clinic. Baseline patient characteristics were similar between the 2 groups (Table 1). Compared to individual counseling, CPAP adherence was greater among those who participated in a group clinic (Table 2). Specifically, group clinic patients used CPAP on 67.2% ± 30.8% of nights, compared with 62.1% ± 37.0% in those receiving individual counseling (p = 0.02). Nightly use of CPAP among group clinic patients was 3.5 ± 1.9 h during all nights compared with 3.1 ± 2.6 h in those receiving individual counseling (p = 0.04). Similarly, during nights CPAP was used, the mean use of CPAP was greater in those undergoing group education (4.3 ± 2.1 versus 3.7 ± 2.8 hours, p = 0.03). Regular use of CPAP tended to be more common in those who participated in a group clinic and was observed in 45.2%, compared with only 40.6% of those receiving individual counseling (p = 0.08).

Table 1—Baseline characteristics of patients receiving individual versus group education

<table>
<thead>
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<th></th>
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<th>Group (n = 1,032)</th>
<th>p-value</th>
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</thead>
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<tr>
<td>Age (years)</td>
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<td>48.0 ± 9.9</td>
<td>0.18</td>
</tr>
<tr>
<td>Gender, male (%)</td>
<td>76.2</td>
<td>77.0</td>
<td>0.14</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>29.6 ± 4.4</td>
<td>29.7 ± 8.2</td>
<td>0.72</td>
</tr>
<tr>
<td>Apnea-hypopnea index</td>
<td>33.8 ± 19.8</td>
<td>32.7 ± 22.2</td>
<td>0.08</td>
</tr>
<tr>
<td>Epworth Sleepiness Scale</td>
<td>13.2 ± 4.8</td>
<td>13.0 ± 5.0</td>
<td>0.55</td>
</tr>
<tr>
<td>Fatigue score</td>
<td>6.5 ± 2.7</td>
<td>6.1 ± 3.2</td>
<td>0.14</td>
</tr>
</tbody>
</table>
In addition, the time between the CPAP titration polysomnography and initiation of CPAP therapy was considerably shorter among those participating in the group clinic (13.2 ± 3.1 versus 24.6 ± 7.4 days, p < 0.001).

Overall, 256 patients (12.6%) discontinued therapy during the first month of treatment. Discontinuation of therapy was significantly less common in the group patients, occurring in 10.6%, compared with 14.5% among those receiving individual counseling (p < 0.001). Patients who discontinued CPAP were more likely to have a lower AHI (23.2 ± 25.8 vs. 31.3 ± 27.3 events/h, p = 0.06), a higher ESS (16.7 ± 5.9 vs. 12.7 ± 2.1, p = 0.02), weighed more (32.0 ± 5.0 vs. 30.4 ± 4.7 kg/m², p = 0.09), and were more likely to be women (35.3% vs. 18.1%, p = 0.01). Furthermore, of those who discontinued therapy, 198 patients (77.3%) had received individual counseling (p < 0.001).

**DISCUSSION**

Despite less time allocated per patient, we found that a group educational strategy resulted in improved acceptance of and adherence to CPAP therapy. Using a group educational setting yielded a three to four-fold increase in the number of patients per unit of time. Further, we did not observe any detriment in subsequent adherence. In fact, objective measures of CPAP use, rates of regular use of CPAP, and discontinuation of therapy were all improved. In addition, group clinics decreased the time between polysomnography and initiation of therapy.

The improvement in CPAP adherence observed in those initiating therapy through a group clinic is likely multifactorial. Both strategies provided the same CPAP device, same clinical evaluations and follow-up care, and similar education regarding OSA and the proper use of CPAP. Given this, it appears that the type of the educational program was the basis for the differences in CPAP use between. Group sessions followed a relatively standard approach to education and shared similar content. While these groups were conducted by different staff physicians, they were based on agreed-upon content and format. Individual sessions, on the other hand, were likely less standardized and may have included variable counseling regarding the effects of non-treatment or emphasis on the benefits of CPAP. Further, group clinics involved participation by a clinic nurse. While the overall content and information provided was similar, having an additional provider likely facilitated a greater emphasis on key points. Regardless, both formats provided similar content, were delivered by the same core group of providers, and all patients received formalized mask selection and fitting, and the same CPAP platform and follow-up care. The dynamic setting of the educational program was the only significant difference and, as such, likely had the greatest impact on our observed outcomes. These improvements may, in part, be a result of reinforcement of the importance of CPAP adherence and strategies for promoting proper usage by several providers. However, we believe it is also largely due to external validation that occurs within a small group environment. Within this setting, patients are encouraged to express concerns, reservations regarding therapy, and personal challenges with their medical condition. In turn, this creates an environment of peer reinforcement of their shared experience and realization that other similar people also have their condition. While this form of external validation and peer support can benefit the acceptance of many disease processes, it is likely more pronounced in disorders like OSA where misconceptions, biases, and images regarding the demographics of apneic patients remain prevalent.

In a similar study, Golay and associates demonstrated improvements in treatment adherence in existing OSA patients on CPAP therapy who underwent additional group educational interventions after an initial period of CPAP use. While the study reported preliminary results, utilized a small cohort, and lacked a control group, it nonetheless demonstrated improvements in the both duration of CPAP use and subjective sleepiness at three months. Likewise, Likar and colleagues observed improvements in CPAP among patients with OSA who participated in group clinics for continuity of care and follow-up assessments at regular time intervals (6 months) over a two-year period.

Group educational strategies have been demonstrated to improve outcomes in several other disease processes. Rickheim et al. showed that group educational programs improved outcomes in the management of diabetes mellitus. Specifically, they observed greater improvements in HbA1c among those who underwent group versus individualized education. Likewise, Barlow and associates demonstrated that group educational clinics positively impacted the management of rheumatoid arthritis and showed improvements in arthritis symptom severity, self-efficacy, and psychological well-being at three- and six-month follow-up assessments.

Our study has several potential limitations. First, our results reflect observations from a performance improvement initiative and not a prospective, randomized trial. Similar to retrospective studies, our study design limits the validity of our findings. However, we included a large number of consecutive patients, which minimizes the potential for bias. In addition, patients were not assigned to either intervention based on any predetermined criteria, which mitigates the potential for selection biases. Patients

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Table 2—Comparison of CPAP use between individual versus group education

<table>
<thead>
<tr>
<th></th>
<th>Individual (n = 1,084)</th>
<th>Group (n = 1,032)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPAP, % nights used</td>
<td>62.1 ± 37.0</td>
<td>67.2 ± 30.8</td>
<td>0.02</td>
</tr>
<tr>
<td>CPAP, hours per night, all nights</td>
<td>3.1 ± 2.6</td>
<td>3.5 ± 1.9</td>
<td>0.04</td>
</tr>
<tr>
<td>CPAP, hours per night, nights used</td>
<td>3.7 ± 2.8</td>
<td>4.3 ± 2.1</td>
<td>0.03</td>
</tr>
<tr>
<td>Regular use of CPAP (%)</td>
<td>40.6</td>
<td>45.2</td>
<td>0.08</td>
</tr>
<tr>
<td>Discontinuation of CPAP (%)</td>
<td>14.5</td>
<td>10.6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CPAP Initiation(days)</td>
<td>24.6 ± 7.4</td>
<td>13.2 ± 3.1</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
had the option of not participating in a group setting, which could also create selection bias. However, this occurred in only 1.3% of those initially designated for a group clinic. Second, both interventions received considerable education, which likely diminished the differences observed between the two groups that could have underestimated the value of this educational model. Overall, regular use of CPAP was low among the cohort. While not dissimilar from other reports, it does highlight the ongoing challenges related to CPAP adherence and emphasizes the need to explore any potentially positive interventions, especially those that are not associated with an increase in costs or resources. Third, while the individual educational counseling adhered to a standardized curriculum endorsed by our clinic, some variations in the educational experience may have occurred. However, in an attempt to minimize this, the physicians responsible for providing the individual educational counseling also co-developed and conducted the group educational program. Further, both educational programs had identical respiratory therapy components conducted by the same specialized respiratory therapists. As such, this impact should have been minimal. We did not include data regarding race or educational level, as our primary focus was the impact of our proposed educational model of adherence, and we limited the information gathered to those items specifically related to sleep and sleep disordered breathing. The impact of these factors on adherence has been explored in prior studies. However, none have been consistently shown to influence adherence. It is possible that we would have identified some additional confounding factor, especially given the size of our study. Finally, while long-term use of CPAP is often predicted by short-term adherence patterns, we only measured CPAP adherence, and we limited the information gathered to those items specifically related to sleep and sleep disordered breathing. It is, therefore, uncertain if these improvements will be sustained.

As the prevalence of OSA and the demand for CPAP continue to increase, fewer resources will likely be available for patients. Through the initiation of a group educational strategy, we were able to decrease the time to therapy while promoting better acceptance of and adherence to therapy. In our institution, group clinics also facilitated a more rapid initiation of therapy and reduced delays in treatment. In addition, group clinics decrease the use of clinic appointments for CPAP initiation which allows for more new and follow-up evaluations. Our results suggest that a group educational setting to initiate patients on CPAP therapy appears to be an effective and productive use of resource that increases clinic availability and therapeutic adherence. The role of this form of educational strategy warrants additional consideration and may be a viable alternative to traditional, individual physician-directed counseling. Further investigation in a prospective randomized trial is needed to validate these findings.

REFERENCES


ACKNOWLEDGMENTS

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SUBMISSION & CORRESPONDENCE INFORMATION

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DISCLOSURE STATEMENT

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ABBREVIATIONS

CPAP, continuous positive airway pressure
OSA, obstructive sleep apnea
BMI, body mass index
AHI, apnea-hypopnea index
ESS, Epworth Sleepiness Scale

Impact of Group Education on CPAP Adherence
A Pilot Study of CPAP Adherence Promotion by Peer Buddies with Sleep Apnea

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Study Objectives: To evaluate patient ratings of the acceptability of a peer buddy system (PBS). To promote continuous positive airway pressure (CPAP) therapy adherence in patients with obstructive sleep apnea (OSA). To obtain preliminary data on the effectiveness of PBS on sleep-specific health-related quality of life and CPAP adherence.

Design: Prospective, randomized, and controlled study.

Setting: Academic Center.

Participants: Thirty-nine patients with OSA and 13 patients with OSA who were experienced CPAP users.

Interventions: Recently diagnosed patients with OSA were randomly assigned to either the PBS to promote CPAP adherence (intervention group) or usual care (control group).

Measurements: Patient satisfaction, Functional Outcomes of Sleep Questionnaire (FOSQ), CPAP adherence, vigilance, self-efficacy, and patient activation were measured.

Results: Ninety-one percent of the subjects rated the PBS as very satisfactory (68%) or satisfactory (23%). During the 90 days of therapy, weekly CPAP adherence was greater in the intervention than the usual care group (MANOVA; F = 2.29; p = 0.04). Patient satisfaction was positively correlated with CPAP adherence ($R^2 = 0.14; p = 0.02$). We did not find any group differences for FOSQ, vigilance, self-efficacy, or patient activation in this pilot study.

Conclusion: Our pilot study suggests that the PBS intervention is feasible and received high patient satisfaction ratings. CPAP adherence may be improved by peer-driven intervention, but a larger, adequately powered study is needed.

Clinical Trial Information: ClinicalTrials.gov identifier: NCT01164683.

Keywords: Adherence, obstructive sleep apnea, sleep apnea, continuous positive airway pressure, adherence, adult, compliance, artificial respiration

Commentary: A commentary on this article appears in this issue on page 551.


Obstructive sleep apnea (OSA) is a highly prevalent condition in veterans with some estimates as high as 47%.1 Poor adherence to the primary treatment of OSA—continuous positive airway pressure (CPAP)—therapy is common, with 29% to 93% of patients being non-adherent to therapy when adherence is defined as greater than 4 hours of CPAP use per night. There remains a paucity of reliable and cost-effective interventions that could promote CPAP adherence. Promoting adherence to therapy through peer-driven intervention is cost-effective and has met with modest success in other chronic conditions such as HIV, heart failure, and diabetes mellitus.2-4 Whether such a peer-driven (“buddy”) system can improve adherence to CPAP therapy is unknown.

We proposed to improve adherence to CPAP therapy using a peer-driven intervention, which, if successful, could have significant impact in improving patient outcomes in OSA. Such a proposal to use trained peers with OSA is both a potentially cost-effective strategy and is grounded on the rationale that veterans as a group are eco-culturally more homogenous than expected for the given level of differences in age, gender, ethnicity, or socioeconomic strata.5 Moreover, there are data to suggest that social support has a favorable effect on promoting CPAP adherence.6-10

Our overall aim was to assess the feasibility and acceptability of a CPAP adherence program driven by trained “peer-buddies” with sleep apnea.11 Our primary objective was to evaluate patient ratings of the acceptability of the peer buddy system (PBS) in veterans receiving CPAP therapy for OSA. Our secondary objective was to obtain preliminary data on the effectiveness of PBS on sleep-specific health-related quality of life (HR-QOL; Functional outcomes in sleep questionnaire [FOSQ]) in veter-
ans receiving CPAP therapy for OSA. Additional objective was to obtain preliminary data on the effect of PBS on CPAP adherence, vigilance, patient activation, and self-efficacy in veterans receiving CPAP therapy for OSA. Patient activation pertains to improving patients’ knowledge, skills, and confidence essential to managing their own health and healthcare.

**METHODS**

**Design and Setting**

This prospective, randomized, parallel group, open label, pilot study randomly assigned patients with OSA who had not yet been initiated on CPAP therapy to the peer-buddy system (PBS) to promote adherence to CPAP therapy (peer-driven intervention group) or be provided with educational brochures regarding OSA and CPAP therapy (usual care group). Both groups received usual care; thus, the only difference between the 2 groups was that the intervention group received interactions with the peer buddy. The study was performed at the Southern Arizona VA Health Care System in Tucson, Arizona (SAVAHCS), with institutional review board approval from the University of Arizona and VA Research and Development Committee. Each participant signed a written informed consent prior to commencing study participation. The duration of the study was one year, although duration of subjects’ participation was for only 3 months.

**Study Sample**

Thirty-nine subjects with OSA who were prescribed CPAP therapy by their physician were recruited from the sleep disorders program at SAVAHCS. Subjects were recruited by posting fliers, distributing brochures at the clinics and sleep laboratory, and by screening clinic attendees following a Health Insurance Portability and Accountability Act (HIPAA) waiver from the Privacy Board. Optimal CPAP pressure was determined by manual titration during a split-night or a CPAP titration polysomnogram. Self-adjusting device was not used for the current study. Subjects were approached if they met the following inclusion and exclusion criteria:

**Inclusion Criteria**

Inclusion criteria were (i) OSA (defined by apnea-hypopnea index [AHI] > 5 per hour; with hypopneas defined as > 30% reduction in airflow with ≥ 4% drop in oxygen saturation as per AASM 2007 criteria1). AHI was determined by full-night or split-night polysomnography. (ii) age between 21 and 85 years. (iii) Stable medical history with no change in medications (including antihypertensives and thyroid replacement) in the previous 4 months. (iv) No regular use (> 3 times/week) of sedative or hypnotic medications in the previous 4 months.

**Exclusion Criteria**

Exclusion criteria were (i) Central sleep apnea (central apnea index > 5 events/h and > 50% of AHI constituted by central apneas and non-obstructive hypopneas1)). (ii) Complex sleep apnea or CPAP emergent central apnea (central apnea index > 5 events/h during CPAP titration with > 50% of apnea-hypopnea index constituted by central apneas and non-obstructive hypopneas). (iii) Required oxygen or bilevel positive airway pressure for treatment of OSA or hypoventilation. (iv) Decompensated cardiac (heart failure or angina) or pulmonary (severe COPD or uncontrolled asthma) disease. (v) Chronic narcotic use. (vi) Nasal obstruction (nasal congestion score > 15)14,15 or enlarged tonsils. (vii) Diagnosis of another sleep disorder in addition to OSA based on PSG (e.g., periodic limb movement disorder [≥ 15 limb movements/h of sleep with arousal], insomnia, obesity hypoventilation syndrome, or narcolepsy). (viii) Previous treatment with positive airway pressure, home oxygen therapy, tracheotomy, uvulopalatopharyngoplasty, or other surgery for OSA. (ix) Night shift workers in situations or occupations where they regularly experience jet lag, or have irregular work schedules by history over the last 6 months. (x) Routine consumption of > 2 alcoholic beverages per day. (xi) Recent or recurring history of recreational drug use leading to tolerance or dependence. (xii) Unable to perform tests due to inability to communicate verbally, inability to write and read in English; less than a 5th grade reading level; visual, hearing, or cognitive impairment (e.g., previous head injury); or upper extremity motor deficit (e.g., previous stroke that prevents patient from using CPAP treatment).

Peer buddies were recruited using fliers in the general clinic areas. Peer buddies had the following inclusion and exclusion criteria:

(a) **Inclusion:** (i) Adherent to CPAP therapy (> 4 h/day of CPAP use); (ii) willing to meet with peer-buddy on 2 occasions in person at SAVAHCS; (iii) able to be contacted by telephone; (iv) willing to undergo a brief training and orientation session with research staff. (b) **Exclusion:** In addition to exclusion criteria for subjects (listed above), patients suffering from major depression or other major psychiatric illness; shift-worker or frequent out of town traveler; unwilling to participate in orientation and training session. The peer-buddies were compensated $300 for the 3-month duration of participation.

**Peer Buddy Training**

Research staff educated the peer buddies and provided them with guidelines for their interactions with the research participants. They were instructed to share their experiences and not to provide medical advice. The sharing of coping strategies fell broadly into the following categories: promoting self-efficacy, promoting outcome expectancies, improving risk perception, and patient activation. At the end of the training, a mock interaction between the peer-buddy and principal investigator (playing the role of the patient with OSA) was undertaken before “certifying” the peer-buddy as competent.

**Protocol**

In the PBS-intervention group, trained peers with OSA who were adherent to CPAP therapy were paired with the newly diagnosed subjects over a 3-month period. During this time the trained peers shared their experiences on coping strategies with CPAP device and equipment (promote self-efficacy), shared their positive experiences (motivational effects and outcome expectancies), shared their knowledge of perceived vulnerabilities due to untreated sleep apnea (promote risk perception), shared methods for improving efficacy of CPAP equipment and interface (patient education) and prepared their subjects for upcoming physician or respiratory therapist appointments.
with their peer buddies.3 Responded to a 25-item questionnaire that was used by Heisler scores was collected at baseline and at 90 days.18 Efficacy with a global score computed from these individual domains that measured perceived risk, outcome expectancies, and self-efficacy.17 Patient characteristics between the participants and non-participants were compared using t-tests or nonparametric equivalent (Mann-Whitney U test). P values less than 0.05 were considered significant. Group comparisons of continuous variables were made by unpaired t-tests or nonparametric equivalent (Mann-Whitney U test). P values less than 0.05 were considered significant. Group comparisons for proportions were made using χ² or Fisher exact tests as appropriate. All data are shown as mean and standard deviation (SD) or median and inter-quartile range (IQR). IBM SPSS Statistics v19.0 (IBM Inc., Armonk NY; for comparisons) and STATA 9.2, College Station, TX (for modeling) was used for statistical analysis.

**Usual Care Description**

All participants in the control (usual care) arm received usual care following initiation of CPAP therapy. Usual care consisted of the newly diagnosed patient with OSA attending a CPAP initiation and education class that was conducted by a dedicated respiratory therapist. At this group clinic, patients were educated about the basics of the care and operation of the device, mask and related equipment. Subsequently, they broke-out into individual sessions wherein they tried on their masks and turned on the machine and mask fitting and readjusting was performed by the respiratory therapist. Following this CPAP initiation and education class, they received instructions to mail-in the CPAP adherence monitoring card (“smart card”) by mail to the therapist about 4 weeks following the initial visit. The adherence information was evaluated and posted in electronic medical records. Patients with OSA were then seen in the sleep clinic at 1 and 3 months following initiation of CPAP therapy.

**Measurements**

(a) Patient ratings of acceptability of PBS: Patients rated their acceptability of the PBS at the end of study participation on a 5-point scale: strongly agree, agree, neutral, disagree, strongly disagree.15 Additionally, patients in the PBS intervention group responded to a 25-item questionnaire that was used by Heisler and colleagues that evaluated various facets of their interaction with their peer buddies.3

(b) Functional Outcomes of Sleep Questionnaire (FOSQ): A disease-specific quality of life questionnaire collected at baseline and at 90 days.16

(c) CPAP adherence downloads: Mean number of hours per day of CPAP use was collected for the entire 90 days through downloads on data 30 and 90.

(d) Patient Activation Measure (PAM): a 22-item measure that assesses patient knowledge, skill, and confidence for self-management;7; and Self-Efficacy Measure for Sleep Apnea (SEMSA), a tool with strong psychometric properties and with the potential for identifying patient perceptions that may indicate those most likely to not adhere to treatment with 3 domains that measured perceived risk, outcome expectancies, and self-efficacy with a global score computed from these individual scores was collected at baseline and at 90 days.18

(e) Nasal congestion score (confounder): a validated questionnaire that assesses nasal congestion using a 5-point Likert scale that was previously administered to patients with sleep disordered breathing and found to be associated with discontinuation of CPAP therapy.11 This questionnaire was used to screen out patients who may be non-adherent due to excessive nasal congestion. A threshold of 15 was chosen to exclude such patients.

(f) Psychomotor vigilance task (PVT): a reproducible measure of vigilance that has been used as an objective assessment of daytime sleepiness was measured at baseline and at 90 days.20

(g) Other confounders: Confounders that may affect adherence to CPAP therapy were collected, such as age, gender, race, severity of OSA (i.e., AHI), body mass index, CPAP level, and highest level of education received.15,21 Another confounder of interest—the Charlson comorbidity index (a well-validated index of comorbid illnesses)—was measured at baseline.22

**Sample Size Estimation**

For CPAP adherence (h/night of CPAP use), we assumed that a difference of 1 h/day of average CPAP use is clinically significant (SD 1.7 h). Using t-test, α of 0.05, and 2-sided, 90% power, we needed 62 subjects per group (a total of 124 patients).23 Other intervention-based trials aimed at improving CPAP adherence have employed sample sizes ranging from 100 to 373 participants.23-27 However, the current pilot study aimed to recruit much less than that to assess feasibility and obtain preliminary data.

**RESULTS**

Thirty-nine subjects—22 in intervention arm and 17 in control arm—and 13 “expert” peer buddies were recruited into the study. Baseline characteristics of the subjects are given in Table 1. Thirty-nine (80%) of the 49 eligible subjects agreed to participate in the study; there was no difference in baseline characteristics between the participants and nonparticipants (Figure 1). In the subjects randomized to the peer-buddy intervention, 63% (n = 14) completed all 10 training sessions; 86% (n = 19) completed 9 of 10 sessions; 91% (n = 20) completed
≥ 8 sessions; and 22 (100%) completed ≥ 7 sessions. Sessions were facilitated by 2 study coordinators to schedule and to ensure that the interactions occurred.

**Patient Ratings**

Twenty (91%) of the 22 subjects in the intervention group were either very satisfied (68%) or satisfied (23%) with the peer-buddies being helpful with regards to managing their underlying disease. For patients in both groups, patient satisfaction was positively correlated with their CPAP adherence (n = 39; $R^2 = 0.14$; $p = 0.02$). In the intervention group, patient ratings of their peer buddies were positively correlated with their CPAP adherence, and a majority of patients rated their peer buddies and the telephone based support very highly (Table 2).

**Outcome Measures**

Subjects receiving PBS intervention did not experience greater improvements in disease specific HR-QOL (FOSQ scores) than patients receiving usual care ($p > 0.4$; Table 3).

During the 90 days of therapy, the average CPAP adherence measured in minutes was greater in the intervention group when

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### Table 1—Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Intervention (n = 22)</th>
<th>Usual Care (n = 17)</th>
<th>p value</th>
<th>All subjects (n = 39)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>53 ± 14</td>
<td>50 ± 14</td>
<td>0.6</td>
<td>52 ± 14</td>
</tr>
<tr>
<td>Gender, % men</td>
<td>100%</td>
<td>100%</td>
<td>1.0</td>
<td>100%</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>35 ± 6</td>
<td>33 ± 5</td>
<td>0.3</td>
<td>34 ± 5</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
<td>0.9</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>17 (77%)</td>
<td>13 (76%)</td>
<td></td>
<td>30 (77%)</td>
</tr>
<tr>
<td>Black</td>
<td>4 (18%)</td>
<td>3 (18%)</td>
<td></td>
<td>7 (18%)</td>
</tr>
<tr>
<td>American Indian/Alaskan Native</td>
<td>1 (5%)</td>
<td>0 (0%)</td>
<td>1 (2.5%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>0 (0%)</td>
<td>1 (6%)</td>
<td></td>
<td>1 (2.5%)</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
<td></td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>19 (86%)</td>
<td>14 (82%)</td>
<td></td>
<td>33 (85%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>3 (14%)</td>
<td>3 (18%)</td>
<td></td>
<td>6 (15%)</td>
</tr>
<tr>
<td>Education, n (%)</td>
<td></td>
<td></td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>&lt; High school</td>
<td>0 (0%)</td>
<td>1 (6%)</td>
<td></td>
<td>1 (2%)</td>
</tr>
<tr>
<td>High school</td>
<td>1 (4%)</td>
<td>4 (26%)</td>
<td></td>
<td>5 (13%)</td>
</tr>
<tr>
<td>Undergrad</td>
<td>18 (82%)</td>
<td>12 (71%)</td>
<td></td>
<td>30 (77%)</td>
</tr>
<tr>
<td>Masters</td>
<td>3 (14%)</td>
<td>0 (0%)</td>
<td></td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Married, n (%)</td>
<td>15 (68%)</td>
<td>10 (59%)</td>
<td>0.8</td>
<td>25 (64%)</td>
</tr>
<tr>
<td>Working, n (%)</td>
<td>9 (41%)</td>
<td>7 (41%)</td>
<td>1.0</td>
<td>16 (41%)</td>
</tr>
<tr>
<td>AHI, mean ± SD</td>
<td>36.7 ± 28.6</td>
<td>37.5 ± 36.9</td>
<td>0.9</td>
<td>37.0 ± 32.1</td>
</tr>
<tr>
<td>AHI, median (IQR)</td>
<td>28 (17, 50)</td>
<td>17 (8, 63)</td>
<td>0.4</td>
<td>26 (11, 56)</td>
</tr>
<tr>
<td>CPAP pressure, mean ± SD</td>
<td>10 ± 2</td>
<td>10 ± 3</td>
<td>0.7</td>
<td>10 ± 2</td>
</tr>
<tr>
<td>Split night, n (%)</td>
<td>(14) 64 %</td>
<td>(10) 59 %</td>
<td>1.0</td>
<td>62%</td>
</tr>
<tr>
<td>NCS, mean ± SD</td>
<td>9.7 ± 4.2</td>
<td>8.6 ± 4.6</td>
<td>0.4</td>
<td>9.3 ± 4.3</td>
</tr>
<tr>
<td>Mask interface, n (%)</td>
<td></td>
<td></td>
<td>0.9</td>
<td></td>
</tr>
<tr>
<td>Nasal mask</td>
<td>14 (64%)</td>
<td>10 (59%)</td>
<td></td>
<td>24 (62%)</td>
</tr>
<tr>
<td>Nasal pillow</td>
<td>2 (9%)</td>
<td>2 (12%)</td>
<td></td>
<td>4 (10%)</td>
</tr>
<tr>
<td>Full face mask</td>
<td>6 (27%)</td>
<td>5 (29%)</td>
<td></td>
<td>11 (28%)</td>
</tr>
<tr>
<td>Charlson Comorbidity Index, median (IQR)</td>
<td>0 (0.0)</td>
<td>0 (0.1)</td>
<td>0.6</td>
<td>0 (0.1)</td>
</tr>
<tr>
<td>Epworth score, mean ± SD</td>
<td>10.5 ± 5.3</td>
<td>11.2 ± 3.8</td>
<td>0.6</td>
<td>10.8 ± 4.7</td>
</tr>
</tbody>
</table>

AHI, apnea-hypopnea index; BMI, body mass index; kg/m², kilograms/meters²; IQR, interquartile range; SD, standard deviation; n, sample size; CPAP, continuous positive airway pressure; NCS, nasal congestion score.
Table 2—Patient evaluations of their peer buddy system

<table>
<thead>
<tr>
<th>Patient evaluation of their peer buddy (intervention group only; total sample = 22)</th>
<th>Proportion that agree or strongly agree, n (%)</th>
<th>Correlation of Likert scores§ with CPAP adherence (minutes/night), R²</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>My peer-support partner listened to me talk about my concerns.</td>
<td>21 (95%)</td>
<td>0.3</td>
<td>0.008*</td>
</tr>
<tr>
<td>My peer-support partner gave me feedback on how I was doing.</td>
<td>21 (95%)</td>
<td>0.3</td>
<td>0.008*</td>
</tr>
<tr>
<td>My peer-support partner helped me solve my problems or concerns.</td>
<td>20 (91%)</td>
<td>0.27</td>
<td>0.01*</td>
</tr>
<tr>
<td>I felt comfortable sharing my feelings with my peer-support partner.</td>
<td>20 (91%)</td>
<td>0.26</td>
<td>0.01*</td>
</tr>
<tr>
<td>My peer-support partner understood my point of view.</td>
<td>19 (86%)</td>
<td>0.27</td>
<td>0.01*</td>
</tr>
<tr>
<td>My peer-support partner pressured me to change.</td>
<td>6 (27%)</td>
<td>0.0</td>
<td>0.8</td>
</tr>
<tr>
<td>My peer-support partner provided me with practical information.</td>
<td>21 (95%)</td>
<td>0.40</td>
<td>0.002*</td>
</tr>
<tr>
<td>My peer-support partner invested time to help me.</td>
<td>21 (95%)</td>
<td>0.50</td>
<td>&lt; 0.0001*</td>
</tr>
<tr>
<td>I was able to talk to my peer-support partner when I needed to.</td>
<td>21 (95%)</td>
<td>0.27</td>
<td>0.01*</td>
</tr>
<tr>
<td>I liked the support over the telephone.</td>
<td>18 (82%)</td>
<td>0.55</td>
<td>&lt; 0.0001*</td>
</tr>
<tr>
<td>My peer-support partner helped me make progress in addressing the self-care issue I had identified as a problem at the beginning of this program.</td>
<td>17 (77%)</td>
<td>0.13</td>
<td>0.09</td>
</tr>
<tr>
<td>I helped my peer-support partner as much as my partner helped me.</td>
<td>7 (32%)</td>
<td>0</td>
<td>0.8</td>
</tr>
<tr>
<td>I helped my peer partner more than he/she helped me.</td>
<td>2 (9%)</td>
<td>0</td>
<td>0.9</td>
</tr>
<tr>
<td>My peer partner helped me in ways that added to the help from my nurse/doctor.</td>
<td>15 (68%)</td>
<td>0.18</td>
<td>0.04</td>
</tr>
<tr>
<td>It was hard to let my partner know when I had something I wanted to talk about.</td>
<td>16 (73%)</td>
<td>0.07</td>
<td>0.2</td>
</tr>
<tr>
<td>The peer support was very helpful for managing my symptoms.</td>
<td>18 (82%)</td>
<td>0.34</td>
<td>0.004*</td>
</tr>
<tr>
<td>I learned something new about how to take care of myself from conversations with my peer-support partner.</td>
<td>19 (86%)</td>
<td>0.22</td>
<td>0.02*</td>
</tr>
<tr>
<td>My partner learned something new about how to take care of himself/herself from talking with me.</td>
<td>5 (23%)</td>
<td>0</td>
<td>0.8</td>
</tr>
<tr>
<td>The calls were a hassle.</td>
<td>10 (45%)</td>
<td>0.34</td>
<td>0.005*</td>
</tr>
<tr>
<td>My peer-support partner helped me do things I need to do to stay healthy.</td>
<td>15 (68%)</td>
<td>0.1</td>
<td>0.15</td>
</tr>
<tr>
<td>I helped my peer-support partner do things he/she needs to do to stay healthy.</td>
<td>3 (13%)</td>
<td>0</td>
<td>0.6</td>
</tr>
<tr>
<td>The messages I heard on the Peer-Support Line were easy to understand.</td>
<td>21 (95%)</td>
<td>0.22</td>
<td>0.02*</td>
</tr>
<tr>
<td>In general, it was easy to use the Peer-Support Line to contact my peer-support partner.</td>
<td>21 (95%)</td>
<td>0.37</td>
<td>0.003*</td>
</tr>
<tr>
<td>It was frustrating to use this system to get through to my peer-support partner.</td>
<td>5 (23%)</td>
<td>0</td>
<td>0.5</td>
</tr>
<tr>
<td>I would be more satisfied with my health care if a peer-support service like this were available to patients.</td>
<td>16 (73%)</td>
<td>0.15</td>
<td>0.07</td>
</tr>
</tbody>
</table>

*Statistically significant, §Likert scores were derived from the respective questions: strongly disagree = 1, disagree = 2, neutral = 3, agree = 4, and strongly agree = 5.

Table 3—Outcome measures

<table>
<thead>
<tr>
<th></th>
<th>Intervention (n = 22)</th>
<th>Usual Care (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>90 days</td>
</tr>
<tr>
<td>FOSQ (global)</td>
<td>15.2 ± 3.7</td>
<td>17.1 ± 3.5</td>
</tr>
<tr>
<td>Activity</td>
<td>3.1 ± 0.8</td>
<td>3.5 ± 0.7</td>
</tr>
<tr>
<td>Vigilance</td>
<td>2.9 ± 0.8</td>
<td>3.4 ± 0.7</td>
</tr>
<tr>
<td>Social</td>
<td>3.2 ± 0.8</td>
<td>3.5 ± 0.7</td>
</tr>
<tr>
<td>Intimacy</td>
<td>3.2 ± 1.0</td>
<td>3.3 ± 0.9</td>
</tr>
<tr>
<td>Mean</td>
<td>3.0 ± 0.7</td>
<td>3.4 ± 0.7</td>
</tr>
<tr>
<td>PAM</td>
<td>68 ± 14</td>
<td>73 ± 14</td>
</tr>
<tr>
<td>SEMSA (global)</td>
<td>8.0 ± 0.1</td>
<td>7.5 ± 0.9</td>
</tr>
<tr>
<td>Risk</td>
<td>2.3 ± 0.5</td>
<td>1.9 ± 0.6</td>
</tr>
<tr>
<td>Outcomes</td>
<td>3.0 ± 0.5</td>
<td>2.9 ± 0.7</td>
</tr>
<tr>
<td>Self-efficacy</td>
<td>2.7 ± 0.5</td>
<td>2.7 ± 0.6</td>
</tr>
<tr>
<td>Epworth score</td>
<td>10.5 ± 5.3</td>
<td>7.1 ± 4.7</td>
</tr>
<tr>
<td>PVT</td>
<td>307 ± 111</td>
<td>287 ± 57</td>
</tr>
</tbody>
</table>

FOSQ, Functional Outcomes Sleep Questionnaire (global and domain scores); SEMSA, self-efficacy in management of sleep apnea (global and domain scores); PAM, patient activation measure; PVT (psychomotor vigilance test; reaction time). None of the baseline or differences achieved statistical significance.
Figure 2—Adherence to continuous positive airway pressure (CPAP) therapy

Expressed as the mean (SD) minutes of CPAP use per day. Subjects assigned to peer buddy system (PBS, closed circles) versus usual care (open circles) is shown for each week of therapy during the 3 months of follow-up. During the 90 days of therapy, Wilks lambda multivariate test of overall differences revealed greater CPAP adherence in the intervention than the usual care group (MANOVA; F = 2.29; p = 0.04).

compared to the usual care group (MANOVA; Wilks Lambda multivariate test of overall differences; F = 2.29; p = 0.04; Figure 2). Differences between groups were apparent at end of first week of therapy wherein, CPAP adherence was 313 ± 119 min/day (5.2 ± 2.0 h/day) in the intervention group tended to be greater than that in the usual care group (238 ± 142 min/day or 4.0 ± 2.4 h/day; p = 0.08). Adherence defined as a categorical variable based upon a threshold of average 4 h (240 min) per day of CPAP use, revealed that 14 (63.6%) of 22 patients in the intervention group were adherent to CPAP, whereas only 6 (40%) of 15 in the usual care group were adherent (p = 0.15; χ²-test). CPAP adherence was not related to any of the confounders (Table 4). We did not find any group differences for self-efficacy or patient activation in this small pilot study (Table 3).

In the intervention group alone, attendance of the sessions with the peer buddy was associated with greater CPAP adherence (R² = 0.36; p = 0.003). Essentially, each peer buddy contact was associated with an additional 88 min/day of CPAP adherence (95% confidence interval 33, 143; standard error = 26; p = 0.003).

DISCUSSION

Our pilot study suggests that the PBS intervention is a feasible and acceptable program with high patient satisfaction ratings. Preliminary data suggest that the peer-buddy system (PBS) was associated with greater CPAP adherence, but a larger adequately powered study is needed.

The acceptability of the PBS intervention was quite high, with 39 of 49 eligible subjects (80%) agreeing to participate in the study. Previously, a system that could promote self-management by the patient—such as group education from a peer-support group or program—has been shown to have the potential to improve adherence to CPAP therapy. However, this approach is limited by the logistics of the patient attending the group sessions and receiving personalized care. We proposed a telephonic system that allowed multiple communications between the patient and the peer buddy over a 3-month period in addition to two face-to-face meetings in the first week following CPAP initiation. Such a telephonic system resulted in good attendance of the sessions, with 100% of subjects in the intervention group completing at least 7 of the 10 interaction sessions with their peer buddies. Moreover, the attendance of sessions with peer buddies was associated with a “dose-effect,” wherein each contact (or session) was associated with an extra 88 minutes per day of CPAP adherence. Interestingly, the adherence in the intervention group tended to be greater at the end of the first week than at the end of the 3-month period (Figure 2), which would suggest that the face-to-face meetings may have had a more favorable effect than the telephonic interactions. However, this is speculative on our part.

There is a paucity of reliable and cost-effective interventions to promote CPAP adherence. While prior intervention-based trials using cognitive-behavioral therapy plus standard education achieved improvement in adherence to PAP therapy when compared to standard education alone, such therapies require a behavioral sleep specialist or health professional, which, in turn, incurs additional costs, and is limited by the shortage of behavioral therapists. If proven by a larger well-powered study, our peer-buddy system would conceivably help promote CPAP adherence while minimizing the burden placed on system resources.

We did not find any statistically significant between group differences in disease-specific health-related quality of life scales, patient activation measures, self-efficacy, or subjective and objective measures of sleepiness. However, this was a small pilot study meant to obtain measures on feasibility, acceptance, and obtain preliminary data that would provide information on efficacy of the intervention, and was underpowered to conclusively test the peer-driven intervention. Of note, the magnitude of changes in the above-mentioned outcome measures was greater...
in the intervention than the control group even though we were not statistically significant (Table 3). Based upon our preliminary data of proportion of subjects who are adherent to CPAP therapy, we would need 75 subjects per group (total of 150 subjects) to be adequately powered to demonstrate an effect of PBS intervention on CPAP adherence (assuming 80% power; \( \alpha = 0.05 \)). In all, our preliminary data would suggest different sample sizes for each of the outcome measures that range from 85 (for patient activation measure) to 230 (for FOSQ) subjects per group.

**Limitations**

This small pilot study suggests that PBS improves CPAP adherence. Larger adequately powered randomized controlled studies are needed to provide proof that this method of promoting CPAP adherence is effective. Moreover, our proposal to use trained peers with OSA can be a potentially cost-effective strategy, but is grounded on the rationale that veterans as a group are eco-culturally more homogenous than expected for the given level of differences in age, gender, ethnicity, or socioeconomic strata. The generalizability of these findings to other populations (such as women and non-veterans) needs to be tested. This is a preliminary experimental study on the feasibility and acceptability of this peer-driven intervention that targeted a homogenous specific population in an experimental study and cannot be as yet generalized to clinical setting.

**CONCLUSIONS**

Our pilot study suggests that the PBS intervention is feasible and received high patient satisfaction ratings. CPAP adherence may be improved by peer-driven intervention, but a larger, adequately powered study is needed. While the magnitude of effect of our peer-driven intervention may not be clinically relevant in our pilot study, the small sample size prohibits us form drawing firm conclusion of the real potential for this intervention. Perhaps greater proportion of face-to-face interactions and rigorous fidelity assessments of the interactions between the peer-buddy and subject may conceivably potentiate the magnitude of benefits on CPAP adherence in such an adequately powered study. Our long term objectives are to build on this pilot project and initiate a randomized, controlled, multi-site, peer-driven, intervention study for enhancing CPAP adherence in veterans with OSA. The ultimate goal of this research is to develop a cost-effective, efficacious, and exportable system of care to promote CPAP adherence in patients with OSA.

**REFERENCES**

ACKNOWLEDGMENTS

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It is well recognized that the effectiveness of continuous positive airway pressure (CPAP) has been limited due to the prevalence of non-adherence to this therapy.\textsuperscript{1,2} Although the pattern of non-adherence was first described in 1993,\textsuperscript{3} approaches employed to date to address this issue, such as education and telephone follow-up calls, have had limited success.\textsuperscript{1} Unfortunately, 29\% to 83\% use their devices less than 4 hours/night, less than the nightly duration required to improve daytime sleepiness and quality of life.\textsuperscript{4} The most promising intervention, a combination of extended hospital stay, education, and home visits, would be prohibitive in our system of health-care reimbursement.\textsuperscript{5}

Interventions to improve disease-specific self-efficacy, or the patient’s confidence in applying CPAP, have demonstrated increased nightly use.\textsuperscript{6} Such studies have employed group cognitive behavioral therapy, which may require expertise not common in most sleep laboratories. In this issue, two articles describe alternative approaches to delivering patient education and support as a means to increase disease-specific self-efficacy. Lettieri and colleagues applied group education to a predominantly military population primarily to enhance the efficiency of the sleep laboratory while promoting treatment adherence.\textsuperscript{7} This study conducted a post hoc comparison of CPAP adherence with group versus individual education. In a pilot study, Parthasarathy and coworkers paired patients receiving care at a Veterans Administration hospital with trained peer buddies to provide support and education compared to usual care that also included individual education.\textsuperscript{8}

The interventions delivered in both of these investigations improved CPAP adherence. Receiving education in a group setting in addition to an individual meeting with the provider resulted in higher levels of adherence at 1 month than those only receiving instruction individually (3.5 ± 1.9 vs 3.1 ± 2.6 h/day, p = 0.04, respectively) and higher proportion of nights used (67.2 ± 30.8 vs 62.1 ± 37.0, p = 0.02, respectively). Across the 3-month study period, overall buddy peer support was well received by patients and enhanced CPAP adherence compared to usual care (p = 0.04) (first week of treatment, 5.2 ± 2 vs 4.0 ± 2.4 h/day, p = 0.08, respectively).

Although these data are promising, don’t start celebrating yet. A close examination of the results suggests that CPAP non-adherence remains a problem. Unfortunately, neither study achieved levels of adherence that would restore normal functioning.\textsuperscript{9} The mean use in both studies was less than 6 h/night; leaving an unprotected airway the remainder of the sleep period. Moreover, what remains unclear is the underlying mechanism that promoted adherence. Both studies indicate that their interventions were based on the need for education and improved self-efficacy. However, only one of the studies systematically measured self-efficacy and did not find statistically reliable differences between intervention groups. However, this may be due to the small sample size and lack of power for this outcome as well as the timing of the assessment. Although Parthasarathy and colleagues employed a validated metric, self-efficacy was not evaluated until after 3 months of treatment when the initial intervention effect may have dissipated. It has been shown that the pattern of adherence is established during the first week of treatment.\textsuperscript{10,11}

We still are at a loss as to how to promote CPAP adherence to levels that will prevent comorbidities and enhance quality of life. Indeed, we do not know whether singular or multiple approaches work best, what type of knowledge—written, oral, video, experiential, or a combination—has the greatest impact and if individual or group-delivered intervention delivers the highest effect. Comparative effectiveness research is needed, employing different interventions to promote CPAP adherence, to determine which method(s) work(s) best and in which patient population, is cost-effective, and easily incorporated into clinical practice. Moreover, it is insufficient to identify what works, we also need to understand the underlying mechanism(s) by which adherence is improved.

As a field, we have yet to develop the comprehensive self-care management and individual-centered care that incorporates interventions to promote adherence for optimal outcomes. Successful with other chronic illnesses, a self-management program addresses patient access to information, continuity and coordination of care across specialties, appropriate infrastructure (home vs in-laboratory studies; short wait time to study), ideal provider mix, and symptom management.\textsuperscript{12,13} Recent studies, such as the two published in this issue, are enriching our understanding of salient components to enhance CPAP adherence. Although further research is needed, what we learn will have limited utility if we fail to develop a comprehensive interprofessional approach to the care of patients with OSA that is designed to build self-management skills.

Don’t Start Celebrating—CPAP Adherence Remains a Problem

Commentary on:


Terri E. Weaver, Ph.D., R.N., FAAN

University of Illinois at Chicago College of Nursing, Chicago, IL

REFERENCES


Comparison of Polysomnographic and Clinical Presentations and Predictors for Cardiovascular-Related Diseases between Non-Obese and Obese Obstructive Sleep Apnea among Asians

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Introduction: Unlike Caucasians, many Asians with obstructive sleep apnea (OSA) are non-obese but are affected by the disease due to predisposing craniofacial structure. Therefore, non-obese and obese OSA may represent different disease entities. The associated risk factors for developing cardiovascular-related diseases, consequently, may be considered separately for the two types of OSA.

Method: We reviewed polysomnographic studies performed in adults (aged ≥ 18 years) diagnosed with OSA (respiratory disturbance index [RDI] ≥ 5). We divided the patients into obese (body mass index [BMI] ≥ 25) and non-obese (BMI < 25) groups. We aimed to determine the differences between these two groups in terms of clinical presentations, polysomnographic findings, and association with cardiovascular-related diseases including hypertension, diabetes mellitus, coronary artery disease, and/or cerebrovascular disease.

Results: Among 194 patients with OSA (RDI ≥ 5), 63.4% were non-obese and 36.6% were obese. Compared with obese OSA patients, non-obese OSA patients were noted to have smaller neck size, less prevalence of hypertension, and less history of frequent nocturia (>3-4/week), with equal prevalence of excessive daytime sleepiness. Overall, non-obese OSA patients were noted to have milder disease indicated by lower total, supine, and non-supine, NREM RDI and higher mean and nadir oxygen saturations. In the non-obese group, only total obstructive apnea index (OAI) was noted to be a predictor for developing any of the cardiovascular-related diseases after controlling for age, sex, and RDI (odds ratio = 9.7). However, in the obese OSA group, frequent snoring (>50% of total sleep time), low sleep efficiency (≤90%), and low mean oxygen saturation (<95%) were noted to be significant predictors of cardiovascular-related diseases (odds ratios = 12.3, 4.2, and 5.2, respectively).

Conclusion: Among Asians, most OSA patients were non-obese. Compared to obese OSA patients, non-obese OSA patients were noted to have less prevalence of hypertension and less history of nocturia. They were also noted to have overall milder OSA. Only OAI was noted to be a significant predictor for cardiovascular-related disease in the non-obese OSA group.

Keywords: Obstructive sleep apnea, obesity

Citation: Chirakalwasan N; Teerapraiaprak B; Simon R; Hirunwiwatkul P; Jaicharanyatam N; Desudchit T; Charakorn N; Wanlapakorn C. Comparison of polysomnographic and clinical presentations and predictors for cardiovascular-related diseases between non-obese and obese obstructive sleep apnea among Asians. J Clin Sleep Med 2013;9(6):553-557.

Obstructive sleep apnea (OSA) is characterized by repetitive episodes of complete (apnea) or partial (hypopnea) upper airway obstruction occurring during sleep. These events often result in reduction in blood oxygen saturation and are usually terminated by brief arousals from sleep. Prior study has shown that obesity is one of the important risk factors for developing OSA. A recent study from a bariatric surgery clinic in which patients had a median BMI of 41.9 showed that 79% of these patients had at least a moderate degree of obstructive sleep apnea. However, unlike Caucasians, many Asians with OSA are not obese. Predisposing craniofacial structure most likely contributes to developing OSA among non-obese Asians. We believe that obese and non-obese OSA may represent different disease entities. Thus, when considering the risk factors for developing cardiovascular-related diseases in the patient, the two types of OSA may present different risk factors.
This is a retrospective study referencing the data of patients aged ≥ 18 years who were referred to a sleep laboratory at the Excellence Center for Sleep Disorders, King Chulalongkorn Memorial Hospital for suspected OSA from January 1, 2010, to June 30, 2010. All polysomnographies conducted in the sleep laboratory were using standard EEG including frontal leads (F1, F2), central leads (C3, C4), occipital leads (O1, O2), and reference leads at mastoids (M1, M2); electromyography, and electrooculography. Oxygen saturation (SpO2) was measured with a finger probe. Air flow was measured by 2 methods: nasal pressure transducer and oral-nasal thermocouple. The thoracic and abdominal respiratory movements were monitored by respiratory inductance plethysmography. The body position was measured by a position sensor, which was attached to the anterior chest wall on the thoracic belt. The sensor differentiated 5 positions, including supine and non-supine position (right, left, prone, and upright position). Sleep stages were scored in 30-sec epochs according to the standard criteria from the AASM Manual for the Scoring of Sleep and Associated Events. Apnea was defined using oral-nasal thermocouple excursion, and hypopnea was defined using nasal pressure transducer excursion. Apnea, hypopnea, and respiratory effort-related arousals (RERAs) were scored using the standard criteria from the AASM manual.

The number of apneas, hypopneas, and RERAs per hour of NREM and REM and total sleep time (TST) were calculated and reported as NREM RDI, REM RDI, and total RDI, respectively. The number of each type of respiratory events per hour of total sleep time were defined including obstructive apnea events, central apnea events, mixed apnea events, and hypopnea event as total OAI, total CAI, total MAI, and total HI, respectively. Parameters of oxygenation included in the study were absolute minimum SpO2, during sleep and mean oxygen saturation during sleep. Arousal/h of TST, arousals/h of during NREM, and arousals/h during REM sleep were reported as total arousal index, NREM arousal index, and REM arousal index, respectively. Sleep efficiency was defined as a ratio of TST over the total recording time in percentage. Time spent in NREM1, NREM2, NREM3, and REM was calculated as percentage of the TST. Periodic limb movement index (PLMI) was calculated using standard criteria.

Demographic and comorbidity data of the patients included age (years), gender, BMI, and neck size (cm). Information regarding cardiovascular-related diseases was obtained from a pretest questionnaire, which all the patients were required to fill out prior to undergoing polysomnographic study. The pretest questionnaire consisted of self-administered “yes” or “no” questions. The patients were asked if they had any cardiovascular-related diseases, including hypertension (HTN), diabetes (DM), coronary artery disease (CAD), or cerebrovascular disease (CVA). Other medical conditions included were congestive heart failure, hyperthyroidism, hypothyroidism, anemia, asthma, cancer, renal disease, iron deficiency, and depression. Using the Epworth Sleepiness Scale (ESS), which was recently validated to Thai language, the measurement of each patient’s sleepiness was obtained from pretest questionnaire. Additionally, patient reports of snoring intensity (mild, moderate, or severe) were obtained from this pretest questionnaire. The patients were also asked about their history of witnessed apnea, habitual snoring, morning headache, nocturia, and morning dry throat.

Patient data collected in the study included technician observation of snoring frequency and intensity. Snoring frequency was divided into 3 categories (< 20%, 20% to 50%, and > 50% of TST). The snoring intensity was also divided into 3 severity levels (low [can only be heard when getting close to the patient], moderate [can be heard when opening the door], and severe [can be heard through the closed door]).

Our exclusion criteria were: (1) RDI < 5, (2) CPAP study, and (3) missing data.

Dividing the patients into obese (BMI ≥ 25) and non-obese (BMI < 25), we aimed to determine the differences between these 2 groups in terms of clinical presentation, polysomnographic findings, and predictors for developing cardiovascular-related diseases including HTN, DM, CAD, and/or CVA.

Our primary aim was to determine the difference between obese and non-obese OSA subjects in terms of:
1. Baseline characteristics: age, sex, and neck size.
2. Clinical presentation: history of witnessed apnea, habitual snoring, morning headache, nocturia, dry throat (> 3-4/week), daytime sleepiness (ESS ≥ 10), and associated comorbidities (CAD, CHF, DM, HTN, CVA, depression).
3. Polysonmographic findings: total RDI, total OAI, total CAI, total HI, total MAI, REM RDI, NREM RDI, mean oxygen saturation, nadir oxygen saturation, sleep latency, REM latency, sleep efficiency, total arousal index, REM arousal index, NREM arousal index, supine sleep time (min), supine REM time (min), supine NREM (min), %NREM1, %NREM2, %NREM3, %REM, supine RDI, non-supine RDI, snoring frequency and intensity, and total PLMI.

Our secondary aim was to determine the association of cardiovascular-related diseases (CAD, CHF, DM, HTN, CVA) with obese and non-obese OSA.

Statistical Analysis

The comparison of the baseline characteristics, clinical presentations, and polysomnographic findings between obese and non-obese OSA subject were statistically analyzed. If the data were observed to have normal distribution, the continuous data were evaluated by Student t-test. If the data did not have normal distribution, a nonparametric method (Mann-Whitney U test) was used for evaluation. The nominal data were evaluated by χ2 test. To identify the association with cardiovascular-related diseases, the data were then evaluated by multivariate regression analysis by stepwise logistic regression analysis. All statistical analysis was performed using statistical software (SPSS for Windows, version 17.0). Our study was approved by the institutional review board, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.

RESULTS

A total of 221 studies of patients ≥ 18 years were reviewed in our laboratory from Jan 1, 2010, to June 30, 2010. We excluded 8 CPAP studies and 19 studies with incomplete questionnaires (missing information on comorbidities). A total of 194 patient records were analyzed. Among these 194 patients with OSA...
63.4% were non-obese and 36.6% were obese. Compared with obese OSA patients, non-obese OSA patients had smaller neck size, less prevalence of hypertension, and less history of frequent nocturia (> 3-4/week), with equal prevalence of excessive daytime sleepiness (Table 1). Overall, non-obese OSA patients had milder disease, indicated by lower total, supine, and non-supine NREM RDIs, and higher mean and nadir oxygen saturations (Tables 2 and 3).

In the non-obese group, only total OAI was noted to be the sole predictor for developing cardiovascular-related diseases after controlling for age, sex, and RDI (odds ratio = 9.7; Table 4). This is in contrast to the obese OSA group, which had multiple predictors: frequent snoring (> 50% of TST), low sleep efficiency (≤ 90%), and low mean oxygen saturation (< 95%) were noted to be significant predictors (odds ratios = 12.3, 4.2, and 5.2, respectively; Table 5).

**DISCUSSION**

Prior studies have shown that obese and non-obese OSA patients are not identical in many aspects. Non-obese OSA patients have generally been noted to have less severe disease, as indicated by less severe oxygen desaturation. Ling et al. published a paper demonstrating that oxygen desaturation index (ODI) is not accurate for diagnosis of OSA in non-obese OSA and should not be used in isolation as a diagnostic test, since this group of OSA patients may not have significant oxygen desaturations. We have confirmed this finding: we found that measurements in non-obese OSA patients, when compared to obese OSA patients, were less severe not only in terms of oxygen desaturations; they were also noted to have lower RDI. However, obesity itself may have unique clinical significance. A prior study has shown that obesity, not RDI, is associated with increased levels of C-reactive protein (CRP)—the marker for cardiovascular-related diseases. We demonstrated that these two groups were had different predictors for cardiovascular-related disease after controlling for age, sex, and RDI. In the non-obese group, total OAI, not oxygen desaturation, was a significant predictor for cardiovascular-related disease. This finding can be explained by higher mean and nadir oxygen saturation in the non-obese group when compared to the obese group. In the non-obese group, only the most severe form of event (obstructive apnea) predicted occurrence of cardiovascular-related diseases. However, due to limited sample size of this study, the association between other predictors and the cardiovascular-related diseases may not be statistically expressed.
We believe our finding is of interest and may be clinically applicable since Asian OSA patients are generally not obese. We found most of our OSA patients to be non-obese (63.4%) when compared to non-obese OSA incidence of 42% in the study of Young et al. We believe that non-obese OSA group in Asian population is unique and differs from obese OSA group found in the Western population. Future prospective studies focusing in this group of patients to identify its clinical significance and specific treatment should be encouraged.

**CONCLUSION**

Among Asians, most OSA patients were not obese. Compared to obese OSA patients, non-obese OSA patients were noted to have less prevalence of hypertension and less history of nocturia. They were also noted to have overall milder OSA. Only OAI was noted to be a significant predictor for cardiovascular-related disease in the non-obese OSA group.

**REFERENCES**


**ACKNOWLEDGMENTS**

The authors thank Mr. Nirun Intarut who was at the time of the study, a statistician at Chulalongkorn Clinical Research Center, Chulalongkorn University, Bangkok, Thailand for his contribution on statistical analyses on this paper as well as Mr. Dittapol...
Munthan, a statistician at the Section for Clinical Epidemiology and Biostatistics, Faculty of Medicine, Ramathibodi Hospital for an additional statistical review.

DISCLOSURE STATEMENT

This was not an industry supported study. The authors have indicated no financial conflicts of interest.
Sleep disturbance is a common and often underdiagnosed complaint in general medical practice,1 which can persist over many years2 and has been shown to result in health problems, greater functional impairment, lost productivity, and excess health care utilization.3-5 The ability of community health resources to treat sleep-related problems appears limited.6 However, insomnia can be a symptom of other conditions, such as depression,7 substance abuse,8 and sleep disordered breathing.9 Currently, the term “primary insomnia” is used to define insomnia in the absence of such conditions.10 Many epidemiological studies in the past have not accounted for these conditions when determining the prevalence of insomnia.11-13

Despite the well-established significance of insomnia, some studies have suggested sleep dissatisfaction is a more accurate predictor than insomnia of the likelihood of seeking medical help, reporting daytime impaired functioning, and of being diagnosed with a sleep or a mental disorder.14-16 Other sleep conditions related to sleep quantity, quality, and excessive daytime sleepiness have also been associated with negative health consequences,17 including injury18 and memory impairment.19 However, large community-based studies utilizing a detailed questionnaire to explore relationships between sleep disorders and complaints and lifestyle behaviors are scant.

The aim of the current analysis was to utilize data from the New Zealand Blood Donors’ Health Study (NZBDHS) to determine the association of multiple sleep related variables with personal and lifestyle factors and evaluate the influence of these factors on primary insomnia and excessive daytime sleepiness.

### Study Objectives

To determine the relationship between sleep complaints, primary insomnia, excessive daytime sleepiness, and lifestyle factors in a large community-based sample.

### Design

Cross-sectional study.

### Setting

Blood donor sites in New Zealand.

### Patients or Participants

22,389 individuals aged 16-84 years volunteering to donate blood.

### Interventions

N/A.

### Measurements

A comprehensive self-administered questionnaire including personal demographics and validated questions assessing sleep disorders (snoring, apnea), sleep complaints (sleep quantity, sleep dissatisfaction), insomnia symptoms, excessive daytime sleepiness, mood, and lifestyle factors such as work patterns, smoking, alcohol, and illicit substance use. Additionally, direct measurements of height and weight were obtained.

### Results

One in three participants report < 7-8 h sleep, 5 or more nights per week, and 60% would like more sleep. Almost half the participants (45%) report suffering the symptoms of insomnia at least once per week, with one in 5 meeting more stringent criteria for primary insomnia. Excessive daytime sleepiness (evident in 9% of this large, predominantly healthy sample) was associated with insomnia (odds ratio [OR] 1.75, 95% confidence interval [CI] 1.50 to 2.05), depression (OR 2.01, CI 1.74 to 2.32), and sleep disordered breathing (OR 1.92, CI 1.59 to 2.32). Long work hours, alcohol dependence, and rotating shift work also increase the risk of daytime sleepiness.

### Conclusions

Even in this relatively young, healthy, non-clinical sample, sleep complaints and primary insomnia with subsequent excess daytime sleepiness were common. There were clear associations between many personal and lifestyle factors—such as depression, long work hours, alcohol dependence, and rotating shift work—and sleep problems or excessive daytime sleepiness.

### BRIEF SUMMARY

**Current Knowledge/Study Rationale:** Insomnia, daytime sleepiness and inadequate sleep are common complaints, but have not been accurately quantified in the past. The current study utilised 22,389 relatively healthy New Zealanders with the ability to control for multiple confounders such as depression, sleep disordered breathing and substance abuse, to more accurately determine how common these sleep complaints are, and to identify the relationship between such sleep complaints, primary insomnia, excessive daytime sleepiness, and lifestyle factors.

**Study Impact:** This study highlights how incredibly common sleep complaints are, even in this relatively young, healthy, nonclinical sample, and identifies some of the common associations such as depression, long work hours, alcohol dependence, and rotating shift work.

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sleepiness in a large, diverse, yet predominantly healthy, community-based sample.

METHODS

Recruitment procedures and methodology of the New Zealand Blood Donors’ Health Study (NZBDHS) are detailed elsewhere. In brief, 22,389 people volunteering to donate blood (81% response rate) aged 16 years or older were recruited into the study from April 1998 to October 1999, at blood collection points managed by the Northern Regional Blood Service in the Northland, Auckland, Waikato, and Bay of Plenty regions of New Zealand. The criteria for accepting volunteer blood donation in New Zealand are in accordance with international guidelines (www.nzblood.co.nz). In general, the donor must be in good health, have a hemoglobin > 120 g/L (females) or 130 g/L (men), and be free from high-risk behaviors to ensure the safety of both the donor and recipient. The study was approved by regional ethics committees, and all participants provided informed consent.

Height, weight, and neck circumference were measured by study staff. A self-administered questionnaire was used to solicit details regarding the presence of snoring, sleep apnea, sleep complaints (satisfaction, quantity, and insomnia), alcohol consumption, smoking, use of marijuana or other illegal drugs, and depression (Appendix). Detailed instruments used in previous research and the pilot study informed its content. Participants were also asked if they had ever been told by a doctor that they have, or have had a heart attack, a stroke, epilepsy, migraine, or diabetes.

The main classification systems for insomnia are the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and International Classification of Sleep Disorders (ICSD). The criteria for defining an insomnia complaint in the current study were consistent with these definitions and previous large-scale studies. To be considered as having an insomnia complaint a subject had to: (i) report difficulty initiating sleep (DIS) or maintaining sleep (DMS), early morning awakening (EMA) with inability to resume sleep, or a complaint of non-restorative sleep (NRS) in spite of adequate sleep duration, ≥ 4 times per month (i.e., once per week) and (ii) claim to be dissatisfied with the amount of his/her sleep, or take a sleep-enhancing medication. These two conditions had to be present together to conclude the presence of an insomnia complaint. “Primary insomnia” was defined as having an insomnia complaint (meeting criteria above) in the absence of alcohol dependence (CAGE), regular cannabis or illicit drug use, depression, and sleep apnea. Insomnia rates vary based on different definitions, including insomnia complaints in the absence of sleep dissatisfaction and more frequent symptoms (e.g., more than every other day); therefore the analysis and reporting is presented with both more liberal and conservative definitions than the DSM-IV and ICSD criteria. Daytime sleepiness was quantified using the Epworth Sleepiness Scale (ESS) and dichotomized into presence (score > 10) or absence (score ≤ 10) of excessive daytime sleepiness, based on evidence indicating scores > 10 have an increased propensity to obstructive sleep apnea syndrome, narcolepsy, or idiopathic hypersomnia. Sleep quantity was collected as a continuous variable based on the number of nights in which ≥ 7-8 h of sleep were obtained, then categorized for logistic regression. Questions relating to depression were based on the CIDI-SFMD and are elaborated in the appendix.

Logistic regression was performed with log odds of insomnia as the dependent variable and adjustment for multiple potential covariates (age, sex, body mass index, neck circumference, sleepiness, sleep quantity, alcohol consumption, smoking, cannabis and illicit drug use, depression, employment status and subsequent primary occupation, hours of work per week, work pattern, education, marital status, and ethnicity). Covariates were kept continuous where possible. Interactions between primary occupation, marital status, insomnia, age, and sex were also assessed. Similar analysis was performed with log odds of excessive daytime sleepiness as the dependent variable. Throughout this paper, OR is used to represent cross-sectional odds ratios. Reported differences are significant at the 0.05 level. All analyses were performed using SPSS version 12.

RESULTS

Demographic data and physical measurements were available from all 22,389 NZBDHS participants (Table 1). Questionnaire responses were received from 96% of the NZBDHS participants. Those who returned questionnaires were similar to those who did not in age (mean difference: 0.1 years) and sex (males comprised 46% of those who returned questionnaires and 47% of those who did not). The percentages of self-reported major illnesses were very low (0.2% reporting a history of heart attack, 0.2% a history of stroke, and 0.4% diabetes), compared with the general population as noted in the New Zealand Health Survey in 2002 (10.4% heart disease, 2.1% stroke, 4.3% diabetes). This study had a higher proportion of participants aged 16-39 years than the New Zealand Health Survey (60% vs 36%, respectively; Table 1).

Sleep Complaints

In this cohort, 7,298 (34%) participants reported not getting at least 7-8 h of sleep 5 or more nights per week. The amount of sleep increased with age (p < 0.001). When asked “How do you feel about the amount of sleep you normally get?’, only 7,503 (34%) responded with “Get the right amount” and 1,429 (6%) with “Get plenty.” Therefore dissatisfaction with the amount of sleep was reported by 60% of the cohort. Women reported being dissatisfied with their sleep more than men (Table 2; p < 0.001), and the percentage reporting sleep dissatisfaction decreased with age (p < 0.001; Table 2). Thus, sleep quantity and subsequently sleep satisfaction, increased with age. The more insomnia symptoms reported, the higher the likelihood of sleep dissatisfaction (Table 3).

After mutually adjusting for multiple risk factors (sleep apnea, age, gender, body mass index, neck circumference, daytime sleepiness, marital status, number of full nights sleep per week, alcohol consumption, smoking, illicit drug use, mood, insomnia symptoms, sleeping tablets, work pattern, and occupation), non-workers were less likely to be dissatisfied with their sleep (OR 0.79, CI 0.67-0.93). Each full night of sleep almost halved the odds of being dissatisfied (OR 0.54, CI 0.53 to 0.56). Factors that increased the risk of sleep dissatisfaction included: night workers (OR 1.30, CI 1.01 to 1.67), taking sleeping tab-
lets ≤ 1 time per week (OR 2.46, CI 1.64 to 3.69), and having 1 (OR 2.38, CI 2.17 to 2.61), 2 (OR 3.23, CI 2.81 to 3.70), 3 (OR 5.32, CI 4.23 to 6.28), or 4 (OR 10.18, CI 6.38 to 16.27) insomnia symptoms (Table 3). Importantly, with adjustment for these multiple confounders, including the number of full nights sleep per week, those with insomnia still report being less satisfied with their sleep. There was an interaction, such that increasing age increased the risk of sleep dissatisfaction for women (OR 1.010 per year, CI 0.985 to 1.015) but decreased the odds for men (OR 0.991 per year, CI 0.985 to 0.996; p < 0.001). Being divorced, separated, or widowed; smoking; or taking sleeping tablets more than weekly did not affect sleep dissatisfaction.

**Sleep Disordered Breathing**

Among participants with sleep disordered breathing, a history of depressive symptoms was reported by 7%. After adjusting for multiple potential confounders, snoring was not associated with depressive symptoms (OR 1.05, CI 0.94 to 1.18). However, sleep apnea increased the odds of having experienced depressive symptoms (OR 1.28, CI 1.05 to 1.56), not surprisingly, being depressed increased the odds of serious suicidal thoughts (OR 5.80, CI 5.12 to 6.58). Importantly, sleep apnea increased the odds of having had serious thoughts of suicide, even after adjusting for depressive symptoms (OR 1.44, CI 1.15 to 1.80).

**Primary Insomnia**

A total of 20,516 (93%, after excluding 321 with missing data) participants reported ≥ 1 of the 4 insomnia symptoms at least once per month; 9,843 (45%) reported ≥ 1 of the 4 insomnia symptoms more than once per week (Figure 1). Of these 9,843 individuals, 7,792 (79%) also reported being dissatisfied with their sleep (or reported taking sleeping tablets more than once per week), that is, 35% of the total cohort. After excluding participants who were alcohol dependent (CAGE ≥ 2), regular cannabis or illicit drug users, reported history of depressive symptoms, or suffering sleep apnea, there were 4,511 (20%) of the original cohort subsequently classified as having “primary insomnia” defined as at least one insomnia symptom more than once per week, with sleep dissatisfaction, not attributable to alternative medical conditions (Figure 1). Primary insomnia was more common reported in women (Table 2).

Of the 4,511 participants with primary insomnia, 1,234 (27%), or approximately 6% of the entire cohort, reported suffering at least one symptom of insomnia > 15 times per month. Among the 4,511 participants with primary insomnia, difficulty initiating sleep (DIS) was reported most commonly (44%), followed by difficulty maintaining sleep ([DMS] 36%) and early morning awakenings (EMA) with inability to resume sleep (34%). A single insomnia symptom was reported by 52% of participants with primary insomnia, 2 symptoms by 27%, and 3 or 4 symptoms by 21%.

The percentage of participants reporting primary insomnia (with sleep dissatisfaction) was high in students (23%), retired women (22%), homemakers (20%), and participants in paid employment (20%) recruited to this study. With respect to work patterns, permanent night workers had the highest proportions of primary insomnia (26%), while daytime workers without rotating shifts had the lowest (19%). For marital status, being “never married” had the highest rates of primary insomnia in both sexes (23%). Divorced men had comparatively low rates (13%), while divorced women had much higher rates (24%).

The odds of suffering insomnia was lower among unemployed participants (OR 0.64, CI 0.44 to 0.94) than workers in paid employment. Higher levels of education also reduced the odds of primary insomnia. The OR comparing university education to primary or secondary school only was 0.78, CI

<table>
<thead>
<tr>
<th>Table 1—Participant characteristics</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>12,012 (54)</td>
</tr>
<tr>
<td>Female</td>
<td>10,377 (46)</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
</tr>
<tr>
<td>16-24</td>
<td>8,040 (36)</td>
</tr>
<tr>
<td>25-39</td>
<td>5,305 (24)</td>
</tr>
<tr>
<td>≥ 40 (maximum 84)</td>
<td>9,041 (41)</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td></td>
</tr>
<tr>
<td>15-19</td>
<td>664 (3)</td>
</tr>
<tr>
<td>20-24</td>
<td>8,901 (40)</td>
</tr>
<tr>
<td>25-29</td>
<td>8,382 (38)</td>
</tr>
<tr>
<td>30-34</td>
<td>3,104 (14)</td>
</tr>
<tr>
<td>≥ 35</td>
<td>1,104 (5)</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
</tr>
<tr>
<td>European</td>
<td>17,457 (81)</td>
</tr>
<tr>
<td>Maori</td>
<td>1,817 (8)</td>
</tr>
<tr>
<td>Pacific Islands</td>
<td>1,040 (5)</td>
</tr>
<tr>
<td>Asian</td>
<td>975 (5)</td>
</tr>
<tr>
<td>Other</td>
<td>322 (1)</td>
</tr>
<tr>
<td><strong>Alcohol (CAGE)†</strong></td>
<td></td>
</tr>
<tr>
<td>Low risk</td>
<td>18,837 (86)</td>
</tr>
<tr>
<td>High risk</td>
<td>3,035 (14)</td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
<td></td>
</tr>
<tr>
<td>Married or living with partner</td>
<td>10,750 (51)</td>
</tr>
<tr>
<td>Divorced/separated/never married</td>
<td>10,395 (49)</td>
</tr>
<tr>
<td><strong>Smoking</strong></td>
<td></td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>17,553 (85)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>3,057 (15)</td>
</tr>
<tr>
<td>Snoring present</td>
<td>7,322 (33)</td>
</tr>
<tr>
<td>Sleep apnea present</td>
<td>1,382 (6)</td>
</tr>
<tr>
<td>Depressed mood</td>
<td>3,633 (17)</td>
</tr>
<tr>
<td><strong>Sleep quantity</strong></td>
<td></td>
</tr>
<tr>
<td>&lt; 1 full night sleep per week</td>
<td>791 (4)</td>
</tr>
<tr>
<td>1 to 6 full nights sleep per week</td>
<td>15,788 (74)</td>
</tr>
<tr>
<td>&gt; 6 full nights sleep per week</td>
<td>4,730 (22)</td>
</tr>
<tr>
<td><strong>Sleep dissatisfaction</strong></td>
<td></td>
</tr>
<tr>
<td>Insomnia present</td>
<td>4,511 (20)</td>
</tr>
<tr>
<td>Daytime sleepiness, sleepy (ESS &gt; 10), mean/median = 5</td>
<td>1,885 (8.8)</td>
</tr>
<tr>
<td><strong>Sleeping tablets per month</strong></td>
<td></td>
</tr>
<tr>
<td>0-1</td>
<td>20,846 (97)</td>
</tr>
<tr>
<td>2-4</td>
<td>370 (2)</td>
</tr>
<tr>
<td>5-15</td>
<td>127 (1)</td>
</tr>
<tr>
<td>16+</td>
<td>111 (1)</td>
</tr>
</tbody>
</table>

†Alcohol dependence assessed by “CAGE” criteria; ESS, Epworth Sleepiness Score.
sleepiness. The OR for a one-unit increase in ESS was 1.03, with post hoc analysis showing a significant difference between each of the groups shown (p < 0.05).

After mutually adjusting for all these potential confounders, each hour of paid work per week increased the odds of reporting excessive daytime sleepiness (OR 1.01, CI 1.007 to 1.015), as did each additional year of age (1.015, CI 1.010 to 1.019). In addition, snoring (1.40, CI 1.24 to 1.58), sleep apnea (1.92, CI 1.59 to 2.32), depression (2.01, CI 1.74 to 2.32), alcohol dependence (1.16, CI 1.09 to 1.16), primary insomnia (1.75, CI 1.50 to 2.05), and working rotating shifts with night shifts (12% v 9%; p = 0.014), 15% v 8%; p < 0.001), be dissatisfied with their sleep (36% v 30%; p < 0.001), smoke (10% v 9%; p = 0.002), be alcohol dependent (12% v 8%; p < 0.001), report having been depressed (15% v 8%; p < 0.001), be dissatisfied with their sleep (11% v 5%; p < 0.001), and work rotating shifts with night shifts (12% v 9%; p = 0.014).

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Discussion

The current study involving a cohort of people presenting to volunteer blood donor sites, was unique in its size and ability to adjust for the effects of secondary causes of insomnia (such as depression, sleep disordered breathing, illicit drug use, and alcohol dependence) to more accurately isolate primary insom-
Insomnia is associated with lost productivity, greater functional impairment, more days of disability due to health problems, and excess health care utilization.4  After excluding participants with confounding conditions to specifically identify primary insomnia, one in five were considered to be suffering from primary insomnia with symptoms at least weekly, and 6% at least every other night. This finding is similar to the prevalence rates previously reported in other large-scale observational studies utilizing DSM-IV criteria (6% to 7%).16,28 However, the prevalence of insomnia varies with the criteria used to define insomnia. Studies defining symptoms of insomnia as “often” or at least three times per week, report prevalence rates between 6% and 15%,34-37 while studies with criteria based on “major complaints of insomnia,” “being bothered by insomnia,” and “having a great or a very great problem with insomnia” reported prevalence rates between 7% and 12%.38-40 Difficulty initiating sleep has been the most commonly reported symptom in all studies to date.28

Our findings are consistent with previous studies which have shown higher rates of insomnia in women,24,41 separated/divorced/widowed individuals, and night workers.14 In our study sample, high proportions of students also reported insomnia. However, after controlling for potential confounders, we found insomnia only increases with age in women. Much of the increased prevalence of insomnia with increasing age in previous studies14 is likely to be associated with increased prevalence of mental and physical conditions associated with insomnia. In the current study and similar studies where primary insomnia has been isolated, the effect of aging has not been so evident.12 The reporting of significant sleep dissatisfaction was high, with 14% of participants getting “nowhere near enough” or “could do with a lot more” sleep, a finding also within the range of previous similar studies (7% to 18%).11,14,16,24,28,43-45 Each full night of sleep halved the odds of reporting sleep dissatisfaction. While other studies have tended to show increased sleep dissatisfaction with increasing age,14,16,28 this was only evident for women in the current project. The discrepancy may reflect the effect of controlling for multiple potential confounders in a larger, more diverse, and relatively healthy cohort, but the possible effect of a non-representative sample cannot be excluded. Almost two of every three participants would like more sleep.

Table 4—Relationship between lifestyle factors and excessive daytime sleepiness, after mutually adjusting for multiple potential confounders*

<table>
<thead>
<tr>
<th>Independent Variables</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Each hour of work per week</td>
<td>1.011 (1.007 to 1.015)</td>
</tr>
<tr>
<td>Each additional year of age</td>
<td>1.015 (1.010 to 1.019)</td>
</tr>
<tr>
<td>Snoring vs non-snorers</td>
<td>1.40 (1.24 to 1.58)</td>
</tr>
<tr>
<td>Sleep apnea vs non-sleep apnea</td>
<td>1.92 (1.59 to 2.32)</td>
</tr>
<tr>
<td>Alcohol dependence vs no dependence</td>
<td>1.16 (1.09 to 1.16)</td>
</tr>
<tr>
<td>Depression vs no depression</td>
<td>2.01 (1.74 to 2.32)</td>
</tr>
<tr>
<td>Primary insomnia vs no insomnia</td>
<td>1.75 (1.50 to 2.05)</td>
</tr>
<tr>
<td>Working rotating shifts with nights vs others</td>
<td>1.36 (1.07 to 1.74)</td>
</tr>
</tbody>
</table>

*Confounders are: age, gender, BMI, neck circumference, sleep apnea, hours of work per week, work pattern, number of full nights sleep, alcohol, depression, sleep dissatisfaction, and occupation. All odds ratios were significant (p < 0.05).

Figure 1—Flow chart for primary insomnia (values are percentages of non-missing values)
sleep, and one in three participants do not get 7 to 8 hours sleep five or more nights per week, with a higher BMI associated with less sleep. Reporting the symptoms of insomnia had a substantial effect on sleep satisfaction independent of the amount of sleep obtained. This supports previous studies indicating an altered perception of sleep quality and quantity in people with insomnia.47

Excessive daytime sleepiness was evident in 9% of this large, healthy cohort. This finding is similar to the control subjects in the original study defining the criteria for excessive daytime sleepiness when developing the Epworth scale,31 and within the range of other studies utilizing the Epworth sleepiness score on school aged students,48 middle-aged bus drivers,46 and middle-aged Polish adults.50 Other studies using less well-validated criteria tend to report a higher prevalence of daytime sleepiness (12% in Irish men,51 15% in middle-aged men,52 and 17% aged > 18 years53 ); however, many of these previous studies have studied specific population subgroups. We have taken a large, diverse group of people and been able to demonstrate that insomnia, depression, suicidal ideation, and sleep disordered breathing are associated with excessive daytime sleepiness, with long work hours, alcohol dependence, and rotating work shifts further increasing the odds of excessive daytime sleepiness.

Our findings must also be interpreted in light of limitations that particularly relate to the recruitment strategy, and the reliance on self-reporting of many lifestyle behaviors and sleep disorders. Most importantly, the study sample was not designed to be representative of the general population or blood donors in New Zealand. The study opportunistically recruited self-selected volunteers reporting to blood donation sites in the study region between 1998 and 1999, some of whom did not meet criteria for blood donation on the day. However, the participants comprise a diverse, nonclinical, community-dwelling sample; and the observed associations between sleep-related factors and other variables of interest in this are likely to be generalizable to other community-based settings. The current survey also had a high response rate (81%) compared with previous studies on the prevalence of insomnia.11,24,38 In addition, we are unlikely to have completely excluded all potential confounding effects when attempting to isolate primary insomnia, such as chronic pain, cardiovascular disease, narcolepsy, delirium, and rarer general medical conditions. However, the possible influence of these factors would be minimal in this relatively young and healthy cohort. The results should also be interpreted in the context of having been collected between 1998 and 1999. Finally, although self-reporting of sleep disorders is likely to underestimate the true magnitude when compared to some direct measurement of sleep quantity and sleep quality, self-report has established accuracy,44,50–54 allows identification of areas for more detailed investigation, and is the only feasible method of measuring sleep variables in very large observational studies such as the NZBDSHS.17,57–59 These potential limitations are offset by accessing the largest cohort examining sleep and insomnia with a high response rate, direct physical measurements, and incorporating a detailed well-validated questionnaire covering multiple personal demographics and lifestyle behaviors.

Even in a large, relatively young and healthy sample, sleep dissatisfaction, inadequate sleep duration, insomnia, and excessive daytime sleepiness are common. The associations of these factors with each other as well as with depression, emphasize the importance of promoting better sleep habits to reduce the risk of adverse health outcomes.

REFERENCES


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SUBMISSION & CORRESPONDENCE INFORMATION

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DISCLOSURE STATEMENT

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APPENDIX

Self-Administered Questionnaire

Sleep disorders (Yes/No)
Have you ever been told that you snore loudly?
Have you ever been told that you stop breathing while you sleep?
Have you ever been told that you appear to choke while you sleep?
Sleep apnea was defined as either stopping breathing or choking whilst asleep.

Sleep complaints

1) Sleep satisfaction
How do you feel about the amount of sleep you normally get?
1. Nowhere near enough
2. Could do with a lot more
3. Could do with a bit more
4. Got the right amount
5. Get plenty
Responses were dichotomized into dissatisfied (1,2,3) and satisfied (4, 5).

2) Sleep quantity
On average, how many nights during a week do you get a full night’s sleep (i.e. at least 7 to 8 hours)?
Responses were categorized as 0 nights per week; 1-6 nights per week; 7 nights per week. For logistic regression categories were < 5 nights per week; and 5-7 nights per week.

3) Insomnia
Please indicate how often (0, 1, 2-4, 5-15, 16-30 times per month) you experience each of the following:
o Have trouble falling asleep.
o Wake up during the night and have difficulty getting back to sleep.
o Wake up too early in the morning and be unable to get back to sleep.
Primary insomnia was defined as having at least one of these sleep complaints at least weekly, and being dissatisfied with sleep, in the absence of depression, alcohol dependence, sleep apnea, or illicit substance use.
Alcohol
Do you currently drink alcohol once a month or more? Yes/No
If yes, how often do you drink alcohol?
- 6-7 days a week
- 4-5 days a week
- 2-3 days a week
- Once a week
- Once every 2 weeks
- Once a month
On an average day when you drink alcohol, how many drinks would you usually have in total?
Alcohol consumption was dichotomized into high and low risk based on the CAGE questionnaire. Two positive answers have a sensitivity exceeding 85% and a specificity approaching 90% for the diagnosis of alcohol abuse or dependence.

Smoking
Do you smoke cigarettes (not cigars/pipe) now? Yes/No
How many manufactured cigarettes do you usually smoke each day?
Non-smokers were assigned ‘0’ where smokers were assigned a value based on the number of cigarettes smoked per day.

Marijuana
During the past 12 months how often did you use marijuana (also known as grass, pot, cannabis, hashish, hash oil)?
- Did not use
- Less than once a month
- Once a month
- Once every 2 weeks
- Once a week or more often

Other illegal drugs
During the past 12 months how often did you use other illegal drugs?
That is, drugs not prescribed by your doctor or bought from a chemist, such as cocaine, LSD, amphetamines or speed, heroin, morphine.
- Did not use
- Less than once a month
- Once a month
- Once every 2 weeks
- Once a week or more often

Health
Have you ever been told by a doctor that you have, or have had:
- a) a heart attack ‘coronary’
  - if yes, were you admitted to hospital?
- b) a stroke
- c) a migraine
- d) epilepsy

Mood
Have you ever had two weeks or more when you felt sad or depressed nearly every day? Yes/No
Did it interfere a lot with your life, work or activities? Yes/No
Subjects who responded positively to both of these questions constituted one group (high risk for depression), all others constituted the other group. Questions relating to depression were based on the CIDI-SFMD. Suicidal ideation was determined by the question: Have you ever seriously thought of committing suicide (that is, taking some action to end your life)? Yes/No
Repetitive thought is an important process that pervades across many disorders.1 Rumination is one such repetitive thought process, which is focused on past failure or the cause of current distress and typically occurs within the context of Major Depressive Disorder.2-4 Whereas rumination is most often associated with depression, it likely plays a role in other disorders as well, especially in those disorders that share similar symptomatology with depression. In particular, insomnia has many overlapping symptoms with depression, such as sleep difficulties, low energy, difficulty concentrating, low mood, and suicidality.5 Further, insomnia and depression are highly comorbid with one another.6 Thus, perhaps rumination plays an important role in insomnia.

As is the case with depression, research has supported a role for cognitive processes in maintaining insomnia.7-10 Harvey's Cognitive Model of Insomnia posits that those with sleep difficulties can suffer from repetitive thinking throughout the 24-hour period.8 This negatively toned mental activity usually focuses on worries about not getting enough sleep and whether it will be possible to function adequately during the following day while suffering from daytime symptoms of insomnia (e.g., fatigue, disturbed mood, concentration difficulties). Such repetitive thought can perpetuate further emotional arousal, and this cycle is thought to perpetuate insomnia. While certain repetitive thought processes, such as worry, have been explored in great depth within the context of insomnia,9 rumination has not received the same degree of attention with respect to its role in sleep disturbance. In the recent past, rumination and worry were used as interchangeable terms, but the content of these two repetitive thought processes are thought to be different (see Carney11 for discussion). Worry is most often associated with thinking about future consequences, e.g., “what is going to happen tomorrow if I feel this way?” whereas rumination is most often concerned with what is causing the current problem; that is, rumination is most often oriented to the past, e.g., “Why am I feeling this way?” Also, worry is more often associated with anxiety whereas rumination is more likely to occur with dysphoria. Whereas other repetitive thought processes, such as worry, have been shown to be sleep-disruptive factors in insomnia,11 worry and rumination are separate but related factors. For example, our previous study suggested that rumination has an important role in insomnia...
minination and worry are distinct constructs since rumination was significantly related to insomnia severity, while worry was not. Despite these observations, there have been no previous efforts to develop an insomnia-specific rumination measure.

Recently, emerging studies have supported the link between rumination and sleep. In an undergraduate sample, there were significant associations between rumination and subjective sleep quality. Similarly, Carney and colleagues found a difference between good and poor sleepers on their tendency to ruminate when feeling low, and this difference was not accounted for by dysphoria. Good and poor sleepers did not differ on other rumination-related constructs, such as distraction (e.g., distracting yourself from depression by doing something fun with a friend) or self-focused rumination (e.g., asking yourself, “why am I reacting this way?”); they differed on a tendency to ruminate on dysphoric symptoms (e.g., thinking about how hard it is to concentrate) only. Thus, whereas those with depression and other disorders are characterized by increased self-focused rumination, those with poor sleep react with repetitive thought in response to insomnia symptoms. Thus, the construct of rumination and more specifically, symptom-focused rumination appears to be a key concept in insomnia.

The rumination characteristic in insomnia focuses on thinking repeatedly about daytime problems, such as poor concentration, low motivation, and low energy. Although insomnia is typically associated with nighttime pathology, a particularly prominent complaint is the resultant daytime fatigue. This daytime pathology, characterized by fatigue, cognitive complaints and low mood, can interfere with daily functioning. Thinking repeatedly about what caused daytime symptoms such as fatigue and poor concentration, can reinforce beliefs of poor sleep self-efficacy, increase anxiety about solving one’s sleep problem, and may lead to maladaptive safety behaviors (e.g., spending more time in bed). However, the current lack of an instrument to measure the symptom-focused rumination process in insomnia limits our ability to scrutinize the role this process plays in perpetuating this form of sleep disorder. Hence, the current series of two studies reported herein describe our efforts to develop and test an insomnia-specific symptom focused rumination scale that includes the common range of daytime symptoms that preoccupy insomnia sufferers. In Study 1, we describe the item content of the scale and report results of psychometric testing with a large sample of mixed good and poor sleepers. We also report our findings in regard to its relationship with other measures of insomnia controlling for coincident levels of depressed mood. In Study 2, we further tested the psychometric properties and predictive validity of our instrument in a sample of individuals with comorbid insomnia and depressive disorders. Our aim was to test the general hypothesis that daytime symptom focus is independently predictive of insomnia over and above what insomnia symptoms might be predicted from coincident levels of depressive mood.

**STUDY 1—METHODS**

**Participants**

The participants consisted of 327 (82% female) undergraduate students enrolled in an introductory psychology course at Ryerson University. Participants ranged in age from 18-49 years (mean = 20.38, SD = 4.60). The students were recruited via SONA, the Psychology Department’s online system. Students who were interested in participating in this study volunteered to participate in partial fulfillment of their introductory psychology course requirements.

**Measures**

**Daytime Insomnia Symptom Response Scale (DISRS)**

Given the emerging evidence for rumination in insomnia, it was important to develop a sleep-specific measure to assess ruminative tendencies in insomnia populations. The rumination measure used in previous studies of sleep and rumination was the Symptom-Focused Rumination Subscale (SYM) from the Response Styles Questionnaire (RSQ). The SYM queries the degree to which one responds to feeling low, with repetitive thinking about: “how hard it is to concentrate” or “feelings of fatigue and achiness.” While these items are associated with depression, they also are common daytime complaints in those with insomnia. Indeed, research has supported that there is substantial overlap between symptoms in depression and those found in insomnia. Given that the SYM is a validated subscale from a validated rumination measure and studies suggested that it was particularly useful in those with disrupted sleep, this 8-item subscale served as the starting point for developing the DISRS. All but one of the 8 original SYM items were retained for inclusion in the new scale. The excluded item from the SYM related to anhedonia (e.g., “Think about how you don’t seem to feel anything anymore”), a cardinal symptom of depression, and one which discriminates between individuals with and without depression. Another item contained in the SYM was a compound item (“Think about your feelings of fatigue and achiness”); this was divided into 2 items (i.e., think about feelings of fatigue” and “think about how achy you feel”) on the DISRS, as there are 2 distinct symptoms of insomnia. Twelve additional items based on daytime symptoms of insomnia were generated by the first author, based on daytime symptoms of insomnia reported elsewhere, including the daytime symptoms listed in Research Diagnostic Criteria for Insomnia. The items were sent to an expert in insomnia (J.D.E.), who provided feedback and approved the items. The result was a 20-item scale in which people are asked how frequently they engage in the behaviors listed when feeling tired, on a 4-point scale ranging from 1 (Almost Never) to 4 (Almost Always). The scale is scored by adding the items and total scores range from 20 to 80, with higher scores indicating higher levels of rumination.

**The Insomnia Severity Index (ISI)**

The ISI is well validated and commonly recommended self-report measure for assessing the severity of insomnia symptoms. It includes 7 items which measure insomnia symptom severity on a 5-point scale ranging from 0 (Not at All) to 4 (Extremely). The ISI score is obtained by adding the individual item scores, resulting in possible values ranging from 0 to 28; within this range, higher scores indicate greater insomnia severity. The ISI has good internal consistency (Cronbach $\alpha = 0.91$) and test-retest reliability ($r = 0.80$). The ISI also demonstrates good concurrent validity, as it correlates with sleep diary measures and polysomnography. A score $\geq 8$ has been shown to differentiate good sleepers from those with insomnia symp-
symptoms\textsuperscript{22} and was used as the division between good and poor sleepers in this study.

**The Beck Depression Inventory, Second Edition (BDI-II)**

The BDI-II\textsuperscript{23} is a 21-item self-report measure that assesses common depressive symptoms, such as depressed mood, hopelessness, suicidal ideation, sleep disturbance, and appetite change. Total scores range from 0 to 63, with higher scores indicating a greater degree of depression. The BDI-II has very good internal consistency (split half Pearson = 0.93). It also has well-established content validity and is good at differentiating between depressed and non-depressed individuals.\textsuperscript{23,24} The BDI-II has been used and validated in insomnia patients; however, there is reason to be cautious in using the BDI-II among those with insomnia because of the high number of non-discriminating items such as those querying insomnia and fatigue.\textsuperscript{5} For the purposes of this study, the highly overlapping insomnia and fatigue items were removed from the total BDI-II score.

**Fatigue Severity Scale (FSS)**

The FSS\textsuperscript{25} is a 9-item scale which is used to measure fatigue symptoms. Items are scored along a 7-point Likert scale ranging from 1 (Strongly Agree) to 7 (Strongly Disagree). The FSS total score is the average of the 9 individual items. The scale has good psychometric properties, as demonstrated by good internal consistency (Cronbach $\alpha = 0.94$) and good test-retest reliability.\textsuperscript{25,26}

**Penn State Worry Questionnaire-Past Week (PSWQ-PW)**

The PSWQ-PW\textsuperscript{27} is an abbreviated version of the original 16-item PSWQ, a common tool which measures the generality, excessiveness, and uncontrollability components of worry. The PSWQ-PW contains 15 items and specifically measures state worry over the past week. Sample items include, “my worries overwhelmed me” and “I worried about projects until they were done.” The PSWQ-PW has good internal consistency (Cronbach $\alpha = 0.91$) and is highly correlated with other state measures of worry.\textsuperscript{27}

**Procedure**

After consenting to participate, participants completed a brief demographic information form, the DISRS, BDI-II, ISI, FSS, and PSWQ.

**STUDY 1—RESULTS**

To test for multivariate normality, histograms were conducted for each of the DISRS items, and all items showed normal distributions. Outliers were screened by obtaining z values for each of the items, and data points were flagged if they had a value exceeding |3.29|.\textsuperscript{28} There were no outliers in this sample, and all data points were well within 3 standard deviations of the mean.

The means and standard deviations for each DISRS item are displayed in Table 1. The mean score on the DISRS in this sample was 41.43, with a standard deviation of 11.42 and a median score of 40. The total scores ranged from 20 to 75 across the sample, with 20 being the minimum possible score and 80 being the highest possible score. The skewness and kurtosis values were 0.30 and -0.48, respectively, well within the |2| and |7| cutoff scores, respectively.\textsuperscript{29} The internal consistency, as measured by Cronbach $\alpha$ was 0.93. The item-total statistics are displayed in Table 1. The item-total correlations range from 0.50 to 0.69, which indicates that each item is adequately cor-
related with the total scale. In addition, the Cronbach α if item deleted statistics did not suggest that any DISRS item should be removed.

An exploratory factor analysis (EFA) was conducted to examine the factor structure of the DISRS. The communalities ranged from 0.34 to 0.77 (as shown in Table 2), but most were within the 0.5 to 0.6 range (mean = 0.59). The inter-item correlation matrix was examined, and most of the correlations ranged from 0.3 to 0.6. There were no correlations greater than 0.8, indicating that multicollinearity is not likely to be a problem.30 The Kaiser-Meyer-Olkin Measure of Sampling Adequacy was 0.94 suggested that the sample size is adequate.31 Bartlett’s test of sphericity $\chi^2(190) = 3,265.78, p = < 0.001$] is significant, indicating that there is a relationship between the variables, and that the correlations are significantly different from zero.30 The EFA was conducted with a principle component extraction method. The rotated factor matrix was obtained using the direct oblimin rotation, a type of oblique rotation, given that all the items, and thus the components, should be correlated with one another, based on previous research.17,18

The EFA revealed a 3-factor solution according to Kaiser’s (1960) criteria. The 3 factors together explain 58.12% of the total variance, and all of the Eigenvalues were > 1.32 The factor loadings for the pattern matrix are displayed in Table 3. All of the factor loadings were > 0.4, a level which meets the current recommended criterion.33 The first factor explains 43.38% of the variance (Eigenvalue = 8.77) and appeared to reflect cognitive and motivation complaints. The second factor, which accounts for 8.54% of the variance (Eigenvalue = 1.71), appeared to relate to negatively valenced state symptoms (e.g., lack of energy, achiness, low mood, irritability). The third factor, accounting for 6.21% of the variance (Eigenvalue = 1.24), consisted of items related to feeling tired. Table 4 displays the correlations between each of the 3 factors.

To investigate the relation between the DISRS and constructs that theoretically should relate, Pearson product moment correlation coefficients were calculated. The DISRS positively

### Table 2—DISRS communalities for exploratory factor analysis

<table>
<thead>
<tr>
<th>Items</th>
<th>Communalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>DISRS1</td>
<td>0.48</td>
</tr>
<tr>
<td>DISRS2</td>
<td>0.60</td>
</tr>
<tr>
<td>DISRS3</td>
<td>0.67</td>
</tr>
<tr>
<td>DISRS4</td>
<td>0.60</td>
</tr>
<tr>
<td>DISRS5</td>
<td>0.54</td>
</tr>
<tr>
<td>DISRS6</td>
<td>0.47</td>
</tr>
<tr>
<td>DISRS7</td>
<td>0.58</td>
</tr>
<tr>
<td>DISRS8</td>
<td>0.67</td>
</tr>
<tr>
<td>DISRS9</td>
<td>0.52</td>
</tr>
<tr>
<td>DISRS10</td>
<td>0.44</td>
</tr>
<tr>
<td>DISRS11</td>
<td>0.66</td>
</tr>
<tr>
<td>DISRS12</td>
<td>0.68</td>
</tr>
<tr>
<td>DISRS13</td>
<td>0.77</td>
</tr>
<tr>
<td>DISRS14</td>
<td>0.62</td>
</tr>
<tr>
<td>DISRS15</td>
<td>0.56</td>
</tr>
<tr>
<td>DISRS16</td>
<td>0.73</td>
</tr>
<tr>
<td>DISRS17</td>
<td>0.61</td>
</tr>
<tr>
<td>DISRS18</td>
<td>0.34</td>
</tr>
<tr>
<td>DISRS19</td>
<td>0.63</td>
</tr>
<tr>
<td>DISRS20</td>
<td>0.59</td>
</tr>
</tbody>
</table>

### Table 3—Factor loadings of exploratory factor analysis with oblique rotation of the DISRS

<table>
<thead>
<tr>
<th>Items</th>
<th>Factor 1 “Cognitive/Motivation”</th>
<th>Factor 2 “Negative State”</th>
<th>Factor 3 “Tired”</th>
</tr>
</thead>
<tbody>
<tr>
<td>3. Think about how hard it is to concentrate</td>
<td>0.84</td>
<td>0.19</td>
<td>0.13</td>
</tr>
<tr>
<td>4. Think about how unmotivated you feel</td>
<td>0.74</td>
<td>-0.06</td>
<td>-0.01</td>
</tr>
<tr>
<td>5. Think about how your thoughts are cloudy</td>
<td>0.58</td>
<td>-0.29</td>
<td>-0.11</td>
</tr>
<tr>
<td>6. Think about how everything requires more effort than usual</td>
<td>0.42</td>
<td>-0.32</td>
<td>0.07</td>
</tr>
<tr>
<td>7. Think, “Why can’t I get going?”</td>
<td>0.72</td>
<td>-0.05</td>
<td>0.10</td>
</tr>
<tr>
<td>12. Think about how hard it is to keep your mind on task</td>
<td>0.84</td>
<td>-0.24</td>
<td>-0.08</td>
</tr>
<tr>
<td>17. Think, “I can’t seem to pay attention”</td>
<td>0.75</td>
<td>0.06</td>
<td>0.11</td>
</tr>
<tr>
<td>18. Think, “I’m so forgetful”</td>
<td>0.50</td>
<td>-0.06</td>
<td>0.09</td>
</tr>
<tr>
<td>1. Think, “I won’t be able to do work because I feel so bad”</td>
<td>0.07</td>
<td>-0.60</td>
<td>0.10</td>
</tr>
<tr>
<td>8. Think about how sad you feel</td>
<td>0.02</td>
<td>-0.84</td>
<td>-0.13</td>
</tr>
<tr>
<td>9. Think about how you don’t feel up to doing anything</td>
<td>0.34</td>
<td>-0.42</td>
<td>0.09</td>
</tr>
<tr>
<td>10. Think about your feelings of achiness</td>
<td>-0.04</td>
<td>-0.43</td>
<td>0.39</td>
</tr>
<tr>
<td>11. Think about how bad you feel</td>
<td>0.05</td>
<td>-0.79</td>
<td>0.01</td>
</tr>
<tr>
<td>14. Think, “I can’t shake this feeling off”</td>
<td>0.30</td>
<td>-0.60</td>
<td>-0.05</td>
</tr>
<tr>
<td>15. Think about how irritable you feel</td>
<td>-0.04</td>
<td>-0.68</td>
<td>0.02</td>
</tr>
<tr>
<td>19. Think, “I can’t be around people when I’m feeling this way”</td>
<td>-0.02</td>
<td>-0.82</td>
<td>-0.05</td>
</tr>
<tr>
<td>20. Think about how you don’t have the energy to get through the day</td>
<td>0.08</td>
<td>-0.45</td>
<td>0.42</td>
</tr>
<tr>
<td>2. Think about your feelings of fatigue</td>
<td>0.29</td>
<td>0.02</td>
<td>0.60</td>
</tr>
<tr>
<td>13. Think about how tired you feel</td>
<td>0.09</td>
<td>-0.06</td>
<td>0.81</td>
</tr>
<tr>
<td>16. Think about how sleepy you feel</td>
<td>-0.01</td>
<td>0.02</td>
<td>0.86</td>
</tr>
</tbody>
</table>

Factor loadings > 0.4 are in bold.
correlated with insomnia severity (ISI) and fatigue (FSS). The means and standard deviations of these measures are shown in Table 5, along with their correlations with the DISRS. An analysis of variance (ANOVA) confirmed that good sleepers (mean = 36.7, SD = 10.9) had significantly lower DISRS scores than poor sleepers (mean = 44.1, SD = 10.8), \( F_{1,323} = 34.69, p < 0.001 \). Discriminant validity is also of importance, particularly with respect to worry, a construct which is theoretically distinct from that of rumination. In order to determine whether the 2 measures were indeed conceptually distinct from one another, we conducted a factor analysis of the DISRS and PSWQ items using a varimax rotation and extracting 2 factors. The rotated matrix can be seen in Table 6. The varimax rotated factor matrix was obtained using the maximum likelihood extraction method. The 2 factors together explain 47.5% of the total variance, and each of the Eigenvalues were > 1. The first factor explained 12.6% of the variance and contains the DISRS rumination items, which load exclusively on this factor. The second factor, which accounted for 4.0% of the variance, contains the worry items from the PSWQ.

The multiple regression found that DISRS significantly predicted the ISI (\( \beta = 0.493; p < 0.001 \)) and accounted for 24% of the variance. Adding the BDI-II without sleep and fatigue items (\( \beta = 0.296; p < 0.001 \)) to the DISRS added marginally to the prediction (\( R^2 \) change = 0.04; \( F \) change score = 0.001); together, depression and rumination accounted for 28% of the variance. The interaction of daytime insomnia symptom rumination and depressed mood was not significant (\( p = 0.618 \)). That is, the contribution of rumination and depression to insomnia is not cumulative, but rather they each contribute to the variance independently.

**Summary**

There was good evidence for internal consistency of the measure, as supported by both Cronbach \( \alpha \) and the item-total correlations. The factor analysis suggests that rumination in insomnia is multidimensional and reflects three domains: rumination about cognitive and motivation problems, negative emotions, and fatigue. Items from the PSWQ loaded exclusively onto the same factor and rumination items loaded onto a separate factor. There was greater rumination about insomnia in those with higher levels of self-reported sleep disturbance. As predicted, insomnia rumination predicted insomnia severity and was not moderated by depression.

**STUDY 2—METHODS**

**Participants**

This study recruited 66 men and women (67% female) aged 20-65 years old (mean = 41.5; SD = 11.8), with complaints of both depression and insomnia (NIH R01-MH076856), solicited from clinics and media advertisements. Sixty-three percent of the sample were Caucasian, 15% did not specify their race/ethnicity, 13% were African American, and 9% were Asian American. These data were collected as part of the baseline measurement package obtained in a larger clinical trial to treat insomnia and depression. Participants were included if they were in good health (determined by medical and psychiatric history, and a physical examination), had insomnia (i.e., met Research Diagnostic Criteria\(^{19} \) for an Insomnia Disorder on the Duke Structured Interview of Sleep Disorders [DSISD]\(^{34} \); had a score \( \geq 15 \) on the Insomnia Severity Index, showed a mean sleep diary total wake time \( \geq 60 \) min/night and a mean sleep diary sleep efficiency \( [SE = (\text{total sleep time} \div \text{time in bed}) \times 100\%] < 85\% \) during a one-week screening period), and met criteria for a Major Depressive Episode (without psychotic features) on the mood module of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID)\(^{35} \) along with a score \( \geq 15 \) on the 17-item Hamilton Rating Scale for Depression (HAM-D).\(^{36} \) Those who had conditions thought to interfere with insomnia or depression treatment were excluded (e.g., those with Obsessive Compulsive Disorder with intrusive nighttime rituals, those with fre-

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**Table 4—Component correlation matrix**

<table>
<thead>
<tr>
<th>Factors</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Cognition/Motivation</td>
<td>-0.54</td>
<td>0.49</td>
<td></td>
</tr>
<tr>
<td>2. Negative State</td>
<td>-0.36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Tired</td>
<td>-</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**Table 5—Descriptive statistics and correlations for convergent validity measures**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>SD</th>
<th>Correlation with DISRS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insomnia Severity Index</td>
<td>9.61</td>
<td>5.07</td>
<td>0.49*</td>
</tr>
<tr>
<td>Fatigue Severity Scale</td>
<td>3.77</td>
<td>1.13</td>
<td>0.53*</td>
</tr>
<tr>
<td>Fear of Fatigue</td>
<td>24.9</td>
<td>13.8</td>
<td>0.62*</td>
</tr>
<tr>
<td>Beck Depression Inventory-II (fatigue and sleep items removed)</td>
<td>9.9</td>
<td>7.2</td>
<td>0.69*</td>
</tr>
<tr>
<td>Raw Beck Depression Inventory-II</td>
<td>14.4</td>
<td>9.9</td>
<td>0.70*</td>
</tr>
<tr>
<td>Study 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insomnia Severity Index</td>
<td>17.5</td>
<td>2.8</td>
<td>0.29*</td>
</tr>
<tr>
<td>MFI-Physical fatigue</td>
<td>12.8</td>
<td>4.2</td>
<td>0.31*</td>
</tr>
<tr>
<td>RSQ-rumination</td>
<td>56.5</td>
<td>10.4</td>
<td>0.62*</td>
</tr>
<tr>
<td>Beck Depression Inventory-II (fatigue and sleep items removed)</td>
<td>27.2</td>
<td>9.4</td>
<td>0.52*</td>
</tr>
<tr>
<td>Raw Beck Depression Inventory-II</td>
<td>29.2</td>
<td>9.5</td>
<td>0.54*</td>
</tr>
</tbody>
</table>

*p < 0.01.
in the previous study, this study used a more comprehensive
measure of fatigue, the Multidimensional Fatigue Inventory (MFI), rather than the FSS.

The Multidimensional Fatigue Inventory (MFI)
The MFI is a 20-item scale to assess dimensions of fatigue, including: general, physical, mental, reduced motivation, and reduced activity.37 These 5 dimensions represent distinct sub-scales of the MFI. Responses range on a 5-point scale from (yes, that is true) to (no, that is not true). The MFI has good internal consistency (Cronbach α = 0.84) and adequate convergent validity, as it has been found to be correlated with visual analog scales measuring fatigue.37 Along with the FSS, the MFI is also a recommended self-report measure for the assessment of fatigue in insomnia studies.21 For comparability to the first study, the Physical Fatigue subscale was used for this study.

Procedures
All study procedures were approved by the Ryerson University Research Ethics Board. Study candidates telephoned the Project Coordinator (PC) in response to study advertising (i.e., advertisements, brochures in clinics), and the PC scheduled an in-lab screening interview. At the screening interview, the participants were told about the study and provided informed consent. After the consent process, participants were interviewed by master’s or doctoral level psychology students with the Duke Structured Interview for Sleep Disorders (DSISD) and the Structured Clinical Interview for DSM disorders (SCID), and they also completed an ISI. Those who met initial entry criteria for depression on the SCID, and insomnia criteria on the DSISD and ISI (≥ 15) were scheduled for (a) a standard medical evaluation that included a physical examination, as well as a Hamilton Rating Scale for Depression (HAMD-17), (b) one night of PSG monitoring, and (c) one week of sleep log monitoring. Those who met entry criteria completed a battery of questionnaires, including the measures of interest for this study: the BDI-II, ISI, Dysfunctional Beliefs and Attitudes about Sleep (DBAS-16), DISRS, Response Styles Questionnaire (RSQ), and MFI. Those who continued to meet all study selection criteria for the parent study were randomized into treatment groups for an 8-week treatment phase wherein combinations of insomnia and depression treatments were tested. The parent study is ongoing and the study variables might be affected by treatment; thus, the present study reports on the baseline measures only.

Because of the relationship between rumination and depression in the previous studies, a regression analysis was conducted to determine whether daytime insomnia symptom rumination predicted insomnia severity and whether depression added any predictive value. The DISRS was entered as a predictor of ISI in the first step of a multiple regression. The BDI-II was added in the second step. Self-focused rumination (e.g., asking myself “why am I reacting this way?”) (shown in previous studies to relate to depression but not insomnia) was added in the next step, to determine if in a comorbid mood sample this form of daytime symptom-focused rumination is important. In the last step, an interaction term was added to test whether the rumination-specific prediction was accounted for by its interaction with depression.

Table 6—Factor loadings of confirmatory factor analysis with varimax rotation of PSWQ and DISRS items

<table>
<thead>
<tr>
<th>Items</th>
<th>PSWQ Items</th>
<th>DISRS Items</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSWQ1</td>
<td>-0.01</td>
<td>0.49</td>
</tr>
<tr>
<td>PSWQ2</td>
<td>0.25</td>
<td>0.76</td>
</tr>
<tr>
<td>PSWQ3</td>
<td>0.07</td>
<td>0.42</td>
</tr>
<tr>
<td>PSWQ4</td>
<td>0.32</td>
<td>0.72</td>
</tr>
<tr>
<td>PSWQ5</td>
<td>0.26</td>
<td>0.79</td>
</tr>
<tr>
<td>PSWQ6</td>
<td>0.22</td>
<td>0.77</td>
</tr>
<tr>
<td>PSWQ7</td>
<td>0.26</td>
<td>0.80</td>
</tr>
<tr>
<td>PSWQ8</td>
<td>0.25</td>
<td>0.53</td>
</tr>
<tr>
<td>PSWQ9</td>
<td>0.11</td>
<td>0.77</td>
</tr>
<tr>
<td>PSWQ10</td>
<td>0.18</td>
<td>0.61</td>
</tr>
<tr>
<td>PSWQ11</td>
<td>0.09</td>
<td>0.45</td>
</tr>
<tr>
<td>PSWQ12</td>
<td>0.26</td>
<td>0.76</td>
</tr>
<tr>
<td>PSWQ13</td>
<td>0.30</td>
<td>0.76</td>
</tr>
<tr>
<td>PSWQ14</td>
<td>0.26</td>
<td>0.81</td>
</tr>
<tr>
<td>PSWQ15</td>
<td>0.10</td>
<td>0.69</td>
</tr>
<tr>
<td>DISRS1</td>
<td>0.62</td>
<td>0.15</td>
</tr>
<tr>
<td>DISRS2</td>
<td>0.62</td>
<td>0.14</td>
</tr>
<tr>
<td>DISRS5</td>
<td>0.65</td>
<td>0.14</td>
</tr>
<tr>
<td>DISRS4</td>
<td>0.70</td>
<td>0.10</td>
</tr>
<tr>
<td>DISRS5</td>
<td>0.67</td>
<td>0.18</td>
</tr>
<tr>
<td>DISRS6</td>
<td>0.66</td>
<td>0.16</td>
</tr>
<tr>
<td>DISRS7</td>
<td>0.67</td>
<td>0.14</td>
</tr>
<tr>
<td>DISRS8</td>
<td>0.60</td>
<td>0.19</td>
</tr>
<tr>
<td>DISRS9</td>
<td>0.70</td>
<td>0.14</td>
</tr>
<tr>
<td>DISRS10</td>
<td>0.58</td>
<td>0.14</td>
</tr>
<tr>
<td>DISRS11</td>
<td>0.67</td>
<td>0.17</td>
</tr>
<tr>
<td>DISRS12</td>
<td>0.69</td>
<td>0.19</td>
</tr>
<tr>
<td>DISRS13</td>
<td>0.64</td>
<td>0.17</td>
</tr>
<tr>
<td>DISRS14</td>
<td>0.69</td>
<td>0.27</td>
</tr>
<tr>
<td>DISRS15</td>
<td>0.62</td>
<td>0.24</td>
</tr>
<tr>
<td>DISRS16</td>
<td>0.52</td>
<td>0.19</td>
</tr>
<tr>
<td>DISRS17</td>
<td>0.66</td>
<td>0.17</td>
</tr>
<tr>
<td>DISRS18</td>
<td>0.53</td>
<td>0.16</td>
</tr>
<tr>
<td>DISRS19</td>
<td>0.61</td>
<td>0.17</td>
</tr>
<tr>
<td>DISRS20</td>
<td>0.71</td>
<td>0.16</td>
</tr>
</tbody>
</table>

Factor loadings > 0.4 are in bold.

quent nocturnal panic). Additionally, those who met criteria for sleep apnea, restless legs syndrome or Circadian Rhythm Sleep Disorder on the basis of the Duke Structured Interview of Sleep Disorders, and/or those with an apnea-hypopnea index ≥ 15 or periodic limb movement-related arousal index ≥ 15/h of sleep during a screening laboratory polysomnogram were also excluded. Those who were hypnotic dependent (i.e., they reported that they were unwilling or unable to abstain from prescription medications for sleep during an 8-week treatment phase of the study) were also excluded from participation.

Measures
In addition to the DISRS, ISI, and BDI-II, which were used in the previous study, this study used a more comprehensive
There were no outliers, and all data points were within 3 standard deviations of the mean. The DISRS mean was 56.2 (SD = 11.6), the median was 55.5, and scores ranged from 29-78. Cronbach α was 0.94. The skewness and kurtosis values (-0.13 and -0.63, respectively) were both within published acceptable cutoff scores. To investigate construct validity, we calculated the bivariate (i.e., Pearson product moment) correlation between the DISRS and daytime fatigue severity, as well as with sleep, general rumination, and depressed mood. The DISRS positively correlated with all of these related measures. The means, standard deviations, and correlations are shown in Table 5. The multiple regression found that the DISRS significantly predicted the ISI (Adjusted R Square = 0.07, β = 0.285; p = 0.02). Adding the BDI-II without sleep and fatigue items to the DISRS did not add to the prediction over and above rumination alone (F change = 0.114, p = 0.74). Adding a depression-specific rumination scale (i.e., self-focused rumination) did not predict insomnia (F change = 0.854, p = 0.36). The interaction of daytime insomnia symptom rumination and depressed mood was not statistically significant (F change = 2.849, p = 0.10).

**Summary**

There was evidence of good internal consistency in this sample. In support of its validity, there were significant correlations with related constructs such as fatigue, mood disturbance, and general rumination. As expected, self-focused rumination, a form of rumination found in previous studies to be depression-specific, was not predictive of insomnia severity. Insomnia rumination was a predictor of insomnia severity and this was not accounted for by the interaction of depressed mood severity and rumination.

**DISCUSSION**

Symptom-focused rumination was characteristic of those with disturbed sleep; a finding consistent with several other earlier studies. Evidence for rumination in those with sleep disturbance also is consistent with Harvey’s cognitive model. The model asserts that the repetitive thought process seen at night (e.g., worry about not sleeping) can occur during the day (e.g., thinking repeatedly about why one is feeling so tired). Namely, that the activation of thoughts and emotions relevant to the insomnia process, e.g., reflecting on the level of daytime fatigue after a poor night’s sleep and feeling upset about it increases subsequent, selective monitoring for evidence of consequences of poor sleep. Such a process increases the likelihood of perceiving such daytime symptoms, which is presumed to lead to increase distress about the insomnia problem and further perpetuates sleep problems. This heightened level of distress may also stimulate activation of the sympathetic nervous system, due to the perceived threat to well being. This, in turn, could lead to increased arousal, as demonstrated in the chronic hyperarousal model of insomnia and the caffeine model of insomnia. This study was not designed to test the paths of all these components, but the data are supportive of aspects of these purported processes. Perhaps the best articulated description of this process in insomnia is seen in Espie’s Attention-Intention Effort model. That is, as one increases attention for daytime threats (e.g., fatigue or concentration problems) associated with the sleep problem, there is resultant effort in trying to “solve” the sleep problem. Rumination is commonly conceptualized as an (ineffective) problem-solving attempt; future studies could more definitively test whether rumination in insomnia can be conceptualized as an example of sleep effort. In these samples, there were increased ruminative tendencies associated with increased sleep disturbance and mood problems, and Espie and colleagues have reported increased sleep effort in those with comorbid mood problems as compared to those with insomnia only. This is particularly worrisome as rumination has been shown to be a difficult process to stop and is an important predictor of depression. It is a repetitive thought process that limits the processing of outside, disconfirming information; that is, someone with a propensity to think negatively would have difficulty integrating more positive information that might disconfirm their deeply ingrained negative beliefs. The current study suggests that those with sleep problems respond to the daytime sequelae of insomnia by thinking about how much it bothers them and this tendency predicts insomnia severity. It has been well established that insomnia increases the risk for episodes of depression; perhaps this common risk factor (i.e., rumination) may be one route by which insomnia increases depressive risk. The possibility of a shared cognitive risk pathway between insomnia and depression could be evaluated in future studies.

While insomnia severity and rumination were correlated in both studies, the size of the relationship between rumination and sleep was smaller in the clinical comorbid sample. Perhaps this may be related to the presence of depression in this sample. However, in the depressed sample, the unique contribution of insomnia symptom rumination to insomnia symptom severity is interesting. Other forms of rumination, namely self-focused rumination, were not related to insomnia severity, thus the content of the rumination was the same as it is in insomnia populations, even when there was a comorbid major depressive disorder. This supports Watkins’ idea suggesting that the repetitive thought process may be trans-diagnostic, albeit the content of the rumination may differ across axis I disorders. Another possible explanation is that those with a comorbid mood problem may have a different array of perpetuating mechanisms that explain their insomnia. Psychological variables appear to relate differently to sleep in those with comorbid insomnias as opposed to those with insomnia only. Future research should continue to explore the role of rumination in those with primary diagnoses of insomnia and depression, in addition to the comorbid populations. Another important finding in the current paper is the support for an insomnia-specific measure. The Daytime Insomnia Symptom Response Scale exhibited similarly reliable characteristics across the two samples, as measured by an internal consistency estimate (Cronbach alphas were > 0.9). Further, the item-total correlations and the alphas if item deleted analyses in Study 1, suggest that there are no items that are considered poor. As such, the internal reliability of the DISRS for use in those with a range of sleep and mood problems is highly acceptable. The confirmatory factor analysis of DISRS and PSQW items re-confirms that insomnia-based rumination and worry are indeed distinct constructs with respect to content.
Correlations between the DISRS and other related measures, along with the finding that the DISRS predicts insomnia severity, supports the convergent validity of the scale for use in those with a range of insomnia symptoms. Given that the DISRS was evaluated against other validated questionnaires in order to establish convergence, future research could evaluate the DISRS with other tests that do not share method variance, i.e., without relying solely on self-report questionnaires.

While these constructs demonstrate appropriate degrees of convergent validity, the correlation between rumination and depression \( (r = 0.71) \) was high in those with preclinical levels of depression and insomnia, and was moderately high in those with clinical insomnia and MDD \( (r = 0.52) \). Given that rumination is a construct implicated in the etiology of depression, and that some of the items were taken from a depression-specific rumination scale (i.e., the symptom-focused rumination scale of the RSQ), it is not surprising that insomnia-symptom rumination is correlated with depression. This may be a nosologic rather than a psychometric issue, as the daytime symptoms of insomnia overlap substantially with symptoms of depression, and depression inventories are confounded by insomnia-symptom items. Nonetheless the prediction of insomnia by insomnia rumination was not moderated by depression, so rumination in insomnia is not a mere vestige of mood pathology.

Alternatively, one could consider refining the DISRS by removing four items on theoretical grounds (i.e., from a face-validity perspective, some may be more closely related to depression). The following items may have the highest association with depression: Items 8 (“Think about how sad you feel”), 11 (“Think about how bad you feel”), 14 (“Think: I can’t shake this feeling off”), and 19 (“Think: I can’t be around people when I’m feeling this way”). Although there are no items that should be removed on empirical grounds, these four items have the highest correlations with the BDI-II, of 0.56, 0.56, 0.57 and 0.55, respectively. The internal consistency of the scale with these items removed was the same as the full scale \( (\alpha = 0.92; \text{mean} = 33.87, \text{SD} = 9.17) \). Ultimately, in order to determine whether the omission of these items is beneficial, this shortened 16-item scale would have to be administered to and validated in another sample. Although these two studies provided psychometric support for this scale, more research is needed.

It is important to consider that this scale was designed to measure a specific construct. That is, the instructions ask about the pervasiveness of the tendency to engage in repetitive thought behaviors in response to the state of “feeling tired.” These instructions were chosen based on a prevailing operational definition of rumination, which conceptualizes rumination as the process through which individuals respond to particular disorder-relevant states by focusing on them and searching for possible causes of the state/symptoms. The relevant cue for rumination in depression is dysphoria, and dysphoria is not a pervasive state in insomnia; thus, using depression scales is inappropriate in this population. Fatigue is the most common symptom complaint in insomnia and the state most related to rumination in insomnia. Therefore, it is important to have a qualifier relevant to insomnia rather than depression to differentiate this state from other states, such as depressed mood, which is relevant to many of the items in the DISRS. Thus, we are not interested in general repetitive thought, or repetitive thoughts relevant to other disorders, and instead are orienting respondents to the specific state of fatigue.

The factor structure suggests that when faced with daytime insomnia symptoms, people with poor sleep tend to increase their thinking about: (1) their thoughts and motivation level, (2) their negative state (e.g., how badly they feel), and (3) tiredness. It is possible that there are other content areas not assessed with this measure, as these three domains accounted for less than two-thirds of the variance. The factor analysis was conducted to understand the construct only. Given that only three items load on the tiredness factor and that the latter two factors do not account for a substantive part of the variance, the use of these factors as subscales is not advisable; instead the total summed score should be used. However, insofar as the factor analysis helps us to further understand the construct, it would also be interesting to see whether and how the factor structure might differ when administering the scale to a clinical sample.

The psychometric properties of this scale in a clinical sample suffering from uncomplicated insomnia without notable comorbidities are yet to be determined. Future studies could evaluate this measure to ensure it is valid in such a population. It is notable that this scale was derived from a smaller set of items shown to be useful in those with clinical insomnia. This study specifically examined those with a range of mood and sleep symptoms to show that rumination is not a mere artifact of mood problems. Comorbid insomnia is the rule rather than the exception in clinical practice, so arguably validation efforts in comorbid insomnia groups are equally if not more important than testing them in those suffering from isolated forms of insomnia. In sum, the present study found evidence in support of an insomnia-specific measure of rumination, and also confirmed previous studies’ findings of symptom focused rumination, in both nonclinical and clinical groups with a range of sleep and mood pathology. In addition to the theoretical implications for understanding perpetuating factors in insomnia and also for models of the risk that insomnia may confer for depression, there also may be clinical implications. The frontline recommended treatment for chronic insomnia is cognitive behavior therapy for insomnia (CBT-I), and this treatment has little to offer with regard to rumination-specific strategies. It is also a treatment that de-emphasizes daytime focused strategies. Future studies could test whether addressing the tendency to respond to daytime symptoms would improve clinical outcomes, or whether improving CBT-I’s effects on daytime symptoms would reduce rumination.

REFERENCES

Insomnia Symptom Rumination

ACKNOWLEDGMENTS

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Authors’ Note: Those interested in using the scale mentioned in this paper can contact Dr. Carney for permission.

SUBMISSION & CORRESPONDENCE INFORMATION

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DISCLOSURE STATEMENT

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Sleep insufficiency is a common disorder that is associated with poor quality of life, depression, and chronic disease. Nevertheless, many US adults continue to obtain insufficient sleep. Approximately 25% of individuals in a recent national sample felt they obtained insufficient rest or sleep on more than half of the preceding 30 days, while an additional nationally representative sample revealed 28% of adults slept ≤ 6 h per night. To address this common and detrimental condition, increasing the proportion of adults who get sufficient sleep is a goal of Healthy People 2020.

Sleep problems are of particular concern among the active duty military population as factors such as inconsistent work hours and deployment may compromise adequate sleep and adversely impact performance. However, few prior studies have investigated whether the prevalence of sleep problems differ between Veterans and demographically similar non-Veterans. The purpose of this study is to investigate whether self-reported insufficient rest or sleep varies in relation to Veteran status and to identify high-risk groups of Veterans. This study used data from the 2009 Behavioral Risk Factor Surveillance System (analyzed in 2011), a state based national telephone survey of non-institutionalized US adults. Inadequate rest was assessed in 411,313 adults aged 21 and older, of whom 55,361 were Veterans. Sleep duration was assessed in 6 states (n = 4,936 Veterans and 30,983 non-Veterans). Model-based direct rate adjustment was used to estimate the prevalence of insufficient rest or sleep while controlling for confounding. Multivariable logistic regression was used to estimate odds ratios of insufficient sleep or rest in subgroups of Veterans.

Results: After multivariable adjustment, insufficient rest or sleep (22.7% vs. 21.1%, p < 0.001) and short sleep duration (< 7 h/night, 34.9% vs. 31.3%, p = 0.026) were more common among Veterans than non-Veterans. When the Veteran group was further divided among newly transitioned (< 12 months) and longer-term Veterans (> 12 months), the overall test for a difference was not statistically significant between groups, mainly because there was little difference in sleep between the two groups of Veterans. High-risk Veteran subgroups included those who were 21-44 years of age (vs. 65-74), women, non-whites, current smokers, obese, unable to work, and those in poor health.

Conclusions: This study suggests that Veterans have a high burden of sleep problems and identifies subgroups that should be targeted to receive interventions and enhanced education regarding insufficient sleep.

Keywords: Insufficient sleep, Veterans health, Behavior Risk Factor Surveillance System

Citation: Faestel PM; Littell CT; Vitiello MV; Forsberg CW; Littman AJ. Perceived insufficient rest or sleep among Veterans: Behavioral Risk Factor Surveillance System 2009. J Clin Sleep Med 2013;9(6):577-584.
mental health conditions such as posttraumatic stress disorder (PTSD)\(^4\) and may be chronic in nature, affecting Veterans up to 20 years after combat exposure.\(^5\) These concerns remain time-
ly, as 37% of Iraq and Afghanistan Veterans entering VA health care from 2002 to 2008 were diagnosed with mental health con-
ditions, while 22% were diagnosed with PTSD.\(^6\) These newly transitioned Veterans may experience high levels of stressors as they make the transition to new employment and a change in lifestyle, thereby potentially altering their sleep patterns. How-
ever, no large-scale studies of sleep health in either newly tran-
sitioned or longer-term Veterans, compared to demographically similar non-Veterans, have been conducted.

The purpose of this study is to investigate whether sleep problems differ among a population-based national sample of Veterans relative to those without any military service history. The first aim of this study is to describe and compare the prevalence of perceived insufficient rest or sleep among Veterans and non-Veterans, and explore factors associated with this outcome among Veterans. The second aim of this study is to describe and compare reported sleep duration in this same paired compar-
son. Description of the prevalence of insufficient sleep among a national sample of Veterans may provide a better understanding of this important component of health and determine whether there are long-term effects of military service on sleep, as well as identify high-risk groups to target for interventions.

**METHODS**

A cross-sectional study was performed utilizing data from the 2009 Behavioral Risk Factor Surveillance System (BRFSS) and analyzed in 2011. This state-based, random-digit-dialed telephone survey of the non-institutionalized US adult population was conducted by state health departments in concert with the Centers for Disease Control and Prevention (CDC).\(^7\) The BRFSS obtained information on preventive health factors and health risk behaviors associated with chronic diseases, injuries, and preventable infectious diseases.\(^8\) Adults aged 18 years and older residing in all 50 states, the District of Columbia, Guam, Puerto Rico, and US Virgin Islands were contacted via a landline telephone during both daytime and evening hours and during each calendar month. The questionnaire comprised a standard set of core questions which queried each respondent about their current health status, including conditions such as diabetes, tobacco use, and demographic characteristics. Optional modules on specific topics such as arthritis management, prostate cancer screening, immunizations, and sleep were included by select states. Twenty-nine optional modules were supported by CDC in 2009; each optional module was included by as few as 2 and as many as 38 states.

The primary exposure evaluated in this study was a history of prior active military service. Individuals were asked the ques-
tion, “Have you ever served on active duty in the United States Armed Forces, either in the regular military or in a National Guard or military Reserve unit?” Respondents who answered yes were asked whether they were currently on active duty, on active duty during the last 12 months but not at the time of the interview, or on active duty in the past but not during the last 12 months. Respondents who answered “no” were asked if they were in a training status for the Reserves or National Guard. Individuals were classified as newly transitioned Veterans if they reported a history of active duty military service during the last 12 months but not at the time of the interview, while individu-
als on active duty in the past but not during the last 12 months were classified as longer-term Veterans. Non-Veterans, defined as individuals without a history of active duty military service, served as the comparison group. Respondents with missing age or between the ages of 18 and 20 were excluded in order to re-
duce residual confounding by age given the presence of a 100-
fold difference in the number of respondents in this age range among comparison groups. Respondents on active duty at the time of the survey were also excluded, as the data were not considered representative of this population, as BRFSS does not sample individuals residing in on-post, government housing
nor those in a deployed or field environment. These factors limited the generalizability among this segment of the population. Individuals who refused to answer the question, were unsure of their status, or had a missing response, as well as those who reported a training status only without ever having received active duty orders were also excluded.

The primary outcome of interest was frequent sleep insuffi-
ciency and was assessed with the response to the core question, “During the past 30 days, for about how many days have you felt you did not get enough rest or sleep?” Responses were recorded as whole numbers between 0 and 30. Due to a non-normal dis-
tribution with multiple modes, responses were dichotomized into < 14 and ≥ 14 days. In agreement with previous research, frequent sleep insufficiency was defined as occurring ≥ 14 days in the past month.\(^1\) The secondary outcome was self-reported average sleep duration and was assessed with the response to the question, “On average, how many hours of sleep do you get in a 24-hour period? Think about the time you actually spend sleeping or napping, not just the amount of sleep you think you should get.” The number of hours of sleep in whole numbers was then entered, rounding ≥ 30 min up to the next hour. Re-
sponses were dichotomized into < 7 and ≥ 7 h.\(^19\) This question was an optional module and was answered in 6 states (Georgia, Hawaii, Illinois, Louisiana, Minnesota, and Wyoming).

Sociodemographic, anthropometric, health, and behavioral characteristics were also elicited during the BRFSS interview, including level of education, marital status, employment status, alcohol consumption, and smoking status. Binge drinking has been associated with short sleep duration\(^1\) and was defined as having ≥ 5 drinks on one occasion in the past 30 days for men, and having ≥ 4 drinks on one occasion in the past 30 days for women. Body mass index (kg/m\(^2\)) as a measure of adiposity was calculated based on self-reported height and weight. Individu-
als were classified as normal weight (< 25 kg/m\(^2\)), overweight (25-29.9 kg/m\(^2\)), obese class I (30-34.9 kg/m\(^2\)), or obese class II (≥ 35 kg/m\(^2\)).\(^20\) Categories of self-reported general health status were collapsed (excellent/very good, good, fair/poor).\(^3\) Subjects were also asked about the presence of stress, depression, and problems with emotion, and were classified as having frequent mental distress if they reported symptoms of poor mental health ≥ 14 days during the past month.\(^1\)

BRFSS survey weights were applied in order to account for unequal probabilities of selection and oversampling. The CDC assigned each respondent a final sampling weight that took into account the overall probability of selection as well as a
post-stratification factor used to adjust for non-coverage and non-response errors. This process allowed for the weighted frequencies to equal the state’s population estimates.

Model-based direct rate adjustment was used to estimate the prevalence of insufficient rest or sleep while controlling for confounding. This method utilized weights from a logistic regression model in order to adjust the outcome measures in the comparison population, using Veterans as the standard population. In order to evaluate whether differences in the prevalence of insufficient rest or sleep and sleep duration between Veterans and non-Veterans were statistically significant, Pearson $\chi^2$ tests corrected for the survey design were conducted. These were converted to an $F$ statistic utilizing STATA 11 (StataCorp LP, College Station, Texas).

To determine the extent to which observed differences were due to differences in demographic and other characteristics, we created nested multivariable models; initial analyses were unadjusted. Subsequent analyses were adjusted for age, sex and race/ethnicity (Model 1); Model 1 factors plus employment and income (Model 2); Model 2 factors plus smoking status (Model 3); and Model 3 factors plus mental health status (Model 4). Age, sex, and race/ethnicity were included as confounders given their associations with varying rates of insufficient sleep, as well as the differences in these characteristics between Veterans and non-Veterans. Prior studies have detected associations between employment status, income and insufficient sleep; consequently, these variables were included as confounders a priori given the differences in employment status and income between Veterans and non-Veterans. Given its association with insufficient sleep and military service, smoking was also included as a confounder. We adjusted for mental health given the potential for significant sleep disturbances related to such disorders as PTSD. Odds ratios were calculated in order to assess how the outcome measure differed among Veterans (pooling newly transitioned and longer-term) by various characteristics. The Veteran groups were combined to better assess factors associated with poor sleep among all Veterans in order to assist with public health interventions in this population. This study was reviewed and approved by the University of Washington Human Subjects Institutional Review Board.

**RESULTS**

The median response rate, defined as the percentage of persons who completed interviews among all eligible persons for the 2009 BRFSS survey was 52.5% (range among states: 37.9% to 66.9%). The median cooperation rate, defined as the percentage of persons who completed interviews among all eligible persons who were contacted, was 75.0% (range: 55.5% to 88.0%).

A total of 432,607 individuals completed the 2009 BRFSS survey. We excluded individuals for the following reasons: between 18 and 20 years of age ($n = 5,878$); refusal to answer the question pertaining to military status, were unsure of their status, or had a missing response ($n = 5,512$); active duty at the time of the survey ($n = 1,923$); in a training status ($n = 4,433$), and those with missing age ($n = 3,548$), leaving 355,952 non-Veterans shown in Table 1. Veterans were more likely to be older, male, married, have more education, and be former smokers, as compared to non-Veterans. Veterans were also more likely to be retired and to report their general health status as fair or poor. A smaller proportion of Veterans were racial/ethnic minorities or from households with children present. The 2 groups were similar with respect to current smoking status, binge drinking, and self-reported poor mental health in the past month.

Table 2 shows the frequency of insufficient rest or sleep among newly transitioned Veterans, longer-term Veterans, and non-Veterans. In unadjusted analyses, newly transitioned Veterans were more likely than both longer-term Veterans and non-Veterans to report frequent insufficient rest or sleep. Following adjustment for sociodemographic factors, this difference was no longer statistically significant, though Veterans reported about a 2-percentage point greater prevalence of sleep problems. A larger proportion of Veterans (both newly transitioned and longer-term) than non-Veterans reported frequent insufficient rest or sleep (22.7% vs. 20.4%). Further adjustment for employment, income, smoking status, and mental health did not appreciably change this relationship.

Based on data from the 6 states that included the optional module on sleep duration ($n = 4,936$ Veterans and 30,983 non-Veterans), Veterans were more likely to report sleep duration less than the recommended 7 h in a 24-h period than their non-Veteran counterparts (34.9% vs. 31.3%) after adjustment for age and gender (data not tabulated).

Table 3 presents the associations of frequent insufficient rest or sleep and selected demographic and other characteristics among both newly transitioned and longer-term Veterans. Insufficient rest or sleep was most strongly associated with age < 65 (compared to those age 65-74), inability to work, decreased income, and frequent mental distress. In addition, current smokers (vs. never smokers) and persons who reported binge drinking on at least one occasion over the past 30 days were also more likely to report frequent insufficient rest or sleep.

**DISCUSSION**

To our knowledge, this is the first study describing the prevalence of insufficient rest or sleep among a population-based, national sample of Veterans relative to those without any military service history. The results corroborate previous research that has identified a high prevalence of insufficient rest or sleep in this population and suggest the continuing need for provider and patient education about sleep hygiene. Even though the overall test for a difference across the three groups (the two groups of Veterans and non-Veterans) was not statistically significant, this was mainly due to the fact that multivariable-adjusted estimates of insufficient rest or sleep in the two groups of Veterans were similar. When considered as a single group, Veterans (newly transitioned and longer-term) were found to have a 23% frequency of insufficient rest or sleep occurring on at least 14 days in the past month. Following adjustment for sociodemographic variables, the difference remained, with Veterans more likely to report frequent insufficient rest or sleep than their non-Veteran counterparts.

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This study also demonstrated that Veterans were less likely to obtain the recommended 7 h of sleep per night when compared to demographically similar non-Veterans. Short sleep duration is associated with limitations in daily activities such as difficulty concentrating\(^1\) and may be a novel risk factor for numerous metabolic conditions including obesity, metabolic syndrome, hypertension, and cardiovascular disease.\(^2\) Chronic sleep loss may also exacerbate depressive symptoms.\(^1\) Addressing sleep health during the clinical encounter for these conditions is an important aspect of comprehensive medical care.

The prevalence of insufficient rest or sleep varied by age in this study, a finding corroborated by research utilizing a similar, national database.\(^1\) Younger Veterans were at a higher risk of insufficient rest or sleep than those 65-74 years of age. As active duty military transition to civilian life, they may be faced with varying challenges including changes in environment, type of health during the clinical encounter for these conditions is an important aspect of comprehensive medical care.

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<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Newly transitioned</th>
<th>Longer-term</th>
<th>Non-Veteran</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N = 2,350)</td>
<td>(N = 53,011)</td>
<td>(N = 355,952)</td>
</tr>
<tr>
<td>Weighted prevalence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21-44</td>
<td>726</td>
<td>4,519</td>
<td>96,397</td>
</tr>
<tr>
<td>45-54</td>
<td>416</td>
<td>6,078</td>
<td>78,367</td>
</tr>
<tr>
<td>55-64</td>
<td>496</td>
<td>13,703</td>
<td>78,489</td>
</tr>
<tr>
<td>65-74</td>
<td>377</td>
<td>13,820</td>
<td>56,967</td>
</tr>
<tr>
<td>≥ 75</td>
<td>333</td>
<td>14,891</td>
<td>45,732</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1,268</td>
<td>49,034</td>
<td>102,844</td>
</tr>
<tr>
<td>Female</td>
<td>1,062</td>
<td>3,977</td>
<td>253,108</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>1,851</td>
<td>44,945</td>
<td>277,495</td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>248</td>
<td>3,332</td>
<td>28,806</td>
</tr>
<tr>
<td>Hispanic</td>
<td>114</td>
<td>1,811</td>
<td>26,680</td>
</tr>
<tr>
<td>Other, non-Hispanic</td>
<td>110</td>
<td>2,733</td>
<td>19,680</td>
</tr>
<tr>
<td>Highest educational level</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than high school</td>
<td>176</td>
<td>3,347</td>
<td>35,363</td>
</tr>
<tr>
<td>High school or equivalent</td>
<td>687</td>
<td>15,852</td>
<td>105,462</td>
</tr>
<tr>
<td>Some college or more</td>
<td>1,485</td>
<td>33,706</td>
<td>214,093</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married or living as married</td>
<td>1,423</td>
<td>34,451</td>
<td>206,705</td>
</tr>
<tr>
<td>Divorced/separated/widowed</td>
<td>671</td>
<td>14,981</td>
<td>108,993</td>
</tr>
<tr>
<td>Never married</td>
<td>248</td>
<td>3,428</td>
<td>39,126</td>
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<tr>
<td>Employment status</td>
<td></td>
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<tr>
<td>Employed</td>
<td>1,238</td>
<td>19,426</td>
<td>185,523</td>
</tr>
<tr>
<td>Unemployed</td>
<td>127</td>
<td>2,175</td>
<td>21,058</td>
</tr>
<tr>
<td>Retired</td>
<td>705</td>
<td>27,658</td>
<td>87,471</td>
</tr>
<tr>
<td>Unable to work</td>
<td>132</td>
<td>3,019</td>
<td>24,959</td>
</tr>
<tr>
<td>Student/homemaker</td>
<td>132</td>
<td>580</td>
<td>35,587</td>
</tr>
<tr>
<td>Income ($)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 15,000</td>
<td>184</td>
<td>3,423</td>
<td>37,508</td>
</tr>
<tr>
<td>15,000-24,999</td>
<td>309</td>
<td>8,339</td>
<td>55,133</td>
</tr>
<tr>
<td>25,000-34,999</td>
<td>283</td>
<td>6,783</td>
<td>36,585</td>
</tr>
<tr>
<td>35,000-49,999</td>
<td>339</td>
<td>8,683</td>
<td>46,305</td>
</tr>
<tr>
<td>≥ 50,000</td>
<td>975</td>
<td>20,386</td>
<td>133,304</td>
</tr>
<tr>
<td>Missing/refused</td>
<td>290</td>
<td>5,397</td>
<td>47,120</td>
</tr>
</tbody>
</table>

BRFSS, Behavioral Risk Factor Surveillance System. \(^1\) Individuals who were discharged from the military in the previous 12 months were classified as Veterans \(\leq 12 \text{ months} \) (newly transitioned), whereas individuals who were discharged from the military \(> 12 \text{ months} \) prior were classified as longer-term Veterans. \(^2\) Unweighted sample size. Categories may not sum to survey total because of missing responses. \(^3\) Never smokers were defined as those who had smoked \(< 100 \text{ cigarettes in lifetime} \). \(^4\) Binge drinking was defined as \(\geq 5 \text{ or } \geq 4 \text{ alcoholic drinks for men and women, respectively, on one occasion in past 30 days}\). \(^5\) Response to question: “On average, how many hours of sleep do you get in a 24-hour period?” Optional module that included this question was used in six states only (Georgia, Hawaii, Illinois, Louisiana, Minnesota, and Wyoming). \(^6\) Estimates are not presented because of small cell sizes (<100) and high imprecision.

Table 1 continues on the following page
work, and loss of camaraderie. Younger Veterans might also have more children in the household than their older counterparts, a factor that may compromise sleep. Finally, younger Veterans would be expected to be closer in time to any significant service-related stressor, such as deployment to a combat zone, which may affect sleep quality and duration. The recognition of these potential risk factors may help clinicians who treat younger Veterans as well as identify those who may benefit from improved sleep hygiene.

A Veteran’s employment status following their military service and this association with frequent insufficient rest or sleep in this study was also noteworthy, especially among those unable to work. Strong associations have been described between overall sleep problems and disability retirement, particularly among individuals with disability related to mental health disorders and musculoskeletal injury. In addition, there is a delay in the return to work among patients with self-reported sleep disturbance. Given the strong association of insufficient sleep and lack of employment, Veterans who are injured as a result of service and who may be limited in their ability to work may benefit from improved education. These methods include addressing mental health problems as well as avoiding tobacco and alcohol in the evening.

In this study, frequent mental distress was also strongly associated with insufficient rest or sleep. Veterans may represent a segment of the population in which this facet of health and its effect on sleep is of particular concern due to the prevalence of mental health disorders, especially among recent Veterans of the wars in Iraq and Afghanistan. Furthermore, the recognition that sleep disorders are a core feature of mental illnesses such as PTSD may assist in earlier screening and treatment.

This study was subject to several limitations. The sleep data were obtained via self-report and may not be comparable to

### Table 1 (continued)—Selected demographic and behavioral characteristics in Veterans and non-Veterans, BRFSS, 2009

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Veteran</th>
<th></th>
<th></th>
<th>Non-Veteran</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Newly transitioned</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>≤ 12 months</td>
<td></td>
<td></td>
<td>&gt; 12 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N = 2,350</td>
<td></td>
<td></td>
<td>N = 53,011</td>
<td></td>
</tr>
<tr>
<td>Smoking statusc</td>
<td></td>
<td>Weighted</td>
<td>Weighted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>1,147</td>
<td>49.8</td>
<td>18,096</td>
<td>36.1</td>
<td>198,844</td>
</tr>
<tr>
<td>Former</td>
<td>790</td>
<td>29.6</td>
<td>26,339</td>
<td>46.0</td>
<td>97,145</td>
</tr>
<tr>
<td>Current</td>
<td>402</td>
<td>20.6</td>
<td>8,272</td>
<td>16.0</td>
<td>57,704</td>
</tr>
<tr>
<td>Binge drinkingd</td>
<td></td>
<td>Weighted</td>
<td>Weighted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1,978</td>
<td>78.3</td>
<td>45,966</td>
<td>86.5</td>
<td>309,412</td>
</tr>
<tr>
<td>Yes</td>
<td>309</td>
<td>21.7</td>
<td>5,377</td>
<td>13.5</td>
<td>36,614</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td></td>
<td>Weighted</td>
<td>Weighted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>650</td>
<td>28.8</td>
<td>14,104</td>
<td>25.3</td>
<td>122,319</td>
</tr>
<tr>
<td>Overweight</td>
<td>1,001</td>
<td>48.5</td>
<td>23,729</td>
<td>44.7</td>
<td>119,742</td>
</tr>
<tr>
<td>Obese, class I</td>
<td>418</td>
<td>16.1</td>
<td>10,165</td>
<td>21.2</td>
<td>59,705</td>
</tr>
<tr>
<td>Obese, class II</td>
<td>204</td>
<td>6.7</td>
<td>4,341</td>
<td>8.8</td>
<td>37,303</td>
</tr>
<tr>
<td>Children in household</td>
<td></td>
<td>Weighted</td>
<td>Weighted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1,641</td>
<td>56.5</td>
<td>45,905</td>
<td>77.0</td>
<td>246,243</td>
</tr>
<tr>
<td>One</td>
<td>285</td>
<td>14.8</td>
<td>3,128</td>
<td>9.5</td>
<td>42,416</td>
</tr>
<tr>
<td>≥ 1</td>
<td>421</td>
<td>28.6</td>
<td>3,901</td>
<td>13.5</td>
<td>66,464</td>
</tr>
<tr>
<td>Self-reported health</td>
<td></td>
<td>Weighted</td>
<td>Weighted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excellent/very good</td>
<td>1,199</td>
<td>58.7</td>
<td>23,179</td>
<td>46.9</td>
<td>178,140</td>
</tr>
<tr>
<td>Good</td>
<td>723</td>
<td>28.5</td>
<td>17,572</td>
<td>33.1</td>
<td>107,833</td>
</tr>
<tr>
<td>Fair/poor</td>
<td>418</td>
<td>12.8</td>
<td>11,917</td>
<td>20.0</td>
<td>68,032</td>
</tr>
<tr>
<td>Poor mental health (days in past month)</td>
<td></td>
<td>Weighted</td>
<td>Weighted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 14</td>
<td>2,085</td>
<td>90.6</td>
<td>47,782</td>
<td>90.8</td>
<td>312,761</td>
</tr>
<tr>
<td>≥ 14</td>
<td>235</td>
<td>9.4</td>
<td>4,394</td>
<td>9.2</td>
<td>37,568</td>
</tr>
<tr>
<td>Sleep duration (h) in a 24-h periode</td>
<td></td>
<td>Weighted</td>
<td>Weighted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 7</td>
<td>–f</td>
<td>–f</td>
<td>1,525</td>
<td>34.5</td>
<td>10,202</td>
</tr>
<tr>
<td>≥ 7</td>
<td>–f</td>
<td>–f</td>
<td>3,251</td>
<td>65.5</td>
<td>20,632</td>
</tr>
</tbody>
</table>

BRFSS, Behavioral Risk Factor Surveillance System. *Individuals who were discharged from the military in the previous 12 months were classified as Veterans ≤ 12 months (newly transitioned), whereas individuals who were discharged from the military > 12 months prior were classified as longer-term Veterans. †Unweighted sample size. Categories may not sum to survey total because of missing responses. ‡Never smokers were defined as those who had smoked < 100 cigarettes in lifetime. §Binge drinking was defined as ≥ 5 or ≥ 4 alcoholic drinks for men and women, respectively, on one occasion in past 30 days. ‡Response to question: “On average, how many hours of sleep do you get in a 24-hour period?” Optional module that included this question was used in six states only (Georgia, Hawaii, Illinois, Louisiana, Minnesota, and Wyoming). Estimates are not presented because of small cell sizes (< 100) and high imprecision.
studies in which sleep was directly measured with methods such as actigraphy or polysomnography. When compared to these objective measurements, subjective assessment underestimates total sleep duration.\(^3\) The cross-sectional nature precludes assessments of the temporal association between characteristics such as employment and sleep problems. The terms “rest” and “sleep” were also used interchangeably. This may have contributed to measurement error as these terms may have differ-

### Table 3—Prevalence and adjusted odds ratio of frequent insufficient rest or sleep among Veterans, by various characteristics, BRFSS, 2009

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Weighted(^d) prevalence of insufficient rest or sleep</th>
<th>Adjusted odds ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>### Adjustments factors*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 0: Nothing</td>
<td>30.2</td>
<td>22.4</td>
<td>27.9</td>
</tr>
<tr>
<td>Model 1: Age, sex, and race/ethnicity</td>
<td>21.3</td>
<td>22.4</td>
<td>20.1</td>
</tr>
<tr>
<td>Model 2: Model 1 factors + employment and income</td>
<td>21.8</td>
<td>22.4</td>
<td>19.8</td>
</tr>
<tr>
<td>Model 3: Model 2 factors + smoking status</td>
<td>21.9</td>
<td>22.4</td>
<td>20.3</td>
</tr>
<tr>
<td>Model 4: Model 3 factors + mental health</td>
<td>22.7</td>
<td>22.4</td>
<td>20.8</td>
</tr>
</tbody>
</table>

*Longer-term Veterans are the reference population.\(^*\)p values are equivalent to a comparison of differences across the 3 groups.\(^*\)Veterans are the reference population (actual percentages are not shown). p value represents the comparison of Veterans (both newly transitioned and longer-term) and non-Veterans.

---

### Table 2—Frequency of insufficient rest or sleep in Veterans and non-Veterans, adjusted for selected combinations of sociodemographic and behavioral characteristics

<table>
<thead>
<tr>
<th>Adjustment factors(^a)</th>
<th>Veterans</th>
<th>Non-Veterans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newly transitioned ≤ 12 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long-term &gt; 12 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>p(^a)</td>
<td>p(^b)</td>
<td></td>
</tr>
<tr>
<td>Model 0: Nothing</td>
<td>30.2</td>
<td>22.4</td>
</tr>
<tr>
<td>Model 1: Age, sex, and race/ethnicity</td>
<td>21.3</td>
<td>22.4</td>
</tr>
<tr>
<td>Model 2: Model 1 factors + employment and income</td>
<td>21.8</td>
<td>22.4</td>
</tr>
<tr>
<td>Model 3: Model 2 factors + smoking status</td>
<td>21.9</td>
<td>22.4</td>
</tr>
<tr>
<td>Model 4: Model 3 factors + mental health</td>
<td>22.7</td>
<td>22.4</td>
</tr>
</tbody>
</table>

Longer-term Veterans are the reference population.\(^*\)p values are equivalent to a comparison of differences across the 3 groups.\(^*\)Veterans are the reference population (actual percentages are not shown). p value represents the comparison of Veterans (both newly transitioned and longer-term) and non-Veterans.
ent meanings among study respondents. In addition, the 2009 BRFSS survey was conducted among households with landline telephones and the findings may not generalize to wireless-only households, who represented an estimated 23.9% of adults in 2009. Although significant health risk differences may exist when comparing these two populations, we have no reason to believe the prevalence of wireless-only households varies significantly by Veteran status.

We were also unable to categorize Veterans into groups that may have helped delineate potential causal factors of their poor sleep. Additional knowledge regarding recent deployment, combat exposure, specific mental health conditions, or the presence of service-connected injury preventing employment would have been helpful in this regard. In addition, there was likely a large amount of heterogeneity among Veterans who served at different time periods. Veterans from specific periods or conflicts may have been exposed to varying military cultures that may have affected their sleep patterns. More in-depth knowledge of these military specific factors would have improved our ability to determine potential reasons for poorer sleep among Veterans in this study.

From a public health perspective, the results of this study suggest that specific subsets of the Veteran population require particular attention when addressing insufficient sleep. Younger Veterans appear to be at higher risk than older Veterans, as well as those who are unable to work or who are experiencing frequent mental distress. Future prospective studies are needed in order to further assess the effects of sleep disorders during the immediate transition period from active service to civilian life, especially among Veterans with a history of musculoskeletal or mental health conditions potentially limiting employability. Given the association with chronic diseases such as diabetes,

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Weighted* prevalence of insufficient rest or sleep</th>
<th>Adjusted odds ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Income ($)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 15,000</td>
<td>27.8</td>
<td>1.67</td>
<td>(1.42, 1.95)</td>
</tr>
<tr>
<td>15,000-24,999</td>
<td>22.9</td>
<td>1.22</td>
<td>(1.08, 1.38)</td>
</tr>
<tr>
<td>25,000-34,999</td>
<td>20.3</td>
<td>0.97</td>
<td>(0.85, 1.11)</td>
</tr>
<tr>
<td>35,000-49,999</td>
<td>20.6</td>
<td>1.03</td>
<td>(0.89, 1.18)</td>
</tr>
<tr>
<td>≥ 50,000</td>
<td>20.5</td>
<td>1.00</td>
<td>Ref</td>
</tr>
<tr>
<td>Smoking status f</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>19.4</td>
<td>1.00</td>
<td>Ref</td>
</tr>
<tr>
<td>Former</td>
<td>19.3</td>
<td>0.95</td>
<td>(0.87, 1.05)</td>
</tr>
<tr>
<td>Current</td>
<td>32.6</td>
<td>2.04</td>
<td>(1.80, 2.31)</td>
</tr>
<tr>
<td>Binge drinking*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>20.7</td>
<td>1.00</td>
<td>Ref</td>
</tr>
<tr>
<td>Yes</td>
<td>26.7</td>
<td>1.35</td>
<td>(1.18, 1.56)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>19.6</td>
<td>0.98</td>
<td>(0.88, 1.10)</td>
</tr>
<tr>
<td>Overweight</td>
<td>19.6</td>
<td>1.00</td>
<td>Ref</td>
</tr>
<tr>
<td>Obese, class I</td>
<td>23.9</td>
<td>1.37</td>
<td>(1.22, 1.55)</td>
</tr>
<tr>
<td>Obese, class II</td>
<td>31.1</td>
<td>1.93</td>
<td>(1.68, 2.21)</td>
</tr>
<tr>
<td>Children in household</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>18.1</td>
<td>1.00</td>
<td>Ref</td>
</tr>
<tr>
<td>One</td>
<td>28.6</td>
<td>2.05</td>
<td>(1.78, 2.35)</td>
</tr>
<tr>
<td>≥ 1</td>
<td>33.1</td>
<td>2.62</td>
<td>(2.28, 3.00)</td>
</tr>
<tr>
<td>Self-reported health</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excellent/very good</td>
<td>16.1</td>
<td>1.00</td>
<td>Ref</td>
</tr>
<tr>
<td>Good</td>
<td>20.7</td>
<td>1.38</td>
<td>(1.24, 1.54)</td>
</tr>
<tr>
<td>Fair/poor</td>
<td>33.9</td>
<td>2.70</td>
<td>(2.42, 3.00)</td>
</tr>
<tr>
<td>Poor mental health (days in past month)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 14</td>
<td>17.8</td>
<td>1.00</td>
<td>Ref</td>
</tr>
<tr>
<td>≥ 14</td>
<td>58.0</td>
<td>6.50</td>
<td>(5.66, 7.47)</td>
</tr>
<tr>
<td>Sleep duration (h) in a 24-h period</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 7</td>
<td>41.4</td>
<td>6.36</td>
<td>(4.74, 8.52)</td>
</tr>
<tr>
<td>≥ 7</td>
<td>9.4</td>
<td>1.00</td>
<td>Ref</td>
</tr>
</tbody>
</table>

BRFSS, Behavioral Risk Factor Surveillance System. CI, confidence interval. *Adjusted for age and gender unless otherwise specified. fAdjusted for gender. Adjusted for age. fNever smokers were defined as those who had smoked < 100 cigarettes in lifetime. gBinge drinking was defined as ≥ 5 or ≥ 4 alcoholic drinks for men and women, respectively, on one occasion in past 30 days. Optional module that included this question was used in six states only (Georgia, Hawaii, Illinois, Louisiana, Minnesota, and Wyoming).
REFERENCES


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DISCLOSURE STATEMENT

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Total Sleep Time and Other Sleep Characteristics Measured by Actigraphy Do Not Predict Incident Hypertension in a Cohort of Community-Dwelling Older Men

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Study Objective: To evaluate whether actigraphy-measured total sleep time and other sleep characteristics predict incident hypertension in older men.

Methods: Study subjects were community-dwelling participants in the ancillary sleep study of the Osteoporotic Fractures in Men Study (MrOS) who were normotensive at the time of actigraphy (based on self-report, lack of antihypertensive medication use, and with systolic blood pressure < 140 mm Hg and diastolic blood pressure < 90 mm Hg). In 853 community-dwelling men 67 years and older (mean 75.1 years), sleep measures (total sleep time [TST], percent sleep [%-sleep], latency, and wake after sleep onset [WASO]) were obtained using validated wrist actigraphy with data collected over a mean duration of 5.2 consecutive 24-h periods. We evaluated incident hypertension (based on self-report, use of antihypertensive medication, or measured systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg) at a follow-up visit an average of 3.4 years later. Baseline prehypertension was defined as a systolic blood pressure 120 to < 140 mm Hg or diastolic blood pressure 80 to < 90 mm Hg.

Results: At follow-up, 31% of initially normotensive men were hypertensive (264 of 853). Those with incident hypertension had higher baseline body mass index (BMI; kg/m²) and were more likely to have had prehypertension at the sleep visit than those who remained normotensive. However, neither TST (reference 6 to < 8 h; < 6 h OR 0.96 [95% CI 0.7, 1.3] and ≥ 8 h OR 0.93 [0.5, 1.7]) nor the other actigraphic-measured sleep variables, including %-sleep (reference > 85%; < 70% OR 1.17 [0.66, 2.08]) and 70% to ≤ 85% OR 1.23 (0.9, 1.68), sleep latency (reference < 30 min; ≥ 30 min OR 1.29 [0.94, 1.76]), or WASO (reference < 30 min; 30 to < 60 min OR 0.7 [0.43, 1.14] and ≥ 60 min OR 0.92 [0.58, 1.47]) differed in those community-dwelling men who developed incident hypertension compared to those who remained normotensive.

Conclusion: TST and other sleep parameters determined by wrist actigraphy were not associated with incident hypertension in community-dwelling older men.

Keywords: Actigraphy, total sleep time, percent sleep, sleep latency, hypertension, older men

Citation: Fung MM; Peters K; Ancoli-Israel S; Redline S; Stone KL; Barrett-Connor E. Total sleep time and other sleep characteristics measured by actigraphy do not predict incident hypertension in a cohort of community-dwelling older men. J Clin Sleep Med 2013;9(6):585-591.

BRIEF SUMMARY

Current Knowledge/Study Rationale: Studies have shown an inconsistent association between total sleep time and hypertension. This prospective study was performed to evaluate this relationship using actigraphy measured sleep variables in community-dwelling older men.

Study Impact: This study indicates that short sleep time and other indicators of poor sleep were not associated with incident hypertension in older men, which is consistent with other studies of older subjects. The effect of reduced sleep may have a greater effect in the development of hypertension in younger individuals.

Short sleep duration has been associated with cardiovascular disease and mortality.4,5 As these studies were entirely observational, cause and effect remain unclear, particularly because the majority of the studies are cross-sectional. Previous studies have also not clarified whether there are potential modifiers of the relationship between sleep and cardiovascular disease that could assist in better delineating the relationship, such as hypertension (HTN).

Studies evaluating HTN as a potential mediator of such cardiovascular morbidity have revealed mixed results.5,6 Study designs have varied widely, often relying on self-reports and questionnaires, and have primarily been cross-sectional in design. Most of the studies that previously revealed an association between shorter sleep durations and HTN were in young populations; in subgroup analyses, the association was not observed in older groups7-9 nor seen in men.10 The relationship between sleep and HTN may be particularly difficult to evaluate in older individuals, given their higher risk for HTN and the high incidence of sleep disorders. Common sleep disorders in older individuals, which may shorten their sleep duration and quality, include insomnia and frequent awakenings, due in part...
to their medications and comorbid conditions, such as urinary frequency and difficulty breathing. However, evaluation of this relationship is important, given that treatment and interventions are available for both sleep disorders and for HTN which could have significant impact in the older populations.

Total sleep time (TST) has been studied extensively, although less commonly in older individuals, but other objective measures of sleep quality, such as sleep latency or percent sleep (%-sleep), have not been commonly investigated to determine whether they are associated with incident HTN. Here, we report TST and these other secondary sleep characteristics using actigraphy obtained objective sleep data to determine whether TST and other characteristics of poor sleep would predict incident HTN in older community-dwelling men. Demonstrating a role for actigraphy in predicting HTN development could have clinical utility since actigraphy is noninvasive and relatively readily available.

METHODS

Study Subjects

Study subjects were participants in the Osteoporotic Fractures in Men Study (MrOS), a cohort of community-dwelling men described previously. Of 5,994 MrOs men, 3,135 (53.3%) participated in the ancillary Outcomes of Sleep Disorders in Older Men Study (MrOS Sleep Study) between 2003 and 2005. Of the original cohort, 2,859 participants did not participate in the sleep study because they were unwilling (N = 1,997), not screened because recruitment goals were met (N = 332), died before the sleep study visit (N = 344), ineligible due to exclusion criteria such as use of mechanical devices during sleep (including positive airway pressure devices, oral appliances for snoring or sleep apnea, or oxygen therapy; N = 150), or quit the MrOS study before the sleep study was offered (N = 36). Of the 3,135 sleep-study enrolled participants, 2,753 had valid actigraphy and follow-up data.

Among these 2,753 older men, 1,860 (67.6%) had a history of HTN, were taking anti-hypertensive medications, or had an elevated systolic blood pressure (SBP) ≥ 140 mm Hg, or diastolic blood pressure (DBP) ≥ 90 mm Hg at baseline and were excluded from the current study of incident HTN; furthermore, 39 participants had missing HTN data at either baseline or follow-up and were also excluded; 1 participant was missing actigraphy measures at baseline, leaving 853 normotensive participants for this analysis. The mean follow-up time was 3.4 (SD 0.46) years.

All protocols were approved by the institutional review boards at the respective enrollment sites, and participants signed informed consent to participate in each visit of the MrOS Sleep Study.

Classification and Measurement of Hypertension (HTN)

At both the baseline and the follow-up visits, HTN was defined as self-reported (“Have you ever had high blood pressure?”), current use of at least one antihypertensive medication, SBP ≥ 140 mm Hg, or DBP ≥ 90 mm Hg. Prehypertension was classified as a SBP 120 to < 140 mm Hg or DBP 80 to < 90 mm Hg. Seated blood pressures were measured in the same manner at each visit. A mercury sphygmomanometer was used at baseline, but a BP Tru automated blood pressure monitor (model BMP-300; Coquitlam, British Columbia, Canada) was used at follow-up, due to prohibition of mercury sphygmomanometers for safety reasons. The BP Tru device, which is commonly used in clinical trials for HTN, has been compared to manual mercury readings and was shown to have high quality and accuracy. Baseline blood pressure was measured at a clinic visit an average of 1.7 (SD 11.1) days before the start of the actigraphy recordings.

Other Measures

Self-administered questionnaires were used at the time of the sleep study to ascertain demographic and lifestyle information and personal and family medical history, including HTN, self-reported diabetes, and cardiovascular disease (history of myocardial infarction, angina, congestive heart failure, coronary bypass surgery, transient ischemic attack, stroke, or rheumatic heart disease). Race/ethnicity was self-reported using a questionnaire with a choice of 5 categories (Caucasian/White, African American/Black, Asian, Hispanic, and Other). Interviews or examinations by trained study staff members included measures of functional status and anthropometric data. Physical activity was assessed using the physical activity scale for the elderly (PASE). Depressed mood was assessed using the Geriatric Depression Scale (GDS), a 15-point scale of yes/no questions; a standard cutpoint ≥ 6 was used to define depression. Participants also reported tobacco use (current, past, or never) and alcohol use (drinks per week). Participants were asked to bring in all prescription and nonprescription medications used within the preceding 30 days, which were entered into an electronic database; 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). Participants were asked whether each medication was used for sleep, and if so, the subject was considered to have “Use of Sleep Medication.” Height (cm) was measured on regularly calibrated Harpenden stadiometers and weight (kg) on calibrated standard balance beam or digital scales. Body mass index (BMI) was calculated as kg/m². Waist, hip, and neck circumferences were measured using a tape measure and standard techniques.

Sleep Duration and Fragmentation

Objective sleep characteristics, including TST, %-sleep (an estimate of sleep efficiency, the % of the sleep period spent asleep), sleep latency, and wake after sleep onset (WASO), were determined by wrist actigraphy (Sleepwatch-O, Ambulatory Monitoring, Inc., Ardsley NY), which measures acceleration using a piezoelectric biomorph-ceramic cantilevered beam and that generates a voltage each time the actigraph is moved. Participants were asked to wear the actigraph on their non-dominant wrist continuously, to be removed only when bathing or doing water sports. Data were averaged over the entire recording period. Data were collected continuously and stored in 1-min epochs. The digital integration mode of data collection, which sums the absolute level of acceleration on a second-by-second basis over each 1-min epoch, was used to quantify the amount of movement in each minute. The University of Cali-
Table 1—Demographic characteristics of the study cohort: overall and by follow-up hypertension (HTN) status.

<table>
<thead>
<tr>
<th>Characteristic, mean (SD)</th>
<th>Overall (N = 853)</th>
<th>Incident HTN (N = 264)</th>
<th>No incident HTN (N = 589)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>75.1 (4.8)</td>
<td>75.6 (5)</td>
<td>74.9 (4.8)</td>
<td>0.07</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.4 (3.5)</td>
<td>26.9 (3.9)</td>
<td>26.2 (3.2)</td>
<td>0.02</td>
</tr>
<tr>
<td>Neck circumference (cm)</td>
<td>39 (2.7)</td>
<td>39.2 (2.9)</td>
<td>38.9 (2.6)</td>
<td>0.15</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>97.4 (10.1)</td>
<td>98.5 (10.8)</td>
<td>96.9 (9.7)</td>
<td>0.04</td>
</tr>
<tr>
<td>Hip circumference (cm)</td>
<td>101.9 (8.3)</td>
<td>102.3 (8.8)</td>
<td>101.7 (8.3)</td>
<td>0.36</td>
</tr>
<tr>
<td>PASE score</td>
<td>160.3 (70.8)</td>
<td>158.7 (72.3)</td>
<td>161.0 (70.2)</td>
<td>0.66</td>
</tr>
<tr>
<td>GDS Score</td>
<td>1.4 (1.9)</td>
<td>1.6 (1.8)</td>
<td>1.3 (2.0)</td>
<td>0.10</td>
</tr>
<tr>
<td>Baseline SBP</td>
<td>120.9 (10.6)</td>
<td>125.2 (9.6)</td>
<td>119 (10.4)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Baseline DBP</td>
<td>67.3 (7.9)</td>
<td>68.8 (7.6)</td>
<td>66.7 (8)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Percentages, N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Caucasian race</td>
<td>78 (9.1)</td>
<td>23 (8.7)</td>
<td>55 (9.3)</td>
<td>0.77</td>
</tr>
<tr>
<td>Education: High school or less</td>
<td>136 (15.9)</td>
<td>52 (19.7)</td>
<td>84 (14.3)</td>
<td>0.032</td>
</tr>
<tr>
<td>Some college/college degree</td>
<td>374 (43.8)</td>
<td>121 (45.8)</td>
<td>253 (43.0)</td>
<td></td>
</tr>
<tr>
<td>Some graduate school/graduate degree</td>
<td>344 (40.2)</td>
<td>91 (34.5)</td>
<td>252 (42.8)</td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>24 (2.8)</td>
<td>5 (1.9)</td>
<td>19 (3.2)</td>
<td>0.28</td>
</tr>
<tr>
<td>Has ≥ 1 alcoholic drink/week</td>
<td>472 (55.7)</td>
<td>144 (55.2)</td>
<td>328 (55.9)</td>
<td>0.85</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>50 (5.9)</td>
<td>20 (7.6)</td>
<td>30 (5.1)</td>
<td>0.15</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>172 (20.2)</td>
<td>70 (26.7)</td>
<td>102 (17.3)</td>
<td>0.0016</td>
</tr>
<tr>
<td>GDS Score ≥ 6</td>
<td>35 (4.1)</td>
<td>8 (3)</td>
<td>27 (4.6)</td>
<td>0.003</td>
</tr>
<tr>
<td>Prehypertensive</td>
<td>518 (60.7)</td>
<td>205 (77.7)</td>
<td>313 (53.1)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Use of sleep medications</td>
<td>85 (10)</td>
<td>23 (8.7)</td>
<td>62 (10.5)</td>
<td>0.41</td>
</tr>
</tbody>
</table>

BMI, body mass index; PASE, physical activity score in the elderly; SBP, systolic blood pressure; DBP, diastolic blood pressure; GDS, geriatric depression scale. p value compares those with and without incident hypertension. Bold p values indicate statistical significance.

While wearing the actigraph, participants completed sleep diaries that included time into and time out of bed and times the actigraph was removed. This information was used in editing the actigraphy data files to set intervals for when the participant was sleeping between from sleep onset to the last minute scored as sleep while in bed. This technique for estimating sleep duration has been validated against polysomnography in this cohort.

TST was determined as the number of minutes asleep in bed after “lights off,” considering only nighttime sleep. Percent sleep (%-sleep), was determined by the percentage of time (0-100) the participant was sleeping between from sleep onset to the last minute scored as sleep while in bed. Sleep latency was the minutes from the time the participant got into bed (based on the sleep diary) to sleep onset, and WASO was the number of minutes scored as wake from sleep onset to the last minute scored as sleep while in bed.

Statistical Analyses
First, the actigraphic sleep variables (primarily TST, followed by %-sleep, sleep latency, and WASO) were evaluated as the predictors. Descriptive and inferential statistics were performed using SAS version 9.2 (SAS Institute, Inc., Cary, NC). Variables potentially related to the actigraphic variables and/or incident HTN were summarized using means and standard deviations for continuous variables and percentages for categorical variables. Potential covariates were identified a priori. ANOVA, Kruskal-Wallis, and χ² tests tested the covariates for association with the sleep characteristics and incident HTN for normal continuous, skewed continuous, and categorical variables, respectively. All predictor variables that were significantly associated with incident HTN and at least one of the sleep variables, with the exception of history of cardiovascular disease, at p < 0.10 in both tests were included in the multivariable model in order to maintain the same straightforward model. BMI, waist circumference, baseline blood pressure, and education level were associated with our primary predictor, TST. Baseline age, categorization of prehypertension, and global depression score (GDS) were included based on their strong association with HTN. The list of preselected potential covariates considered is shown in Table 1. Pearson corre-
lationship coefficients were assessed for correlation between the sleep characteristics.

The actigraphic exposure variables were expressed as clinically determined ranges (for TST < 6, 6 to < 8, ≥ 8 h; for %-sleep < 70%, 70% to 85%, ≥ 85%; for sleep latency < 30 min, ≥ 30 min; and for WASO < 30, 30 to < 60, and ≥ 60 min) and by quartiles. Logistic regression modeling with incident HTN as the outcome was performed using indicator variables for the clinically determined ranges and for each quartile, using the most optimal sleep category as the reference group. Models were first constructed accounting only for age and non-Caucasian race. Then BMI, mean DBP, education level, prehypertensive, waist circumference, the 15-point GDS, and history of cardiovascular disease were added.

Power was estimated using SAS proc power. More than 99% power was present to detect an odds ratio (OR) > 1.33 given our sample size of ~850 men, assuming an α of 0.025 and the power was present to detect an odds ratio (OR) > 1.33 given our sample size of ~850 men, assuming an α of 0.025 and the proportion exposed was 31%. Under these assumptions, this study has 80% power to detect an OR > 1.23.

RESULTS

Baseline Characteristics

The 853 normotensive men at baseline had a mean age of 75.1 (SD 4.8) years and mean BMI of 26.4 (3.5); 90.9% were Caucasian. Baseline characteristics are shown in Table 1.

The participants wore the actigraph for an average of 5.2 ± 0.9 nights. As shown in Table 2, participants had a mean TST of 389 min (69.5) or 6.5 h (1.2) and a mean sleep latency of 28.7 min (29.2) at baseline. Mean WASO was 70.7 min (39.8) with a mean %-sleep of 84.1% (9.6%). These sleep characteristics were highly correlated, particularly %-sleep with both WASO (r = -0.94, p < 0.001) and TST (r = 0.72, p < 0.001). Only 6.2% of the participants (N = 53) had an average TST ≥ 8 h; 64.5% slept 6 to < 8 h (N = 550); and 29.3% had an average < 6 h (N = 250). There were no differences in baseline age, SBP, DBP, race, or use of sleep medications between these common categories of TST. However, BMI, neck circumference, and waist circumference were the highest in the < 6 h TST group (p < 0.001 for all). Those in the < 6 h TST group had the lowest amount of %-sleep, the longest sleep latency, and the highest WASO (p < 0.001 for all).

Overall, 7.2% of the men had %-sleep < 70% (N = 61), 36.1% between 70% and < 85% (N = 308), and 56.7% ≥ 85% (N = 484). Lower %-sleep was associated with higher BMI, neck circumference, and waist circumferences (p < 0.001 for all). Those with < 70% sleep were most likely to be Caucasian (p = 0.013) and smokers (p = 0.030). Lower %-sleep was associated with shorter TST and greater sleep latency and WASO (p < 0.001 for all).

Of the entire sample, 29.1% had ≥ 30 min sleep latency (N = 248). Compared to those with < 30 min sleep latency, those with ≥ 30 min had higher BMI, neck circumference, and waist circumference (all p < 0.001). Smokers and prehypertensive men were also more likely to have sleep latency ≥ 30 min (p = 0.022 and p = 0.026, respectively). Similarly, those with ≥ 60 min of WASO (N = 452; 53.0%) had greater BMI (p = 0.004), and neck (p = 0.0053) and waist circumference (p = 0.0068) than those with < 30 (N = 96; 11.3%) or 30 to < 60 min (N = 305; 35.8%).

Similar trends were noted when evaluating TST, %-sleep, sleep latency, and WASO by quartile (data not shown).

Incident Hypertension and Actigraphic Sleep Variables

At a mean of 3.4 (0.46) years follow-up, 264 men (31%) had developed incident HTN. Those with incident HTN had a greater baseline BMI (26.9 versus 26.2, p = 0.019), and were more likely to report cardiovascular disease (26.7% versus 17.3%, p = 0.0016). However, as shown in Table 2, incident HTN was not associated with the primary predictor TST, nor with the other sleep variables %-sleep, sleep latency, or WASO. Logistic regression by clinically determined ranges, shown in Figure 1, or by quartiles (data not shown), was not associated with incident HTN when adjusted for age and non-Caucasian race. Additional models, which included covariates that were associated with the sleep characteristics and/or incident HTN at a statistical level of p < 0.10, such as the Geriatric Depression Score, baseline blood pressures, BMI, education level, and history of cardiovascular disease failed to show any significant associations between these sleep variables and incident HTN.

DISCUSSION

In this study, we did not find any association between the actigraphically defined measure of TST, nor the secondary predictors of poor quality sleep including %-sleep, latency, or WASO with HTN in community-dwelling older men. To our knowledge, this is the first prospective study evaluating the association between sleep and blood pressure using objectively measured estimates of both sleep duration and quality together in older men.

Both cross-sectional and prospective studies have assessed the relationship between sleep and HTN, but in different popu-
lations and with varying study designs and measurements of sleep. Cross-sectional study results, looking over a number of age ranges, have revealed inconsistent results. The Sleep Heart Health Study (of participants aged 40-100 years, with mean 63.1 years) reported that sleep above or below the mean of 7-8 hours per night determined by polysomnography was cross-sectionally associated with an increased prevalence of HTN. However, the Rotterdam study (participants aged 58-98 years) failed to detect such an association, which was also confirmed in a subset of the participants who had actigraphy-validated sleep times. One study reported an association with HTN only in subjects < 65 years of age; another used polysomnographic (PSG) data and noted that short sleep duration was associated with HTN only when accompanied with a sleep complaint of insomnia or poor quality. A small study of healthy adolescents found an association of actigraphy-measured sleep time and prehypertension.

Prospective studies of younger subjects have generally shown more consistent associations between total sleep duration and incident HTN, whereas studies of older adults, particularly with male patients, more comparable to this one, generally have not reported such associations. The Coronary Artery Risk Development in Young Adults (CARDIA) Study, which included 41% African Americans, reported that actigraphic-measured sleep duration was associated with HTN 5 years later in participants aged 33-45 years, though the association was attenuated with covariate adjustment. In NHANES after 8-10 years of follow-up, self-reported sleep time was associated with incident HTN; however, subgroup analysis using age-defined strata showed no association with short sleep duration among individuals aged 60-85 years, although an association with long sleep (> 9 h duration) was observed. The 5-year prospective Whitehall II study reported that women with a self-reported sleep duration < 5 hours were most likely to have HTN, with some attenuation of the association after accounting for cardiovascular risk factors and psychiatric comorbidities; no association was observed in men. Lastly, a Spanish study of older men (mean age 71.8 years), most similar to the cohort studied in this report, reported no relationship between prevalent or incident HTN and self-reported sleep duration.

Differences between these previous studies and this current report may be partially explained by the prevalence of HTN in older men. In our cohort, 67.6% of those with valid actigraphy data were already hypertensive at baseline and excluded from this analysis of incident HTN. With many potential contributors to blood pressure, including molecular mechanisms which may be specific to older individuals such as telomeres shortening, progenitor cells, circulating microparticles, and epigenetic factors, sleep characteristics may only play a minor role in the development of HTN in older men.

The increased risk of HTN in short sleep duration may be at least partially attributable to neurohormonal changes, which may be more apparent in younger populations where stronger associations have previously been noted and less so in older populations such as ours. Older individuals may have decreased production or desensitization to neurohormones. Also, men who tend to have less overall fat mass than women, may have lower production of neurohormones such as leptin which is produced in adipose tissue.

<table>
<thead>
<tr>
<th>Total sleep time</th>
<th>&lt; 6 h</th>
<th>6 - &lt; 8 h</th>
<th>≥ 8 h</th>
<th>≤ 60 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>WASO</td>
<td>≥ 60 min</td>
<td>30 - ≤ 60 min</td>
<td>≤ 30 min</td>
<td>Ref</td>
</tr>
<tr>
<td>Percent sleep</td>
<td>≥ 85%</td>
<td>&lt; 85%</td>
<td>≤ 30%</td>
<td>Ref</td>
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<tr>
<td>Sleep latency</td>
<td>≥ 30 min</td>
<td>&lt; 30 min</td>
<td>≤ 20 min</td>
<td>Ref</td>
</tr>
<tr>
<td>Sleep efficiency</td>
<td>≥ 85%</td>
<td>&lt; 85%</td>
<td>≤ 30%</td>
<td>Ref</td>
</tr>
</tbody>
</table>

Figure 1—Adjusted odds ratios of incident hypertension (HTN) in the actigraph measured sleep variables by clinical categories

Short TST, low % sleep, high sleep latency, and high WASO were all associated with higher BMI in this study. The relationship between total sleep duration and BMI in both cross-sectional studies, including this MrOs cohort of older men and in prospective studies, has been demonstrated repeatedly, such that short sleep duration (< 5 h) is associated with increased obesity. Studies have suggested that short sleep time may affect neurohormonal pathways, such as in leptin and ghrelin, leading to metabolic and endocrinologic changes that increase the risk of diabetes and obesity.

Prior work using PSG in the MrOs sleep cohort has shown that decreased time spent in slow wave sleep (stage N3 sleep) was associated with incident HTN, but not total sleep duration. These findings suggest that time in specific neurophysiological states (such as those associated with different levels of sympathetic activity) may influence the development of future HTN. If it is confirmed that it is the time in such neurophysiological states that influences the development of future HTN, then actigraphy may not be sensitive enough to detect these changes, thus explaining the lack of the association between indices of sleep and wake duration seen in this study.

Few studies have evaluated sleep efficiency or latency or WASO as measures of sleep quality and fragmentation and their association with blood pressure; these studies have all been of cross-sectional design. While our study examined % sleep rather than sleep efficiency (the ratio of time spent asleep to total sleep time) to the amount of time spent in bed), we would have expected the results to be similar. Reduced sleep efficiency has been associated with HTN and prehypertension prevalence as well as resistant HTN. Self-reported sleep latency has been associated with blood pressure and antihypertensive medication usage in postmenopausal women.
Previous studies of TST have relied predominantly on self-reported sleep time and did not assess whether other measures of sleep quality or continuity were associated with HTN. Subjective reports have been shown to be moderately correlated with objective measures, though differences may exist for a number of reasons. In older individuals, particularly, misperceptions of sleep quality may occur associated with chronicity of problems. The strengths of this study include the use of an objective and validated tool for assessing sleep and characterizing sleep latency and fragmentation.20,42,43 Advantages of using the actigraph over PSG is that it can be used for longer periods of time and is averaged over a number of nights of sleep as opposed to only one night of the more disruptive and expensive PSG.

Limitations of this study include its potential limited generalizability to other groups, including women and non-Caucasian men. Participants in cohort studies tend to be healthier and more educated than the general population and only those who survived to the follow-up visit were included in the analysis. Also, by focusing on incident cases, it is possible that those men most susceptible to sleep-associated HTN were excluded with the exclusion of prevalent HTN cases. Only nighttime sleep, not including daytime napping, was considered in this analysis of TST. We evaluated sleep efficiency as the percent time sleeping rather than the more-often-used definition of percent time asleep in a given duration. We also did not employ 24-hour blood pressure monitoring to better define HTN and its diurnal patterns. Diagnosis of HTN in 24% of subjects with incident HTN was based on only one clinic visit, though was made using an average of two blood pressure measurements. Lastly, an additional limitation to this cohort study was the power. Our sample size allowed only 80% power to detect an OR > 1.2 (effect size of approximately 20% or greater) between TST and incident HTN.

In conclusion, this study demonstrated that short TST was cross-sectionally associated with higher BMI but was not associated with incident HTN in older men, despite known associations with cardiovascular disease and mortality. Similarly, the other sleep predictors of poor quality sleep including low %-sleep at night, long sleep latency, and high WASO showed consistent results, but upon close examination, studies of older men were less likely to demonstrate an association with either prevalent or incident HTN. This may be attributed to the high prevalence of HTN in older men and the many pathophysiologic contributors that may operate over many years to influence vascular tone and responses. Reduced sleep duration may have a larger effect on the development of HTN in younger individuals, before the development of arteriosclerosis or significant vascular remodeling.

REFERENCES

Total Sleep Time Does Not Predict Incident Hypertension

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This was not an industry supported study. Dr. Fung has received funding from Forest Laboratories, and currently works and owns stock at Amgen. Dr. Ancoli-Israel has served as a consultant or serves on the scientific advisory board from Astra Zeneca, Ferring Pharmaceuticals, Inc., GlaxoSmithKline, Hynocore, Johnson & Johnson, Merck, NeuroVigil, Inc., Pfizer, Purdue Pharma LP, and Sanofi-Aventis. Dr. Barrett-Conner has received grant support and/or consulting fees from the NIH, the NIA, and the NCCR, Merck, and Roche. Dr. Redline has received equipment from Philips-Respironics and ResMed Inc. and received a grant from ResMed Inc. The other authors have indicated no financial conflicts of interest.
Diopathic pulmonary fibrosis (IPF) is a chronic progressive fibrosing interstitial pneumonia of unknown cause associated with the histopathologic and/or radiologic pattern of usual interstitial pneumonia (UIP). The disease is always lethal, and its natural history is characterized by either rapid or slow deterioration of respiratory function, often accelerated by the unpredictable development of acute exacerbations. Pharmacologic therapy is lacking, and all patients will die from respiratory failure or complicating comorbidities such as coronary vascular disease, pulmonary hypertension, gas troesophageal reflux disease (GERD), and obstructive sleep apnea (OSA).

Obstructive sleep apnea and more generally, sleep breathing disorders (SBDs) that include increased sleep fragmentation, decreased slow wave and REM sleep, as well as sleep oxygen desaturation characterizing poor sleep quality, are frequent in IPF. Poor sleep quality has been shown to further influence quality of life in IPF patients who already suffer from an impaired quality of life due to low energy levels, fatigue, and exertional dyspnea. The latter, is the most prominent and disabling symptom in IPF and is attributed to several factors including deranged lung mechanics, gas exchange abnormalities, pulmonary vascular disease, myocardial dysfunction, and peripheral muscle weakness. Moreover, exertional dyspnea and oxygen desaturation during exercise are parameters that negatively influence the outcome in IPF.

Sleep Oxygen Desaturation Predicts Survival in Idiopathic Pulmonary Fibrosis

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Background: Recent studies suggest poor sleep quality in patients with idiopathic pulmonary fibrosis (IPF). However, so far, the impact of IPF-related sleep breathing disorders (SBDs) on survival has not been extensively studied.

Methods: In a cohort of 31 (24 males) treatment-naïve, newly diagnosed consecutive IPF patients, we prospectively investigated the relationship of SBD parameters such as apnea-hypopnea index (AHI), maximal exercise saturation between wakefulness and sleep (maxdiff SpO2), and lowest oxygen saturation (lowest SpO2) with clinical (survival, dyspnea, daytime sleepiness), pulmonary function, submaximal and maximal exercise variables (6MWT) and maximal exercise variables (cardiopulmonary exercise test [CPET]), and right ventricular systolic pressure (RVSP).

Results: Sleep oxygen desaturation exceeded significantly that of maximal exercise (p < 0.001). Maxdiff SpO2 was inversely related to survival, DLCO%, and SpO2 after 6MWT, and directly with dyspnea, AHI, and RVSP. The lowest SpO2 was directly related to survival and to functional (TLC%, DLCO%) as well as submaximal and maximal exercise variables (6MWT).

Conclusions: Sleep oxygen desaturation significantly exceeds that of maximal exercise and is associated with survival in IPF patients. Furthermore, they imply the existence of a link between lung damage and apnea events resulting to the induction and severity of intermittent sleep oxygen desaturation that aggravate pulmonary arterial hypertension and influence IPF survival.

Citation: Kolilekas L; Manali E; Vlami KA; Lyberopoulos P; Triantaffilidou C; Kagouridis K; Baou K; Gyftopoulos S; Vougas KN; Karakatsani A; Alchanatis M; Papiris S. Sleep oxygen desaturation predicts survival in idiopathic pulmonary fibrosis. J Clin Sleep Med 2013;9(6):593-601.
In the present study we hypothesized that sleep oxygen desaturation and eventually OSA or their physiological consequences also have a negative impact on IPF survival. To examine this hypothesis we prospectively investigated the relationship of several SBD parameters with clinical and pulmonary function variables as well as with right ventricular systolic pressure (RVSP).

METHODS

Subjects
We prospectively recruited 31 consecutive patients referred to our department’s Outpatient Interstitial Lung Disease Unit over a period of one year. Written informed consent was obtained from each patient. All patients fulfilled the criteria of both previous and—as retrospectively evaluated—new guidelines of the American Thoracic Society, European Respiratory Society and the American College of Chest Physicians for the diagnosis of IPF.1 Of 31 patients, only 6 were diagnosed using lung biopsy; the other 25 were diagnosed by fulfilling typical clinico-radiographic criteria. Secondary causes of lung fibrosis were excluded based on history, absence of relevant occupational or environmental exposures, clinical examination, and serology tests. The study was approved by the Medical Ethics Committee of Attikon University Hospital, National and Kapodistrian University of Athens, Greece. Written informed consent was obtained from each subject.

Dyspnea
Chronic exertional dyspnea was assessed at presentation by the responsible physicians (LK, EM) using the modified Medical Research Council (mMRC) chronic dyspnea self-administered questionnaire consisting of 6 questions about perceived breathlessness.6

Pulmonary Functional Tests (PFTs)
PFTs were performed either at diagnosis or after a short interval not exceeding 10-15 days from the 6MWT and the CPET. Specifically, forced expiratory volume at the first second (FEV1), forced vital capacity (FVC), total lung capacity (TLC), and single-breath carbon monoxide diffusing capacity (DLCO) were assessed by MasterScreen apparatus (Erich Jaeger GmbH, Wurzburg, Germany). The following parameters were recorded: heart rate (HR), minute ventilation, tidal volume (TV), peak oxygen consumption (VO2 peak), peak oxygen consumption/kg (VO2 peak/kg), %VO2 predicted, minute ventilation-carbon dioxide production relationship (VE/VCO2 slope), VE/VCO2 slope at anaerobic threshold, respiratory rate (RR), total ventilation (VE), oxygen pulse (O2P), oxygen saturation at peak exercise (SpO2 peak), anaerobic threshold (AT), breathing reserve (BR), heart rate recovery (HRR), and heart rate reserve (HRRs).

Polysomnography
All participants underwent full-night polysomnography (PSG) according to standard techniques, including sleep staging by monitoring of central and occipital channels of electroencephalogram (C4-A1,C3-A2,O1-A2,O2-A1), electrooculogram and electromyograms (submental and anterior tibialis). Airflow was monitored by combined thermistor and nasal pressure transducer signals. Electrocardiogram and heart rate were monitored using the standard limb leads. Respiratory efforts were monitored with piezoelectric transducers placed around the chest and the abdomen. Arterial oxygen saturation (SpO2) was measured continuously by pulse oximetry using a finger probe. Body position was assessed with a body position sensor. All variables were recorded by a computerized system (Alice 5, Philips Respironics, USA). Manual scoring was done in all cases, according to the American Academy of Sleep Medicine recommendations.10,11 Apnea was defined as the reduction in airflow ≥ 90% of baseline, lasting ≥ 10s. It was classified as an obstructive apnea when associated with the presence of an inspiratory effort, as central apnea in the absence of an inspiratory effort, or as mixed apnea if inspiratory effort was absent in the initial part of the event and present at the final part. Hypopnea was defined as the reduction in baseline airflow or in thoracoabdominal movement ≥ 30% with ≥ 4% desaturation, lasting ≥ 10s. The apnea-hypopnea index (AHI) was calculated as the number of apnea and hypopnea events per hour of sleep. All PSGs were scored by the registered sleep technologist of our laboratory (SG) and reviewed by the responsible authors (LK, KAV).

Journal of Clinical Sleep Medicine, Vol. 9, No. 6, 2013
CPAP titration was done manually under the surveillance of a technician. Based on the monitoring of oxygen saturation during sleep the following parameters were furthermore calculated for each patient:

1. The maximal difference in oxygen saturation between wakefulness and sleep (maxdiff-SpO2) evaluated as stated in previous publications.12,13
2. The lowest sleep oxygen saturation (lowest SpO2)

**Questionnaires**

All patients completed the Epworth Sleepiness Scale (ESS) before performing PSG.14

**Echocardiography**

Trans-thoracic echocardiography was performed in all patients. Right atrial pressure was estimated on the basis of the inferior vena cava size and movement on respiration. The simplified Bernoulli equation was used to calculate right ventricular systolic pressure (RVSP).15 An RVSP value < 35 mm Hg was considered normal.16

**Survival**

During the time of data acquisition of the present study, 10 of 31 patients succumbed to IPF. All deaths were attributable to the disease, as verified by the death certificates. Finally, 21 of the 31 patients who were still alive at the reporting of this work were censored for survival analysis.

**Statistical Analysis**

Data are presented either as mean ± standard deviation (± SD) or as median with interquartile range. The Mann-Whitney test is used for 2-group comparison. The Pearson and Spearman correlation coefficients were both utilized to describe the relationships between variables, since the first one shows a strong bias towards linear relationships while the other one presents a more generic behavior towards any relationship. Having calculated both coefficients, we can distinguish the relationships tending to be linear from the non-linear ones. The factors of the current study were individually evaluated for relevance to the overall survival through Cox proportional hazards models. More specifically, each of these models were evaluated by 3 independent and asymptotically equivalent tests, the Wald test, the Likelihood ratio test and the Score (logrank) test, each calculating a p-value for the null hypothesis that the factor coefficients are equal to zero. A mean p-value was calculated by averaging the p-values of the aforementioned tests, and this was used as the final criterion for the determination of relevance to the overall survival. Lowest SpO2 during sleep and SpO2 peak during CPET were checked for normality with the Kolmogorov-Smirnov test of normality, and having been found normally distributed, they were compared for difference in their mean values with the paired t-test.

All statistical analysis was carried out using R and SPSS. A cox proportional hazard modelling was performed utilizing the ‘Survival’ R-package. The nonparametric Spearman correlation coefficient was calculated by using SPSS v.13.0.0 (Chicago, IL). A p-value ≤ 0.05 was considered significant.17

### RESULTS

**Epidemiological, Functional, Exercise Capacity, and Sleep Characteristics of the Study Group**

Thirty one patients (77.4 % male) with a mean age (SD) of 68 (7.88) years and body mass index (BMI) of 28.66 (± 4.3) were studied and followed-up for a mean time of 495.39 (266.07) days and a median time of 530 days. Seven patients (22.6%) had moderate to severe dyspnea, with MRC scores of 3 and 4. Smoking habits and further anthropometric and clinical data of the study group are shown in Table 1. More than two-thirds of patients presented with GERD; all of them received specific treatment after enrollment. Patients walked during the 6MWT a mean distance of 375.60 (159.07) m or 58.9% (24.26%) of predicted distance and desaturated at a minimum SpO2 of 89.6% (6.05%).

| Table 1—Demographic, anthropometric, and clinical data of the study population |
|-------------------------------|-------------------|
| Variables (n)                  | Values            |
| Age, years (31 pts)            | 67.96 (± 7.88)    |
| Sex (M/F)                      | 24/7              |
| BMI (kg/m²)                    | 28.66 (± 4.3)     |
| Neck circumference, cm (30 pts)| 40.25 (± 4.19)    |
| Smoking history                |                   |
| Ex-smokers                     | 18 (58.1)         |
| Nonsmokers                     | 12 (38.7)         |
| Current smokers                | 1 (3.2)           |
| MRC chronic dyspnea score      |                   |
| 0.0                            | 2 (6.5)           |
| 1.0                            | 9 (29)            |
| 2.0                            | 13 (41.9)         |
| 3.0                            | 5 (16.1)          |
| 4.0                            | 2 (6.5)           |
| GERD                           |                   |
| No                             | 6 (19.3)          |
| Yes                            | 25 (80.7)         |
| AHI                            |                   |
| < 5                            | 3 (9.7)           |
| 5-15                           | 12 (38.7)         |
| > 15                           | 16 (51.6)         |
| Epworth Sleepiness Scale       |                   |
| Score < 10                     | 22 (78.6)         |
| Score > 10                     | 6 (21.4)          |
| RVSP (N = 31)                  |                   |
| < 35 mm Hg                     | 15 (48.4)         |
| ≥ 35 mm Hg                     | 16 (51.6)         |
| Oxygen supplementation at home | 0                 |
| Oxygen supplementation after enrolment | 2          |

Pts, patients; BMI, body mass index; MRC, medical research council; GERD, gastroesophageal reflux disease; AHI, apnea-hypopnea index; RVSP, right ventricular systolic pressure. Values are expressed as mean ± SD, or absolute numbers and percentage of total.
The mean value (SD) of max diff SpO2 during sleep was 10.32% (5.83%). Six patients (21.4%) had an ESS > 10. The mean value of SpO2 peak during CPET was 88.67 (6.01). When both variables were compared, the difference in their means was found to be statistically significant (p value < 0.001).

### Table 2—Functional and exercise testing characteristics of the study group

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<tr>
<td>PFT</td>
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<td>77.6 ± 17.06</td>
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<tr>
<td></td>
<td>TLC % pr</td>
<td>29</td>
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<td></td>
<td>DLCO % pr</td>
<td>29</td>
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<td></td>
<td>TIF (FEV/FVC %)</td>
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<td></td>
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<td>SpO2 after %</td>
<td>30</td>
<td>89.6 ± 4.90</td>
</tr>
</tbody>
</table>

PFT, pulmonary function testing; pr, predicted; CPET, cardiopulmonary exercise testing; 6MWT, 6-min walk test; TLC, total lung capacity; DLCO, diffusion capacity of the lung for carbon monoxide; TIF, Tiffeneau index; SpO2, oxygen saturation; VO2 peak, oxygen uptake at peak exercise; AT, anaerobic threshold; VE, peak minute ventilation at peak exercise; BR, breathing reserve; VE/VO2 slope, slope of minute ventilation-carbon dioxide production relationship; HR, heart rate.

Survival Plot and Correlations between Sleep Architecture Characteristics and Survival and Clinical, Functional, Physiological Exercise Testing, and Pulmonary Hypertension Variables of the Study Population

The cumulative Kaplan-Meier survival plot for the study population is shown in Figure 1. Survival was associated with SpO2 peak during CPET exercise (p = 0.032 HR = 0.764, CI [95%] = 0.584-0.999) as well as with RVSP calculated by Doppler echocardiography (p = 0.001 HR = 1.1, CI [95%] = 1.036-1.167). Among sleep characteristics, the max diff SpO2 was inversely related to survival (p = 0.011 HR = 0.764, CI [95%] = 0.584-0.999) as well as with RVSP (Figure 2, DLCO% and SpO2 after 6MWT and directly with MRC, AHI, and RVSP (Table 4). Lowest SpO2 was directly related to survival (p = 0.009 HR = 0.897, CI [95%] = 0.827-0.972) (Figure 3) and to functional (TLC%, DLCO%), physiological exercise testing parameters (6MWT distance, SpO2 after 6MWT, VO2 peak/kg, SpO2 peak) and inversely with MRC score, AHI, and RVSP (Table 5). AHI itself was not related to survival in IPF patients when the entire study population was examined. After excluding the subgroup of IPF patients that were assigned to treatment with CPAP for OSA, AHI was found to be significantly correlated with decreased survival, (p = 0.043, HR = 1.02, CI [95%] = 1.001-1.048) (Figure 4). It is of note that all outcome correlations were further adjusted for lung volumes and resting SpO2, and we found that none of them contributed in a statistically significant way (p < 0.05).
to the initial Cox proportional hazards models. Furthermore, AHI in this group of IPF patients was significantly correlated with neck circumference (r = 0.45, p = 0.013) and hip diameter (r = 0.38, p = 0.039), but not with BMI. Among the clinical, functional, exercise physiological, and pulmonary hypertension parameters, the only significant correlations of AHI found were with VO₂ peak and VO₂ peak/kg from CPET.

When IPF patients with excessive daytime sleepiness were compared with those that presented lower ESS scores no significant difference was noticed regarding survival, pulmonary function, submaximal and maximal exercise variables, RVSP, or BMI (data not shown).

**DISCUSSION**

The main finding of the present study is that in IPF patients, intermittent sleep oxygen desaturation exceeds that of maximal exercise and is associated with survival. Both sleep oxygen desaturation variables (maxdiff SpO₂, lowest SpO₂) we studied were related to lung damage, as reflected by functional parameters (TLC%, DLCO%), sleep apnea events, exercise oxygen desaturation, dyspnea, and right ventricular systolic pressure. These results imply a link between lung damage and apnea events in the induction and severity of intermittent sleep oxygen desaturation and a role of the latter on aggravating pulmonary arterial hypertension and its negative effect on IPF survival.

![Figure 1](image1) — Survival of 31 patients with usual interstitial pneumonia/idiopathic pulmonary fibrosis (UIP/IPF)

All patients were followed until death (uncensored n = 10) or until reporting of the study (censored n = 21). Shown are cumulative Kaplan-Meier survival plot, sample size, and survival (median survival = 525 days).

![Figure 2](image2) — Maximal fall in saturation of oxygen during sleep

Kaplan-Meier survival curves for various values of maximal fall in saturation of oxygen (maxdiff SpO₂) during sleep, as predicted by the respective statistically significant Cox proportional hazards model for the entire study population (n = 31). Correlation is significant at p ≤ 0.05.

![Figure 3](image3) — Lowest oxygen saturation during sleep

Kaplan-Meier survival curves for various values of lowest saturation during sleep (lowest SpO₂), as predicted by the respective statistically significant Cox proportional hazards model for the entire study population (n = 31). Correlation is significant at p ≤ 0.05.

**Table 4** — Statistically significant correlations (either Pearson r or Spearman r) of maximal fall of oxygen saturation during sleep (maxdiff SpO₂) with functional, clinical, exercise testing, and sleep variables of the study group (n = 31)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pearson r</th>
<th>Pearson r, p value</th>
<th>Spearman r</th>
<th>Spearman r, p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLCO%</td>
<td>-0.388</td>
<td>0.037</td>
<td>-0.373</td>
<td>0.046</td>
</tr>
<tr>
<td>SpO₂ a 6-MWT</td>
<td>-0.365</td>
<td>0.047</td>
<td>-0.338</td>
<td>0.068</td>
</tr>
<tr>
<td>MRC</td>
<td>0.461</td>
<td>0.009</td>
<td>0.479</td>
<td>0.006</td>
</tr>
<tr>
<td>AHI</td>
<td>0.702</td>
<td>&lt; 0.001</td>
<td>0.598</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>RVSP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DLCO%, diffusion capacity of the lung for carbon monoxide per cent predicted; SpO₂, oxygen saturation; a, after; 6-MWT, 6 min walking test; MRC, medical research council; AHI, apnea-hypopnea index; RVSP, Right ventricular systolic pressure. Correlation is significant at p ≤ 0.05.
So far nocturnal hypoxemia in idiopathic pulmonary fibrosis has been associated with decreased energy levels and impaired daytime social and physical functioning. To the best of our knowledge, this is the first study supporting the negative impact of sleep desaturation on survival in a population of pure IPF patients. Moreover, our findings are consistent with the results of a recent retrospective study, in which a mixed ILD population (including IPF patients) was studied by overnight oximetry, showing that an elevated nocturnal desaturation index is predictive of mortality.

An advantage of our study is the use of formal polysomnography. We showed that sleep oxygen desaturation was linked to the severity of the underlying lung damage of IPF and the coexistence of OSA, as disclosed by the relationship between both desaturation parameters used with both DLCO% and AHI. The significantly greatest magnitude of the sleep lowest SpO₂ compared to that of maximal exercise emphasizes the fact that sleeping in IPF is a stressful “practice,” even more intense to that of maximal exercise, both conducted under hypoxic conditions. The relevance of exercise oxygen desaturation in the clinical course of IPF patients has become clearly evident in chronic obstructive pulmonary disease (COPD), rendering the term “overlap” syndrome even more appropriate for the coexistence of OSA and IPF. This high occurrence, however, is not related to the BMI of the population studied, which appears even lower of that of previous publications. Furthermore, it cannot be attributed to the treatment effect of corticosteroid use because all were treatment-naïve patients. Factors other than obesity are implicated in the disturbed sleep architecture in IPF, such as the interaction between pharyngeal patency and lung volume. Prior studies have shown that during both wakefulness and sleep, there is increased pharyngeal collapsibility and airway resistance when lung volume is reduced. Moreover, the desaturation-reoxygenation sequence characterizing intermittent hypoxia constitutes a major stimulus, even more potent than continuous hypoxia, which leads to oxidative stress, systemic inflammation, and generalized vascular endothelial damage adversely affecting myocardial function.

The present study also shows that SBDs and especially OSA is common in IPF extending previous observations. This rate of occurrence is even higher from the 10% of OSA encountered in chronic obstructive pulmonary disease (COPD), rendering the term “overlap” syndrome even more appropriate for the coexistence of OSA and IPF. This high occurrence, however, is not related to the BMI of the population studied, which appears even lower of that of previous publications. Furthermore, it cannot be attributed to the treatment effect of corticosteroid use because all were treatment-naïve patients. Factors other than obesity are implicated in the disturbed sleep architecture in IPF, such as the interaction between pharyngeal patency and lung volume. Prior studies have shown that during both wakefulness and sleep, there is increased pharyngeal collapsibility and airway resistance when lung volume is reduced. Moreover, the lung volume dependence appears to be more pronounced in patients with OSA, probably due to loss of caudal traction on upper airway and subsequent airway instability. This effect of decreased lung volume during sleep may be even more pronounced in IPF patients than in those with COPD, rendering the term “overlap” syndrome even more appropriate for the coexistence of OSA and IPF. The potential mechanisms linking sleep and exercise oxygen desaturation with the development of PH may relate to different mechanisms, such as the hypoxia-mediated endothelial dysfunction and the rise in arterial endothelin-1 levels—a potent mediator of pulmonary vascular remodelling—as well as to the resetting of peripheral chemoreceptors due to hypoxia and the resulting lowering of the hypoxic drive, which might aggrivate sleep oxygen desaturation by delaying arousal.

### Table 5—Statistically significant correlations (either Pearson r or Spearman r) of lowest oxygen saturation during sleep with functional, clinical, exercise testing, and sleep parameters of the study group (n = 25)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pearson r</th>
<th>Pearson p value</th>
<th>Spearman r</th>
<th>Spearman p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLC%</td>
<td>0.294</td>
<td>0.121</td>
<td>0.396</td>
<td>0.033</td>
</tr>
<tr>
<td>DLCO%</td>
<td>0.467</td>
<td>0.01</td>
<td>0.489</td>
<td>0.007</td>
</tr>
<tr>
<td>6-MWT distance</td>
<td>0.463</td>
<td>0.01</td>
<td>0.494</td>
<td>0.005</td>
</tr>
<tr>
<td>SpO₂ b 6-MWT</td>
<td>0.502</td>
<td>0.005</td>
<td>0.572</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>SpO₂ a 6-MWT</td>
<td>0.55</td>
<td>0.002</td>
<td>0.573</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>MRC score</td>
<td>-0.477</td>
<td>0.007</td>
<td>-0.417</td>
<td>0.019</td>
</tr>
<tr>
<td>VO₂ peak/kg</td>
<td>0.286</td>
<td>0.147</td>
<td>0.377</td>
<td>0.05</td>
</tr>
<tr>
<td>SpO₂ peak</td>
<td>0.291</td>
<td>0.141</td>
<td>0.402</td>
<td>0.037</td>
</tr>
<tr>
<td>AHI</td>
<td>-0.465</td>
<td>0.008</td>
<td>-0.542</td>
<td>0.002</td>
</tr>
<tr>
<td>RV/SP</td>
<td>-0.732</td>
<td>&lt; 0.001</td>
<td>-0.662</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

TLC, total lung capacity; DLCO, diffusion capacity of the lung for carbon monoxide; 6-MWT, 6-min walking test; SpO₂, oxygen saturation; b, before; a, after; MRC, medical research council; VO₂, oxygen uptake at peak exercise; AHI, apnea-hypopnea index; RV/SP, Right ventricular systolic pressure; Correlation is significant at p ≤ 0.05.

### Figure 4—Apnea-hypopnea index

Kaplan-Meier survival curves for various values of apnea-hypopnea index (AHI) as predicted by the respective statistically significant Cox proportional hazards model for IPF patients of the study population not receiving treatment with continuous positive airway pressure (CPAP) (n = 25). Correlation is significant at p ≤ 0.05.
important in supine subjects with restrictive disorders such as IPF. Another implicated factor could be the rapid, shallow breathing pattern characterizing these patients, considered to be a reflex response to stiff lungs mediated by vagal afferents. The decrease of rapid, shallow breathing pattern during sleep, especially during REM sleep, may worsen hypoxemia, which in turn leads to sleep fragmentation and impairment of sleep quality. In fact, in the study group, both lung volumes and saturation during sleep were decreased.

Another finding of the present study is that sleep architecture presented impaired efficiency characterized by a predominance of S2 sleep, a decrease of REM sleep, and an increase in the arousal index. Sleep disturbances, no matter how common or severe in IPF, were not found to cause excessive daytime sleepiness, with only one-fifth of our patients showing high ESS scores. We could speculate that IPF patients report important tiredness and fatigue more often than excessive daytime sleepiness. In the literature, daytime sleepiness in OSAS patients is suggestive of hyperglycemia and hyperinsulinemia. However, when IPF patients with excessive daytime sleepiness were compared with those with lower ESS scores, no significant difference was noticed regarding survival, pulmonary function, submaximal and maximal exercise variables, RVSP or BMI.

To further understand the significance of SBDs in IPF, we examined the associations of SBD parameters with clinical, functional, submaximal and maximal exercise testing parameters. We found that AHI, the most representative of SBD parameters, was not related to the majority of clinical and physiological parameters of severity, such as the MRC chronic dyspnea scale and the dynamic and static lung volumes. Among the exercise parameters, AHI was only related to cardiopulmonary exercise testing. Data on the relationships of sleep disordered breathing and its physiological derangements with exercise are scarce. Based on the literature, there is evidence that the distance walked at 6MWT in severe OSA is related to BMI but not to AHI. As far as cardiopulmonary exercise testing is concerned, OSA patients have a decrease of peak oxygen uptake and an increased cardiovascular response related to the severity of OSA. Despite the importance of exercise in the evaluation of severity and outcome in IPF, no data exist as far as we know on the impact of OSA on exercise capacity of these patients. The present study shows an association of AHI with peak oxygen uptake in IPF, and to the best of our knowledge demonstrates for the first time in the literature that among SBD parameters, it is the lowest saturation during sleep that best correlates with clinical, functional and physiological parameters of disease severity and outcome. It is already known that hypoxemia during sleep induces brainstem depression and is one mechanism leading to sleep disordered breathing. Desaturation during sleep has been well studied in chronic respiratory diseases such as COPD and lymphangioleiomyomatosis (LAM), but it has been poorly studied in IPF. It was shown that patients with mild daytime hypoxemia may be particularly vulnerable to desaturation during sleep because they often reside on the steep portion of the oxyhemoglobin dissociation curve. COPD-OSA overlap syndrome patients have more pronounced nocturnal hypoxemia and are at increased risk of death. As far as interstitial lung disease is concerned, a single study more than 20 years ago, pointed out that oxygen desaturation during sleep was less severe than during exercise. In the present study population, saturation at rest and wakefulness were significantly related with the lowest saturation during sleep. The fact that the lowest SpO2 was related to major parameters known to reflect ventilatory impairment, exercise limitation, extent of disease, and pulmonary hypertension in IPF could provide further explanation on the prognostic significance of this parameter in IPF.

The major clinical implication of our findings would be the management of oxygen desaturation in combined IPF and OSA patients with continuous positive airway pressure (CPAP), seeking for a survival benefit. Based on the latest guidelines, IPF patients with severe resting hypoxemia are advised to use long-term oxygen therapy, based partly on indirect information from patients with obstructive lung disease. So far, CPAP treatment is shown to have a beneficial impact on hospitalizations and survival of OSA and of COPD-OSA “overlap” patients, while data for combined IPF and OSA are completely lacking. In our study population, only four patients were treated with CPAP, and they were all alive at the reporting of the study. No significant conclusions could be drawn yet because of the very small number of patients treated, although one could speculate that CPAP in this group of patients might relate to the survival benefit.

Our study has a number of limitations, the most important being the moderate number of patients included, reflecting the rarity of the disease in Greece—3.4 cases per 100,000 inhabitants. However, it is a prospective, single-center study, based on a well-selected group of newly diagnosed IPF patients; none had received treatment for IPF. In conclusion, in IPF, intermittent sleep oxygen desaturation exceeds significantly that of maximal exercise and is associated with survival. Both sleep oxygen desaturation variables studied were related to lung damage, sleep apnea events, exercise oxygen desaturation, dyspnea, and right ventricular systolic pressure. Moreover, our results imply the existence of a link between lung damage and apnea events in the induction and severity of intermittent sleep oxygen desaturation that aggravate pulmonary arterial hypertension and influence IPF survival. Further studies are needed to clarify this issue and underlying pathophysiological mechanisms.

**ABBREVIATIONS**

6MWT, 6 minute walking test  
AHI, apnea-hypopnea index  
AT, anaerobic threshold  
ATS/ACCP, American Thoracic Society/American College of Chest Physicians  
BR, breathing reserve  
BMI, body mass index  
CPET, cardiopulmonary exercise testing  
COPD, chronic obstructive pulmonary disease  
CPAP, continuous positive airway pressure  
ESS, Epworth Sleepiness Scale  
FEV1, Forced expiratory volume at the first second of expiration  
FVC, Forced vital capacity  
GERD, gastroesophageal reflux disease  
HR, heart rate
L Kolilekas, E Manali, KA Vlami et al

HRR, heart rate recovery
HRRres, heart rate reserve
IPF, idiopathic pulmonary fibrosis
IQR, interquartile range
LAM, lymphangioleiomyomatosis
Lowest SpO₂, lowest oxygen saturation during sleep
Maxdiff SpO₂, maximal difference in oxygen saturation between wakefulness and sleep
VE/VO₂ slope, Slope of minute ventilation-carbon dioxide production relationship
MRC, Medical Research Council
OSA, obstructive sleep apnea
O₂ P, oxygen pulse
SpO₂ peak, oxygen saturation at peak exercise
VO₂ peak, peak oxygen consumption
VO₂ peak/kg, peak oxygen consumption/kg
PSG, polysomnography
PFTs, pulmonary function tests
PH, pulmonary hypertension
RR, respiratory rate
RVSP, right ventricular systolic pressure
SpO₂ saturation of oxygen
DLCO, Single-breath carbon monoxide diffusing capacity
SBDs, sleep breathing disorders
TLC, total lung capacity
VE, total ventilation
TV, tidal volume
UIP, usual interstitial pneumonia

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600

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SUBMISSION & CORRESPONDENCE INFORMATION

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DISCLOSURE STATEMENT

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Idiopathic pulmonary fibrosis (IPF) is a specific form of chronic, progressive, fibrosing interstitial pneumonia of unknown cause, occurring in adults and confined to the lungs. Clinical trials of potential treatments have failed to affect the progression of disease or the survival of patients with IPF, despite substantial advances in immunomodulatory and antifibrotic therapies.1,2

Interestingly, the clinical course of IPF is variable, with some patients deteriorating rapidly and others remaining in a relatively stable condition. The prognosis of IPF is poor with a median survival of 2 to 3 years from the time of diagnosis1-3 and is equivalent to that of many forms of cancer. This shortened survival has been associated with several factors such as: older age at presentation, extensive cigarette smoking, lower body mass index (BMI), more severe physiologic impairment, greater radiologic extent of disease, and the development of other complications or conditions, e.g., pulmonary hypertension, emphysema, pulmonary embolism, and bronchogenic cancer.1,4

In this issue of Journal of Clinical Sleep Medicine, Kolilekas et al.5 have prospectively examined the impact of several parameters of sleep disordered breathing on survival of 31 consecutive treatment naive patients with IPF. The authors have highlighted that sleep in IPF is a stressful hypoxemic “practice” even more intense to that of maximal exercise, as assessed by cardiopulmonary exercise test. Sleep oxygen desaturation was linked to the severity of the underlying lung damage and the coexistence of obstructive sleep apnea (OSA).

In agreement with previous reports,6,8 prevalence of OSA is high in IPF patients and has atypical characteristics, such as the lack of association between BMI and AHI and the reported tiredness or fatigue instead of daytime sleepiness. This high prevalence of OSA can be attributed to other factors, such as the reduction of lung volume in IPF patients, which increases pharyngeal collapsibility and airway resistance. Indeed, lung volume dependence seems to be more pronounced in OSA patients.9

What is more important about this study is that it proposes novel markers for predicting survival in IPF patients, which are easily obtained with a polysomnographic study. Repeated desaturations and extended periods of low saturation during sleep may contribute to the pathological and pathophysiologic changes in the pulmonary tissue, negatively affecting patients’ prognosis through aggravation of pulmonary arterial hypertension. Awareness of these parameters in patients with IPF can potentially help in discriminating those with a lower life expectancy. Accurate risk prediction is essential both for the patient and the attending physician. The patient needs to know the disease prognosis in order to plan his/her remaining time, while the physician has to estimate the right time to propose the appropriate therapeutic intervention. Finally, risk stratification in IPF might be helpful for the design of clinical trials, where the outcome of therapeutic interventions in patients with good or poor prognosis could be compared.

The real value of this study, though, is that it raises an important question: Could the amelioration of oxygen desaturation with CPAP in IPF patients with concomitant OSA have a survival benefit, especially under the spectrum of the absence of an effective treatment for IPF? Indeed, CPAP treatment has been effective in ameliorating systemic inflammatory markers and markers of tissue hypoxia in OSA patients10 and in improving quality of life in IPF patients with OSA11 despite therapeutic difficulties or poor compliance.12

This study, despite its limitations, makes an important contribution to literature by identifying, for the first time, sleep parameters as predictors of survival in IPF. Future studies are necessary in order to confirm and possibly to expand these results by demonstrating which of the sleep parameters can reliably add predictive value to current prediction models for survival. Additional work through randomized controlled trials is also required to shed light to this important question: can CPAP treatment delay lung fibrosis or prolong survival in IPF patients with OSA?

Can We Predict the Survival of Idiopathic Pulmonary Fibrosis Patients? Sleep Must Be Re-appreciated


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REFERENCES

Sleep Duration and Reported Functional Capacity among Black and White US Adults

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**Objective:** Evidence suggests that individuals reporting sleeping below or above the population’s modal sleep duration are at risk for diabetes, hypertension, and other cardiovascular diseases. Sleep data also indicates that individuals with these conditions have reduced functional capacity. We assessed whether reported sleep duration and functional capacity are independently associated and whether individuals’ race/ethnicity has an effect on this association.

**Method:** Data were obtained from 29,818 black and white Americans (age range: 18-85 years) who participated in the 2005 National Health Interview Survey (NHIS). The NHIS uses a multistage area probability design sampling of non-institutionalized representatives of the US civilian population. Of the sample, 85% were white and 56% were women.

**Results:** Univariate logistic regression analysis showed that individuals sleeping < 6 h were 3.55 times more likely than those sleeping 6-8 h to be functionally impaired (34% vs 13%; p < 0.001). Likewise, those sleeping > 8 h were 3.77 times more likely to be functionally impaired (36% vs 13%; p < 0.001). Individuals of the black race/ethnicity were more likely to be functionally impaired than their white counterparts (23% vs 19%; p < 0.001). Multivariate-adjusted regression analyses showed significant interactions between individuals’ race/ethnicity and long sleep with respect to functional capacity (black: OR = 2.78, p < 0.0001; white: OR = 2.30, p < 0.0001). Significant interactions between race/ethnicity and short sleep were also observed (black: OR = 2.43, p < 0.001; white: OR = 2.63, p < 0.001).

**Conclusion:** Our findings suggest that individuals’ habitual sleep duration and their race/ethnicity are significant predictors of their functional capacity.

**Keywords:** Sleep duration, functional capacity, race/ethnicity

*Citation:* Brimah P; Oulds F; Olafiranye O; Ceide M; Dillon S; Awoniyi O; Nunes J; Jean-Louis G. Sleep duration and reported functional capacity among black and white US adults. J Clin Sleep Med 2013;9(6):605-609.
Our sample included a total of 29,818 black and white Americans (age range: 18-85 years) who participated in the survey, and provided valid data for the present analysis. Of the sample, 85% were of white race/ethnicity and 15% of black race/ethnicity. Adults of both sexes were represented; 44% of the volunteers were men and 56% were women.

PROCEDURES

NHIS is an ongoing, cross-sectional, in-person household interview survey conducted annually by the National Center for Health Statistics of the Centers for Disease Control and Prevention. The NHIS uses a multistage area probability design sampling of non-institutionalized representatives of the US civilian population. Probability samples of the adult population of all 50 states and the District of Columbia were obtained. The final sample was characterized by a response rate of 69%. As the response rate was relatively low, we compared demographic characteristics between responders and non-responders, finding no significant differences. Details on sample design can be found in Design and Estimation for the National Health Interview Survey, 1995-2005.

During face-to-face interviews conducted by trained interviewers from the US Census Bureau, volunteers provided sociodemographic data and information about physician-diagnosed chronic conditions. The chronic conditions included hypertension, heart disease, cancer, diabetes, and arthritis. Participants also estimated habitual sleep duration (using full-hour increments i.e., 5 h, 6 h, 7 h, with instructions to round 30 min or more up to the next whole hour, and dropping ≤ 29 min. Self-reported sleep duration was assessed with the following question: “On average, how many hours of sleep do you get in a 24-hour period?” No information on specific sleep disorders was elicited during the interview. Participants also reported depressed moods (i.e., feeling of sadness, hopelessness, or worthlessness, and poor effort) experienced in the past 30 days. Functional capacity was assessed by asking respondents whether they were able to walk a quarter of a mile without assistance; respondents were classified as “limited” if they answered “very difficult” or “unable” to perform this activity, or “not limited” if they were able to do it. Obesity was defined as BMI ≥ 30 kg/m².

Surveys were conducted using computer-assisted personal interviewing (CAPI), which utilizes a computer program for data collection that guides the interviewer through the questionnaire. The interviewer enters survey responses directly into the computer. The program determines through a computer algorithm whether data entered by the user match against all possible responses to specific questions; the program also checks for consistency against other data collected during the interview and saves the responses into a survey data file.

RESULTS

Individuals of black race/ethnicity were slightly younger than their white counterparts (Table 1). During the face-to-face interview, fewer blacks reported that they completed at least high school, and fewer blacks reported household income ≥ $35,000 than their white counterparts. White Americans were more likely to report a diagnosis of arthritis and heart disease, while black Americans were characterized by a greater likelihood of reporting a diagnosis of hypertension or diabetes, depressed moods, or being obese. Altogether, 20% of the sample reported sleeping < 6 h, and 22% reported sleeping longer than 8 hours.

Results of univariate logistic regression analysis showed that individuals sleeping < 6 h were 3.55 times more likely than those sleeping 6-8 h to be functionally impaired (34% vs 13%; p < 0.001). Likewise, those sleeping > 8 h were 3.77 times more likely to be functionally impaired (36% vs 13%; p < 0.001). Individuals of black race/ethnicity were more likely to be functionally impaired than their white counterparts (23% vs 19%; p < 0.001).

In the multivariate-adjusted regression models, we ascertained independent associations of short sleep (Model A) and long sleep (Model B) with functional capacity, while examining potential interactions between race/ethnicity and sleep duration. As shown in Table 2, significant interactions between race/ethnicity and short sleep with respect to function-
al capacity were noted (black: OR = 2.78, p < 0.0001; white: OR = 2.30, p < 0.0001). Results also showed significant interactions between race/ethnicity and long sleep (black: OR = 2.43, p < 0.001; white: OR = 2.63, p < 0.001). Associations of each of the adjusted sociodemographic and medical factors in the models are also provided in Table 2.

**DISCUSSION**

A plethora of studies have evidenced that sleep loss is associated with daytime performance decrements, excessive daytime sleepiness, negative moods, weight gain, and poor quality of life.27-32 One expectation from the gradual sleep reduction in population sleep time has been a commensurate increase in daytime functional impairment among US adults. Indeed, a recent report has indicated that the number of Americans reporting sleeping eight hours habitually, the recommended sleep time, has decreased from 38% in 2001 to 28% in 2009.33 The main finding of our study is that individuals’ habitual sleep duration, as well as their race/ethnicity, is a significant predictor of their functional capacity.

Our analyses indicated that both short (< 6 h) and long sleepers (> 8 h) were more likely to be functionally impaired, compared with individuals sleeping 6-8 h. These findings are in tandem with epidemiologic evidence showing a U-shaped relationship between sleep duration and medical/psychological health, indicating that both short and long sleepers are at increased risk for adverse health outcomes.34-36 Evidently, directionality cannot be established given the correlational nature of these observations. The findings of the present study indicating that black short and long sleepers were more likely to be functionally impaired than their white counterparts corroborate previous observations suggesting that blacks show greater functional impairment than their white counterparts.19,37 Further, they point to two other important observations. First, after adjusting all the factors that are known to cause functional impairment, both short and long sleep remained associated with reduced functional capacity. Hence, one could reasonably expect that a substantial variability in functional capacity may be uniquely associated with sleep duration itself. Second, black short sleepers had greater odds of being functionally impaired than their white counterparts. Conversely, white long sleepers had greater odds of being functionally impaired, although ORs for black and white long sleepers were less discrepant than they were for short sleep. These findings are very interesting, warranting further analysis in large-scale studies. While waiting for replication of these findings, one can reasonably posit that short and long sleep might have differential race/ethnic-based effects on individual functional capacity.

Available data provides ample evidence supporting our observation of an interaction between race/ethnicity and short sleep with regard to functional capacity. Epidemiologic evidence shows that individuals of black race/ethnicity are three times as likely as those of white race/ethnicity to meet criteria for obstructive sleep apnea.38-40 Individuals with obstructive sleep apnea, a condition that causes significant nocturnal sleep disturbances and excessive daytime sleepiness, have shown worse functional capacity than healthy controls.41,42 Among 5,301 African American adults, a recent report from Jackson Heart study showed an independent association between sleep disorders-breathing symptoms and sleep duration.43 It is conceivable that a significant number of blacks reporting short sleep might have untreated sleep apnea, likely causing daytime functional impairment either directly or through exacerbation of comorbid conditions (e.g., hypertension, diabetes, heart disease).44-47 However, the relationship between sleep apnea and sleep duration in blacks has not been well studied, suggesting the need for further research in this area.

In conclusion, our data suggest that individuals’ habitual sleep duration and their race/ethnicity are significant predictors of their reported functional capacity. One important limitation of our study is that the influence of sleep apnea on our analy-
sis could not be determined since the NHIS did not screen respondents for the presence of sleep apnea. Another limitation relates to the fact that the measure we used to assess functional capacity, the ability to walk a quarter mile without assistance, is highly subjective. Future studies should attempt to verify our results using objective methods of assessing functional capacity and sleep duration.

REFERENCES


ACKNOWLEDGMENTS

This research was supported by funding from the NIH (R25HL105444, R01HL095799 and R01MD004113).
Narcolepsy with cataplexy (NC) is a rare hypersomnia of central origin characterized by daytime sleepiness, cataplexy (sudden losses of muscle tone triggered by emotions, pathognomonic symptom), and other REM sleep disturbances. Reduced levels of cerebrospinal hypocretin-1 (hcrt-1 < 110 pg/mL) or ≥ 2 sleep onset REM periods (SOREMP) at MSLT should, “whenever possible” confirm NC diagnosis according to the International Classification of Sleep Disorders (ICSD-2).1 We report two ambiguous cases who were sent to our center for narcolepsy, pseudo cataplexy, video polysomnography.

Keywords: Childhood, hypocretin-1, narcolepsy with cataplexy, pseudo cataplexy, video polysomnography

Citation: Pizza F; Vandi S; Poli F; Moghadam KK; Franceschini C; Bellucci C; Cipolli C; Ingravallo F; Natalini G; Mignot E; Plazzi G. Narcolepsy with cataplexy mimicry: the strange case of two sisters. J Clin Sleep Med 2013;9(6):611-612.

We report on two sisters, 17 and 12 years of age, with clinical features suggesting narcolepsy with cataplexy (NC): daytime sleepiness, spontaneous and emotionally triggered sudden falls to the ground, and overweight/obesity. MSLT showed borderline sleep latency, with 1 and 0 sleep onset REM periods. HLA typing disclosed the DQB1*0602 allele. Video polygraphy of pseudo-cataplexy, together with normal cerebrospinal hypocretin-1 levels.

Our cases emphasize the need of a clear depiction of cataplexy pattern at the different ages, the usefulness of examining ictal neurophysiology, and collecting all available disease markers in ambiguous cases.

Video polygraphy of pseudo-cataplexy

Video 1 shows an instance where Patient 1 was standing while a placebo suggestion was performed. She abruptly fell on the ground—EMG showed initially increased then persistent muscle tone, and EEG, partially masked by artifacts, showed wake activity. While Patient 1 was recumbent and apparently unconscious, brisk reflexes could be easily evoked, confirming the non-cataplectic nature of the spell. The episode ended after another suggestion maneuver and while the doctor was reassuring Patient 1 that the episode would soon vanish. Polygraphic montage included EEG (C3-A2; O1-A2; Cz-A2), EOG (ROC-A1; LOC-A1), EMG (chin, right masseter, nuchal, right sternocleidomastoid, right and left deltoid, right and left carpus extensor, right and left anterior tibial muscles), ECG, and thoraco-abdominal belt from the top to the bottom.
Patient 2

Patient 2, the 12-year-old sister of Patient 1, had sudden episodes of vertigo followed by apparent brief loss of consciousness and falls to the ground with unresponsiveness to external stimuli for a few seconds to some minutes since 11 years of age. These episodes, after an initial cluster of 10 per day over a week, decreased to 1-2 per day. According to parent’s report, the episodes were similar to those of Patient 1. Psychiatric evaluation disclosed attention deficit hyperactivity disorder (ADHD), and normal head-up tilt table test excluded vasovagal syncope. At our evaluation, she complained mild restless legs symptoms and daytime sleepiness (ESS score of 15); sleep talking since childhood was reported. Her BMI was 29.7 kg/m². MSLT showed borderline sleep latency (9 min 12 sec). No SOREMP occurred during daytime or nighttime sleep on 48-h PSG (AHI = 0/h). She was HLA-DQB1*0602 positive and had normal brain MRI. Video-PSG of a spell occurring while watching funny videos showed persistence of wake EEG activity, EMG muscle tone, and deep tendon reflexes (Video 2). Hcrt-1 was in the normal range (253.7 pg/mL). Atomoxetine was given for ADHD, and she reported improved daytime sleepiness and significant spells reduction (1-2 per month).

Video polygraphy of pseudo-cataplexy

Video 2 shows an instance where Patient 2 was standing and watching funny videos and abruptly fell on the ground—EMG initially showed a reinforcement then a persistence of muscle tone and EEG, masked by artifacts, wake activity. While Patient 2 was recumbent and unresponsive to external stimuli, osteo-tendinous reflexes could be easily evoked, also when muscle tone was apparently of low amplitude on EMG channels. Polygraphic montage included EEG (C3-A2; O1-A2; Cz-A2), EOG (ROC-A1; LOC-A1), EMG (chin, right masseter, nuchal, right sternocleidomastoid, right and left deltoid, right and left carpus extensor, right and left anterior tibial muscles), ECG, and thoraco-abdominal belt from the top to the bottom.

DISCUSSION

Our cases show that the diagnosis of cataplexy based on clinical history alone may be misleading and suggest the need to further frame cataplexy and its mimics by documenting the episodes in the diagnostic work-up of suspected NC. According to ICSD-2, MSLT should be performed in the absence of a definite history of cataplexy, and HLA typing is neither sensitive nor specific for NC diagnosis confirmation. Indeed, as cataplexy is easy to document and peculiar, especially in children close to disease onset, we suggest the need to search for it considering ictal video-PSG useful in uncertain cases, and also for phenotype-genotype research purposes. NC objective biomarkers, namely SOREMPs and low/undetectable hcrt-1, have to be investigated in all challenging patients, and normal hcrt-1 may occur only in peculiar cases. Differential diagnosis of cataplexy should include a careful work-up to rule out cardiovascular conditions such as vasovagal syncope, drop attacks, and epilepsy. Misdiagnosing as NC other neurologic or psychiatric disorders, or cases of malingering, may have serious consequences for patients and their families, as well as high costs for the society. Overlaps between NC and psychiatric traits or disorders may also exist and require multidisciplinary approach and further investigations.

REFERENCES


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DISCLOSURE STATEMENT

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Nonarteritic anterior ischemic optic neuropathy (NAION) is the most prevalent optic nerve disorder among patients over 50 years of age, characterized by sudden onset, painless visual loss, with an accompanying relative afferent pupillary defect and optic disc edema. Although the pathophysiology of NAION has not been fully elucidated, several risk factors have been considered, including advanced age, systemic hypertension, diabetes mellitus, and certain optic disc morphologies. An association between obstructive sleep apnea (OSA) and NAION has also been recognized. One prospective cohort study indicated that the relative risk of OSA among patients with NAION was 4.9; a later retrospective cohort study demonstrated that patients with OSA not treated with continuous positive airway pressure (CPAP) had a 16% increased hazard of developing NAION compared to patients without OSA. The following review will discuss the most recent understanding of the relationship between OSA and NAION, with implications for further research and prevention strategies.

Keywords: Optic nerve diseases, anterior ischemic optic neuropathy, sleep disorders, obstructive sleep apnea.


BACKGROUND

Clinical Characteristics of NAION

Nonarteritic anterior ischemic optic neuropathy (NAION) is an ischemic insult to the anterior portion of the optic nerve, though an exact pathophysiology remains unclear. Classically, NAION presents with sudden, painless, monocular visual loss, most often in patients over the age of 50. Visual loss may affect central vision, peripheral fields, or both. Visual field deficits vary, but commonly, patients present with superior or inferior altitudinal field defects evident on automated perimetry. Interestingly, vision loss is most often noted upon awakening. Visual acuity on presentation may range from 20/20 to no light perception. Dyschromatopsia may be associated with NAION, with the level of color vision impairment coinciding with the degree of visual acuity deficit. Pain with eye movements is not a classic feature of NAION.

For a diagnosis of NAION to be made, the affected eye must exhibit a relative afferent pupillary defect. If bilateral NAION is present, a relative afferent pupillary defect will be absent, yet both pupils will react sluggishly to light. Optic disc edema evident on fundoscopy is another requirement for a diagnosis of NAION. The optic disc edema may be localized or diffuse, and the edematous area may be hyperemic or mildly pale (though not as pale as with arteritic anterior ischemic optic neuropathy). Nerve fiber layer hemorrhages are often visualized at the optic disc margins. In general, optic disc edema associated with NAION resolves in 4 to 8 weeks; if it fails to do so, an alternative diagnosis should be considered.

In a subset of NAION patients, the acute visual loss continues to decline over the following days to weeks. In the Ischemic Optic Neuropathy Decompression Trial (IONDT), 45% of patients reported a subjective worsening of their vision over the course of 30 days; whereas other studies have indicated continued deterioration of vision in approximately 30% of affected patients. But this is not to say that a significant portion of NAION patients do not exhibit visual improvement. The IONDT also demonstrated that at 6 months following the initial onset of visual loss, 42.7% of patients improved ≥ 3 lines of visual acuity, versus 44.9% with little to no change and 12.4% with worsening of vision by ≥ 3 lines.

The rate of recurrent NAION, meaning a second, distinct ischemic event in the same eye, is low; in one study, 53 of 829 (3.6%) eyes experienced a recurrent NAION in 3-year follow-up. A sequential NAION, a separate ischemic event in the contralateral eye, is more common. In one published series, 24% of 83 patients with NAION developed sequential involvement of the contralateral eye in an average time of 2.9 years; similar rates of sequential NAION were found during the IONDT.

Epidemiology of NAION

NAION can occur at any age but is most prevalent among patients older than 50 years of age. The annual incidence of NAION among patients 50 years and older is between 2.3 and 10.2 per 100,000, with a prevalence of 0.54 per 100,000 patients of all ages. No specific gender predilection has been found, with both men and women affected equally. The majority of NAION patients, though, are Caucasian.

Risk Factors Associated with NAION

Several risk factors for the development of NAION have been proposed, including systemic vasculopathic risks such as systemic arterial hypertension, diabetes mellitus, hyperhomo-
Obstructive sleep apnea (OSA), characterized by recurrent episodes of partial or complete upper airway obstruction causing cessation of breathing during sleep, is also a significant risk factor for the development of NAION. In their influential 1993 publication, Young et al. reported that of 602 middle-aged persons undergoing overnight polysomnography, 9% of middle-aged women and 24% of middle-aged men suffered from undiagnosed sleep disordered breathing (≥ 5 episodes of apnea or hypopnea/h of sleep). The authors also concluded that 4% of men and 2% of women in this age group “met minimal criteria for the sleep apnea syndrome,” indicating an apnea-hypopnea score > 5 and self-reported sleepiness. A more recent analysis of data collected from the 2005 National Sleep Foundation’s Sleep in America Poll revealed that of 1,506 respondents, 31% of men and 21% of women were at high risk for OSA according to the Berlin questionnaire. The percentage of respondents at high risk for OSA increased with increasing BMI, with 59% of individuals with BMI > 30 at high risk. The risk of OSA also increased linearly with increasing age. Additional risk factors for OSA include large neck circumference, craniofacial abnormalities, nasal obstruction, and increased pharyngeal tissue. The severity of sleep apnea may be increased by smoking, consuming alcohol, sleeping in the supine position, or engaging in minimal physical activity. Airway obstruction is corrected only after arousal from sleep, when airway muscle tone increases.

OSA is recognized as an independent risk factor in the development of daytime hypertension, with a recent study indicating a linear relationship between the odds of hypertension and severity of OSA. The Wisconsin Sleep Cohort Study provided prospective confirmation of this association, reporting that the apnea-hypopnea index (the average number of disordered breathing events per hour of sleep) is an independent predictor of daytime hypertension, with an odds ratio of 2.89 among patients with an apnea-hypopnea index > 15/hour. Notably, apnea-hypopnea indices also correlate directly with body mass index (BMI), insulin resistance, and systolic and diastolic dysfunction. The incidence of cardiac arrhythmias was found to be elevated among OSA patients, while a matched case-control study concluded that OSA is an independent predictor of coronary artery disease, with an odds ratio of 3.1. In addition, strong evidence exists to substantiate OSA as a risk factor for the development of cerebrovascular accidents.

Recently, the link between OSA and oculovascular health has been investigated, particularly the association between OSA and NAION, glaucoma, papilledema, and floppy eyelid syndrome.

Mojon and colleagues published a seminal case-control cross-sectional study that sought to determine the prevalence of sleep apnea among patients diagnosed with NAION. Seventeen patients diagnosed with NAION (mean age: 64.6 ± 11.7 years), recruited from Switzerland and Boston, agreed to undergo overnight polysomnography, along with 17 control patients (mean age: 63.3 ± 11.0) who were referred for suspected restless leg syndrome; controls were matched according to age, gender, and cardiovascular risk factors. Sleep apnea syndrome was diagnosed and graded according to respiratory disturbance index (Normal, RDI < 10; Mild sleep apnea, RDI 10-20; Moderate sleep apnea, RDI 20-40; Severe sleep apnea, RDI > 40).

Twelve (71%) of 17 NAION patients were diagnosed with OSA, versus only 18% among matched controls. The elevated mean RDI among NAION patients compared with restless leg syndrome controls was statistically significant (25.3 ± 21.9 versus 9.2 ± 20.8, respectively). Mojon et al. also compared their OSA prevalence results to those of a larger random sample of men (741 subjects), aged 20-100 years of age and without NAION, published previously by Bixler et al. The prevalence of OSA among NAION patients in the study by Mojon et al. was significantly higher than the prevalence calculated from sleep studies among Bixler et al. subjects. In light of their comparisons between a previously reported control group and a current control group (restless leg syndrome suspects), in addition to similar prevalence rates obtained in two independent eye clinics (both Switzerland and Boston), the authors concluded that the elevated prevalence of OSA among NAION patients was “real and clinically significant.”

Palombi and colleagues further pursued the association between sleep apnea and NAION. Twenty-seven patients (18 men, 9 women, mean age 65 years), newly diagnosed with NAION, where recruited to undergo polysomnography. The authors found that “NAION was nearly always associated with sleep apnea,” with 89% of patients having an apnea-hypopnea index > 15 per hour. The prevalence of OSA among NAION patients was compared to the prevalence of OSA in the general population (5,615 subjects), published in a 2002 study completed by Young et al. The relative risk of OSA among NAION patients compared to members of the general population was 4.9. Although the gold standard for diagnosing OSA is polysomnography, such sleep studies are time-consuming, fairly expensive, and include a variety of invasive recordings. Therefore, Li and colleagues attempted to quantify the prevalence of OSA among NAION patients via telephone questionnaires (SA-SDQ), which have been validated against full polysomnography in terms of sensitivity and specificity. Seventy-three patients diagnosed with NAION, along with 73 age- and gender-matched controls, were given the verbal questionnaire. Questions addressed symptoms of OSA, as well as current weight, BMI, smoking status, etc.; a score of 36 for men and 32 for women served as the diagnostic cutoff for OSA (a score closer to 60 indicated a higher likelihood of OSA). Thirty percent of the NAION patients scored in the OSA range, whereas only 17.8% did so among the control group. Statistical analysis indicated that patients with NAION were 2.62 times more likely to have a SA-SDQ score consistent with OSA. These findings were consistent with results from the previously mentioned studies, though the magnitude of association was not as great.

The three preceding studies examined the prevalence of OSA among patients with NAION. Stein et al. investigated the con-
Table 1—Summary of published epidemiological investigations regarding the association between OSA and NAION

<table>
<thead>
<tr>
<th>Authors</th>
<th>Type of Study</th>
<th>Results</th>
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<tbody>
<tr>
<td>Prevalence of OSA among patients diagnosed with NAION</td>
<td></td>
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<tr>
<td>Mojon et al.³</td>
<td>Case-control, cross-sectional</td>
<td>12 (71%) of 17 NAION patients diagnosed with OSA by polysomnography. 3 (18%) of 17 restless leg syndrome controls diagnosed with OSA by polysomnography.</td>
</tr>
<tr>
<td>Palombi et al.⁴</td>
<td>Prospective, cohort</td>
<td>24 (89%) of 27 NAION patients diagnosed with OSA by polysomnography. Relative risk of OSA among NAION patients: 4.9, compared to prevalence of OSA among general population.</td>
</tr>
<tr>
<td>Li et al.¹⁴</td>
<td>Case-control</td>
<td>30% of 73 NAION patients qualified as suffering from OSA by SA-SDQ (questionnaire). 17.8% of controls qualified as suffering from OSA by SA-SDQ. NAION patients 2.62 times more likely to have SA-SDQ score consistent with OSA, when adjusted for glaucoma, high cholesterol, and smoking.</td>
</tr>
<tr>
<td>Prevalence of NAION among patients diagnosed with OSA</td>
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<tr>
<td>Stein et al.¹⁵</td>
<td>Retrospective, longitudinal cohort</td>
<td>From approximately 2 million billing records, incidence of NAION determined and stratified by OSA status. If patient had OSA and was not treated with CPAP, 16% increase in hazard of experiencing NAION compared to controls.</td>
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</table>

verse association—the prevalence of NAION among patients previously diagnosed with OSA. Stein et al. completed a retrospective, longitudinal cohort study utilizing billing records of 2.2 million managed care recipients in the United States. The incidence of NAION was determined among patients older than 40 years of age, who had been with the managed care network for at least one year, with at least one visit to an eye care provider during that time. Included patients must have received a diagnosis of sleep apnea prior to experiencing an NAION event.

Stein and colleagues found, after adjustment for confounding variables, that individuals diagnosed with sleep apnea and not treated with continuous positive airway pressure (CPAP) had a 16% increase in the hazard of developing NAION when compared to controls without sleep apnea. Otherwise, the adjusted hazard of developing NAION was not significantly different between those sleep apnea patients receiving CPAP treatment and controls without sleep apnea. Authors concluded that it may be beneficial for newly diagnosed sleep apnea patients to have a thorough ophthalmic examination to assess the possibility of coexistent optic neuropathy, especially those not treated with CPAP. Unfortunately, due to a lack of access to medical records, the incidence of NAION was not quantified based upon the severity of sleep apnea, and possible differences among those patients using and not using CPAP, with regards to their severity of sleep apnea, was not noted.

The current standard of treatment for OSA remains CPAP during sleep, which serves as an airway splint to keep the airway patent. It has been demonstrated that the use of CPAP eliminates apneic episodes, improves fragmented sleep, and minimizes hemodynamic changes associated with OSA. Studies have also revealed that CPAP use improves blood pressure, alleviates the recurrence of cardiac arrhythmias and lessens the excess mortality among OSA patients who have suffered a stroke. In light of the abovementioned association between OSA and NAION, it is reasonable to hypothesize that if a patient with OSA is treated with CPAP, the probability of developing NAION would be less than if CPAP was not utilized. The findings of Stein and his colleagues substantiated this supposition.

The value of CPAP treatment in the prevention of NAION was questioned by Behbehani et al. in their 2005 case reports. At Wills Eye Hospital in Philadelphia, PA, between 2002 and 2003, 108 patients were newly diagnosed with NAION. Three of those patients had been using CPAP prior to the diagnosis of NAION: (1) a 55-year-old male, treated for 2 years with a nasal CPAP machine at home; (2) a 57-year-old male treated for 6 years with a nasal CPAP machine; (3) a 50-year-old male treated with CPAP for 4 months prior to visual loss. All 3 patients suffered from hypertension; 2 had hypercholesterolemia, and 1 had diabetes. With no further studies investigating whether CPAP prevents NAION development, the utility of CPAP use for prevention of ocular complications of OSA remains speculative.

Blaivas and Uddin most recently published a novel case report of a 79-year-old male diagnosed with bilateral NAION, whose past medical history was significant for OSA and a euthyroid goiter for which the patient refused surgery for several years. Authors proposed that the goiter, demonstrated to deviate and narrow the trachea on chest radiograph, interfered with the physiologic tracheal tug present in normal supine individuals. The tracheal tug refers to the slight caudal movement of the trachea during tidal breathing, which "tenses the upper airway soft tissues, serving to counter inspiratory upper airway collapse." In light of the patient’s BMI of 25 and his normal craniofacial structure, it was concluded that the patient experienced a rare cause of OSA, which ultimately resulted in bilateral NAION.

Table 1 provides a summary of the published epidemiological studies regarding the association between OSA and NAION.

PROPOSED PATHOPHYSIOLOGY LINKING OSA AND NAION

Nocturnal hypotension has long been implicated in the development of NAION, serving as the “final insult” among compromised optic discs. Hayreh et al. published a prospective report of 275 individuals with anterior ischemic optic neuropathy (AION), normal tension glaucoma, or primary open angle glaucoma who underwent 24-h ambulatory blood pressure monitoring. When all 3 optic nerve diseases were considered together, those individuals with visual field deterioration had sig-
of NAION among OSA patients. Hypertensive individuals on antihypertensive medications had significantly lower mean nocturnal systolic blood pressure, in addition to a larger mean percentage decrease in systolic, diastolic, and mean blood pressures during the night. The authors concluded that in an optic nerve head that is susceptible to vascular insufficiency, whether from altered autoregulation, arteriosclerosis, vasospastic disorders, systemic hypertension, or diabetes mellitus, nocturnal hypotension may no longer be simply a physiologic process; instead, may serve as “the straw that broke the camel’s back.”

In contrast, a study published by Landau et al. revealed contradictory results, indicating no significant difference in mean nocturnal decreases in blood pressure among NAION patients and controls. Thus, the role of nocturnal hypotension in NAION is not certain. Moreover, if nocturnal hypotension did play a role in the development of NAION, it may not be the reason as to why OSA, in particular, causes optic nerve damage. Previous studies have indicated that patients with OSA experience no nocturnal decrease in blood pressure, suggesting a limited or no role for nocturnal hypotension in the development of NAION among OSA patients.

Though extensively documented among cases of arteritic anterior ischemic optic neuropathy, Arnold found that histopathological evidence for infarction in the paralaminar regions of the optic nerve head, as well as occlusion of the short posterior ciliary arteries (SPCAs), in NAION is lacking. From the limited histopathological specimens of NAION that do exist in the literature, Arnold drew two conclusions regarding the pathogenesis of NAION: (a) Optic nerve head infarction is generally located in the retrolaminar region, implying that SPCA branches directly supplying the optic disc may be involved, rather than a primary role of the choroidal circulation. (b) A significant amount of NAION cases revealed cavernous degeneration, with accompanying mucopolysaccharide deposit that displaces optic nerve axons. The latter observation may imply focal compression as a contributing pathologic factor in the development of NAION.

Arnold described how fluorescein angiographic studies of NAION subjects report delayed filling of the prelaminar optic disc compared with normal controls and subjects with nonischemic optic disc edema. This finding suggests circulatory impairment in NAION as a primary process, rather than secondary to optic disc edema. Interestingly, fluorescein angiography also revealed, via “poorly correlated” filling of the optic disc and adjacent choroidal segments, that the level of vascular occlusion in NAION is located within the paraoptic branches of the SPCAs, after separating from the choroidal branches.

Proposed etiologies of NAION are summarized in Table 2.

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<tr>
<th>Proposed Etiology</th>
<th>Authors</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Ischemic</td>
<td>Arnold</td>
<td>Vascular occlusion within paraoptic branches of short posterior ciliary arteries after separating from choroidal branches.</td>
</tr>
<tr>
<td>- Nocturnal Hypotension</td>
<td>Hayreh et al., Landau et al.</td>
<td>Contradictory results regarding difference in mean nocturnal decrease in blood pressure between NAION patients and controls.</td>
</tr>
<tr>
<td>Compressive</td>
<td>Arnold, Tesser et al.</td>
<td>Ischemic insult drives subsequent edema formation, contributing to optic nerve compression and infarction.</td>
</tr>
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</table>

Tesser et al. analyzed 3-dimensionally reconstructed serial sections of an optic nerve with NAION from a 70-year-old male who had a past medical history significant for peripheral vascular disease, congestive heart failure, and hypertension. The patient died 20 days after diagnosed with NAION. Results were indicative of a compartment syndrome mechanism of NAION development, similar to a possible compressive etiology suggested by Arnold. The resulting infarct was widest anteriorly, nearest to the optic nerve head, and confined to the intrascleral portion of the optic nerve. The infarct did not correlate to any one single vascular territory and vascular inflammatory infiltrates or emboli were not evident. Though the results suggested a compartment syndrome pathogenesis of NAION, it is still believed that an initial ischemic event leads to edema formation within the confined space of the sclera, ultimately leading to mechanical compression of optic nerve fibers. Subsequently, it would appear that surgical decompression of the optic nerve may be beneficial in the prevention and/or treatment of NAION, yet previous publications demonstrated no benefit.

Though observational studies have indicated an epidemiological association between OSA and NAION, as described above, a causal relationship cannot be presumed. Today, research continues to more clearly define the way in which OSA may specifically contribute to an isolated vascular insult and/or compartment syndrome of the optic nerve disc. How OSA affects homeostatic, physiologic mechanisms may serve as guidance in efforts to deduce the exact role OSA plays within the pathogenesis of NAION. The following are proposed mechanisms by which OSA may contribute to the development of NAION (also outlined in Table 3).

1. It has been hypothesized that direct exposure of the optic nerve to OSA-induced hypoxia can lead to optic nerve damage. Interestingly, due to the excellent buffering capacity of the human body, changes in PaCO₂ and pH during apneic episodes generally remain insignificant compared to changes in PaO₂.

2. It is suspected that OSA leads to vascular dysregulation of the optic nerve. Nocturnal hypoxia secondary to repetitive apneic episodes is detected by carotid chemoreceptors, which subsequently fuels hemodynamic changes, particularly an elevation in blood pressure. Inspiratory efforts against collapsed airways decrease intrathoracic pressures, leading to increased venous return and subsequent increases in stroke volume and cardiac output. The same inspiratory efforts lead to arousal from sleep, with even further activation of the sympathetic system. Due to these intermittent sympathetic surges, transient elevations in blood pressure are evident in OSA, often accom-
Table 3—Summary of proposed pathophysiologic mechanisms linking OSA and NAION

1. Direct exposure of optic nerve to OSA-induced hypoxia.2,10
2. Intermittent sympathetic surges secondary to repetitive apneic episodes leads to changes in cardiovascular functioning → arteriosclerosis and altered vascular autoregulation of optic nerve.3,10,19
3. Hypoxia-reoxygenation pattern associated with OSA contributes to oxidative stress → vascular endothelial damage → autoregulatory dysfunction.4
4. Hypoxia-induced cerebral vasodilation may further impair autoregulation of optic nerve due to decreased cerebral perfusion pressure.10
5. Increased intracranial pressure during apneic episodes may contribute to optic nerve damage directly, or by circulatory compression.1,2
6. Suspected imbalance of vasoactive substances (increased concentrations of VEGF and endothelin-1 among OSA patients).4

To date, it is believed that large variations in the concentration of blood oxygen and carbon dioxide may metabolically stress the autoregulatory ability of the optic nerve head. Riva et al. found that by autoregulation, through increased blood volume secondary to increased vascular capacitance, via recruitment of capillaries and/or increased in venous diameter, blood flow to the optic nerve head can remain steady until ocular perfusion pressure decreases to 15-20 mm Hg (or an intraocular pressure of 40-45 mm Hg is obtained).10 For the optic disc to experience hypoperfusion persistent enough to damage axonal fibers, impairment of this autoregulatory process, whether via arteriosclerosis or vasospasm, may very well play a role in NAION development.8 In addition, the hypoxia-reoxygenation pattern associated with OSA contributes to oxidative stress with the production of reactive oxygen species, therefore allowing vascular endothelial damage.4 Optic nerve vascular dysregulation secondary to OSA may also be due to an imbalance between vasoactive substances, especially nitric oxide and endothelin. Vascular endothelial growth factor (VEGF) and endothelin-1 have been found at high serum concentrations among OSA patients.4 Hypoxia-induced cerebral vasodilation may further impair autoregulation due to decreased cerebral perfusion pressure.10

3. Elevated intracranial pressure during apneic spells may contribute to optic nerve head damage, directly or by circulatory compression.3 In one retrospective review of 18 adult males with idiopathic intracranial hypertension (IIH), 6 (33%) patients were identified as suffering from OSA; this prevalence was higher than the previously reported prevalence of OSA among the general male population.20 Also documented in the literature are 3 case reports of OSA patients with normal intracranial pressure during the day and “marked, frequent, and episodic elevation” in cerebrospinal fluid pressure over night (from 50 to 750 mm of water).20 Of importance, each episode of elevated intracranial pressure was preceded by an apneic or hypopneic episode. The authors proposed 3 possible mechanisms by which OSA may lead to elevated intracranial pressure, including (a) elevated central venous pressure leading to increased cerebrovascular volume, (b) increased systemic arterial blood pressure with accompanying elevated cerebrovascular perfusion pressure, and lastly, (c) hypercapnia-induced cerebral vasodilation and ensuing decreased vascular resistance and increased cerebral blood flow.20 Questions remain as to whether OSA and IIH may be associated not by a causal relationship, instead, by their link to obesity.

Recognizing the association between OSA and NAION, though not fully clarified, has considerable implications for current medical practice. Ophthalmologists should be vigilant to ask NAION patients OSA screening questions and when necessary, to refer patients for polysomnographic studies. Simple screening questions are effective in differentiating what patients are most at risk of suffering from OSA, such as, “Are you sleepy during the day?” “Do you fall asleep more easily than normal?” “Does your partner comment that you snore loudly?” “Does your partner notice you gasping or choking at night during sleep?” “Has your partner witnessed any episodes where you stop breathing over night?” A general medical examination completed by an ophthalmologist may also raise suspicion for underlying OSA, including systemic hypertension, obesity, increased neck circumference, large soft palate, and enlarged tonsils. But it is important to recognize that not all OSA patients are obese; instead, upper airway changes and retriglottis may indicate the diagnosis.1 Screening as described above is essential in preventing the profound cardiovascular and cerebrovascular effects secondary to OSA with the use of CPAP; the beneficial oculovascular effects of CPAP are not as definitive.

Likewise, general medical practitioners, pulmonologists, and sleep specialists should be cognizant of the risk of severe visual loss due to NAION among patients with OSA. Screening questions regarding visual function and early ophthalmic examinations are prudent, but what remains frustrating is the lack of prevention and treatment strategies.

This review highlights the need for further research. Larger sample size, retrospective or case-control studies to further quantify the association between OSA and NAION would be valuable but is not of imminent concern, for the association has been fairly well documented in the literature. The greatest need is for a more detailed understanding of the etiology of NAION and its pathophysiological link to OSA. It would be beneficial to examine more NAION eye specimens for histopathologic information which may guide new pathophysiological hypotheses, in addition to considering the role individual differences in VEGF responses may have in this disease. Further investigation into the preventative measures of NAION is also necessary, especially a more thorough quantification of the prevalence of NAION among patients treated with CPAP. A closer look is needed, too, at the efficacy of preventing NAION with antihypertensives and diabtic medications. Additional research should be pursued so to one day provide protection for those at
risk, and defense from progression or hope of reversal for those already affected by this potentially devastating disease.

REFERENCES


SUBMISSION & CORRESPONDENCE INFORMATION

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DISCLOSURE STATEMENT

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A 29-year-old male with no medical or family history presented with excessive daytime somnolence (Epworth Sleepiness Scale score 22/24) for more than a year, including falling asleep while driving. He endorsed taking frequent naps during the day with sleep paralysis (SP) upon awakening. He reported seeing shadows in his room when falling asleep consistent with hypnagogic hallucinations. The patient also endorsed brief episodes of cataplexy characterized by muscle weakness, such as dropping objects even if held in both hands, and bilateral leg weakness at the knees, triggered by laughter and lasting several seconds. Cataplexy and sleep paralysis were his most distressing symptoms due to recurrent daytime episodes. Furthermore, his wife complained of the patient shaking or twitching while he slept. Physical examination was normal. Cataplexy could not be induced during the clinic visit.

Diagnostic polysomnography (PSG) preceding a multiple sleep latency test (MSLT) showed 80% sleep efficiency and sleep onset of 13.5 min. REM latency was prolonged at 185.5 min, and the patient spent 20% of the night in stage R. Apnea-hypopnea index was unremarkable. On EEG, apparent spikes occurring singly and in semi-rhythmic runs up to 30 s were seen over the left hemisphere during 4 different 10- to 15-minute periods (Figure 1). One episode was present in stage N2 and the remainder in REM sleep. Review of the video showed intermittent rhythmic rolling and side-to-side head shaking while the patient lay supine with his head tilted to the left. After awakening, the patient was unaware these movements occurred. On MSLT, the mean sleep latency (MSL) was 15.8 min with no sleep onset REM periods (SOREMPs).

QUESTION: What is your diagnosis?
Figure 1—Initial polysomnography

(A) 30-s epoch with the patient lying supine but with head tilted to his left side showing stage R prior to the start of rhythmic movements. (B) 30-s epoch showing stage R during rhythmic movements associated with apparent spikes and lasting approximately 20 sec. (C) 30-s epoch showing stage R approximately 2 min after the rhythmic movements in B. Note the absence of arousal or increased slow activity. (D) 10-s epoch of rhythmic movements shown in B. Note the apparent spikes are located in the left-sided electrodes (F3, C3, O1). EOG: E1-M2, E2-M1. EEG: F3-M2, F4-M1, C3-M2, C4-M1, O1-M2, O2-M1. EMG: Chin1-Chin2, LAT (left anterior tibialis), RAT (right anterior tibialis). EKG, electrocardiogram; HR, heart rate; SaO2, oxygen saturation; Therm, thermistor; Pres-ss, nasal air pressure sensor; Abd, abdomen.
Despite the MSLT findings, narcolepsy with cataplexy (NC) was strongly suspected by history. A repeat MSLT was recommended to the patient, but was not pursued at his request. He was distressed over daily episodes of sleep paralysis and/or cataplexy and did not want to delay treatment despite attempts to provide reassurance. The International Classification of Sleep Disorders second edition (ICSD-2) does not require an MSLT to show MSL < 8 min and 2 SOREMPs or a cerebrospinal fluid (CSF) hypocretin level < 110 pg/mL to diagnose NC if there is a definite history of cataplexy.

Both MSLT and CSF hypocretin level are recommended but not required for the diagnosis of NC because neither test provides additional diagnostic value over the clinical history of definite cataplexy.

In a large retrospective study of 2,472 MSLTs, 170 subjects were diagnosed with narcolepsy based on either of the following diagnostic criteria: (1) a complaint of, or history compatible with, excessive sleepiness and definite cataplexy, or (2) MSL < 8 min, ≥ 2 SOREMPs, and no other medical, psychiatric, or other sleep disorder sufficiently severe to account for sleepiness, associated symptoms, and SOREMPs. Of the patients with NC studied with a MSLT, 13% did not have any SOREMPs and 29% did not have MSL < 8 min and ≥ 2 SOREMPs. Further, 6/15 (40%) patients with NC who underwent 2 MSLTs did not have MSL < 5 min or ≥ 2 SOREMPs on either study. The authors concluded that overemphasizing MSLT results “may prevent the diagnosis of narcolepsy in some patients who actually have the diagnosis.”

CSF hypocretin levels are also recommended but not required by ICSD-2 for the diagnosis of NC, but this test was validated against the diagnostic criteria of a history of cataplexy, the same standard as used in our patient. Based on this evidence, no further evaluation was justified clinically for our patient, and the diagnosis of NC was based on the clinical history of excessive sleepiness and definite cataplexy. He was started on sodium oxybate.

Although the diagnosis of NC was not in doubt, the head rolling movements raised the possibility of a second diagnosis. Classifying nocturnal movements as simple or complex, and if present in either NREM or REM sleep, assists with narrowing the differential diagnosis. Motor activity in REM sleep is not frequent but has been described in REM sleep behavior disorder (RBD) and epilepsy. Furthermore, NC has been associated with RBD, periodic limb movements during sleep, and sleep-related rhythmic movements (SRMs). RBD was not suspected in this patient due to lack of complex movements. While the assumed cause of the EEG abnormalities was movement artifact, the waveform morphology appeared epileptiform-like on the limited EEG montage of the PSG. Further, simple movements associated with interictal spike-wave discharges have been reported during both NREM and REM sleep.

Repeat PSG with full montage EEG using the international 10-20 system showed a normal waking background with good organization and reactivity. Stereotypic head rolling occurred only in stage R with the patient lying on his right side. SRMs were associated with high amplitude 4-5 Hz theta activity throughout the right hemisphere (Figure 2) without increased slowing or arousal on EEG. The full montage EEG PSG demonstrated that there was no epileptiform-like activity and that the apparently abnormal waveforms represented movement artifact.

SRMs observed in this case were similar to those seen in sleep-related rhythmic movement disorder (SRMD). SRMD is rarely seen in adults or REM sleep, and must result in sleep impairment and not be explained by another diagnosis. The patient did not meet criteria for SRMD because daytime sleepiness, cataplexy, and SRMs improved after starting sodium oxybate for NC, suggesting the SRMs were related to NC. In a recent report, three patients with NC had intermittent SRMs of the head, legs, and/or body coinciding with stage R and SP on PSG. SRMs in stage N2 were not seen. The authors found that two of three patients recalled initiating the movements to

**Figure 2—Full EEG polysomnography**

(A) 30-s epoch showing stage R during rhythmic head movements. (B) 10-s epoch showing stage R during rhythmic movements. In both A and B, the EEG shows 90-130 µV theta activity with a sinusoidal morphology in right-sided electrodes only (maximal Fp2-F8, F4-F8, Cz-C4, C4-T4, Pz-P4, P4-T6, O1-O2, O2-T6). There is myogenic artifact, primarily in T4-M2. EOG: E1-M2, E2-M1. EEG (transverse montage): F7-Fp1, Fp1-Fp2, Fp2-F8, F7-F3, F3-Fz, Fz-F4, F4-F8, M1-T3, T3-C3, C3-Cz, Cz-C4, C4-T4, T4-M2, T5-F3, P3-Pz, Pz-P4, P4-T6, T5-O1, O1-O2, O2-T6. EMG: Chin3-Chin2, LAT (left anterior tibialis), RAT (right anterior tibialis). EKG, electrocardiogram; SaO2, oxygen saturation; Airflow, thermistor; Abd, abdomen.

**ANSWER:** Narcolepsy with cataplexy associated with sleep-related rhythmic movements.
“shake out” of SP. Treatment for NC led to improvement in the SRMs. A similar phenomenon may account for the findings in this case.

Treatment for NC with sodium oxybate led to improvement in the SRMs for this patient. At 8 months follow-up, the patient was tolerating 3 grams of sodium oxybate twice per night without side effects and endorsed no episodes of cataplexy, rare sleep paralysis, and an estimated 90% reduction in daytime sleepiness (Epworth Sleepiness Scale score 7/24). His wife stated that she no longer observed any nocturnal movements.

CLINICAL PEARLS

1. The diagnosis of narcolepsy with cataplexy may be made based on clinical criteria if there is a definite history of cataplexy. An MSLT and/or CSF hypocretin level are recommended but not required for diagnosis.
2. Motor findings in REM sleep occur infrequently and may be caused by REM sleep behavior disorder, epilepsy, or sleep-related rhythmic movements.
3. Defining abnormal movements during sleep as simple or complex can assist in narrowing the differential diagnosis.
4. Narcolepsy with cataplexy is associated with abnormal movements during REM sleep that can be either simple (e.g., periodic limb movements during sleep) or complex (e.g., REM sleep behavior disorder).
5. Treatment of narcolepsy with cataplexy may help relieve symptoms of sleep-related rhythmic movements when they coexist.
6. Differentiating seizures from primary sleep disorders may require a full montage EEG PSG.

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CITATION

Primary vs. Specialist Care in Management of Sleep Apnea


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Summary of Primary Care vs. Specialist Sleep Center Management of Obstructive Sleep Apnea and Daytime Sleepiness and Quality of Life: A Randomized Trial

Question: Is a primary care led, ambulatory, simplified approach to diagnosis and treatment of obstructive sleep apnea (OSA) similar in clinical efficacy to specialist sleep center care?

Design: Randomized, controlled, non-inferiority trial; anzctr.org.au Identifier: ACTRN12608000514303.

Allocation: Randomization was conducted by a telephone call to a clinical trials pharmacist independent of the study, using a computer-generated random numbers list.

Blinding: The investigators and participants were not blinded to study arm assignment.

Follow-Up Period: 6 months.

Setting: Participants were recruited from 4 geographical locations in South Australia (metropolitan and rural primary care and nurse led community practices, and a university hospital sleep center in a metropolitan region).

Subjects: 155 adults, mean age 57.2 (n = 81, Primary care) and 54.5 (n = 74, Specialist sleep center), 69% and 57% male, respectively, were randomized. Inclusion Criteria: A high diagnostic likelihood of moderate to severe OSA defined as a score of ≥ 5 on a screening questionnaire and an overnight 3% desaturation index (3%ODI) of ≥ 16 events per hour, and an Epworth Sleepiness Scale (ESS) score ≥ 8 or persistent hypertension despite taking 2 or more antihypertensive agents. Exclusion Criteria: 1) Body mass index (BMI) > 50; 2) neuromuscular disease; 3) unstable psychiatric disease or cognitive impairment considered likely to interfere with adherence to instructions, completing the study or managing CPAP; 4) hospitalization in the previous 3 months for myocardial infarction, unstable angina, cardiac failure, or cerebrovascular accident or New York Heart Association class III or IV symptoms; or 5) lung disease with awake resting oxygen saturation of less than 92%.

Intervention: Patients meeting eligibility criteria were randomized into either primary care management or standard care offered at a specialist sleep center. Both plans included treatment of OSA with continuous positive airway pressure, mandibular advancement splints, or conservative measures only. The primary care physician and community nurse participated in a 6 hour educational program on OSA and its management prior to treating patients. Additionally, the community nurse received 5 days of in-service training with specialist nurses at the tertiary sleep center. Home Auto-titrating CPAP was used over 3 consecutive nights to determine a fixed treatment pressure based on the 90th or 95th (S8 AutoSet Spirit) percentile pressure. CPAP devices were converted to a fixed pressure mode for the remainder of the study.

In the sleep specialist arm, in lab baseline, CPAP titration, or split night polysomnography decisions were left to the discretion of the treating physician. Follow-up phone and clinic visit contact was identical in both arms.

Outcomes: The primary outcome was the change in ESS score from baseline to 6 months. Secondary outcome measures were 6 month changes in the Functional Outcomes of Sleep Questionnaire (FOSQ), Sleep Apnea Symptoms Questionnaire (SASQ), Short-Form 36 Health Survey (SF-36) vitality and mental health components, CPAP adherence, blood pressure, and weight. Within trial sleep diagnostic and treatment costs were collected and compared during the 6-month follow-up.

The sample size was calculated to show the non-inferiority of the primary care arm relative to the specialist group in the mean change in ESS scores after 6 months using an a priori determined non-inferiority margin of -2.0 (based on past studies of minimal clinically important differences for health related quality of life instruments). Clinical studies of variations in ESS scores and ESS responses to placebo CPAP in patients with OSA), assuming 90% power, a one sided type I error of 5%, and a standard deviation of 4.0 for the change in ESS score.

Patient Follow-Up: Intention to treat analysis with replacement of missing values by multiple imputations; 17 of 81 withdrew from primary care arm (79% completed follow-up), 6 of 74 withdrew from specialist arm (92% completed follow-up).

Main Results: There were no statistically significant differences between the groups in the primary outcome. Both management arms showed improvement in ESS after 6 months of therapy. In the primary care group, the mean baseline score of 12.8 decreased to 7.0 at 6 months (p < 0.001), and in the specialist group, the score decreased from a mean of 12.5 to 7.0 (p < 0.001). Primary care management was non-inferior to specialist management with a mean change in ESS score of 5.8 vs. 5.4 (adjusted p = 0.43). There were no differences in secondary outcome measures between groups. Total average costs per patient were estimated at US $1,819.44 in the primary care group and US $3,067.86 in the specialist group.

Conclusion: In adults with at least mild symptoms of daytime sleepiness, a primary care led, ambulatory, simplified approach to diagnosis and treatment of obstructive sleep apnea similar in clinical efficacy to specialist sleep center care.
sleepiness, moderate to severe oxygen desaturation index, and no significant pulmonary, cardiac or cognitive co-morbidities, a simplified management strategy for OSA based in primary care was not clinically inferior to specialist sleep center care in improving symptoms of daytime sleepiness.

Sources of Funding: The study was funded by Project Grant 426744 from the National Health and Medical Research Council of Australia and a small grant from the Flinders Medical Centre Foundation. Equipment donations were received from ResMed (oximetry monitors and CPAP machines), Philips Respironics (CPAP machines), and SomnoMed (mandibular advancement splints).

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COMMENTARY

Various estimates of the prevalence of obstructive sleep apnea (OSA) in the U.S. are available and they range from as low as 2% to as high as 28% of the adult population. Examining specific patient populations such as those with hypertension, obesity, diabetes, stroke or ischemic heart disease would show much higher prevalences. So there is no doubt that primary care physicians seeing adult patients are managing a high percentage of patients with obstructive sleep apnea, and most of them are undiagnosed. I believe every sleep specialist in the U.S. would be ecstatic if the primary care physicians in their area routinely screened for OSA; but they don’t.

One could speculate why they don’t – too busy, too much hassle, the impression that patients won’t wear CPAP, that it isn’t an important diagnosis to make, the testing is too cumbersome, etc. But no matter what the reason, most patients in primary care clinics are not being routinely evaluated for OSA.

In the presented study, the authors show that teaching primary care physicians and their nurses about OSA can result in “non-inferior” outcomes compared to sleep specialists with the primary measure outcome being an Epworth Sleepiness Scale score (ESS). I applaud their efforts to show that such an endeavor can be successful; however, there are a few problems with the study and with translating its results to a U.S. model (the study was performed in Australia).

The study was a “noninferiority” study. It is much easier to show that a treatment is “not worse” than it is to show a treatment is better or even equivalent. A noninferiority study only has to show that a minimal level of effectiveness is present. The authors chose a 2 point improvement in ESS as their primary outcome. Is this the right outcome? ESS scores have been shown to vary quite a bit from day-to-day but it is frequently used scale that has validity (and was developed in Australia). We check ESS scores regularly in our clinic and while it is interesting information, it doesn’t usually help much in management and a multidimensional evaluation such as the FOSQ, may have been a more appropriate primary outcome measure to assess true improvement. The secondary outcomes were also considered “noninferior” although a margin for each of these was not set. It should be kept in mind that such a study does not show that this approach is equivalent, just that it is not significantly worse than the “standard” treatment.

Another aspect of the study was that the sleep specialists were more likely to use different treatments compared to the patients cared for by the primary care team; 1/3 of the specialist’s patients received an alternative therapy. This is probably because the sleep specialists are specifically trained to manage OSA and not just blindly apply CPAP to every patient. They would have the expertise to know which patients may be better candidates for CPAP, dental appliances or conservative treatments – isn’t this why we have specialization in medicine? Additionally, the patients who saw sleep specialists were less likely to stop using CPAP – perhaps because they were better at educating them or choosing them – and, less likely to withdraw from the study. These important distinctions are buried in the details and not noted in the “headlines” of such a paper.

All those issues aside, what would be barriers to doing this in the U.S., outside of a research setting? First, you would have to start by convincing primary care doctors that this was important. Getting them to attend a 5 hour class about sleep apnea in between seeing patients, running an office, taking calls, documentation, etc, etc. We know that most don’t ask about sleep symptoms and have not had adequate education in medical school or during CME sessions on sleep/wake disorders. If you could convince them to attend a class, then you would need to get them to rearrange their office practice so it could screen patients systematically, perform or at a minimum, order home sleep tests (HST), work with the myriad of DME providers who provide CPAP (as often third party payers have preferred providers), teach their office staff to do CPAP prescriptions and downloads. The home sleep testing and CPAP will require insurance approvals and follow-up visits. Additionally the physician will need to review the HST report, discuss options with the patient, order the auto PAP – which then has to be delivered, used and that data downloaded. The primary care provider needs to get the data and give an order to switch the machine to fixed PAP. And then the follow-up visit with someone – nurse or physician – to troubleshoot problems and document usage. Sure, this could be done, but given the constraints on most primary care practices in the U.S., I am not sure this will be seen as a high enough priority.

The model in the paper uses nurses to perform many of these tasks, which is fine, but where does the income come from? The nurse will not get paid for visits (or only at a low level), the staff will not get paid for the home sleep test (unless they do them themselves which sets up another whole level of complexity) nor for CPAP’s, and the doctor visits are usually not reimbursed enough to take care of the overhead. Sleep Centers are much better equipped to perform these tasks and are the experts in diagnosis and treatment. Can it be done in primary care offices? Yes. The likelihood of this happening in most U.S. primary care offices – nil (in my humble opinion).

In conclusion, I wholeheartedly agree that primary care physicians should take a more active role in diagnosing, and even managing OSA. However, until education about sleep disorders is taught in medical schools and residencies and primary care physicians are knowledgeable about the diagnosis and management of OSA, the care of OSA should stay with the sleep specialist.

Response from Chai-Coetzter CL, Antic N and McEvoy D to Commentary by Collop N.

The science of the study was extensively canvassed during journal review and we do not think it particularly helpful to re-
visit Dr. Collop’s criticisms concerning the statistical approach used, change in ESS as the primary endpoint etc. However, we do think it important to comment on the broader translational issues that she has raised. Dr. Collop wholeheartedly agrees that “primary care physicians should take a more active role in diagnosing, and even managing OSA” but then lists a series of perceived barriers. These include that PCPs and their nurses are already too busy and OSA diagnosis and management is too complex for them to be concerned with sleep apnea, that they lack the necessary education and that reimbursement models are not aligned with primary care management. She argues for maintenance of the status quo whereby sleep medicine specialists remain the sole providers of OSA diagnosis and management.

We believe the high prevalence of OSA in the developed and the developing world means we must change our approach to the diagnosis and management of OSA. Decades ago endocrinologists and internists provided the evidence, protocols and training for PCPs and specialist nurses to become actively involved with them in the management of diabetes, a disorder of comparable prevalence to OSA. Sleep medicine specialists are at similar point in history and in our view need to embrace and lead similar changes. Undoubtedly there are challenges ahead in evolving both the skills and knowledge of PCPs and nurse specialists in sleep medicine (incidentally, this applies to Australia as much as it does in the US) but if we dismiss this as all too hard we may miss a generational opportunity. Surely the way forward is to embrace the need for change and to lead the policy discussions and the education programs that build the necessary skills and knowledge, be this in medical and nursing schools, residency programs or amongst primary care physicians and nurses. New funding streams will obviously need to be developed to support these new models of care using evidence from our study, and others, that simplified diagnostic and management approaches to the care of OSA sufferers can provide care more cheaply without jeopardizing patient outcomes.

If we believe OSA is an important disease we must change our ways. Change can be difficult and at times confronting but as the evidence linking OSA with adverse health outcomes mounts we have a responsibility to our patients to make evidenced based diagnosis and management of OSA accessible to as many patients as we possibly can. Furthermore if the Sleep Medicine field does not lead the evolution of new models of care other groups will inevitably do so.

Response to Chai-Coetzter et al., from Collop N.
Contrary to what is written in this response, I did not “argue for maintenance of the status quo.” Nowhere did I state that the current environment is ideal – what I did state in my last paragraph is that I “wholeheartedly agree that primary care physicians should take a more active role in diagnosing, and even managing OSA.” On a personal note, I have been very proactive regarding education about OSA by speaking at our local primary care offices, on a national and regional level at internist and family practice physician’s meetings and in medical schools and internal medicine residencies core lectures series. As AASM president, I organized a taskforce in the AASM to examine inclusion of PA and APN’s in sleep centers; I have developed electives for internal medicine residents in sleep centers; we are in the process of setting up an online educational program for our nursing school to introduce sleep topics. No, I also disagree with the “status quo” and have spent a career teaching various groups about sleep and sleep disorders. But this is not going to happen overnight and the efforts must be aimed at further education of medical students, nursing students, advanced practice providers and in primary care residency programs. Sleep medicine specialists should be leading the way in this effort to educate these groups – which will lead to more patients with OSA getting appropriately diagnosed and treated. Interdisciplinary models of care are the way of the future and sleep centers will also need to figure out how best to facilitate the critical interface with primary care providers to provide the best outcomes for patients with sleep apnea.

CITATION

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LETTER TO THE EDITOR

The editorial “A Warning Shot Across the Bow: The Changing Face of Sleep Medicine” is a cautionary tale. It would seem that a “warning shot” is an understatement. This comes on top of another cautionary tale that 25% of sleep medicine fellowships did not fill up last year, i.e., before recent events. None of this should come as a surprise since the writing has been on the wall for some time (see commentary I wrote in December 2011).

We should not have positioned sleep medicine as a diagnostic discipline based on one test for one diagnosis. The perception of our field nationally is that we simply make money by testing, if not over-testing. It is a perception that we need to counter by accreditation standards to avoid over-testing.

Sleep medicine is a chronic care management discipline with management of many highly prevalent chronic disorders. Accreditation should be based on outcomes of care, not diagnostic criteria, as recommended by the Institute of Medicine report in 2006 (Recommendation 9.2).4

The positive aspect is that as medicine moves to emphasizing patient-centered outcomes, we are in a field that has major assets: (a) highly prevalent disorders that directly affect patient lives, and (b) effective treatments that directly benefit patients. We need, however, a new vision for this field. We need new accreditation standards that help implement this vision and emphasize outcomes of care and comprehensive management of all sleep disorders, based on a team approach, not just sleep apnea. Given “dead canaries” and “warning shots,” we need change now before the next editorial is about an even more catastrophic event.

CITATION


REFERENCES

With interest we read the findings of Shepherd et al., \(^1\) “Symptoms of Aerophagia are Common in Patients on Continuous Positive Airway Pressure Therapy and are Related to the Presence of Nighttime Gastroesophageal Reflux.” Shepherd et al. examined the prevalence of continuous positive airway pressure (CPAP)-associated aerophagia utilizing patient questionnaires to identify symptoms of gastroesophageal reflux (GER) and aerophagia in CPAP users. One of the authors’ conclusions is that the presence of aerophagia symptoms is the strongest predictor of GER symptoms and vice versa. Authors further conclude that aerophagia induced by CPAP may precipitate GER. However, we feel that the authors failed to discuss prior data suggesting evidence to the contrary. The study by Bredenoord et al.\(^2\) is especially important as it sheds more light on the connection between aerophagia and GER.

In Bredenoord’s study, esophageal impedance, pH, and pressure were monitored in patients with and without gastroesophageal reflux disease (GERD) before and after inflation of air into the gastric cavity, an experimental surrogate for physiologic aerophagia. Air infusion increased the incidence of gas reflux; however there was no increase in acid reflux episodes. These findings are supported by Sifrim et al., who also concluded that the liquid component of GER occurred as a primary event and not associated with gas.\(^3\) In light of this contradictory evidence, we should be cautious to assume that aerophagia precipitates GER, and in fact the opposite may be true.

Furthermore, in data sub-analysis by Shepherd et al., patients with preexisting GER showed no more aerophagia after CPAP than non-GER patients. This finding is also at odds with Bredenoord et al.,\(^2\) who reported that in patients with GERD, the rate of belching is 60% higher than healthy subjects. GERD patients may be more prone to belching due to increased air swallows,\(^2\) baseline deficiency in lower esophageal sphincter (LES) tone, or increased rate of transient LES relaxation.\(^4\) The lack of aerophagia in GERD patients after CPAP raises the question, does CPAP actually improve baseline aerophagia in GERD patients?

Given conflicting evidence in the literature regarding the relationship between GER, aerophagia, and CPAP, it may be premature to assume causality among these entities. The directionality of this link has consequences in the way we approach and treat CPAP users with symptoms of aerophagia.

CITATION

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DISCLOSURE STATEMENT
This was not an industry supported study. The authors have indicated no financial conflicts of interest.
LETTER TO THE EDITOR

We appreciate the interest shown in our paper by Snapp and Sharma but disagree with their suggestion that the findings in two previous studies to which they refer contradict our own. Both these other studies investigated reflux events in individuals who were awake and upright. Our study was of new symptoms of aerophagia and reflux in individuals commenced on continuous positive airway pressure (CPAP) therapy for obstructive sleep apnea. This therapy, which is known to be associated with aerophagia, is applied overnight when the subjects are predominantly recumbent and asleep. In the Bredenoord et al. study, aerophagia was induced by infusing 600 mL of air into the stomachs of individuals with and without gastroesophageal reflux disease (GERD). In the Sifrim et al. study, a meal was used to induce postprandial reflux in healthy young volunteers. It is unclear what relevance, if any, the findings of these studies have to questionnaire responses regarding GER symptoms in obstructive sleep apnea patients following commencement of CPAP.

Comparing findings between studies in upright and recumbent subjects is unproductive. Several studies have reported that reflux episodes which occur in the upright position are primarily gas episodes, while the majority of those which occur in the recumbent position are liquid in nature. This is likely due to the esophago-gastric junction being “submerged” in liquid stomach contents when recumbent, whereas the junction is in air when upright. In the sleeping subjects of our study, the CPAP therapy associated aerophagia will occur almost exclusively in the recumbent position, increasing the likelihood of liquid reflux episodes and therefore GER symptoms.

In our paper we recognize the difficulty in assigning directionality to an association between GER and aerophagia symptoms referred to by Snapp and Sharma and state clearly that our data cannot directly answer whether it is aerophagia that precipitates GER or the reverse. Our sub-analysis of individuals before and after CPAP treatment showed that reflux that pre-exists CPAP does not predispose to aerophagia when on CPAP. However the occurrence of GERD symptoms after institution of CPAP is associated with a significant increase in aerophagia symptoms. On this basis we speculated that CPAP-induced aerophagia might precipitate GER, particularly overnight. We reiterate that the association we found between symptoms of aerophagia and symptoms of GER in those on CPAP therapy is strong and warrants further attention.

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REFERENCES

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Rapid Eye Movement Sleep: Regulation and Function is an expertly crafted treatise on rapid eye movement (REM) sleep, aimed at the reader with particular interest in this phenomenon. The discovery of REM sleep serves as an important lesson in the role of “thinking outside of the box” in the advance of science. Prior to 1951, the prevailing thought in academic circles was that sleep was a passive phenomenon. Our knowledge of sleep physiology took a quantum leap forward in that year when University of Chicago graduate student Eugene Aserinsky, using an aging Offner Dynograph, enlisted his 8-year-old son, Armond, for a recording of the youngster’s electroencephalogram and electrooculogram during sleep. Later in the night, the recording appeared to show that his son was awake and looking around, prompting Aserinsky to check on Armond’s well-being. Rather than awake, on the contrary he found Armond with his eyes closed and clearly asleep. Aserinsky and his mentor Nathaniel Kleitman went on to publish a brief report of this intriguing finding in the journal Science, and the field of rapid eye movement sleep was born. Since this initial discovery, the images, ideas, sensations, and emotions associated with REM sleep have been the topic of philosophical, religious, and scientific speculation, and a burgeoning amount of research has appeared aimed at identifying and defining the unique characteristics of this physiologically different phase of sleep. Rapid Eye Movement Sleep: Regulation and Function serves as a compilation of both the extant body of scientific research on REM sleep (and dreaming), as well as touching on some of the psychological and philosophical implications of this state of being.

This is a weighty volume of 478 pages, divided into six provocative sections. The introductory chapters present a history of the science of dreaming and REM sleep, a discussion of the inexact temporal association between REM sleep and dreaming, and philosophical musings on the phenomenology of dreaming. Chapters on the hard science of REM follow, with extensive discussions of general biology in section II (including evolutionary development, a systems approach to REM sleep, and circadian considerations), and then chapters in sections III, IV, and V exploring topics such as the interactions between various neuroanatomical locations that regulate and control REM, the neurochemistry of REM, and the functional significance of REM. There are detailed descriptions of the research that has led to our current understanding of the neuroanatomy and neurochemistry of REM; the interested reader will be fascinated by the descriptions of these painstaking investigations. The book also describes certain specific CNS locations that are activated by REM sleep, presumably leading to the experiencing of emotions or memories during this sleep state. After extensive coverage of normal REM sleep, section VI concludes the text by discussing what can go wrong in REM sleep, particularly narcolepsy, REM sleep behavior disorder (RBD), and multi-directional interactions between psychiatric illness, REM sleep, and dreaming. Although the title of the book implies that the focus is on REM sleep alone, many subjects that are important to the regulation of NREM sleep and of wakefulness appear throughout the text as well. Particularly noteworthy are concise discussions of the neurotransmitters that are essential to the regulation of wake, NREM sleep, and REM sleep. Accompanying all of this material are exceptional colored pictures, graphs, MRI scans, slides, and other excellent visual learning aids.

Rapid Eye Movement Sleep: Regulation and Function condenses nearly 60 years of research and academic thought into a well-written and nicely illustrated review of virtually every aspect of this intriguing state of being. Although there are books that speak to the subjects of sleep and dreaming, most are not scientifically rigorous. This book is unique in view of its meticulous, scientifically precise focus. While this approach may appear daunting at first, the body of knowledge presented is in fact easily accessible and consequently presents an opportunity for the reader to be exceptionally well versed in a fascinating aspect of sleep medicine. Definitely an excellent addition to the sleep specialist’s library.

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