Sleep, 20(6):423–487

An American Sleep Disorders Association Review

The Indications for Polysomnography and Related Procedures

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Summary: This paper is a review of the literature on the use of polysomnography in the diagnosis of sleep disorders in the adult. It is based on a search of MEDLINE from January 1966 through April 1996. It has been reviewed and approved by the Board of Directors of the American Sleep Disorders Association and provides the background for the accompanying ASDA Standards of Practice Committee's Parameters for the Practice of Sleep Medicine in North America. The diagnostic categories reviewed are: sleep-related breathing disorders; other respiratory disorders; narcolepsy; parasomnias and sleep-related epilepsy; restless legs syndrome and periodic limb movement disorders; insomnia; and circadian rhythm sleep disorders. Where appropriate, previously published practice parameters papers are cited and discussed. The relevant published peer-reviewed literature used as the basis for critical decisions was compiled into accompanying evidence tables and is analyzed in the text. In the section on the assessment of sleep apnea syndrome, options for estimating pretest probability to select high risk patients are also reviewed. Sleep-testing procedures other than standard polysomnography are also addressed (daytime polysomnography, split-night studies, oximetry, limited full respiratory recordings, and less-than-full respiratory recording) and treatment-related follow-up studies are discussed. **Key Words:** Practice parameters—Practice guidelines—Standards of practice—Polysomnography—Sleep apnea syndrome—Sleep disorders—Narcolepsy—Parasomnias—Restless legs syndrome—Periodic limb movement disorder—Insomnia—Circadian rhythm disorders.

1.0 INTRODUCTION

Polysomnography (PSG) is a recording of multiple physiologic parameters relevant to sleep. Traditionally, clinical studies have used a typical recording montage that includes electroencephalography (EEG), electrooculography (EOG), chin electromyography (EMG), respiratory effort, airflow, electrocardiography (ECG), oximetry, and anterior tibialis EMG (1); one or several channels of each of these parameters allow for necessary data acquisition. Recently, however, sleep-testing procedures performed with fewer channels have been proposed as adequate to diagnose some sleep disorders (2–25). The purpose of this background paper is to evaluate the literature to determine when PSG or other sleep-testing procedures are indicated for the diagnosis of a variety of sleep disorders and what the necessary recording variables are for each specific diagnosis.

Accepted for publication March 1997.

2.0 HISTORIC INFORMATION

PSG and clinical sleep medicine originated in the late 1950s and have evolved together. Their beginnings were precipitated by the discoveries and characterizations of rapid eye movement (REM) sleep and sleep apnea. Rapid eye movement sleep was first described by Kleitman, Aserinsky, and Dement in Chicago (26,27) and subsequently by Jouvet, Michel, and Mounier in France (28). In the mid-1960s, two groups of European researchers (29,30) made observations about the correlations between upper airway obstruction and disturbed sleep, thereby discovering sleep apnea.

During the burgeoning clinical and basic research that followed the discoveries of REM sleep and sleep apnea, PSG was the essential tool to investigate sleep and its disorders and became the accepted standard for clinical practice. Efficient clinical use of PSG increasingly became an issue in the late 1980s, partly because of concerns over rapidly rising healthcare costs in the United States. Because of the simultaneous development of PSG and sleep medicine, the great majority

of sleep experts consider that PSG is the de facto standard for diagnosing sleep disorders. Nevertheless, PSG as a clinical tool has not undergone the same evaluation of its accuracy, reliability, and validity that is now demanded for newer diagnostic tests in all fields of medicine.

Practice guidelines for the use of clinical PSG have been published by specialty societies, such as the American Thoracic Society (ATS) (31), the American Academy of Neurology (AAN) (32), and the American Electroencephalographic Society (AEEGS) (33), and by the American Association of Respiratory Care (AARC) and the Association of Polysomnographic Technologists (APT) (34). These guidelines used primarily consensus–conference approaches to determine PSG indications. In 1992, the Agency of Health Care Policy and Research's (AHCPR) Office of Technology Assessment performed an evidence-based assessment of PSG and the multiple sleep latency test (MSLT) and found that insufficient published, peer-reviewed information was available to recommend any polysomnographic techniques other than standard in-laboratory PSG and MSLT (35). Since these technology assessments were released, new information has become available. Therefore, the Board of Directors of the American Sleep Disorders Association (ASDA) appointed a task force comprised of the Standards of Practice Committee and additional experts, whose mission included reviewing the published, peer-reviewed literature regarding PSG and other sleep-testing procedures. Based upon a critical analysis of that literature, the task force forged a set of indications for the use of PSG in the more common sleep disorders.

The diagnostic categories selected for review included: sleep-related breathing disorders, other respiratory disorders, narcolepsy, parasomnias and sleep-related epilepsy, restless legs syndrome (RLS) and periodic limb movement disorder (PLMD), insomnia, and circadian rhythm sleep disorders.

3.0 METHODS

3.1 MEDLINE search

MEDLINE searches covered publications from January 1966 to April 1996. Each section of this paper used the search terms *polysomnography, polysomnogram,* and *sleep studies*; further inclusion and exclusion criteria and additional relevant search terms for topics are listed in each section. Articles published in English that included adult subjects (age greater than 18 years) were retrieved and reviewed. Reviews, case reports, editorials, abstracts, and letters were excluded from the evidence-based evaluation. Reviewers were consulted concerning the thoroughness, comprehensiveness, and accuracy of the literature review and of the interpretation. At a national conference and on multiple conference calls, the PSG task force discussed and assimilated the evidence-based background data and developed practice parameters and algorithms for the use of PSG and some additional sleep-testing procedures (36). The final document was approved by all authors and the ASDA Board of Directors.

3.2 Definition of measures

A glossary of the terms referred to in this paper is included in the appendix (Appendix A, terms pertinent to sleep disorders medicine; Appendix B, terms pertinent to biases and validity).

4.0 SLEEP-RELATED BREATHING DISORDERS (SLEEP APNEA AND UPPER AIRWAY RESISTANCE SYNDROME)

4.1 Overview

The typical sleep apnea–hypopnea syndrome (SAS) consists of symptoms that affect patients during times of both wake and sleep. The diagnosis of SAS is based on the demonstration of apneas or hypopneas or both during sleep. The symptoms usually include excessive daytime sleepiness (EDS) and loud snoring. In addition, patients may have cognitive deficits, systemic hypertension, and complications of hypoxemia. The patients are typically male, but a substantial number of women, particularly postmenopausal women, have been diagnosed with the syndrome (37). Most apneas and hypopneas are of an obstructive or mixed type, but they may also be central in nature (i.e. with absence of or decrease in respiratory effort). An associated sleep-related breathing disorder is the upper airway resistance syndrome (UARS), in which partial obstruction of the upper airway during sleep produces arousals, snoring, and EDS without apneas or hypopneas (37).

The evolution of an understanding of SAS began with the study of the Pickwickian syndrome, in which patients have EDS and cardiorespiratory failure (38). Studies of such patients led to the discovery of apnea and its effects on sleep (29). It soon became apparent that many obese snorers without cardiorespiratory failure also had sleep apnea and EDS and that SAS was much more common than the Pickwickian syndrome (39).

Attended PSG is the time-honored technique for confirming a diagnosis of sleep-related breathing disorders. Recently, a number of studies have examined the utility of more limited techniques, i.e. respiratory and cardiorespiratory sleep studies with less-than-full

PSG montages, unattended studies, or studies performed in the patient's home (40). Alternative approaches to traditional EEG, EMG, and EOG staging of sleep also have been examined.

Sleep apnea syndrome is relatively common in adults; it also occurs in children, but the prevalence has not been defined. A recent estimate in Wisconsin is that 4% of men and 2% of women aged 30 to 60 years have SAS, as defined by an apnea–hypopnea index (AHI) of at least five events per hour of sleep plus reported sleepiness (41). In adults, the prevalence is positively correlated with age.

Treatment strategies include tracheostomy and other operations of the upper airway, weight loss, continuous positive airway pressure (CPAP), and the use of oral appliances (42). Studies have shown that treatment of sleep-related breathing disorders improves patients' symptoms of EDS and their survival (37, 42–47).

Because recently published practice parameters describe indications for PSG in patients using oral appliances (48) or treated by laser-assisted uvulopalatopharyngoplasty (LAUP) (49), surgical modifications (50), or other surgical procedures, those subjects have not been reevaluated for this paper.

4.2 MEDLINE search terms and review of papers

The additional specific MEDLINE search terms for this section included *sleep apnea, snoring, insomnia, excessive daytime sleepiness, central sleep apnea* (CSA), *tracheostomy, multiple sleep latency test, wakefulness test,* and *sleepiness.* References from selected articles were also retrieved, as were references from standard textbooks.

The inclusion criteria for reviewing the literature were as follows: 1) studies that included 10 or more subjects, unless the study was a randomized controlled trial, in which case any number of subjects was acceptable (because the design of randomized studies makes them interpretable with fewer subjects); 2) in the absence of better evidence and where there were several studies with smaller numbers of patients but similar and consistent results, these studies were accepted for some topics of interest; and 3) studies that validated devices other than usual nocturnal polysomnography, including unattended studies and limited studies (i.e. oximetry, full respiratory recording, and less-than-full respiratory recording) by comparing the devices to attended polysomnography. The initial literature search revealed 91 potential articles. In reviewing these articles, 34 were deleted because they were reviews, isolated reports, or case reports, or did not include at least 10 subjects. All of the remaining studies were reviewed in detail. An additional 30 studies were excluded because they attempted to validate alternative devices (e.g. unattended or limited studies) without comparison to attended PSG, or because they used these devices as the tool of investigation and were not validation studies. The final analysis included 27 studies meeting all three inclusion criteria: three daytime PSG studies, eight oximetry studies, eight less-than-full respiratory studies, and eight full respiratory studies.

4.3 Evidence-based literature for PSG and other sleep medicine procedures

4.3.1 Central sleep apnea

Texts such as *Principles and Practice of Sleep Medicine* (51) and the *International Classification of Sleep Disorders* (ICSD) (52) divide SAS into CSA and obstructive sleep apnea (OSA). Review of the literature, however, suggests that except in cases of "pure" central apnea (as might occur in patients with abnormal brainstem function), the causes, significance, and treatment of central apneas in most patients are not clearly distinct from those of obstructive apneas.

Evidence suggests a relationship between central apneas and upper airway obstruction: central apneic events are commonly seen in patients with OSA, and patients with predominantly central apnea have symptoms similar to those of patients with predominantly obstructive apneas (53–55); various mixtures of obstructive, mixed, and central apneas may occur in an individual patient (although it is rare for central apneas to predominate); CSA may be position dependent (54); central apneic events may convert to obstructive events with oxygen administration (56); and central apneas often improve with the use of nasal CPAP (54).

Although insomnia has been proposed as a characteristic symptom of CSA, this association has been described in only a few cases (54,56,57) and, in fact, the symptom is not specific for respiratory disturbance of any type.

Case reports have been published that included results of documented assessments of patients with CSA; however, no studies met our inclusion criteria that identified specific presenting symptoms that would reliably differentiate patients with CSA from those with OSA. Therefore, the indications for PSG, and the general monitoring techniques required, are essentially the same for both conditions, and these disorders are included in discussions of SAS in subsequent sections of this paper.

4.3.2 Sleep apnea syndrome

4.3.2.1 Symptoms and associated risk factors. The main symptoms of SAS are loud snoring and EDS

(37). Other findings and associated risk factors include obesity, ECG changes, and insomnia. We examined the literature to determine the degree to which these features, individually or in combination, indicate a need for PSG. Section 4.3.2.2 will review multivariate analyses of symptoms and other factors that assess a patient's pretest probability for having SAS.

4.3.2.1.1 Snoring and observed apneas. A history of snoring and observed apneas (i.e. breath holding) during sleep is strongly associated with a subsequent diagnosis of SAS; a standard text lists these symptoms as useful initial criteria in determining which patients are likely to have sleep apnea (37). In most studies looking at snoring, the data tend to be similar, and the evaluation of snoring typically is part of a multifactorial analysis of symptoms. One very large study, which looked at snoring and breathing pauses in 1,409 patients, documented that the greater the frequency of reported snoring or observed breath holding, the more likely the patient is to have SAS (58). The symptoms of both snoring and breath holding are more often associated with the diagnosis of SAS in men than in women.

4.3.2.1.2 Excessive daytime sleepiness. Sixteen articles that address various assessments of EDS in patients with EDS symptoms are listed in Table 1. Results of these studies indicate 1) that there is a high prevalence of SAS in patients with EDS who are referred to sleep disorders centers (59); 2) that, in general, EDS (as measured in a variety of ways) correlates well with arousals, AHI, AI, and arterial oxygen desaturations (60–72); and 3) that CPAP therapy improves EDS (45,62,73).

One study specifically examined the prevalence of SAS among patients with a history of EDS who were referred to a sleep laboratory and found an 84% prevalence among men and a 60% prevalence among women (59). In patients referred to sleep disorders centers with suspected SAS (but not specifically with EDS), EDS prevalence rates range from 22% to 73% (4,7,9,10,12,74–80). These reports suggest that, in patients referred to sleep disorders centers, EDS is a frequent but not specific finding, suggestive of SAS.

Several studies used the multiple sleep latency test (MSLT), the maintenance of wakefulness test (MWT), and responses to the Epworth Sleepiness Scale (ESS) as measures of EDS; these studies generally revealed correlations of test results with the degree of sleep disturbance (as measured by PSG) in patients with SAS. In four studies, EDS (as measured by MSLT) correlated better with arousals than with decreases in oxygen saturation (SaO_2) (65,67,68,81). In one study (60), MSLT correlated better with SaO_2 than with arousals, and in another study, EDS (as measured by responses to an unvalidated questionnaire) correlated better with SaO_2 than with arousals. In two other studies, the AHI (71) and short arousals (70) correlated with EDS (as measured by MSLT); SaO_2 was not measured in either of these studies. Two additional studies (66,73) found that EDS (as measured by the MWT) was significantly correlated with various respiratory disturbances during sleep. Respiratory arousals and decreases in SaO_2 correlated with the degree of sleepiness (66), whereas the use of CPAP was associated with a decrease in sleepiness (73).

The ESS, a questionnaire-derived measure of EDS, has been validated in four studies by one investigator (61–64). These articles provide credible evidence, including significant correlation with MSLT in several circumstances, that patients' responses to this questionnaire could distinguish excessively sleepy patients from normal subjects and from patients with insomnia. The ESS could also distinguish among patients with various severities of SAS, as defined by AHI. These studies also found that levels of AHI between 5 and 15 were associated with EDS and that an AHI less than 5 was still associated with significant sleepiness in primary snorers, a finding that may be relevant to patients with UARS (as will be described in section 4.3.3). The ESS also documented improvement after treatment with CPAP (62).

These combined data suggest that the predictive value of EDS for a specific level of SAS severity (based on SaO_2 changes or specific respiratory-event frequency) is variable. EDS is, however, a reliable predictor of the likelihood of the presence of SAS and of the need for a diagnostic sleep study.

4.3.2.1.3 Obesity. Obesity has been identified as a risk factor for sleep apnea, and a number of authors have reported on the positive relationship between body weight or body mass index (BMI) and apnea severity (75,82–90). These reports raise the questions of whether excess weight alone could be an indication for PSG and whether weight fluctuations, either with or without changes in other symptoms, should be an indication for repeat PSG or CPAP recalibrations.

These studies suggest that only in combination with other symptoms is obesity an indication for PSG. Various authors (80,83,90–95) have tried to correlate the pattern of fat distribution with RDI or number of desaturations. Results of these studies are mixed, but correlation with neck circumference appears to be more promising than are correlations with other specific locations of obesity (e.g. abdominal girth). Again, however, the symptom of obesity alone is not sufficiently specific to be predictive of which patients are in need of further evaluation. The combination of BMI with other features, however, can be used to predict high pretest probability for SAS (see section 4.3.2.2).

The efficacy of weight reduction as a treatment for

TABLE 1. *Evidence for sleep-related breathing disorders and excessive daytime sleepiness*

Reference	Study design/ location	# of patients	Monitoring channels	Study parameters	Bias	Diagnostic value of testing procedure
App et al. 1990 (59)	CoS/lab	1,000	SS CR EMG_2 SaO_2 MSLT	All presented with EDS, AI not defined as a number but probably an AI ≥ 5. 84.1% of men and 59.6% of women had sleep apnea as a final diagnosis.	Patient-selection bias, errors in measurement of outcomes, population bias	Sleepiness in patients referred to sleep centers is usually due to sleep apnea.
Bédard et al. 1991 (60)	NCT/lab	20	SS CR EMG_2 SaO_2 MSLT	AI > 10. EDS. SaO_2 < 80%.	Patient-selection bias	MSLT correlates with minimum SaO_2 during sleep.
Guilleminault et al. 1993 (45)	NCT/lab	48 (15 OSA)	SS CR MSLT	UARS patients, arousal index > 10, MSLT < 10	Patient-selection bias, population bias	MSLT increased from 5.3 ± 1.5 to 13.5 ± 2.1 with CPAP.
Johns 1991 (61)	CCS, CoS/ lab	180 completed questionnaire 150 patients, 30 controls	SS CR EMG_2 SaO_2 Sound Body position	RDI > 5, mild OSA 5 ≤ 15, moderate 15 ≤ 30, severe > 30. ESS used to measure sleepiness.	Patient-selection bias, population bias	Patients with all levels of RDI had significant sleepiness compared to controls and primary snorers. Patients with severe OSA were significantly sleepier than those with mild or moderate OSA. Those with mild and moderate OSA were not significantly different from each other.
Johns 1992 (62)	NCT/lab	308	SS CR EMG_2 SaO_2 Sound Body position	ESS is measured in patients with RDI ≥ 4 (average 27.1) for CPAP titration (n = 54), medical students (n = 104 with 87 follow-up), and 150 with various sleep disorders from Johns 1991.	Patient-selection bias, confounding factors, population bias	High level of reliability of ESS, high level of consistency over 5 months. ESS measures reduction in sleepiness with CPAP therapy.
Johns 1993 (63)	NCT, CoS/ lab	273 108 snorers, 165 OSA	SS CR EMG_2 SaO_2 Sound Video Body position	RDI ≥ 5, stratified into mild (RDI 5 ≤ 24.9), moderate (RDI 25 ≤ 49.9), and severe (RDI ≥ 50). Primary snorers and nonsnoring controls.	Population bias	Patients with all levels of RDI were sleepy. Snorers were sleepy despite an RDI < 5. ESS level was less in snorers and consistent with level of severity of sleep apnea.
Johns 1994 (64)	NCT/lab	381 331 patients with 50 spouses	SS CR EMG_2 SaO_2 Sound Body position MSLT in 44	RDI ≥ 5; 44 with MSLT had diagnoses of: 8, OSA; 4, PLMD; 10, narcolepsy; 12, idiopathic hypersomnia; 9, psychophysiologic hypersomnia; 1, head trauma. MSLT and ESS significantly correlated, explaining 40% of variance in MSLT.	Errors in measurement of outcomes, population bias	ESS provides a subjective measure of sleepiness that is consistent with an independent observer (i.e. the spouse) and an independent objective measure (i.e. MSLT).
Phillips et al. 1990 (65)	Blinded crossover RCT/lab	8	SS CR SaO_2	AHI ≥ 5, AHI of 21 at baseline, MSLT averages > 10 minutes at baseline	Random error, population bias	Oxygen therapy had no effect on sleep latency. The use of CPAP significantly increased latency.
Poceta et al. 1992 (66)	CSS/lab	322	SS CR	RDI SaO_2 MWT	Population bias	MWT correlates with various measures of sleep disturbance from OSA and shows improvement with CPAP.

TABLE 1. *Continued*

Reference	Study design/ location	# of patients	Monitoring channels	Study parameters	Bias	Diagnostic value of testing procedure
Roehrs et al. 1989 (67)	NCT/lab	466	SS CR SaO_2 MSLT	AI > 5, AI mean 42, MSLT of 5.87 minutes	Population bias	Respiratory arousals correlate best with MSLT. SaO_2 events correlate but provide no independent predictive information.
Sangal et al. 1992 (73)	NCT/lab	47	SS CR MSLT MWT	MWT measure before and after treatment in a variety of sleep disorders.	Population bias, confounding factors	MWT measures improvement with CPAP treatment (from 23.4 ± 14 to 30.0 ± 12).
Sforza and Lugaresi 1995 (68)	NCT/lab	30	SS AF RE SaO_2 Esophageal balloon MSLT	Severe OSA with range of AHI of 35.2 to 108.6. Four studies with baseline and CPAP and with CPAP and off CPAP after 1 year.	Patient-selection bias, population bias	MSLT improvement was correlated with fewer arousals during sleep with CPAP at 1-year follow-up.
Sink et al. 1986 (69)	CoS, CCS/ lab	37	SS EMG_2 CR SaO_2	AHI > 10, sleepiness based on questionnaire and only those with high levels of sleepiness were considered positive.	Errors in measurement of outcomes, population bias	SaO_2 is best associated with high levels of sleepiness in patients with sleep apnea.
Stepanski et al. 1984 (70)	CCS/lab	55	SS EMG_2 CR SaO_2 MSLT	AI > 5, groups included OSA, PLMs, normals, and insomnia patients; OSA patients had equivalent of 4-minute sleep latency on average.	Population bias	Increasing number of short arousals is related to increasing sleepiness on the MSLT in OSA patients. Normals did not have a relationship between sleepiness and arousals.
Valencia-Flores et al. 1993 (71)	CoS/lab	31	SS EMG_2 CR MSLT	Women over age 60 unselected for sleepiness or likely apnea. After PSG and MSLT study, groups included AHI ≤ 5, AHI 5–20, AHI > 20, and a sleepy group with a low AHI (on average of 5.5).	Random error, population bias	Elderly women with sleepiness and apnea during sleep are more likely to have an AHI > 20. However, low levels of apnea may also be associated with sleepiness in some patients.
Zorick et al. 1983 (72)	NCT, CoS/ lab	31	SS AF RE SaO_2 MSLT	AI rather than AHI used—AI > 5. PSG and MSLT performed before and after UPPP. Number of arousals and AI negatively correlated with MSLT. Responders had reduced AI to 11.7 from 64.4, and sleep latency went from 3.4 minutes to 9.6 minutes.	Population bias	Measures of sleep fragmentation are best predictors of MSLT. MSLT not fully normal in responders.

CoS, cohort study; SS, sleep staging includes EEG (electroencephalogram), EOG (electrooculogram), and EMG_1 (chin electromyogram); CR, cardiorespiratory monitoring includes AF (airflow), RE (respiratory effort), and heart rate or ECG (electrocardiogram); EMG_2, anterior tibialis electromyogram; SaO_2, arterial oxygen saturation; MSLT, multiple sleep latency test; EDS, excessive daytime sleepiness; AI, apnea index; NCT, nonrandomized controlled trial; OSA, obstructive sleep apnea; UARS, upper airway resistance syndrome; CPAP, continuous positive airway pressure; CCS, case control study; RDI, respiratory disturbance index; ESS, Epworth sleepiness scale; PLMD, periodic limb movement disorder; RCT, randomized controlled trial; AHI, apnea–hypopnea index; CSS, cross-sectional study; MWT, maintenance of wakefulness test; PSG, polysomnography.

Table 2. *Evidence for predictive questionnaires*

Reference	Study design/ location	# of patients	Monitoring channels	Study parameters	Bias	Diagnostic value of testing procedure
Crocker et al. 1990 (78)	CoS/lab	214	SS AF RE SaO_2	AHI > 15 for OSA. Developed probability equation using observed apnea, BMI, age, hypertension. Self-administered.	Population bias	Equation may be used to stratify patients to a high probability group for AHI > 15. If probability is 15% or less, sensitivity is 92%, specificity is 51%. If probability at least 70%, sensitivity is 46%, specificity near 100%.
Dealberto et al. 1994 (75)	CoS/lab	129	SS CR SaO_2 $tcPO_2$ $tcPCO_2$	AHI ≥ 10 for OSA. Age, sex, BMI, and snoring used for probability. Self-administered.	Population bias	Problematic to exclude because of issue of UARS. If probability 25% or less, sensitivity is 94% and specificity is 62%.
Deegan and McNicholas 1996 (76)	Blinded CoS/lab	250	SS CR SaO_2	AHI ≥ 15. Observed apneas, use of alcohol, BMI ≥ 30, and age used in probability equation. Self-administered.	Errors of ascertainment of exposure to an intervention, population bias	High probability may be used to stratify to AHI ≥ 15. If probability 26% or less, sensitivity for AHI ≥ 15 is 100%, specificity 16%. If probability at least 70%, sensitivity is 36%, specificity 90%.
Douglass et al. 1994 (112)	Preliminary NCT/ home	519	SS EMG_2 CR SaO_2	AI > 5 probably used for OSA. Questionnaire for OSA, narcolepsy, PLMD, and psychiatric disorders. Twelve items for OSA used in score. Score > 36 in men and 32 in women used as cutoff. Administered by staff.	Patient-selection bias	May be useful to stratify to high probability group for AI > 5. Use for exclusion of patients is problematic because of UARS issue. Sensitivity of score for men is about 85%, with a specificity of about 93%. For women, it is about 80% and greater than 95%, respectively.
Flemons et al. 1994 (80)	CoS Blind/lab	200 (180 completed PSG)	SS CR SaO_2	AHI > 10 for OSA. Used habitual snoring, neck circumference, reports of choking or gasping during sleep, and hypertension to develop score. Probably administered by staff.	Errors of ascertainment of exposure to an intervention, population bias	Low posttest probability made problematic by issue of UARS. High posttest probability is lower for AHI > 20 than for > 10, making use for stratification problematic. If score ≤ 5, this substantially decreases the probability of AHI of 10 or 20. If score is ≥ 15, this substantially increases the probability of AHI of 10 or 20.
Haraldsson et al. 1992 (113)	CoS/lab	42	SS AF RE SaO_2	AI > 5 for OSA. Used responses to snoring, observed apnea, mid-sleep awakenings, difficulty falling asleep initially or after awakening, and EDS to determine a high likelihood of sleep apnea. Not clear who administered.	Population bias	Low specificity makes use for stratification problematic. Use to exclude patients made problematic by issue of UARS. If questionnaire positive, sensitivity and specificity for AI > 5 were 80% and 78%, for AI > 10 were 91% and 74%.
Rauscher et al. 1993 (77)	CoS/lab	338	SS CR SaO_2	AHI ≥ 10 for OSA. Equation used gender, weight, falling asleep while reading, observed apnea. Self-administered.	Population bias	May be used to stratify to high probability group for having AHI ≥ 10. For probability of 31% or less, sensitivity and specificity were 94% and 49%. For probability of at least 70%, respective values were 38% and 87%.

Table 2. *Continued*

Reference	Study design/ Location	# of Patients	Monitoring Channels	Study parameters	Bias	Diagnostic value of testing procedure
Viner et al. 1991 (79)	CoS, blinded/lab	410	SS CR SaO_2	AHI > 10. Developed probability from questionnaire using age, gender, BMI, habitual snoring. Administered by a physician.	Errors of ascertainment of exposure to an intervention, population bias	Ability to exclude made problematic by issue of UARS. May be used to stratify to high probability group for AHI > 10. If probability 20% or less, sensitivity and specificity were 94% and 28%. If probability at least 70%, respective values were 28% and 95%.

CoS, cohort study; SS, sleep staging includes EEG (electroencephalogram), EOG (electrooculogram), and EMG_1 (chin electromyogram); CR, cardiorespiratory monitoring includes airflow (AF), respiratory effort (RE), and heart rate or ECG (electrocardiogram); SaO_2, arterial oxygen saturation; AHI, apnea–hypopnea index; OSA, obstructive sleep apnea; BMI, body mass index; $tcPO_2$, transcutaneous arterial oxygen tension; $tcPCO_2$, transcutaneous arterial carbon dioxide tension; UARS, upperairway resistance syndrome; NCT, nonrandomized controlled trial; EMG_2, anterior tibialis electromyogram; AI, apnea index; PLMD, periodic limb movement disorder; PSG, polysomnography; EDS, excessive daytime sleepiness.

SAS in obese patients is variable, implying that factors other than weight are involved. Noseda et al. (96) used PSG to evaluate the effects of weight reduction in 39 patients with SAS who had used CPAP for 1 year. The decrease in the AHI at 1 year correlated significantly with reduction in BMI and was negatively correlated with baseline AHI.

Peiser et al. (97) followed 15 morbidly obese SAS patients for up to 12 months after the patients underwent gastric bypass operations to achieve weight reduction and found no particular correlation between the reduction in weight and the decrease in the AI. A later study at the same institution (98), however, showed promising results with weight reduction for the treatment of SAS. At a mean follow-up of 43 weeks, 47 patients were found to have a mean reduction in AI from 60 per hour to 8 per hour, with 72.3% of the patients having a postoperative AI of less than 10 per hour, and 40.4% of the patients having no apneas. However, stepwise multiple regression analysis revealed that only 19% of the variance in postoperative AI was accounted for by percentage of body weight lost, preoperative AI, and time interval between the operation and the postoperative PSG. Of the six followed up long term, three had regained considerable weight, and these three all had severe SAS at follow-up.

Pillar et al. (99) reported that five of 14 morbidly obese patients with SAS had a recurrence of sleep apnea without concomitant weight increase 7.5 years after they had undergone gastric bypass operations and vertical-banded gastroplasty. The authors concluded that obesity is not the only causative factor in SAS in the morbidly obese; aging may contribute to the later recurrence of SAS.

In summary, obesity alone (without the presence of other risk factors for, or symptoms of, SAS) is not a good predictor of SAS. Significant weight loss in obese patients with SAS can result in improvement or a resolution of the sleep apnea (factors other than the obesity, however, may contribute to sleep apnea and the variability of weight loss results, and SAS may recur at a later date even if the patient does not have a significant weight gain). The limited available data regarding the use of CPAP and weight changes suggest that it is not possible to predict a change in pressure requirement (or elimination of the need for CPAP altogether) based only on known weight loss or gain.

4.3.2.1.4 Insomnia. Six articles addressed insomnia as a symptom of SAS (100–105). All were case control, cohort, or nonrandomized controlled trials. In five reports covering thousands of patients, the prevalence of SAS in patients referred to various sleep disorders centers for assessment of insomnia ranged from 0% to 7% (100–102,104,105). Another study found no dif-

ference in AHI levels between controls and patients with insomnia (103). These studies indicate that insomnia is not a frequent presenting symptom of SAS.

Some evidence indicates that women with SAS complain more of insomnia than do men, but this evidence is insufficient to lead to firm conclusions. In one study (100), 14 of 16 patients with SAS and insomnia were women. An additional case series report (106) showed that insomnia usually coexists with other, more typical symptoms of SAS (such as snoring and EDS); therefore, the diagnostic work-up for women should be similar to the work-up for men.

4.3.2.1.5 ECG changes. It is known that ECG changes occur in patients with SAS. Five cohort studies have documented that these changes include premature ventricular contractions, atrial arrhythmias, and manifestations of myocardial infarction (93,107–110); one randomized controlled trial has documented the presence of ST-segment depression (111). These changes do not occur specifically during sleep, however, and they also occur with regular frequency in the general population.

Conversely, little or no information documents the prevalence of SAS in patients presenting with ECG changes. Thus, there is little evidence to support the presence of ECG changes as a general indication for PSG. However, if arrhythmias are present and are secondary to sleep apnea, they will usually resolve with treatment such as CPAP and tracheostomy (107,110). At least one study suggests that tracheostomy should be considered as primary therapy for patients with potentially life-threatening arrhythmias caused by SAS (107), but this study was undertaken before the advent of CPAP.

4.3.2.2 Estimating pretest probability

Eight published studies used multifactorial analysis to determine a patient's pretest probability of having SAS (75–80,112,113) (Table 2). All of the studies were performed in referral centers. One study determined the accuracy with which various questions can be used to identify patients with a variety of diagnoses (112). The questionnaires were developed in different ways—some prospectively, some retrospectively, and some retrospectively and then administered prospectively. One study developed a probability formula to predict SAS (78) but, in a subsequent study (3), the formula was found to have less predictive ability than was originally reported. Studies differed in their definitions of significant sleep apnea, requiring a minimum AHI of somewhere between 10 and 20. Some studies analyzed sleep apnea at more than one AHI.

Taken together, these studies came to two conclusions based on symptoms and questionnaire responses: the assignment to a high probability group cannot be made with enough certainty to eliminate the need for PSG; and assignment to a low probability group reduces the likelihood that a patient has SAS to between 0% and 17%. Ten percent to 33% of patients currently referred to sleep disorders centers would be classified as low probability. The possibility that such low probability patients had UARS was not addressed in these studies. Another study (79) compared the pretest predictive capabilities of an expert physician to that of a questionnaire and found that the questionnaire was superior.

These same studies also suggest that patients assigned to a high pretest probability group (compared to patients assigned to a low pretest probability group) are more likely to have SAS (defined as an AHI of at least 10) and are more likely to have severe apnea (defined as an AHI of at least 40). In general, pretest probabilities of at least 70% (i.e. high probability of having SAS) give a sensitivity of about 30% and a specificity of about 90%. That is, the high pretest probability group will include about 30% of all patients with an AHI of at least 10, most of whom will have an AHI of at least 40. The high pretest probability group will also include about 10% of patients with an AHI of less than 10.

In another study (12), PSG performed on patients assigned to a high pretest probability group (determined by high BMI and a history of observed apneas and habitual snoring) also revealed a high prevalence of severe SAS (based on AHI). Two other studies found that although some patients in the high probability group had an initial PSG that was negative for a diagnosis of SAS, a repeat PSG was positive in 50% of cases (114,115).

4.3.2.3 Testing

4.3.2.3.1 Daytime PSG. Three studies used various approaches to assess PSG performed at times other than the patients' usual sleep period (i.e. performed in the daytime). Patients had all been referred to sleep disorders centers with symptoms of SAS. One nonrandomized controlled study compared 90 or more minutes of daytime PSG, obtained after 24 hours of sleep deprivation, to nocturnal PSG. The AI for each was calculated (hypopneas were not counted) (113). The sensitivity was 80% for an AI of at least 5 and 100% for an AI of at least 10; specificities were 67% and 62%, respectively. The AI was higher on the daytime study. The authors concluded that a patient with a negative daytime PSG is unlikely to have sleep apnea, as defined on the nighttime PSG by an AHI of at least 10. The issue of sleep deprivation may influence conclusions in this study.

A second nonrandomized controlled study measured 1 hour of morning sleep in 306 non–sleep-deprived patients (116) and used a finding of more than three apneas on the daytime PSG as predictive of more than 30 apneas, or an AHI of at least 5, on nocturnal PSG; 89 patients were found to have SAS, defined as having an AHI of at least 5. The negative studies included 31 subjects who did not sleep. The sensitivity of daytime PSG was 66% for an AHI of at least 5, 81% for an AHI of at least 10, and 89% for an AHI of at least 20. Specificities were 88%, 87%, and 83%, respectively. At an AHI of at least 10, a negative study had a negative predictive value of 95%. A positive study needed to be repeated because of the high ratio of false positives to true positives.

The third study compared nocturnal PSG to a 5-hour (noon to 5:00 p.m.) study in 35 non–sleep-deprived patients (117), using an AI of at least 5 or an AHI of at least 10 as the diagnostic criterion. One of these patients did not sleep during the day and was excluded from the analysis. This randomized, controlled trial included 25 patients with SAS. The sensitivity was 88%, and the specificity was 100%. Apneas and hypopneas were highly correlated between the day and night studies; sleep architecture was not well correlated between the day and night studies. The three patients whose apnea was missed by daytime PSG had mild sleep apnea, and REM sleep was not recorded in two of these patients. This study concludes that 5-hour daytime PSG can be sensitive and specific, but a negative study that does not detect REM sleep might need to be repeated.

4.3.2.3.2 Number of nights required to diagnose SAS. Of 11 studies reviewed, seven were nonrandomized controlled trials (41,75,114,115,118–120), and four were cohort studies (58,121–123). Because such studies cannot be performed in a randomized manner, the best evidence comes from prospective studies, when subjects are chosen randomly and interpretation is blinded. Though the authors of each of these 11 studies addressed some of these methodologic issues, they did not all address each issue. In general, there were no significant group differences between the first and subsequent nights of study in terms of AHI, and few patients were reclassified by the use of more than one night of PSG. Several studies showed a first night effect in sleep measures, such as a shorter sleep time and poorer efficiency, but this effect did not appear to affect the patients' AHI or subsequent diagnosis of SAS.

An epidemiologic study of 30- to 60-year-old patients with minimal apnea showed no difference in diagnostic outcome between PSG recordings obtained on the first and second nights (41). In a study of middle-aged patients suspected of having a sleep disorder (75), no systematic difference was found between nights; the diagnosis would have changed for eight of 68 patients (using an AHI of at least 10), but the direction of change was unpredictable (i.e. some had an increase and some had a decrease in AHI). A study of elderly men (119) showed no systematic difference in AHI, but five of 14 individuals would have been reclassified (using a cutoff of an AHI of at least 5) on the basis of the second night, again without a predictable direction of change. Using an AHI of at least 10, two of 14 studies would have been negative on the second night, but both were close to the threshold. A study of middle-aged African-American women (120) who were part of an ambulatory blood pressure recording study revealed no differences in AHI between nights, but apnea levels were low in this group (mean AHI, 6). The results of this study were confounded by the fact that blood pressure recording was performed only on the second night of study.

4.3.2.3.3 Split-night studies. The authors of three studies performed PSG over an entire night and subsequently scored the resultant polysomnograms for a portion of the night and for the whole night (Table 3). Scharf et al. (124) showed that scoring the first 90 minutes of the recording had a low sensitivity and a high specificity for correctly diagnosing SAS. Another study of patients with a suspected diagnosis of SAS (125) indicated that if the results were positive in first half of the night (average of 134 minutes), they would remain positive for whole night; if initially negative, the results could become positive over last half of the night. The sensitivity of the first half of the night for a diagnosis of SAS was about 90%. In the final study (126), only patients with an AHI of at least 40 were studied, and the AHI was compared between consecutive quartiles over the course of the night (i.e. using four periods of about 100 minutes each). In this group, no major differences were found, except that the group with the highest AHI had an increase in AHI over the course of the night. The authors concluded that a positive partial-night study is truly positive and that a negative partial-night study requires the whole night to confirm or exclude the diagnosis. That is, an AHI of at least 40 in the first 2 hours of the night is indicative of at least that level for the rest of the night. Also, the greatest number of apneas or hypopneas is likely to occur in the last quarter of the night in patients with the most severe SAS.

Three studies that examined the efficacy of a partial night of CPAP titration concluded that CPAP titration can be successfully carried out during a portion of the night in some patients. In one study (127), 412 patients with an AI [not an AHI or what they called a respiratory disturbance index (RDI)] of more than 20 were studied. The authors required that baseline PSG in the

TABLE 3. *Evidence for split-night studies of diagnosis and CPAP titration*

Reference	Study design/ location	# of patients	Monitoring channels	Study parameters	Bias	Diagnostic value of testing procedure
Charbonneau et al. 1994 (126)	NCT/lab	66	SS CR SaO_2	Only patients with an AHI ≥ 40. Divided night into quarters that averaged 100 minutes.	Population bias	First quarter of night generally representative of AHI of whole night except when AHI is at least 85. At that level, AHI increases over the course of the night.
Iber et al. 1991 (127)	NCT/lab	412	SS CR SaO_2	Patients with AI ≥ 20 proceed to CPAP titration at 2.5-cm increments. 78% successful, 10% had inadequate sleep, 12% did not tolerate CPAP on first night. All unsuccessfully titrated were repeated as many times as necessary, usually one more night.	Confounding factors, population bias	Diagnosis and CPAP titration can be carried out in one night in most patients with an AI ≥ 20. There are potential cost savings compared to one night of diagnosis and one night of titration.
Sanders et al. 1991 (125)	NCT/lab	50	SS CR SaO_2 Body position	AHI ≥ 5 or ≥ 10. Compared first half to whole night. Half sleep period time was 168 minutes.	Population bias	If positive for AHI ≥ 5 in about 3 hours of recording, then high probability of same or higher for full night. If negative, then full night will lead to some becoming positive. At an AHI ≥ 5, sensitivity and specificity of half sleep time for whole night was 93% and 100%; at AI ≥ 10, respective values were 86% and 95%. There were at most three false positives at AHI and AI ≥ 5 and 10.
Sanders et al. 1993 (129)	NCT/lab	50	SS CR SaO_2	AHI average of 77. Diagnostic period of 120 minutes and CPAP titration time of 132 minutes on first night. Pressure increased or decreased in 2.5-cm changes. Followed by a second full night for titration.	Patient-selection bias, errors in measurement of outcomes population bias	Suggests that partial night titrations are accurate in about half of patients who stay with the same interface and CPAP. Full night needed to determine level of CPAP, interface, or BiPAP® in a number of patients. Thirty-one patients had CPAP and same interface on both nights. Sixteen had no difference, 1 had a decrease of 2.5 cm, 11 had an increase of 2.5 cm, and 3 had an increment of 5 cm. Nineteen patients changed interface, mode (CPAP or BiPAP®), or both.
Scharf et al. 1990 (124)	NCT/lab	40	SS CR SaO_2	AHI ≥ 10, hypertension a requirement for entry into study.	Population bias	If AHI ≥ 10 in the first 90 minutes, then indicative of AHI ≥ 10 for the whole night. Sensitivity of first 90 minutes for AHI ≥ 10 for whole night is 42% with a specificity of 100%.

TABLE 3. *Continued*

Reference	Study design/ Location	# of patients	Monitoring channels	Study Parameters	Bias	Diagnostic value of testing procedure
Yamashiro et al. 1995 (128)	NCT/lab	107	SS EMG_2 CR SaO_2	Two consecutive nights, no specific AHI to titrate, but stratified after analysis. First night split between diagnosis and titration. Second night, full titration. Increments or decrements of CPAP in 1- to 2-cm intervals, starting at 3 cm on both nights.	Population bias	If AHI ≥ 40 and titration period at least 3 hours, split night similar to full night of titration.

NCT, nonrandomized controlled trial; SS, sleep staging includes EEG (electroencephalogram), EOG (electrooculogram), and EMG_1 (chin electromyogram); CR, cardiorespiratory monitoring includes airflow (AF), respiratory effort (RE), and heart rate or ECG (electrocardiogram); SaO_2, arterial oxygen saturation; AHI, apnea–hypopnea index; AI, apnea index; CPAP, continuous positive airway pressure; BiPAP© bi-level positive airway pressure; EMG_2, anterior tibialis electromyogram.

first part of the night, including both non-REM (NREM) and REM sleep, be recorded before instituting CPAP titration and that CPAP titration include time with the patient in REM sleep in the supine position. The authors' criterion for success was a reduction in RDI (apneas and hypopneas) on CPAP to less than 20 or a reduction of more than 50% in the AI that was measured before CPAP, whichever value (RDI or AI) was lower. Seventy-eight percent of patients met the criterion, and CPAP was successfully titrated. In these patients, the RDI was reduced to an average of 1 from an average AI of 67. For 10% of patients, time was insufficient to complete titration; an additional 12% of patients did not tolerate CPAP. Repeat studies were performed in most of these patients, most of whom required two studies, but a few of whom required three or more studies to achieve successful CPAP titration.

A second study (128) compared a partial night of CPAP titration to a full night of CPAP titration; during the partial night, CPAP titration followed 3- to 4-hour diagnostic PSG. In the 20 patients with an AHI of at least 40, final pressures were not significantly different on the two nights, being only 0.4 cm H_2O greater on the full night. In the 18 patients with an AHI of 20 to 40, the final pressures on the two nights were also not significantly different, but the sample size was small; the patients averaged a 2.1 cm H_2O greater requirement on the full night, and five patients required at least an additional 3.0 cm H_2O on the full night. In the 69 patients with an AHI of less than 20, final pressures were significantly higher by 1.5 cm H_2O on the second (i.e. full) night. CPAP titration that occurred for longer than 3 hours on the partial night resulted in greater night-to-night consistency of final pressure levels. Eight patients were switched to BiPAP© and were excluded from the analysis of pressure differences.

In a third study of 50 patients with an average AHI of 77 (129), CPAP was titrated after an average of 2 hours of diagnostic PSG. Total CPAP titration time at the final combination of pressure, interface (i.e. nasal mask), and modality (CPAP or BiPAP) averaged 2 hours and 12 minutes. Results were compared to those achieved on a second full night of CPAP titration, and significant differences were found. However, besides changing patients' CPAP levels, technicians also made changes in the nasal interface and in CPAP versus BiPAP. The short lengths of the diagnostic and titration periods also may have influenced the pressure level obtained on the first night. In addition, pressure was changed in increments of 2.5 cm H_2O, causing difficulties when making comparisons with the Yamashiro study, in which pressures were changed in 1- to 2-cm H_2O steps. Finally, during the second night of study, the CPAP was begun at the pressure level from the

TABLE 4. *Evidence for oximetry*

Reference	Study design/ location	# of patients	Monitoring channels	Study parameters	Bias	Diagnostic value of testing procedure
Cooper et al. 1991 (2)	NCT blind/lab	41	SS AF RE SaO_2	AHI ≥ 5, two nights in laboratory, pattern of repetitive 5% desaturations to diagnose OSA.	Errors in measurement of outcomes, population bias	Value difficult to assess partly because of uninterpretable records. Sensitivity of 60% and specificity of 95% for AHI ≥ 5, sensitivity of 100% and specificity of 80% for AHI ≥ 25, sensitivity of 75% and specificity of 86% for AHI ≥ 15.
Gyulay et al. 1993 (3)	NCT/lab, home	98	SS CR SaO_2	AHI ≥ 15, PSG in lab, oximetry for SaO_2 in home.	Population bias	Because of high specificity of 4% desaturations, this may allow stratification to high probability group. Use of saturation time problematic because of issue of UARS. 4% desaturations at least 15 per hour give sensitivity of 40% and specificity of 98% for AHI ≥ 15. If more than 1% of time below 90% saturation used, sensitivity is 93% and specificity is 51%.
Levy et al. 1996 (4)	CoS/lab	301	SS CR SaO_2	RDI ≥ 15, 12-second intervals of change in SaO_2 called a delta index.	Population bias	The higher index could be used to stratify patients with high probability of OSA. The lower index used to exclude patients is problematic because of issue of UARS. At delta index of 0.6, sensitivity of 98%, specificity of 46%. At delta index of 1.8, there is 46% sensitivity and 100% specificity.
Rauscher et al. 1991 (5)	CCS, computer blinded/ lab	53	SS CR SaO_2	AHI > 100 per night, compared 3% desaturations to 4% desaturations in habitual snorers and patients with sleep apnea.	Population bias	Limited because no attempt to determine sensitivity and specificity for diagnosis of sleep apnea.
Ryan et al. 1995 (6)	NCT/PSG, lab; oximetry, home	100	SS CR SaO_2 Body position by video	Inclusion criteria: AHI ≥ 15 on PSG, 4% desaturations at least 15 per hour on oximetry, awake saturation greater than 90%.	Population bias	High specificity could be used to stratify positives to high probability group. Sensitivity of 31%, specificity of 100%.
Sériès et al. 1993 (7)	CoS/oximetry, home; PSG, lab	240	SS AF RE SaO_2 Esophageal balloon	AHI ≥ 10, pattern recognition of repetitive cyclical desaturations, 8% needed repeat testing. At AHI ≥ 10, 98% sensitivity, 48% specificity. At AHI ≥ 20, sensitivity of 100%, specificity of 39%.	Population bias	Issue of UARS makes use problematic to exclude patients.
Williams et al. 1991 (8)	NCT/lab	40	SS AF RE SaO_2	AHI ≥ 10. On oximetry, cyclical desaturations of at least 4%, each to a level of at least 90% saturation. 10% failure rate plus 7.5% more indeterminate.	Population bias	Might be used to stratify to high probability group, but use is problematic because of indeterminate and failed recordings. Sensitivity of 58%, specificity 93%.

TABLE 4. *Continued*

Reference	Study design/ location	# of patients	Monitoring channels	Study parameters	Bias	Diagnostic value of testing procedure
Yamashiro et al. 1995 (9)	NCT blinded/lab	300	SS AF RE SaO_2	Oximetry desaturation index of greater than five 3% desaturaetions per hour for diagnosis of OSA. UARS by cyclical desaturations of less than 3% on oximetry and by respiratory arousals of greater than 10 per hour with less than 3% desaturations on PSG. AHI on PSG for diagnosis of OSA is greater than 5 per hour.	Population bias	Oximetry is of low sensitivity for UARS and of borderline specificity for OSA with AHI $\geq$ 20. Sensitivity for OSA is 94.2% and specificity is 90.2% (includes UARS criteria on oximetry as normal). Sensitivity for UARS is 69%, with specificity of 73.2%. Sensitivity for AHI $\geq$ 20 identified by greater than 20 desaturations per hour on oximetry is sensitivity of 100%, specificity of 81.5%. SRBD has a sensitivity of 100%, a specificity of 75%, a PPV of 92.6%, and an NPV of 45.5%. OSA has a sensitivity of 94.2%, a specificity of 73.5%, a PPV of 78.7%, and an NPV of 92.4%.

NCT, nonrandomized controlled trial; SS, sleep staging includes EEG (electroencephalogram), EOG (electrooculogram), and EMG_1 (chin electromyogram); CR, cardiorespiratory monitoring includes airflow (AF), respiratory effort (RE), and heart rate or ECG (electrocardiogram); SaO_2, arterial oxygen saturation; AHI, apnea–hypopnea index; OSA, obstructive sleep apnea; PSG, polysomnography; UARS, upperairway resistance syndrome; CoS, cohort study; RDI, respiratory disturbance index; CCS, case control study; PPV, positive predictive value; NPV, negative predictive value; SRBD, sleep-related breathing disorder.

first night so that, in effect, part of the titration had already been performed.

4.3.2.3.4 Oximetry. Eight oximetry studies were performed at referral centers (Table 4). Most of the studies took place on two separate nights—one night with oximetry alone, often at home, and one night with PSG. Two of these studies examined the correlation between rapid desaturations and RDI (5,130). One study used a qualitative *yes* or *no* for an oximetry pattern that was consistent with sleep apnea (7). The other authors analyzed data as a specific quantitative measure, such as number of 3% or 4% desaturations per hour (3,6,9) or as cyclical 4% (8) or 5% desaturations (2). One study examined the ability of oximetry alone to make the diagnosis of UARS as well as of SAS (9).

The sensitivity of the qualitative approach (7) was 98%, with a specificity of 48%; 8% of the overnight oximetry studies had to be repeated, presumably for technical reasons. Four quantitative studies had sensitivities of detecting SAS of 94%, 59%, 40%, and 31% (3,6,8,9); specificities were 74%, 93%, 98%, and 100%, respectively. One study used computer scoring. All of these oximetry studies used number of desaturations per hour divided by total recording time. When UARS patients were included, the overall sensitivity fell to 90%, and among UARS-only patients, the sensitivity was 69% (9). Failure rates, which were reported in two studies, were 10% (8,9).

One quantitative study (2) compared several levels of AHI from PSG to 5% desaturations on oximetry. At an AHI of more than 25, the sensitivity of oximetry was 100% and the specificity was 80%. At an AHI of more than 5, sensitivity and specificity were 60% and 95%, respectively.

Another study, which was computer scored, looked at a delta index of absolute 12-second changes in SaO_2 divided by the number of 12-second intervals (4). At a delta index of 0.6, sensitivity was 98% and specificity was 46%; at 1.8, respective values were 46% and 100%.

Those studies that show that oximetry has a high sensitivity suggest that oximetry studies can exclude a minority of patients (those with negative studies) from further study for SAS. However, this group appears to include a substantial number of patients with UARS (9). The studies also suggest that another group of patients can be classified as having a high probability of having SAS by using the same oximetry data but analyzing it with different criteria. That is, stratification to a high probability group for SAS can be achieved. The specificity of this approach is only marginally better, however, than the use of predictive questionnaires, and there is about a 10% failure rate requiring retesting. No studies of CPAP titration that use oximetry alone have been published.

TABLE 5. *Evidence for limited study—full respiratory*

Reference	Study design/ location	# of patients	Monitoring channels	Study parameters	Bias	Diagnostic value of testing procedure
Douglas et al. 1992 (10)	Simultaneous, blinded NCT/lab	200	SS EMG_2 AF RE SaO_2	AHI ≥ 15, attended in laboratory. Sleep time was time in bed.	Population bias	Sleep staging adds little to determining AHI and diagnosing sleep apnea on that basis. UARS not addressed.
Emsellem et al. 1990 (11)	Simultaneous NCT/lab	67	SS EMG_2 CR SaO_2 Four-channel portable system used CR, SaO_2	AHI ≥ 5. Desaturation not required on portable system for an apnea or hypopnea. Sleep time was quiet recording time.	Population bias	Attended portable respiratory monitoring is similar to PSG for diagnosis of sleep apnea. UARS not addressed. Sensitivity 93%, specificity 96%. No difference in total number of events between PSG and portable. All misclassifications were at low AHI levels.
Gyulay 1987 (17)	Simultaneous, blinded NCT/lab	14	SS CR SaO_2 Portable used RE, ECG, SaO_2, actigraphy, tidal volume, and inductance plethysmography	RDI ≥ 5, CPAP applied after 3.6 hours in 11 patients. Records hand-scored, two records technically lost, apneas and hypopneas on portable and PSG were 15 seconds. *r* for RDI was 0.7.	Patient-selection bias, population bias	Not adequate for diagnosis of central apneas; diagnostic accuracy for respiratory events has poor sensitivity and specificity not well assessed. Use of CPAP may have influenced results. Relevance to UARS uncertain. Sensitivity for detection of respiratory events was 59%. Sensitivity for diagnosis of RDI ≥ 5 was 100%. Specificity was 0% (0 of 2).
Man 1995 (12)	Simultaneous, blinded NCT/lab	104	SS EMG_2 CR SaO_2 Portable system used CR, SaO_2, and body position	Sleep time on portable not defined. AHI ≥ 5 or ≥ 15. Stratified by questionnaire and BMI into high, medium, and low probability.	Intensity bias	Stratification to high probability led to selection of patients with AHI average of 42. Overall diagnostic ability is excellent, especially at higher AHIs. UARS not addressed. Sensitivity of portable system was 83%, specificity of 86% at AHI ≥ 5; at AHI ≥ 15, values are 91% and 95% respectively. *r* values were excellent for AI and AHI.
Montserrat 1995 (13)	RCT/lab	41	SS AF RE SaO_2 Portable system used AF, RE, and SaO_2	Previously diagnosed sleep apnea with average AHI of 53. CPAP applied after 1 hour. At least one prolonged period of sleep supine. Each patient spent one night on PSG and one night on portable system in randomized fashion.	Population bias	CPAP pressures same with PSG and portable system. One patient had a 5-cm increase on portable system. UARS not addressed.
Orr 1994 (14)	NCT/lab	40	SS EMG_2 AF RE SaO_2 Portable system used EEG, EOG, EMG_2,	RDI ≥ 15. Simultaneous monitoring.	Population bias	Attended portable system with measure of sleep comparable to PSG for diagnosis of RDI ≥ 15. UARS not addressed. RDI ≥ 15, sensitivity and specificity of portable system is 100% and 93.3%. *r* values higher than 0.9 for RDI with portable system.

TABLE 5. *Continued*

Reference	Study design/ location	# of patients	Monitoring channels	Study parameters	Bias	Diagnostic value of testing procedure
			RE, SaO_2, wrist actigraphy, and tracheal noise			
Redline et al. 1991 (15)	Simultaneous NCT/lab, home	51	SS AF RE SaO_2 Portable system used CR and SaO_2. Same system as used by Emsellem.	RDI ≥ 10. *r* values for simultaneous in-laboratory portable in 20 studies combined with laboratory-to-home in 5 was 0.96 for RDI; sensitivity and specificity for RDI ≥ 10 was 96% and 100%. *r* for night-to-night in home was 0.94 with reclassification of one subject at an RDI ≥ 10.	Confounding factors, population bias	Attended in-laboratory portable study comparable to PSG for RDI ≥ 10. Unattended home studies have a high degree of reproducibility for RDI. No independent comparison of unattended portable in-home to attended PSG in-lab. UARS not addressed.
White et al. 1995 (16)	Simultaneous NCT in lab for portable system in phase 1, partial RCT for lab-to-home for phase 2	30 in phase 1, 70 in phase 2	SS EMG_2 CR SaO_2 Body position by video Portable system used eye sensor, body position and movement, leg movement, SaO_2, CR	Sleep staging done by eye and movement sensors on portable system.	Confounding factors, population bias	Attended in-laboratory system not fully comparable to PSG, possibly because of different analysis techniques and overestimate of sleep time on portable system. Unattended in-home system provides different results compared to attended in-laboratory, possibly because of different analysis techniques, more supine sleep at home, and overestimate of sleep time by portable system. Relevance to UARS not certain. Phase 1 in lab—AHI ≥ 10. Sensitivity and specificity for AHI ≥ 10 were 100% and 64%, AHI ≥ 20 were 77% and 88%, respectively. AHI and saturation *r* value > 0.94. Phase 2 lab-to-home—AHI ≥ 10 with two failures and modem monitored by technician at remote location. AHI slightly but significantly higher on portable system at home. Sensitivity and specificity for AHI ≥ 10 were 90% and 86%; for AHI ≥ 20 were 70% and 83%, respectively. AHI *r* at 0.92, saturation minimum at 0.78 and mean saturation at 0.93.

NCT, nonrandomized controlled trial; SS, sleep staging includes EEG (electroencephalogram), EOG (electrooculogram), and EMG_1 (chin electromyogram); EMG_2, anterior tibialis electromyogram; CR, cardiorespiratory monitoring includes airflow (AF), respiratory effort (RE), and heart rate or ECG (electrocardiogram); SaO_2, arterial oxygen saturation; AHI, apnea–hypopnea index; UARS, upperairway resistance syndrome; PSG, polysomnography; RDI, respiratory disturbance index; CPAP, continuous positive airway pressure; BMI, body mass index; AI, apnea index; RCT, randomized controlled trial.

TABLE 6. *Evidence for limited study (less-than-full respiratory)*

Reference	Study design/ location	# of patients	Monitoring channels	Study parameters	Bias	Diagnostic value of testing procedure
Ajilore et al. 1995 (18)	NCT/lab-home	10	SS Portable system with eye sensor, body sensor, and movement detector	No respiratory monitoring.	Patient-selection bias	In normals, sleep staging comparable in lab but not in home to PSG. In-lab comparison not significantly different. Lab-to-home comparison had significant REM differences with shorter REM latency, longer REM time, and shorter REM cycle in the home.
Ancoli-Israel et al. 1981 (19)	Simultaneous NCT/lab, RCT/home	36	SS CR EMG_2 SaO_2 Portable system used thorax and abdomen RE, leg, and wrist actigraphy	Sleep apnea at least 30 apneas per night. Thirty-six had PSG and simultaneous portable in lab, 36 had portable in home. There were eight lab portable failures and nine in-home portable failures.	Confounding factors, errors in measurement of outcomes	Attended portable comparable to PSG for 30 apneas per night. However, correlation is relatively poor for apneas between portable and PSG. Portable reproducibility from night to night is excellent. Relevance to UARS uncertain. r for lab portable to PSG was 0.68 for apnea. r for home portable to lab portable was 0.94. Sensitivity and specificity for 30 apneas per night were 100% and 95% on lab portable and 78% and 86% on home portable compared to PSG.
Hida et al. 1993 (20)	CoS/lab	520	Not well described. Portable system used tracheal sounds, AF, ECG	AI > 5, no correlations given for respiratory events between systems.	Population bias	Uncertain, but specificities at higher AI are low and failure rate not given. Sensitivity varied between 91% and 94% and specificity between 68% and 88% for varying AI from 5 to 20 for 170 patients. r for portable in-home on two nights was 0.81 in 182 patients.
Issa et al. 1993 (21)	Simultaneous NCT/lab	129	SS CR SaO_2 Portable system used tracheal sounds, oximetry, and computer scoring	Portable used snoring to determine which 3% desaturations were respiratory. RDI ≥ 7.	Population bias	High specificity may be useful in stratifying patients to high probability group possible. No full explanation for difference between portable system and oximetry. Relevance to UARS uncertain. Sensitivity and specificity at RDI ≥ 7 were 89% and 95%, at ≥ 10 were 84% and 97%, at ≥ 15 were 87% and 96%, at ≥ 20 were 90% and 98%. r between portable and PSG RDI was 0.94. Oximetry had a much lower sensitivity and specificity.
Stoohs and Guilleminault 1992 (22)	Simultaneous NCT/lab	56	SS CR EMG_2 SaO_2 Portable system used heart rate, breathing sounds, SaO_2, and body position	RDI ≥ 10.	Population bias	Highly sensitive and specific but is essentially performing as an oximeter with better results than other studies. Only oximetry had reasonable sensitivity and specificity of 92% and 97%. Three percent desaturations per hour of sleep vs. RDI was r of 0.8[c].

TABLE 6. *Continued*

Reference	Study design/ location	# of patients	Monitoring channels	Study parameters	Bias	Diagnostic value of testing procedure
Svanborg et al. 1990 (23)	Simultaneous NCT/lab	94	SS CR SaO_2 Portable system used oximetry and static-charge sensitive bed for movements	AI ≥ 5, diamond-shaped movements for respiratory movement. No diamond-shaped movements in controls. Use of combination of movements and desaturations to define sleep apnea.	Population bias	Uncertain, but specificity of 86% at AI > 20 may allow for stratification to high probability group. Relevance to UARS uncertain. Sensitivity and specificity dependant on criteria used; for AI ≥ 5 were 67% and 100%; for AI > 20 were 94% and 86%. Use of different criteria for this AI gave sensitivity and specificity of 100% and 67%. *r* value of 0.64 for AI and oxygen desaturations.
Van Surell et al. 1995 (24)	Simultaneous blinded NCT/lab	50	SS CR Diaphragmatic EMG SaO_2 Portable system used tracheal sounds, body position, SaO_2, and computer scoring	Used AHI ≥ 5, ≥ 10, ≥ 15, and ≥ 20. RDI from ambulatory compared to PSG.	Population bias	May be useful for stratifying to high probability group for sleep apnea. Sensitivities too low for general diagnostic purposes. Relevance to UARS uncertain. Using a threshold of RDI ≥ 5 for portable system, sensitivity and specificity at AHI of 5, 10, 15, and 20 generally less than 75% except for a specificity of 88% at AHI of 5 and a sensitivity of 83% at an AHI of 20. Using a threshold of portable RDI ≥ 15, sensitivities were 41% or less and specificities were 94% to 100% for AHI of at least 10, 15, or 20. *r* value for apneas between portable device and PSG was 0.68.
White et al. 1994 (25)	Simultaneous blinded NCT/lab	37	SS AF RE SaO_2 Portable system used SaO_2 and snoring	AHI ≥ 10, oximetry scored by pattern, many equivocal records on oximetry alone. Addition of snoring decreased number of equivocal records.	Population bias	Lack of standardization makes usefulness uncertain. Relevance to UARS uncertain. Sensitivity and specificity of oximetry were 30% and 100% at AHI ≥ 10, 71% and 94% at AHI ≥ 15, and 100% and 94% at AHI ≥ 20. With snoring added, sensitivity at AHI at 10 and 15 increased, but specificity decreased at 15 and 20.

NCT, nonrandomized controlled trial; SS, sleep staging includes EEG (electroencephalogram), EOG (electrooculogram), and EMG_1 (chin electromyogram); PSG, polysomnography; REM, rapid eye movement; RCT, randomized controlled trial; CR, cardiorespiratory monitoring includes airflow (AF), respiratory effort (RE), and heart rate or ECG (electrocardiogram); EMG_2, anterior tibialis electromyogram; SaO_2, arterial oxygen saturation; UARS, upperairway resistance syndrome; CoS, cohort study; AHI, apnea–hypopnea index; AI, apnea index.

4.3.2.3.5 Limited studies. Limited studies to diagnose SAS can be divided into three groups: those with at least full respiratory recording (Table 5), those with less-than-full respiratory recording (Table 6), and those that use daytime PSG. None of the studies addresses UARS.

4.3.2.3.5.1 Full respiratory recording. Eight studies (10–17) assessed the capabilities of at least full respiratory recording, which includes airflow (or tidal volume by inductance plethysmography) (17) or tracheal sounds (14); respiratory effort; arterial oxygen saturation; and, usually, heart rate. Six studies used manual scoring (10–13,15,17); one used computer scoring (14); and one used computer scoring that was checked by a technician (16). All of the authors compared the results of limited studies to PSG.

Most of these studies examined systems designed to be fully portable and to be used in an unattended fashion (11,12,14–17), one compared the respiratory channels on PSG to the PSG as a whole (10), and one used a combination of a portable system plus a PSG channel (13).

In five studies (10–12,15,17), the validation part of the study compared simultaneous in-laboratory recordings to PSG; in all cases, the scoring was blinded, making each the equivalent of a randomized, double-blind, controlled trial. In one of these five studies (15), there was an unattended in-home recording that showed excellent reproducibility. It was not clear if the false negatives in one study were near threshold (12); they were near threshold in another study (17). The number of failures of portable systems ranged from 4% to 14%. When correlations for concordance between PSG and the portable systems were performed, r values were over 0.9, except in one study, which showed 0.7 (17).

A sixth full respiratory study used a randomized controlled design to examine CPAP titration (13), finding that CPAP pressures were essentially the same in 40 of 41 patients when respiratory recording alone was compared to full PSG.

A seventh study (14) of in-laboratory comparison between PSG and a limited study using EEG, EOG, EMG, tracheal sounds, wrist activity, SaO_2, and two respiratory-effort belts had a sensitivity of 100% and a specificity of 93% for an AHI of at least 15. Correlations between PSG and the portable device were over 0.9.

The eighth study used an indirect measure of sleep (16) and had two components. In the first, an in-laboratory comparison was run simultaneously with PSG. Sleep parameters were correlated but not highly so, and the portable system recorded more sleep time. The sensitivity and specificity for an AHI of at least 10 were 100% and 64%, respectively; at an AHI of at least 20, they were 77% and 88%. Some of the misclassification represented *recognition* of hypopnea on the portable system that was not seen on PSG, and some reflected an overestimation of sleep time, which subsequently reduced the AHI below the diagnostic threshold.

In the second component of this study, in-laboratory PSG was compared to an in-home study performed within 10 days of the PSG. Though designed as a randomized study, the randomization protocol was not always followed. There were two failures out of 70 portable studies, and 57 telephone calls were made to a family member in the home by a technician who monitored the studies in the laboratory via modem. The correlations for sleep were low but significant. The AHI was significantly higher on the portable system. Sensitivity and specificity for an AHI of at least 10 were 91% and 70%, respectively; for an AHI of at least 20, they were 86% and 83%. At an AHI of at least 10, three of the false positives had more supine sleep at home, making it indeed possible that the difference was real. In the other five false positives, and in all the false negatives, the AHIs were near the diagnostic threshold. At an AHI of at least 20, two of the four false negatives were near the threshold, as were five of the seven false positives. Two false positives had more supine sleep at home. Two false negatives could not be explained.

These studies indicate that substituting total in-bed time (sometimes modified by subtracting artifact time and diary-indicated awake time) for total sleep time results in a high degree of concordance between full respiratory recording and PSG for the diagnosis of SAS. The use of partial or indirect sleep recording does not appear to add substantially to the determination of clear-cut respiratory events or to substantially improve the sensitivity and specificity of this type of recording.

4.3.2.3.5.2 Less-than-full respiratory recording. All of the eight studies of less-than-full respiratory recording had a component of simultaneous recording, most were scored by clinicians blinded to the results of PSG, and one (19) used a randomized controlled design for comparing a portable in-laboratory study to home study. No study addressed CPAP titration. Four of these systems were generally of too low a sensitivity or specificity to be substituted for PSG or full respiratory recording, although some approaches could be used to stratify patients to a high probability group (20,23–25).

Ajilore et al. (18) evaluated the same equipment that White et al. (16) used in their study (an indirect sleep-staging system), but Ajilore et al. did not include respiratory recording. The in-laboratory limited study showed good correlation with the simultaneously re-

corded PSG study in the laboratory, but did not show good correlation between a subsequent home study and PSG in the laboratory in normal subjects. This difference may have been due to variation in patients' sleep between the two nights, or it may have been due to a technical effect of the different recording conditions.

One study of a portable system (19) showed a failure rate of 25% in the laboratory and 22% at home. Simultaneous study in the laboratory had a sensitivity of 100% (for recognition of patients with a total number of apneas per night of more than 30) and a specificity of 95%. This criterion for an apnea level is no longer realistic. The r value for apnea was 0.8 with PSG. Night-to-night correlation of apneas recorded by the portable system in the home compared to the portable system in the laboratory was $r = 0.94$.

A second study of a portable system used computer-analyzed snoring and oximetry to diagnose SAS (21). Total sleep time was equated with quiet recording time. The sensitivities and specificities of this approach were 84% to 90% and 95% to 98%, respectively, depending on the AHI or desaturation index (the number of 3% drops in oxygen saturation per hour of sleep) level for a diagnosis of SAS. If confirmed, the high correlations between polysomnographic RDI and portable RDI could be used to identify patients in need of further study or therapy. Of note, oximetry alone (without computer scoring) had a lower sensitivity and specificity, and the reason was unclear.

A third study (22) of a portable system used a combination of snoring, oximetry, heart rate, and body position; proprietary computer software analysis was used. To summarize, only oximetry provided acceptable sensitivities (92%) and specificities (97%) for an AHI of at least 10. Total sleep time was equated with recording time minus diary-recorded awake time. This study is essentially an oximetry study with results superior to those of any other oximetry study reported. Rauscher et al. (130), using oximetry, heart rate and snoring, also confirmed that oximetry results are the only ones with any diagnostic accuracy.

4.3.3 Evidence for upper airway resistance syndrome

Three articles from one group of researchers describe UARS (Table 7). In these studies, patients were classified as having UARS if they had EDS and respiratory disturbances during sleep that could not be classified as either apneas or hypopneas; therefore, the patients had an AHI of less than 5. These studies did not address the issue of patients who have mild SAS but also have additional symptoms caused by upper airway resistance. The initial definition of UARS required that the patient have EDS and flow limitation and increased respiratory efforts with arousal just following peak negative inspiratory esophageal pressure, documented by esophageal pressure recording (46). A subsequent description in women did not include arousals as part of the definition (47). The studies correlated MSLT and ESS information with CPAP treatment and showed a highly significant lengthening of the MSLT sleep latency or decrease in the ESS score after treatment. The UARS tended to occur in patients who weighed less and were younger than the usual SAS patient. The prevalence was 11% of the female patients with suspected sleep apnea, and 15 of 48 patients with an initial diagnosis of idiopathic hypersomnia were found to have UARS (45,47). Eleven of the 38 women with UARS did not have an increased number of arousals despite their being sleepy and showing improvement with CPAP therapy (47).

In a study of 46 men who snored and had a wide spectrum of AHIs, the Stanford Sleepiness Scale correlated with the number of apneas and hypopneas even in patients with an AHI of less than 5 (131).

In a study of 257 patients with suspected sleep apnea, 139 had an AHI of at least 5, and 118 habitual snorers had an AHI of less than 5 (74). Fifty-nine of the 118 snorers had a symptom score on a scale similar to the ESS that indicated sleepiness, giving a possible prevalence of 50% for snoring causing EDS. Forty-eight of these patients refused CPAP treatment. Eleven of those who refused CPAP treatment underwent uvulopalatopharyngoplasty. In the 11 who accepted CPAP treatment, the symptom score improved significantly in the group as a whole, and in eight of the 11, the number of arousals per hour of sleep declined from 20 to five; of the three for whom CPAP did not improve sleepiness, two had very poor compliance with CPAP. This study suggests that for those patients who are habitual snorers, are sleepy, and comply with therapy, CPAP is effective for treating EDS; however, fewer than 40% of those patients with possible UARS desire therapy, including fewer than 20% who will accept treatment with CPAP.

In a study of 300 patients with suspected sleep apnea, 106 had AHIs below the threshold for SAS (9). Of these, 65 snored or had disordered breathing with at least 10 arousals per hour and with desaturations of less than 3%, giving a prevalence of UARS of 61% in patients who have suspected sleep apnea and an AHI of less than 5.

In another study looking at the ESS scores of primary snorers, 26% of patients had scores indicating sleepiness (63). In another study from the same author, however, the highest ESS score of any primary snorer was only slightly higher than that of controls (61).

In conclusion, there is a substantial prevalence of

TABLE 7. *Evidence for upper airway resistance syndrome*

Reference	Study design/ location	# of patients	Monitoring channels	Study parameters	Bias	Diagnostic value of testing
Berry et al. 1986 (131)	CoS/lab	46	SS AF RE SaO_2	AHI classified into 0, < 5, and ≥ 5. Sleepiness measured with SSS.	Random error, population bias	Suggests that there is no readily defined threshold for sleepiness based on AHI. Desaturations and AHI correlate with number of naps during the day. AI and AHI correlate with SSS even when AHI < 5.
Guilleminault et al. 1991 (46)	Blinded NCT/lab	15	SS EMG_2 CR SaO_2 Pneumotachograph for tidal volume Esophageal balloon for RE, MESAM 4 for snoring, MSLT	Male heavy snorers, RDI < 5, measured short respiratory-event arousals. Measured PSG and MSLT before and after treatment with CPAP for two nights.	Patient-selection bias, population bias	Respiratory arousals are related to mild sleepiness, which can be improved with nasal CPAP. Respiratory arousals went from 17 to one per hour. MSLT went from 11.3 to 14.5 minutes. Both were statistically significant.
Guilleminault et al. 1993 (45)	NCT for CPAP CoS for diagnosis/lab three nights, home one	48	SS EMG_2 CR SaO_2 Esophageal balloon Pneumotachograph MSLT MESAM 4 at home for snoring	48 patients with diagnosis of idiopathic hypersomnia. 15 fit criteria for UARS of respiratory-related arousals including RDI < 5 and more than 10 arousals per hour. MSLT less than 10 minutes. All patients had at least 14 respiratory arousals before and 10 or less after CPAP.	Patient-selection bias, population bias	Respiratory arousals are related to moderate to severe sleepiness that can be reversed with CPAP. Final MSLT after 4 weeks of CPAP. Arousals went from 31 to eight with CPAP. MSLT went from 5.3 to 13.5 minutes with CPAP. Both are statistically significant.
Guilleminault et al. 1995 (47)	Retrospective CoS/lab	334	SS EMG_2 CR SaO_2 Body position Pneumotachograph Esophageal balloon and MSLT in many	38 women had UARS with respiratory disturbances not qualifying as apnea or hypopnea and an RDI < 5. Sleepiness measured with either MSLT or ESS. Clinical improvement with CPAP or BiPAP® required to make diagnosis of UARS.	Patient-selection bias	UARS prevalence among females with sleep-related breathing disorders was 11%. Respiratory arousals ranged from four to 30 per hour, with a subgroup of 11 of the 38 having minimal arousals despite MSLT of 7.7 minutes and response to CPAP.
Johns 1991 (61)	CCS, CoS/lab	180 completed questionnaires 150 patients, 30 controls	SS CR EMG_2 SaO_2 Sound Body position	RDI > 5, mild OSA 5 ≤ 15, moderate 15 ≤ 30, severe > 30. ESS used to measure sleepiness.	Patient-selection bias, population bias	Patients with all levels of RDI had significant sleepiness compared to controls and primary snorers. Patients with severe OSA were significantly sleepier than those with mild or moderate OSA. Those with mild and moderate OSA were not significantly different from each other.

TABLE 7. *Continued*

Reference	Study design/ location	# of patients	Monitoring channels	Study parameters	Bias	Diagnostic value of testing
Johns 1993 (63)	NCT, CoS/lab	273 108 snorers, 165 OSA	SS CR EMG_2 SaO_2 Sound Video Body position	RDI ≥ 5, stratified into mild (RDI 5 ≤ 24.9), moderate (RDI 25 ≤ 49.9), and severe (RDI ≥ 50). Primary snorers and nonsnoring controls.	Population bias	Patients with all levels of RDI were sleepy. Snorers were sleepy despite an RDI < 5. ESS level was less in snorers and consistent with level of severity of sleep apnea.
Rauscher et al. 1995 (74)	CoS/lab	265	SS CR SaO_2 Video	257 had suspected sleep apnea, all were probably snorers. 118 had an AHI < 5, and 59/118 had a sleepiness score that was greater than normal.	Patient-selection bias, population bias	In this study, about 50% of habitual snorers with AHI < 5 are mild to severely sleepy, and those who accept CPAP and are compliant reverse the sleepiness to near normal or normal levels.
Yamashiro and Kryger 1995 (9)	NCT blinded/ lab	300	SS AF RE SaO_2	Oximetry desaturation index of greater than five 3% desaturations per hour for diagnosis of OSA. UARS by cyclical desaturations of less than 3% on oximetry and by respiratory arousals of greater than 10 per hour with less than 3% desaturations on PSG. AHI on PSG for diagnosis of OSA is greater than five per hour.	Population bias	Oximetry is of low sensitivity for UARS and of borderline specificity for OSA with AHI ≥ 20. Sensitivity for OSA is 94.2% and specificity is 90.2% (includes UARS criteria on oximetry as normal). Sensitivity for UARS is 69%, with specificity of 73.2%. Sensitivity for AHI ≥ 20 identified by greater than 20 desaturations per hour on oximetry is sensitivity of 100%, specificity of 81.5%. SRBD has a sensitivity of 100%, a specificity of 75%, a PPV of 92.6%, and an NPV of 45.5%. OSA has a sensitivity of 94.2%, a specificity of 73.5%, a PPV of 78.7%, and an NPV of 92.4%.

CoS, cohort study; SS, sleep staging includes EEG (electroencephalogram), EOG (electrooculogram), and EMG_1(chin electromyogram); CR, cardiorespiratory monitoring includes airflow (AF), respiratory effort (RE), and heart rate or ECG (electrocardiogram); SaO_2, arterial oxygen saturation; AHI, apnea–hypopnea index; SSS, Stanford sleepiness scale; AI, apnea index; NCT, nonrandomized controlled trial; EMG_2, anterior tibialis electromyogram; MSLT, multiple sleep latency test; RDI, respiratory disturbance index; PSG, polysomnography; CPAP, continuous positive airway pressure; UARS, upper airway resistance syndrome; ESS, Epworth sleepiness scale; BiPAP© bi-level positive airway pressure; CCS, case control study; OSA, obstructive sleep apnea; PPV, positive predicitive value; NPV, negative predictive value; SRBD, sleep-related breathing disorder.

sleepiness in habitual snorers presenting for medical care who do not have obvious apneas or hypopneas. These individuals may have partial upper airway obstruction with arousals, as indicated by increased respiratory effort (i.e. abdominal–thoracic paradox or a cyclical decrease in esophageal pressure) followed by arousals. A sleep latency on MSLT of less than or equal to 10 minutes or an ESS score of at least 9 (47), or a symptom score similar to an ESS score of at least 10 (74), is associated with a respiratory-arousal index of at least 10 per hour of sleep (45–47,74). Another study used at least 10 respiratory arousals per hour (9) to define UARS but did not specifically report on sleepiness. Patients with UARS can benefit from treatment with CPAP (45–47,74), with a reduction in arousals to 10 or less (45,74).

4.4 Future research

We now recognize that respiratory events other than obvious apneas and hypopneas can produce arousals during sleep and concomitant daytime sleepiness. Refinement of the approach to diagnosis needs to be delineated in those cases that do not cause obvious arousals but still produce sleepiness that is reversed by CPAP therapy. Understanding more about relationships between arousals and apneas will also be key to further exploring the utility of cardiorespiratory recording without sleep staging to titrate CPAP. Study of the possibility of a split-night diagnosis and CPAP titration with cardiorespiratory recording needs to be further addressed to explore the success of this approach before economic impact can be assessed.

The current approaches to the diagnosis of EDS by questionnaire should be refined; predictive questionnaires should be developed that take into account not only SAS, but also UARS and nonrespiratory diagnoses such as narcolepsy. Ideally, we will have a screening questionnaire that provides pretest probabilities for a variety of diagnoses and triages these patients to the type of confirmatory study needed. If the questionnaire could be time effective to administer and interpret, it could become part of each patient's initial work-up by primary care physicians. Use of such a questionnaire could lead to more awareness of sleep disorders and appropriate therapy at the primary care level and referral to sleep disorders specialists of the more complex cases.

Home recording needs to be better defined and validated. Such a natural environment may actually lead to better diagnostic clarity, but insufficient numbers of studies have addressed this issue. In addition, the use of unattended recording needs to be addressed with more studies. Intuitively, it should be possible to obtain reproducible data that can diagnose obvious SAS from unattended respiratory recording in the home or other environments; however, sufficient evidence to fully support this concept is lacking.

5.0 OTHER RESPIRATORY DISORDERS

5.1 Overview

While SAS and UARS are the respiratory disorders most commonly evaluated in sleep laboratories, other respiratory disorders are also known to cause sleep disturbance. Studies with PSG have produced significant insights into the pathophysiology of sleep disorders related to chronic obstructive pulmonary disease (COPD), asthma, and a variety of chronic restrictive lung diseases. These studies suggest that any condition causing substantial impairment of lung function will be associated with sleep disturbance.

The modern study of sleep-related breathing disorders began with the study of arterial blood gases during sleep in normal subjects and in patients with COPD (132,133). Following the development of reliable oximeters, Flick and Block (134) demonstrated a characteristic nocturnal pattern of oxyhemoglobin desaturation in patients with COPD, consisting of moderate reduction in saturation after sleep onset and severe intermittent drops in oxygen saturation. Polysomnography was used to relate the severe "dips" in oxygen saturation to REM sleep in patients with COPD, emphysema, and cystic fibrosis (135–138); to define the mechanisms of hypoxemia during sleep (139,140); to study respiratory factors contributing to arousal (140); and to study the relationship of COPD to SAS (141–143).

The modern study of nocturnal asthma began with the demonstration of an abnormal decrease of expiratory lung function during the sleep period (144). Polysomnography has been used to investigate the relationship of nocturnal asthma attacks and lung function changes to sleep stage (145,146). Other chronic lung disorders that have been investigated with PSG include those associated with kyphoscoliosis, interstitial lung disease, and pulmonary fibrosis (147–150). Patients with neuromuscular diseases, including patients with substantial restriction of lung function due to weak muscles, have also been studied with PSG (151–158).

Obstructive and restrictive lung diseases are common; COPD occurs in 3% of adults, and asthma occurs in 5% (159). Interstitial lung diseases such as pulmonary fibrosis occur in 0.1% of the population (160), and neuromuscular diseases occur in 0.5% of the population (161).

5.2 MEDLINE search terms and review of papers

The additional MEDLINE search terms for this section included *chronic obstructive lung disease, asthma,*

interstitial lung disease, restrictive lung disease, neuromuscular disease, diagnosis, and *oxygen desaturation.* The inclusion criteria for selection of literature required that a minimum of five patients be studied and that at least sleep staging and a cardiorespiratory sleep study be used for evaluation. All articles identified by the literature search that included a well-defined diagnosis of lung disease and PSG were reviewed.

5.3 Evidence-based PSG literature

The diagnosis of respiratory disorders other than sleep apnea is based on clinical examination, radiographic studies, and pulmonary function tests. Although PSG has produced insights into the interaction between sleep and breathing in these disorders, PSG is not essential to the diagnosis of these conditions.

5.3.1 Chronic obstructive pulmonary disease

In many chronic lung disorders, hypoxemia is a major abnormality during sleep, especially during REM sleep (135–137). The investigation of this specific complication in COPD does not require a definition of sleep stage or other parameters of sleep to make decisions about oxygen treatment; oximetry during sleep can be used to adequately characterize oxygenation without specific measurement of sleep stage (162). The treatment of hypoxemia that occurs only during sleep has not been shown to have a significant impact on mortality (163). Investigations of the hypoxemia of patients with other respiratory disorders are more limited than are the studies of patients with COPD; the studies that are available have not identified a diagnostic strategy that includes sleep staging to be of benefit.

Sleep complaints are common in patients with chronic lung disease and occur more frequently in this group of patients than in control populations (164,165). In COPD, symptoms of sleep disturbance are usually related to respiratory insufficiency, i.e. hypoxemia, hypercapnia, increased respiratory resistance and effort, or cough (140,166–168). The routine clinical examination often provides sufficient clues to attribute the sleep disturbance to the underlying respiratory condition. The severity of nocturnal oxygen desaturation has been correlated with the degree of daytime hypoxemia (140,167,169), but nocturnal desaturations also occur in patients with relatively normal awake SaO_2 (170). Sleep apnea is uncommon in unselected patients with COPD (141). When the examination suggests concomitant SAS, however, PSG is required to diagnose the cause of the sleep disturbance and to plan the correct treatment (see sections 4.0–4.4 of this paper) (Table 8). Because chronic lung disease can cause hypopneas with oxygen desaturation (137,139,140,168,169), oximetry is not a reliable tool to distinguish SAS from COPD. For this reason, PSG is required to accurately distinguish upper airway disorders from other types of respiratory effects on sleep.

5.3.2 Asthma

In patients with asthma, sleep disturbance is prevalent, principally because patients frequently awaken with attacks of bronchospasm (165); PSG has demonstrated that these attacks occur in all sleep stages (145,171). Transient hypoxemia does occur in patients with asthma but is usually modest compared to the hypoxemia that occurs in patients with COPD (145,171). Obstructive sleep apnea has not been a feature in the several small case series of asthmatics that have been studied for other reasons (145,146,171,172) (Table 9). The author of one report suggests that the nocturnal asthma of patients who have concomitant SAS improves when the SAS is treated with nasal CPAP (173). These observations are uncontrolled, however, and have not been confirmed by other authors. These studies indicate that sleep disturbance in patients with asthma should be attributed to inadequately controlled asthma unless more specific indications for other sleep-related breathing disorders exist.

5.3.3 Other chronic lung diseases

Polysomnography has been used to investigate breathing during sleep in other chronic lung disorders, including those associated with cystic fibrosis (138), kyphoscoliosis (147), and interstitial lung disease and fibrosis (148–150). All studies show that the patients have hypoxemia during sleep and that the hypoxemia is worse during REM sleep. Polysomnography has not been shown to offer other significant insights in the diagnosis of these diseases (Table 10).

5.3.4 Neuromuscular diseases

Patients with various types of neuromuscular disease often develop respiratory insufficiency and, by this mechanism, may have disturbed sleep. A relatively large amount of literature, examples of which are cited selectively in this paper, has described sleep disturbance and sleep-disturbed breathing in samples of patients with neuromuscular diseases in general (151) and with specific diagnoses, including muscular dystrophy (156), myotonic dystrophy (152), myasthenia gravis (155), amyotrophic lateral sclerosis (153), and

TABLE 8. *Evidence for other respiratory disorders and COPD*

Reference	Study design/ location	# of patients	Monitoring channels	Bias	Diagnostic value of testing procedure
Calverley et al. 1982 (166)	CCS/lab	29	SS AF RE SaO_2	Patient-selection bias, population bias	In COPD, sleep disruption is related to arousal. Failure to arouse may account for severe hypoxemia in "blue and bloated" patients.
Catterall et al. 1983 (141)	CCS/lab	40	SS AF RE SaO_2	Patient-selection bias	Sleep apnea is uncommon in COPD and does not account for hypoxemia.
Chaouat et al. 1995 (143)	CIS/lab	265	SS AF RE SaO_2	Patient-selection bias	In a case series of OSA, 11% of patients had obstructive spirometry and relatively lower PaO_2 and higher $PaCO_2$ and pulmonary artery pressure.
Coccagna and Lugaresi 1978 (135)	CCS/lab	33	SS AF RE SVP PVP	Patient-selection bias	In COPD, alveolar hypoventilation and pulmonary hypertension worsen with sleep and are worst in REM sleep.
Cormick et al. 1986 (167)	CCS/lab	90	SS AF RE SaO_2	Population bias, confounding factors	Symptoms of poor sleep more prevalent in COPD. Sleep characterized by hypoxemia and arousals.
Douglas et al. 1979 (136)	CCS/lab	16	SS AF RE SaO_2	Patient-selection bias, population bias	Transient hypoxemia during sleep occurs in "blue bloaters" and is worst during REM sleep.
Fleetham et al. 1982 (140)	CCS/lab	24	SS CR SaO_2	Patient-selection bias, intensity bias, ascertainment bias	Poor sleep (arousals) is not corrected with oxygen therapy.
Fletcher et al. 1983 (139)	CIS/lab	7	SS RE SaO_2 AF	Patient-selection bias	Decreased tidal volume in REM sleep.
Fletcher et al. 1987 (170)	CIS/lab	152 (135 PSG; 17 had OSA or no sleep)	SS CR SaO_2	Patient-selection bias	Oxygen desaturation occurs in patients with $PaO_2 > 60$ awake and can be detected with continuous oximetry during sleep.
Guilleminault et al. 1980 (142)	CIS/lab	26	SS CR SaO_2	Patient-selection bias	Obstructive sleep apnea is a frequent occurrence (81%) in sleepy patients with COPD.
Littner et al. 1980 (168)	CIS/lab	14	SS CR SaO_2	Patient-selection bias	During REM, partial upper airway obstruction contributes to oxygen desaturation.
Wynne et al. 1979 (137)	CIS/lab	7	SS CR SaO_2	Patient-selection bias	Hypopneas and oxygen desaturation prevalent in COPD.

CSS, cross-sectional study; SS, sleep staging includes EEG (electroencephalogram), EOG (electrooculogram), and EMG_1 (chin electromyogram); CR, cardiorespiratory monitoring includes AF (airflow), RE (respiratory effort), and heart rate or ECG (electrocardiogram); SaO_2, arterial oxygen saturation; COPD, chronic obstructive pulmonary disease; CIS, clinical series; OSA, obstructive sleep apnea; PaO_2, arterial oxygen tension; $PaCO_2$, arterial carbon dioxide tension; SVP, systemic vascular pressures; PVP, pulmonary vascular pressure; REM, rapid eye movement; PSG, polysomnography.

TABLE 9. *Evidence for other respiratory disorders and asthma*

Reference	Study design/ location	# of patients	Monitoring channels	Bias	Diagnostic value of testing procedure
Ballard et al. 1989 (146)	CCS/lab	10	SS AF RE SaO_2	Patient-selection bias	In patients with asthma with nocturnal attacks, nocturnal bronchoconstriction occurs without sleep, but is worse with sleep.
Bellia et al. 1989 (172)	CCS/lab	12	SS AF RE	Patient-selection bias	Airway resistance is highest in stages 3 and 4 sleep.
Chan et al. 1988 (173)	ClS/lab	9	SS CR SaO_2	Patient-selection bias, intensity bias	Nasal CPAP improves asthma, especially nocturnal attacks.
Issa and Sullivan 1985 (171)	ClS/lab	10	SS CR SaO_2	Patient-selection bias	Nocturnal asthma attacks are not stage specific.
Montplaisir et al. 1982 (145)	ClS/lab	16	SS AF RE SaO_2	Population bias, patient-selection bias, confounding factors, intensity bias	Asthmatics have lower sleep efficiency. Nocturnal attacks are not stage specific.

CCS, case control study; SS, sleep staging includes EEG (electroencephalogram), EOG (electrooculogram), and EMG_1 (chin electromyogram); CR, cardiorespiratory monitoring includes AF (airflow), RE (respiratory effort), and heart rate or ECG (electrocardiogram); SaO_2, arterial oxygen saturation; ClS, clinical series; CPAP, continuous positive airway pressure.

TABLE 10. *Evidence for other respiratory disorders and diseases*

Reference	Study design/ location	# of patients	Monitoring channels	Bias	Diagnostic value of testing procedure
Bye et al. 1984 (148)	CoS/lab	13	SS AF RE SaO_2	Population bias, patient-selection bias	Hypoxemia during sleep is prevalent in ILD.
Guilleminault et al. 1981 (147)	ClS/lab	5	SS CR SaO_2	Patient-selection bias	Oxygen desaturation is worst during REM sleep.
McNicholas et al. 1986 (149)	ClS/lab	7	SS AF RE SaO_2	Patient-selection bias	Oxygen desaturation in ILD is moderate even in REM sleep.
Müller et al. 1980 (138)	CCS/lab	25	SS AF RE SaO_2	Patient-selection bias, intensity bias	Oxygen desaturation during REM sleep is greater than in healthy subjects.
Perez-Padilla et al. 1985 (150)	CCS/lab	22	SS CR Sound SaO_2	Patient-selection bias	Oxygen desaturation during REM sleep is increased in ILD.

CoS, cohort study; SS, sleep staging includes EEG (electroencephalogram), EOG (electroculogram), and EMG_1 (chin electromyogram); CR, cardiorespiratory monitoring includes airflow (AF), respiratory effort (RE), and heart rate or ECG (electrocardiogram); SaO_2, arterial oxygen saturation; ILD, interstitial lung disease; ClS, clinical series; REM, rapid eye movement; CCS, case control study.

postpolio syndrome (157). Polysomnography has been used in many of these investigations (Table 11).

Although some features of sleep disturbance in patients with neuromuscular diseases may be specific to certain diseases, several general observations can be made in this context of respiratory disorders. As in other respiratory conditions, hypoxemia, especially during REM sleep, is commonly found. Nighttime abnormalities may be difficult to predict based on waking observations. Nocturnal oxygen desaturation was correlated to the degree of spirometric restriction in one study (151). Hypoventilation is frequently the cause of hypoxemia (153,156). Increased frequencies of apnea and hypopnea, usually of the nonobstructive type, have been prevalent in several series (152). Steljes et al. (157) found sleep fragmentation, hypoventilation, or obstructive apnea in 13 patients with postpolio syndrome, and these patients improved with the use of nasal ventilation or CPAP. Sleep disturbance and hypoxemia are not always explained by respiratory abnormalities, as for example in patients with myotonic dystrophy, in whom a condition similar to idiopathic hypersomnia has been described (158).

It has been argued that oximetry alone is sufficient to investigate hypoxemia in patients with neuromuscular disease (162). In patients with complaints of disturbed sleep or hypersomnolence or both, however, PSG can be used to investigate sleep apnea of either the central or obstructive type and to identify other factors contributing to sleep fragmentation. Furthermore, these findings can lead to significant therapeutic interventions (157,174). Ventilation during sleep by means of a nasal airway and a bi-level pressure-support ventilator can be an effective intervention (174). The combined evidence of three case series (151,152,157) suggests that the diagnostic yield of PSG in these circumstances is high and may offer a significant therapeutic opportunity.

5.4 Future research

Future studies should address the use of PSG in the evaluation and diagnosis of patients with respiratory insufficiency of any cause, with special focus on whether treatment interventions affect outcome variables.

6.0 NARCOLEPSY AND IDIOPATHIC HYPERSOMNIA

6.1 Overview

6.1.1 Narcolepsy

A clinical description of narcolepsy first appeared in 1880 (175), but it was not until the discovery of REM sleep and the identification of the abnormalities in its control that the electrophysiologic features of narcolepsy became recognized. The first international symposium on narcolepsy was held in 1975 and defined the clinical syndrome (176). Narcolepsy is a neurologic disorder characterized predominantly by abnormalities of REM sleep and by excessive sleepiness that cannot be fully relieved by any amount of sleep (177).

In narcolepsy, the individual components of REM sleep (sleep, motor inhibition, and dreams) can become dissociated and appear independently of one another. This dissociation accounts for the clinical tetrad of narcolepsy: sleep attacks, cataplexy, sleep paralysis, and hallucinations. Narcoleptic patients often report broken sleep, and fragmented sleep patterns are typically seen when narcoleptics' sleep is studied. The onset of symptoms of narcolepsy typically occurs between adolescence and young adulthood, but the range is very broad. The associated features of narcolepsy generally begin when the hypersomnolence begins but may develop years before or after the primary symptom of hypersomnolence. The ICSD (178) defines narcolepsy as: 1) a complaint of EDS or sudden muscle weakness (cataplexy) that has associated features such as sleep paralysis, hypnagogic hallucinations, automatic behavior, and disrupted major sleep episode; in which 2) polygraphic findings frequently include a sleep latency less than 10 minutes, with an early onset REM period, and the MSLT typically shows a mean sleep latency less than 5 minutes and two or more sleep-onset REM periods (SOREMPs); and in which 3) no other medical, psychiatric, or sleep disorders are the primary cause of the symptoms. Genetic factors have been shown to play an important but not well-defined role in the development of narcolepsy. There is a strong association (up to >95%) between narcolepsy and HLA (human leukocyte antigen) DR2 DQw1 (new nomenclature: DRw15 DQw6) in people of Caucasian and Mongolian descent (179). Narcolepsy occasionally develops at a time of emotional stress or after an acute brain trauma or tumor, often involving the hypothalamus (180).

There is little disagreement among sleep clinicians concerning the diagnosis of classic narcolepsy when the history of hypersomnolence, cataplexy, sleep paralysis, and hallucinations is present and when PSG shows short sleep latencies and early onset of REM sleep and the MSLT shows a short sleep latency and the presence of REM sleep on two or more daytime naps; however, all of these findings are present only 50% of the time (181). It is often a diagnostic challenge to identify the disease in patients with some but not all of these findings.

The prevalence of narcolepsy varies worldwide

TABLE 11. *Evidence for other respiratory disorders and neuromuscular diseases*

Reference	Study design/ location	# of patients	Monitoring channels	Bias	Diagnostic value of testing procedure
Bye et al. 1990 (151)	CIS/lab	20	SS ECG SaO_2	Patient-selection bias	REM sleep oxygen desaturation correlates with vital capacity and arterial blood gases.
Carroll et al. 1991 (162)	CIS/lab	10	SS AF RE SaO_2	Patient-selection bias, population bias, intensity bias	Home oximetry is satisfactory for defining sleep-related oxygen desaturation.
Cirignotta et al. 1987 (152)	CIS/lab	8	SS CR SaO_2	Patient-selection bias, population bias	Central apneas are prevalent in MD.
Gay et al. 1991 (153)	CSS/lab	21	SS AF RE SaO_2	Patient-selection bias	Oxygen desaturation is caused by hypoventilation, not OSA.
Khan et al. 1996 (154)	CIS/lab	8	SS AF RE SaO_2	Patient-selection bias, population bias, intensity bias	Polysomnography demonstrates hypoxemia plans sleep fragmentation, which are reverted with nocturnal nasal ventilation.
Quera-Salvá et al. 1992 (155)	CIS/lab	20	SS CR SaO_2 Esophageal pressure	Patient-selection bias, intensity bias	Patients with MG may have sleep-related breathing disorders even if properly treated.
Smith et al. 1989 (156)	RCT/lab	6	SS CR SaO_2	Population bias	Hyperventilation is prevalent during sleep in DMD. Diaphragmatic dysfunction predicts REM desaturation.
Steljes et al. 1990 (157)	CSS/lab	13	SS AF RE SaO_2	Patient-selection bias, population bias, intensity bias	Poor sleep may be due to OSA and can be improved with CPAP.
van der Meché et al. 1994 (158)	CIS/lab	32	SS AF RE $tcPO_2$	Patient-selection bias	Polysomnography performed on 17/22 patients, 10 controls. OSA explains sleepiness in only three of 17 patients with myotonic dystrophy.

CIS, clinical series; SS, sleep staging includes EEG (electroencephalogram), EOG (electrooculogram), and EMG_1 (chin electromyogram); CR, cardiorespiratory monitoring includes airflow (AF), respiratory effort (RE), and heart rate or ECG (electrocardiogram); SaO_2, arterial oxygen saturation; MD, muscular dystrophy; CSS, cross-sectional study; OSA, obstructive sleep apnea; MG, myasthenia gravis; RCT, randomized controlled trial; DMD, Duchenne's muscular dystrophy; REM, rapid eye movement; CPAP, continuous positive airway pressure; $tcPO_2$, transcutaneous oxygen tension.

from as little as 0.0002% in Israel to 0.16% in Japan. In North America and Europe, the prevalence varies from 0.03% to 0.06% (182).

6.1.2 Idiopathic hypersomnia

Idiopathic hypersomnia is a disorder of presumed central nervous system (CNS) cause that is associated with a normal or prolonged major sleep episode and EDS (183). The indications for PSG and MSLT for the evaluation of idiopathic hypersomnia are the same as for narcolepsy. Aldrich (184) found that apart from the REM sleep measure, there were no major differences in clinical or polygraphic features between subjects with narcolepsy without cataplexy and those patients with idiopathic hypersomnia. Care must be taken to exclude UARS or any CNS structural anomaly as the cause of hypersomnia in patients for whom the diagnosis of idiopathic hypersomnia is being considered (45,183).

In a patient with EDS, the following findings are consistent with the diagnosis of idiopathic hypersomnia: an MSLT demonstrating a sleep latency of less than 10 minutes (typically less than 5 minutes) and fewer than two SOREMPs; polysomnographic testing performed on the night preceding the MSLT not demonstrating sleep fragmentation; and no other medical or psychiatric disorder accounting for the patient's EDS. Treatment generally requires stimulant medication.

6.2 MEDLINE search terms and review of papers

The additional MEDLINE search terms for this section included *narcolepsy, hypersomnolence, multiple sleep latency test, wakefulness,* and *excessive daytime sleepiness.* The inclusion criteria for selection of literature included studies that evaluated a minimum of eight patients and that used at least cardiorespiratory recording, sleep staging, and MSLT for the evaluation. Few case-controlled PSG studies of patients with narcolepsy have been published.

6.3 Evidence-based literature for PSG and other sleep medicine procedures

The most pervasive and sometimes initially the only symptom of narcolepsy is EDS. However, narcolepsy is only one of many causes of hypersomnolence. Other sleep disorders that affect quality of sleep (SAS and periodic limb movement disorder [PLMD]), quantity of sleep (insufficient sleep syndrome), or the circadian phase of sleep (circadian rhythm disorder) may also result in EDS (72,185).

The presence and severity of these other disorders cannot always be reliably evaluated by clinical history or physical examination alone. The treatment of many of these disorders is entirely different from the treatment of narcolepsy. Narcolepsy, as well as some of the other causes of EDS such as idiopathic hypersomnia, once diagnosed, require long-term intervention with stimulant medication. Because of all these issues, it is incumbent on the clinician to first accurately assess the severity of the EDS and to diagnosis its cause before proceeding to treatment. For this assessment, it has become accepted procedure to objectively evaluate the nighttime sleep by all-night PSG the night before a daytime MSLT (Table 12). The diagnosis and management of narcolepsy is further complicated by the fact that patients with narcolepsy often have increased periodic leg movements (PLMs), sleep-disordered breathing, and unexplained arousals, although none of these findings is generally severe enough to explain the patient's level of EDS (186,187).

Historically, PSG and MSLT have been used together to evaluate suspected narcolepsy (188): PSG to assess for appropriate quantity and quality of nighttime sleep (and to exclude other disorders that might disrupt sleep and create EDS), and MSLT the following day to quantify EDS and to document the presence of SOREMPs.

A finding on MSLT of a mean sleep latency of less than 5 minutes and two or more SOREMPs is considered diagnostic for narcolepsy when the clinical history is indicative of a diagnosis of narcolepsy and sleep fragmentation due to other sleep disorders is not present on all-night PSG (72,189). In up to 30% to 50% of patients with severe narcolepsy, one or more of the classic findings of narcolepsy is absent—e.g. there may be no symptoms of cataplexy; or, despite the presence of short sleep latencies, there may be no SOREMPs on MSLT (184,186); or the sleep latency may not be as severely shortened as to the level of less than 5 minutes. Furthermore, other sleep disorders that cause hypersomnolence by fragmenting nighttime sleep may lead to a mean sleep latency of less than 5 minutes with two or more SOREMPs on MSLT (72). In such cases, clinical judgment is important in establishing the diagnosis and in planning treatment.

Mitler et al. (189) reported that 40 of 40 patients with narcolepsy had two or more SOREMPs in a five-nap protocol on the MSLT. None of 14 controls had any SOREMPs. Moscovitch et al. (186) reported that two or more SOREMPs were more likely in patients with narcolepsy with cataplexy than in patients with narcolepsy without cataplexy. Amira et al. (185) noted that two or more SOREMPs on MSLT had a specificity of 99% and a sensitivity of 84% for the diagnosis of narcolepsy.

TABLE 12. *Evidence for narcolepsy*

Reference	Study design/ location	# of patients	Monitoring channels	Bias	Diagnostic value of testing procedure
Aldrich and Chervin 1995 (197)	Data review	1,602 176 narcolepsy, 1,426 other sleep disorders	SS CR MSLT		In patients with clinical narcolepsy, ≥ two SOREMs, sensitivity is 76% and predictive value is 57%. With > three SOREMs, sensitivity is 41% and predictive value is 79%. Specificity is 98.8% and negative predictive value is 94%. Seven percent of OSA patients and 5% of other sleep disorders patients had two SOREMs on MSLT; leads to low predictive value for narcolepsy.
Amira et al. 1985 (185)	ClS/lab	144 MSLT and PSG, 64 PSG	CR SS MSLT	Patient-selection bias, population bias	Three different groups of EDS patients: 1) less than or equal to two SOREMs, MSLT of less than 5 minutes, 51 narcolepsy, one apnea 2) one SOREMs, MSLT mean of 8 minutes, nine narcolepsy, one apnea, one idiopathic hypersomnolence 3) 0 SOREMs, mean MSLT of 11.5 minutes, one narcolepsy Sensitivity ≥ two or more SOREMs, 84%; specificity ≥ two or more SOREMs, 99%.
Broughton et al. 1988 (198)	CCS/ home	20	CR SS MSLT	Patient-selection bias, population bias	Night sleep in narcolepsy has increased sleep fragmentation and decreased sleep efficiency. Daytime sleep has increase in amount, increase in number of SOREMs, number of SOREMs variable in day. Both narcolepsy patients and controls had likelihood of sleep in midafternoon.
Mitler et al. 1979 (189)	ClS/lab	40	CR SS MSLT	Patient-selection bias, population bias	Documented SOREMs in clinical narcolepsy. 11/40 had two SOREMs, 5/40 had three SOREMs, 11/40 had four SOREMs, 13/40 had five SOREMs.
Mitler et al. 1993 (193)	RCT/lab	16	CR SS MSLT		Used PSG as assessment of placebo and stimulant medication. Narcoleptic patients have short sleep latency at night, and during MSLT, the latencies increase in both groups with treatment in a dose-dependent manner. Performance improves as latencies decrease.
Moscovitch et al. 1993 (186)	Data review	306	SS CR MSLT		Cataplexy present in 92% of patients with EDS. In patients with narcolepsy based on clinical criteria (cataplexy) and two SOREMs, sensitivity is 83% and specificity is 49%. Subgroup of patients with two or more SOREMs was older women with PLMs. EDS and cataplexy and two SOREMs had the greatest likelihood of DR2 DQw1-positive narcolepsy.
Richardson et al. 1978 (199)	CCS/lab	41	CR SS MSLT	Patient-selection bias, population bias	Narcolepsy patients: shorter sleep latency, shorter TST, less REM sleep, increased WASO, increased body movements and arousals. MSLT: allowing 10 minutes of sleep after sleep onsets did not affect sleep latencies compared to 1 minute of sleep.
Rosenthal et al. 1990 (181)	ClS/lab	119	CR SS MSLT	Patient-selection bias, population bias	Clinical symptoms in narcolepsy: 79.3% of patients had cataplexy. 67% had hypnogogic hallucinations. 64% had sleep paralysis. 48% had entire tetrad. 10% had isolated EDS.

TABLE 12. *Continued*

Reference	Study design/ location	# of patients	Monitoring channels	Bias	Diagnostic value of testing procedure
Uchiyama et al. 1994 (200)	CIS/lab	10	CR SS MSLT	Patient-selection bias, population bias	Measured effect of extending time in bed from 8 hours to 12 hours resulting in 1) increased TST (7 hours to 10 hours), 2) longer mean MSLT (4.1 minutes to 8.2 minutes), and 3) no change in REM latency at night or SOREMs on naps.
van den Hoed et al. 1981 (187)	CIS/lab	100	CR SS MSLT	Patient-selection bias	Patients with narcolepsy: 89% had cataplexy, 85% had two SOREMs, mean MSLT 3.3 min. Night sleep: frequent PLMs, frequent arousals Non-narcoleptics: idiopathic hypersomnolence, 17%; psychiatric disease, 18%; insufficient sleep or irregular sleep, 18%; drug use or abuse, 9%; mean MSLT of 9 minutes. Sensitivity for 2 SOREMs 85%, specificity 87%.
Zorick et al. 1982 (72)	CIS/lab	161	CR SS MSLT	Patient-selection bias, population bias	MSLT of less than 4 minutes: diagnosis of narcolepsy or OSA. MSLT of 5 to 8 minutes: diagnosis of PLMs or insufficient sleep. MSLT of greater than 9 minutes: diagnosis of psychiatric disorders or no objective findings. Only narcolepsy patients had two or more SOREMs. All other diagnoses have some patients with one SOREM.

SS, sleep staging includes EEG (electroencephalogram), EOG (electrooculogram), and EMG_1 (chin electromyogram); CR, cardiorespiratory monitoring includes AF (airflow), RE (respiratory effort), and heart rate or ECG (electrocardiogram); MSLT, multiple sleep latency test; SOREMs, sleep-onset rapid eye movement periods; OSA, obstructive sleep apnea; CIS, clinical series; PSG, polysomnography; EDS, excessive daytime sleepiness; CCS, case control study; RCT, randomized controlled trial; PLMs, periodic limb movements in sleep; TST, total sleep time; REM, rapid eye movement; WASO, wake after sleep onset.

No body of accumulated data has validated MWT, limited or partial PSG, portable recording, isolated MSLT, or separately performed PSG and MSLT as an alternative to the "gold standard" of nocturnal PSG with an MSLT on the following day for the diagnosis of narcolepsy. While MSLT measures a patient's sleep propensity, the MWT performed under conditions similar to those of the MSLT, i.e. in a quiet, sleep-inducing environment, measures the patient's ability to remain awake. Therefore, because this test allows for the determination of sleep latency, MWT does offer the ability to measure treatment effects and has been validated for this use (190–192). However, the MWT has not been validated as an alternative for the diagnosis of narcolepsy (192) because, though MWT does record REM sleep, no scoring mechanism of SOREMPs has been established for use in MWT. Both MSLT (193) and MWT (190) may have some usefulness in documenting response to stimulant medicine in narcoleptic patients with an established diagnosis. Pupillography and 24-hour ambulatory EEG have been evaluated in the past as possible alternative tests, but neither is in current clinical use.

The PSG and MSLT findings of narcolepsy can be obscured by psychiatric disease, insufficient sleep, or sleep apnea; and sleep apnea, depression, insufficient sleep syndrome, and circadian rhythm disturbances can masquerade as narcolepsy (184,194,195). Before the full syndrome of narcolepsy develops, partial symptoms may occur before characteristic PSG or MSLT findings can be seen, particularly in children or adolescents (196). A careful medical and sleep history, sleep diary, and physical and neurologic examination can help minimize misdiagnosis.

6.4 Future research

MWT, limited or partial PSG, ambulatory recording, isolated MSLT, or separately performed PSG and MSLT should be validated by comparison to the traditional "gold standard" of nocturnal PSG with MSLT the following day for diagnosing narcolepsy.

The MWT is an alternative tool for which some data are available for evaluating daytime alertness, but MWT has not been validated for diagnosing narcolepsy or for identifying SOREMPs. How the MWT data differ from the MSLT data needs to be clarified.

7.0 PARASOMNIAS AND SLEEP-RELATED EPILEPSY

7.1 Overview

Parasomnias are undesirable physiologic phenomena that occur predominantly during sleep and can be

associated with a number of sleep disorder diagnoses described in the ICSD (201). This section primarily concerns those parasomnias (principally the arousal disorders, such as sleepwalking and sleep terrors, and REM sleep behavior disorder [RBD]) that are potentially violent, can be injurious to the patient and others, and can produce serious disruption of sleep and family functioning. Although not classified in the ICSD as parasomnias, sleep-related epilepsy (202,203) and sleep-related psychiatric disorders (such as panic and dissociative disorders) also must be considered in the differential diagnosis (204–206). Polysomnographic studies of sleepwalking first appeared in 1963 (207), and studies of the sleep of patients with panic and dissociative disorders initially were reported in 1984 and 1989 (206,208). The first systematic report of RBD was published in 1986 (209). Sleep-related violence, including sleep-related homicide, also has been described (210,211).

Sleepwalking occurs in up to 30% of healthy children, peaking at 11 to 12 years of age, and 2% to 3% of these children may have frequent episodes; sleepwalking also occurs in 2.5% of adults (212–215). Sleep terrors occur in 1% to 6% of prepubertal children and in 1% of adults (216). The prevalence of RBD is not known; at least 290 cases have been reported in the world's literature (217).

Epilepsy is a common disorder, affecting nearly 4% of the population at some time in their lives (218). In 15% to 20% of epileptics, seizures occur mostly or exclusively at night, a condition termed "sleep-related epilepsy" (202,203). Sleep-related epilepsy, however, is a heterogeneous category. In fact, EEG abnormalities increase during sleep in almost every subtype of epilepsy (219,220). Except for the preponderance of seizures during the usual sleeping periods, there are no distinctive biologic characteristics of sleep-related epilepsy that distinguish it from a diurnal seizure disorder or that require specialized diagnostic techniques or unique types of therapy.

Between 6% and 14% of people in college and community populations will report at least one uncued panic attack. Panic disorder has a prevalence of 2.5% of the general population. Approximately 18% of panic attacks begin during the sleeping state; 2.5% of these attacks occur exclusively at night. In a group of patients with panic disorder, 71% experience at least one nocturnal panic attack (221,222). A number of PSG studies have reported on the sleep of patients with panic disorder. Panic attacks tend to arise from NREM sleep stages 2 and 3; they occur occasionally at sleep onset (208,223–228). Sleep-related dissociative disorders, although not classified as parasomnias in the ICSD, may mimic parasomnias. Nocturnal dissociative behaviors generally occur in patients already carrying the diagnosis of a diurnal dissociative disorder. Although these patients appear behaviorally to be asleep when these events occur, PSG recording demonstrates wakefulness (206). The prevalence of sleep-related dissociative disorders is unknown (206).

7.2 MEDLINE search terms and review of papers

The additional MEDLINE and Psychinfo search terms for this section included *aggressiveness; attitudes toward health; cost-benefit; cost-effectiveness; economics; electroencephalography; epilepsy; outcomes; processes; parasomnias; pavor nocturnus; REM sleep behavior disorder; reproducibility of results; sleep-related violence; sleep terrors*; and *sleepwalking*. For inclusion in this literature review, papers had to report the study of at least four subjects and the measurement of at least the basic sleep-staging channels of EEG, EOG, and EMG. Abstracts, review articles, and case reports (even with documented PSG) were excluded from the evidence tables for decision-making concerning indications for sleep-testing procedures. However, two articles without full EMG data are included because of their historic importance (229,230).

7.3 Evidence-based literature for PSG and other sleep medicine procedures

Polysomnography can be diagnostic for parasomnias and epilepsy if the event occurs during the study. However, because events often do not occur nightly, the failure to record an event per se does not assist the clinician in making or excluding the diagnosis. In such cases, ancillary findings still may be helpful [e.g. the characteristic augmentation of the EMG tone, or excessive phasic twitching, that occurs during REM sleep in RBD (201,209,231–234) or the presence of interictal paroxysmal abnormalities that commonly occur in patients with sleep-related epilepsy]. Seizure-induced behaviors may closely resemble other parasomnias and make differential diagnosis difficult (235,236). "Episodic nocturnal wandering" is a term often used for disorders of suspected ictal etiology that may or may not be accompanied by epileptiform EEG activity during events and may be clinically indistinguishable from disorders of arousal (237–242). One group uses this term for sleep-related ambulatory behaviors when the etiology is not conclusively epileptic (237).

Disorders of arousal occur during partial arousals from sleep. Typically, they occur from the deeper stages of NREM sleep (230,243–245). Less commonly, they arise from stage 2 sleep (237,246–250). Pa-

tients may have unremarkable PSG studies, and the ICSD does not list any particular interspell PSG markers that are pathognomonic of disorders of arousal. When recorded by PSG, these events appear as abrupt arousals with EEG admixtures of sleep and wakefulness. These arousals may be manifested only electrophysiologically or may include movement, vocalization, or more complex behavior. They often fail to appear during recorded sleep in the laboratory (229,235,237,243,244,247–255). The likelihood that the arousals will be recorded correlates with the patient's reported frequency of symptomatic spells (235). Difficulty establishing a diagnosis is greater when several syndromes or findings coexist, such as sleep terrors and seizures, RBD, SAS, or PLMD (236,247,250,256).

7.3.1 Seizures, disorders of arousal, REM-sleep behavior disorder, dissociative disorders

Polysomnographic findings can serve to identify obvious seizures, sleepwalking, sleep terrors, RBD, or dissociative disorders (235,237,247,250) (Table 13). Typical sleepwalking or sleep terrors—with onset in childhood, a positive family history, occurrence during the first third of the night, amnesia for the events, prompt return to sleep following the events, and relatively benign automatistic behaviors—may be diagnosed on the basis of their historic clinical features. This conclusion is based upon very consistent descriptive literature (205,207,212,230,243,245,253). Polysomnographic evaluation becomes important in any of the following circumstances (when the events are not typical of benign partial arousals and where other diagnoses, prognoses, and interventions must be considered): when the behaviors are injurious to the patient or others, began at an unusual age, are repetitive and stereotypical, occur with an unusual frequency or duration or at an unusual time of night, or seriously disturb the patient's home life; when EDS is present; or when there are forensic concerns. Polysomnography is then performed to help document the presence of a disorder of arousal, sleep-associated seizure disorder, REM sleep parasomnia, or sleep-related manifestation of a psychiatric disorder and to recognize other predisposing sleep disorders such as OSA or PLMs. Precise diagnosis is important because the significance and treatment of these various disorders are often quite different (205,210,211,217,237,238,241,247,250,255, 257,258).

7.3.2 Sleep-related epilepsy

There is limited direct evidence supporting the diagnosis of sleep-related epilepsy by PSG. In a retrospective study of nocturnal arousals of uncertain etiology, the PSG format that was used emphasized video recording and an expanded EEG montage (235). (The study did include a spectrum of patients who turned out to have various parasomnias and nocturnal seizures.) Of 122 reported cases, 41% of a subgroup with minor motor manifestations, and 69% with prominent motor activity, had recordings that demonstrated epilepsy. Some of the epilepsy diagnoses were based on findings of increased amounts of interictal EEG abnormality despite the absence of other physiologic abnormalities on PSG. The limitations of this study are lack of detail about the clinical "gold standard" for diagnosis, lack of blind interpretation of the PSGs, lack of validity and reliability information regarding PSG, limited consideration of the effect of the prerecording attack frequency on the success of PSG recording, and lack of information about outcomes.

The lack of data from PSG studies on sleep-related epilepsy may be partially addressed by referring to published information about a related recording method, video-EEG telemetry. Video-EEG telemetry does not record sleep staging, respiratory, or limb movement channels, but its EEG coverage and video capability are similar to those of PSG with video recording. A prospective evaluation using video-EEG telemetry recorded ictal events in 57 of 64 patients (89%) with intractable seizures. As a result of the video-EEG recording, these patients had marked improvement of seizure control and a reduction in the number of anticonvulsant medications used during a 2-year follow-up period (259).

7.3.3 Other parasomnias

The literature supporting the use of PSG for other parasomnias is summarized in the evidence tables (Tables 13–15). Only three articles dealing with disorders of arousal (243,251,260) and two for RBD (232,234) include comparison data for normal controls. Most articles supporting the utility of PSG are limited by biases inherent in uncontrolled clinical reports. Clinical series and cohort studies all share patient-selection biases due to differing laboratory sites (i.e. research, clinical, neurology, or psychiatry settings) and severities of the disorders selected. Standard PSG scoring is based upon the criteria of Rechtschaffen and Kales (261), but there are no assessments of interrater reliability across studies. Furthermore, although the differences between sleep in the laboratory and sleep in the home may influence the findings, this issue is addressed in only one report (which indicates that full parasomnia events are more likely to be recorded at home) (237). PSG performed in the laboratory revealed no episodes of sleepwalking, but somniloquy

TABLE 13. *Evidence for seizures, generally noninjurious parasomnias, and disorders of arousal*

Reference	Study design/ location	# of patients	Monitoring channels	Bias	Diagnostic value of testing procedure
Aldrich and Jahnke 1991 (235)	CIS/lab	122	SS AF RE SaO_2 EMG_2 Expanded EEG Video	*a*	PSG with concurrent video and capability for increased paper speed yielded diagnostic (35%) or supportive studies in two thirds of cases, multiple diagnoses. Expanded, bilateral EEG montage and concurrent video increase diagnostic value.
Blatt et al. 1991 (251)	Blinded CCS/lab	36 (24 patients, 12 controls)	SS AF RE EMG_2 Video	Patient-selection bias	No full parasomnia events in lab. Behavioral events in bed in 29% of DoA patients, not controls. Increased hypersynchronous delta in patients, not controls. Interruptions of stages 3 and 4 greater in patients.
Crisp et al. 1990 (252)	CIS/lab	12 10 had PSG	SS Video	*a*	Behavioral events recorded in 70% of patients with DoA. Signs (behavioral events) recorded in 50%.
Fisher et al. 1973 (229)	NCT, single blind/lab	6	SS CR	Population bias	5/6 patients had more than 1 DoA event per study night off drug. PSG demonstrates decreased frequency of events on diazepam.
Fisher et al. 1973 (230)	CoS/lab	11	SS CR	Patient-selection bias	Unspecified number of events on specific nights of study for DoA. Events rarely emerged from stage 2 sleep. More awakenings from all stages of sleep in patients with DoA compared to patients with REM nightmare.
Guilleminault et al. 1995 (237)	CoS/lab and home	41	*Lab* SS CR SaO_2 Sound Pes in some Paper speed 10 mm/sec *Home* SS	Patient-selection bias, confounding factors	No full parasomnia events recorded in lab. PSG made presumptive diagnoses of associated sleep disorders in 7/41 cases; somniloquy ± movement in another 11/41 cases. Events were demonstrated in all of the 37 cases studied in the home after a mean of 6.5 nights.
Halász et al. 1985 (260)	CSS/lab	17 9 patients, 8 controls	SS ECG Expanded EEG Video	Patient-selection bias	No DoA events recorded by PSG. Microarousals preceded by synchronous slow-wave activity in patients greater than controls.
Jacobson et al. 1965 (244)	CSS/lab	9	SS	Patient-selection bias	74 DoA events recorded in SWS during 47 study nights.
Kales et al. 1966 (243)	CSS/lab	9 4 child patients 1 adult patient 4 child controls	SS	Patient-selection bias	15 DoA events recorded from SWS during 12 study nights in four child patients, none from adults or controls.
Kavey et al. 1990 (247)	CIS/lab	10	SS RE ECG Expanded EEG Video	*a*	DoA events recorded in 80% of patients. Three patients had multiple events in single night.
Llorente et al. 1992 (254)	CIS/lab	11 10 had PSG	SS CR SaO_2	*a*	All DoA patients demonstrated EEG arousals with motor activity. Sleep-terror events recorded in 60%.

TABLE 13. *Continued.*

Reference	Study design/ location	# of patients	Monitoring channels	Bias	Diagnostic value of testing procedure
Moldofsky et al. 1995 (248)	ClS/lab	64	SS ECG RE in some SaO_2 in some EMG_2 in some Paper speed 15 mm/sec Video	*a*	Behavioral events recorded 31% of cases during NREM sleep. Two patients also demonstrated arousals with vocalization from REM sleep.
Popoviciu et al. 1990 (249)	ClS/lab	27	SS ECG AF Actigraphy Video	*a*	At least two events with motor and verbal behaviors recorded in all patients.
Schenck et al. 1989 (250)	ClS/lab	100	SS AF ECG RE in some EMG_2 Expanded EEG Paper speed 15 mm/sec (30 mm/sec intervals) Video	*a*	Over multiple diagnoses, PSG was diagnostic in 65% of cases and supportive in 26% of cases.
Vela et al. 1982 (255)	CoS/lab	6	SS ECG	Patient-selection bias	Events recorded in 50% of patients but none before third night of study. No events recorded in three patients during 10 nights of study.

ClS, clinical series; SS, sleep staging includes EEG (electroencephalogram), EOG (electrooculogram), and EMG_1 (chin electromyogram); CR, cardiorespiratory sleep study includes AF (airflow), RE (respiratory effort), and heart rate or ECG (electrocardiogram); SaO_2, arterial oxygen saturation; EMG_2, anterior tibialis electromyogram; CCS, case control study; DoA, disorders of arousal; PSG, polysomnography; NCT, nonrandomized controlled trial; REM, rapid eye movement; CoS, cohort study; CSS, cross sectional study; SWS, slow-wave sleep; NREM, nonrapid eye movement.

[a] Several biases are common to clinical series: patient-selection bias, lack of blinding, lack of controls/comparison data, errors in measurement of outcomes, bias to external validity.

TABLE 14. *Evidence for parasomnias for REM-sleep behavior disorders*

Reference	Study design/ location	# of patients	Monitoring channels	Bias	Diagnostic value of testing procedure
Culebras and Moore 1989 (231)	CIS/lab	6	SS ECG EMG_2 Video	*a*	All PSGs demonstrated tonic and phasic EMG elevations during REM sleep. Aperiodic twitching and motor restlessness during REM sleep. Periodic and aperiodic EMG activity during NREM sleep. Complex behaviors recorded during REM sleep in 50% of patients.
Lapierre and Montplaisir 1992 (232)	CCS/lab	10 5 patients 5 controls	SS ECG EMG_2 AF	Patient-selection bias	Elevation of tonic and phasic EMG activity during REM in all patients. Quantitative scoring of phasic EMG activity presented. Phasic activity decreased with use of clonazepam.
Schenck et al. 1986 (209)	CIS/lab	5	SS AF ECG RE in some EMG_2 Expanded EEG in some Paper speed 10 mm/sec (15 and 30 in one case) Video	*a*	Fluctuating augmentation of EMG tone during REM sleep in all patients. Jerky movements and some complex behaviors during REM sleep. REM-related behaviors represent dream enactment.
Schenck and Mahowald 1990 (233)	CIS/lab	70	SS ECG EMG_2 AF RE in some SaO_2 in some Expanded EEG Paper speed 15 mm/sec (30 mm/second intervals) Video	*a*	All PSGs diagnostic of RBD.
Schenck and Mahowald 1991 (275)	CIS/lab	20	SS CR EMG_2 SaO_2 Expanded EEG Paper speed 15 mm/sec (30 mm/second intervals) Video	*a*	17/20 PSGs diagnostic of RBD; 3/20 diagnostic of DoA.
Schenck et al. 1993 (217)	CIS/lab	96	SS CR EMG_2 SaO_2 Expanded EEG Paper speed 15 mm/sec (30 mm/second intervals) Video	*a*	Review paper.

TABLE 14. *Continued*

Reference	Study design/ location	# of patients	Monitoring channels	Bias	Diagnostic value of testing procedure
Sforza et al. 1988 (276)	CIS/lab	6	SS EMG_2 CR SaO_2	*a*	All PSGs diagnostic of RBD.
Tachibana et al. 1991 (234)	CCS/lab	21 7 patients 14 controls	SS ECG EMG_2 Video	Patient-selection bias	RBD events recorded in 86% of patients. All patients had elevated tonic and phasic EMG activity during REM sleep.

CIS, clinical series; SS, sleep staging includes EEG (electroencephalogram), EOG (electrooculogram), and EMG_1 (chin electromyogram); CR, cardiorespiratory sleep study includes AF (airflow), RE (respiratory effort), and heart rate or ECG (electrocardiogram); EMG_2, anterior tibialis electromyogram; PSG, polysomnography; REM, rapid eye movement; NREM, nonrapid eye movement; CCS, case control study; SaO_2, arterial oxygen saturation; RBD, REM sleep behavior disorder; DoA, disorders of arousal.

[a] Several biases are common to clinical series: patient-selection bias, lack of blinding, lack of controls/comparison data, errors in measurement of outcomes, bias to external validity.

TABLE 15. *Evidence for parasomnias for episodic nocturnal wandering and paroxysmal arousals*

Reference	Study design/ location	# of patients	Monitoring channels	Bias	Diagnostic value of testing procedure
Maselli et al. 1988 (238)	CIS/lab	12	SS ECG RE Expanded EEG	*a*	Events unaccompanied by epileptiform EEG changes recorded in two cases. Interictal epileptiform activity recorded in four cases.
Montagna et al. 1990 (239)	CIS/lab	6	SS ECG EMG_2 RE Video Expanded EEG	*a*	Brief paroxysmal arousals with motor activation recorded during NREM in all patients. Epileptiform EEG activity recorded in one patient during an event.
Pedley and Guilleminault 1977 (241)	CIS/lab	6	SS Video	*a*	Behavioral events were recorded during NREM sleep in two patients. No EEG abnormality detected on PSG.
Plazzi et al. 1995 (242)	Crpt/lab	4	SS Expanded EEG Video	Population bias	Behavioral events were recorded in all cases with associated ictal epileptiform EEG activity.

CIS, clinical series; SS, sleep staging includes EEG (electroencephalogram), EOG (electrooculogram), and EMG_1 (chin electromyogram); CR, cardiorespiratory sleep study includes AF (airflow), RE (respiratory effort), and heart rate or ECG (electrocardiogram); EMG_2, anterior tibialis electromyogram; NREM, nonrapid eye movement; PSG, polysomnography; Crpt, case report.

[a] Several biases are common to clinical series: patient-selection bias, lack of blinding, lack of controls/comparison data, errors in measurement of outcomes, bias to external validity.

was recorded in 11 cases, eight of which included motor activity; four cases of sleep-disordered breathing were identified, with sleep terrors precipitated by respiratory events in two cases; and RBD was identified in three PSGs. In summary, laboratory-based PSG yielded supportive diagnostic information in 20 of 41 cases, but none of the laboratory studies yielded definitive results, i.e. there were no recordings of full events as described in the patient's history. In contrast, all of the studies performed in the home-recorded somnambulistic parasomnias after 4 to 10 nights (mean of 6.5). Two other discrepancies were noted between ambulatory and laboratory recordings—in one case, events occurred from REM sleep in the laboratory and from stage 2 sleep at home; in the other case, different stages of NREM sleep immediately preceded the events.

7.3.4 Technical considerations

Distinguishing sleep-related epilepsy from other parasomnias is a crucial and difficult problem clinically; therefore, PSG technical requirements must be suitable for confident identification of seizures. The requirements include an expanded, bilateral scalp montage (as opposed to the usual three-channel EEG used for sleep staging). Although standard PSG may be nearly as sensitive as PSG with an expanded bilateral EEG montage, it will be considerably less specific for detecting epileptic attacks (if conclusions from research on ambulatory EEG apply to PSG) (262).

A second important issue about both PSG and video-EEG telemetry is the frequent failure of scalp recordings to detect subtle seizures and simple partial seizures. In some of these cases, video recording demonstrates the stereotyped nature of the behavior, suggesting that the events are ictal in origin and not pseudoseizures or nonepileptic parasomnias (263). The improvement in detection rate gained from video recording has not been quantified.

Third, recording speed, pen responses, and digital sampling rate must be sufficient to detect spike and wave activity, paroxysmal fast activity, and electrodecremental events that signal seizures or show interictal paroxysmal abnormalities. The technical requirements are spelled out in publications from the AEEGS and generally include a paper speed of 30 mm per second (264) or a sampling rate of 200 Hz (265).

Fourth, the presence of a technician capable of testing the responsiveness of the patient, adjusting the equipment settings, and replacing PSG connections disrupted by movement is essential for adequate seizure diagnosis (235).

Finally, the record must be interpreted by a clinician skilled in recognizing paroxysmal discharges, identifying recorded seizures and other sleep events, and staging sleep (235).

These technical factors lead directly to the question of whether diagnostic methods other than PSG will be sufficient for the diagnosis of complex parasomnias. Daytime video-EEG telemetry is irrelevant for use in diagnosing sleep disorders, and nighttime video-EEG telemetry would not be expected to be as useful as PSG with video recording for differentiating epilepsy from other parasomnias. Another alternative, ambulatory recording, would not allow simultaneous video-physiologic recording, technician interaction with the patient, or correction of artifacts from movements that displace leads. Because much of the diagnostic capability of PSG and video-EEG telemetry arise from viewing the behavior and associated physiologic events together and having an opportunity for the technician to interact with the patient, it is unlikely that portable sleep studies, ambulatory EEG, or daytime video-EEG telemetry will be effective alternatives to PSG with video recording (235,259,263,266–273).

It is also important to know how often spells or attacks must occur to be reasonably detectable by recording, whether by PSG or by video-EEG telemetry. Two case series of video-EEG recording for epilepsy (266,268) demanded event frequencies of two per week before recording was considered. Other investigators have correlated prerecording event frequencies with recording success. Success rates for 6- to 8-hour sessions of daytime recording ranged from 33% to 74%, depending on whether the patient's spells occurred weekly or daily (274). In another center, spontaneous seizures were recorded within 48 hours in 85% of patients whose prerecording seizure frequency was at least one per week (259).

A number of PSG studies have provided ample description of disorders of arousal in laboratory settings. These studies document that the percentage of patients whose PSG recorded the behavioral events varied widely and ranged from 0% to 80% (235,237,244,247, 250–252,254); in addition, the events recorded were often milder than were those reported by history and often occurred without the patient leaving the bed. Milder events, such as vocalizations, limb movement, and sitting up in bed are often designated as supportive rather than diagnostic findings, although they do not occur in normal controls (243,251,260). Six studies describe increased frequency of arousals from NREM sleep (230,235,249,250,251,254), and one study demonstrated no difference from control values for microarousals unless the arousals were associated with slow-wave synchronization, in which case the microarousals occurred significantly more frequently in patients than in controls (260). The presence of hypersynchronous high-voltage delta activity in the

EEG of patients with arousal disorders is often described and may reflect cerebral immaturity (237,243,244,247,251,260). There is no consistent pattern of sleep-architecture alteration reported in the arousal-disorder literature. One study reports diminution of percentage of slow-wave sleep (250), and another shows a trend toward an elevation (251). Fisher et al. (230) reported that arousal-disorder events are more severe after longer preceding periods of slow-wave sleep. There are no consistent quantitative criteria or sensitivity and specificity data yet established for severity of events, frequency of microarousals or hypersynchronous delta EEG activity, or specific sleep-architecture alterations in disorders of arousal.

The reported studies of RBD clearly indicate that the diagnosis is based upon polygraphic findings of variably elevated EMG tone and increased phasic EMG activity during REM sleep. Inasmuch as the concordance of extremity movement and dream mentation is documented by reported descriptions, the recording of EMG from the extremities is important (209,217,231–234,275,276).

With regard to diagnostic usefulness, the two clinical series (each including over 100 cases of patients with various parasomnias) indicate that PSG was diagnostic in 35% and 65% and supportive in another 26% and 30% of cases, for an overall yield of clinical utility in 65% and 91% of cases (235,250).

7.3.5 Alternative tools

The clinical interview and physical examination are the primary tools for the diagnosis of epilepsy. Standard EEG, preferably including a daytime nap, is performed in nearly all epileptics. Imaging studies may show an area of altered structure or brain metabolism that can be correlated with partial epileptic attacks, but imaging studies do not provide direct diagnostic evidence of epilepsy (277). These initial investigations are sufficient to establish the diagnosis of sleep-related epilepsy in the vast majority of instances.

7.4 Future research

A multicenter cooperative effort could identify a large population of individuals with histories of sleep-related violence and describe the behaviors systematically and polysomnographically in a prospective manner to better understand the utility and limitations of PSG. Controlled studies can evaluate the actual significance of hypersynchronous delta EEG activity and microarousals in disorders of arousal.

Likewise, a multicenter prospective evaluation of outcomes could address the health benefits of treating parasomnias. Extensive clinical experience documents the long-term efficacy of clonazepam for the treatment of RBD, anticonvulsants for the treatment of sleep-related epilepsy, and benzodiazepines for the treatment of parasomnias. Treatment has not been addressed by randomized, controlled clinical trials. The extent of overlapping parasomnias in individual patients has not yet been clarified, and it will be important to learn whether any common thread of motor or autonomic dysregulation can be found.

8.0 RESTLESS LEGS SYNDROME AND PERIODIC LIMB MOVEMENT DISORDER

8.1 Overview

Restless legs syndrome (RLS) is a disorder characterized by disagreeable leg sensations that usually occur prior to sleep onset and cause an irresistible urge to move the legs (278). Willis (279) provided the earliest description of restless legs in 1685. In 1945, Ekbom (280) proposed the term "restless legs syndrome" and gave the first modern description of the disorder. A recent large-scale telephone survey (281) found that 15% of respondents complained of restless legs, with the prevalence significantly increasing with age—9% in the group between 18 and 29 years of age versus 23% in those over 60 years of age.

The minimum criteria for the diagnosis of RLS suggested by the International RLS Study Group (282) include: the desire to move the limbs, often associated with paresthesias or dysesthesias; motor restlessness while awake; symptoms present only or especially at rest; symptoms alleviated by motor activity; and symptoms worse in the evening or at night. Additional but not required symptoms include involuntary periodic or aperiodic leg jerks or leg twitches while awake, sleep disturbances, and periodic limb movements (PLMs) occurring during sleep (282). These PLMs are periodic, repetitive, and stereotypic limb movements that occur during sleep; the movements usually involve both of the legs and occasionally the arms, and may shift from side to side or may be asymmetrical (282–287). Periodic limb movements of sleep can be an incidental finding without RLS in individuals without sleep–wake complaints. Patients with periodic limb movement disorder (PLMD) are those who have PLMs that cause arousals and who have symptoms of insomnia, frequent awakenings, unrefreshing sleep, or EDS, and have no other sleep-related medical or psychiatric disorder that is significant enough to account for their symptoms (278).

In PLMD, the limb movements are often associated with arousals or awakenings, although the patient may

be unaware of the limb movements or the associated sleep fragmentation. A clear association between RLS and PLMs has been described. Most patients (70% to 80%) with RLS have PLMs, but a much smaller proportion of patients with PLMs complain of RLS symptoms (284,288). Lugaresi et al. (288,289) were the first to polygraphically record the sleep and EMG activity of patients with PLMs.

Restless legs syndrome and PLMs have been reported to be associated with a variety of other medical, neurologic, and sleep disorders and with the use of, or withdrawal from, some medications. However, few of these studies were controlled, and many were based only on case reports or small series. The strongest associations in the peer-reviewed literature are for RLS with anemia (290–292), diabetic neuropathy (293), impotence (294), Parkinson's disease (295), pregnancy (296,297), and uremia (298–301), or occurring postgastrectomy (302,303).

8.2 MEDLINE search terms and review of papers

The additional MEDLINE search terms in this section included *restless legs, sleep myoclonus, nocturnal myoclonus, periodic limb movements, periodic movements in sleep,* and *periodic limb movement disorder.* The inclusion criteria for selection of evidence-based literature included studies of at least six patients and those that provided sufficient detail concerning the patients, recording techniques, polysomnographic recording techniques, scoring criteria, and results to allow comparison with other studies.

8.3 Evidence-based PSG literature

8.3.1 Restless legs syndrome

Because the principal symptoms of RLS occur while the patient is awake (104,284,285,290,304–308), an experienced clinician with knowledge of the disorder can often make the diagnosis of RLS by obtaining a clinical history and performing a physical examination. Actual observation of the RLS patient sitting or lying, particularly while simultaneously recording time-locked videotape EMG recording, can be useful (282,286,309,310), but these observations cannot measure the impact of the RLS activity on the patient's sleep, nor can they diagnose or define PLMs that occur.

In patients with RLS, PSG can document the presence and severity of the sleep disturbances, document the presence of PLMs, and exclude other treatable sleep disorders, but PSG is not required to diagnose RLS (104,284,285,304,306–308) (Table 16).

Polysomnographic studies of limb activity in patients with RLS show that anterior tibial EMG activity may increase before sleep onset, may occur as aperiodic or periodic bursts lasting longer than 5 to 10 seconds, and may be accompanied by excessive muscle activity or high-amplitude tonic activity, or both (285,287,310). Polysomnography demonstrates that patients with moderate-to-severe RLS often have a prolonged sleep latency (285,304,308), decreased sleep efficiency, increased number of awakenings (305,311,312), increased amounts of stage 1 sleep, and decreased amounts of stages 3 and 4 sleep (304,308).

8.3.2 Periodic limb movement disorder

Investigators have found that PLMs are best recorded in the PSG from anterior tibialis muscles (104,283,285,308). Movements typically last 2 to 3 seconds (range, 0.5 to 5.0 seconds) and occur at periodic intervals, usually 20 to 40 seconds (range, 5 to 120 seconds) (104,283,288,308) (Table 17). The anterior tibialis EMG activity of PLMs can vary from a sustained tonic contraction to a polyclonic burst with a frequency of approximately 5 Hz (284). Periodic limb movements of sleep occur most frequently during stages 1 and 2 sleep, decrease in stages 3 and 4 sleep, and are usually absent in REM sleep (285,288,289,313,314). Coleman et al. (283) reported that patients with PLMs have significantly lower sleep efficiencies than do controls, and they found that the total sleep time and minutes of REM sleep were negatively correlated with the patient's PLM index (the number of periodic limb movements per hour of sleep).

Several studies have focused on the prevalence and impact of PLMs in the elderly (315–319). Ancoli-Israel et al. (320) found that seniors with sleep–wake complaints and PLMs had significantly more awakenings per hour of sleep, more stage 1 sleep, and less REM sleep than did those patients with sleep-wake complaints but no PLMs. Mosko et al. (319) found that seniors with PLMs had significantly more time awake after sleep onset, more sleep-stage changes, more awakenings, a higher percentage of stage 1 sleep, and a lower percentage of stage 2 sleep when compared to those without PLMs, and the seniors with PLMs reported less satisfaction with their sleep (being troubled by kicking at night and leg jerks that disturbed sleep) (320). These authors also found that the historic factor that correlated most strongly with PSG changes was the patient's estimate of the number of awakenings. One study demonstrated that patients with narcolepsy and PLMs had more awakenings, increased stage 1 sleep, and increased wake after sleep onset than had patients with narcolepsy alone (321). Patients with OSA treated with nasal CPAP who had PLMs

TABLE 16. *Evidence for restless legs syndrome*

Reference	Study design/ location	# of patients	Monitoring channels	PLMs/RLS scoring criteria	Bias	Diagnostic value of testing procedure
Coccagna and Lugaresi 1981 (304)	CCS/lab	40 32 RLS patients and 8 NM patients	SS EMG_2 RE	Criteria for PLMs not specified.	Patient-selection bias	RLS patients compared to controls had reduced TST, reduced sleep efficiency, prolonged sleep latencies, increased stage 1 sleep, decreased stages 3 and 4 sleep, and increased nocturnal awakenings. Among eight NM patients, slight insignificant increase in stage 1 sleep.
Pelletier et al. 1992 (306)	CCS/lab	10 RLS patients	RE AF Bilateral EMG_2	≥4 consecutive movements separated by at least 4 but no more than 90 seconds. PLM index = number of PLMs/TST.	Patient-selection bias, errors of measurement of outcomes, population bias, intensity bias	10 RLS patients had mean PLMs index of 32.1/h of sleep with mean IEI 28.0 seconds. 9/10 had PLMs index > 5/h on their nocturnal PSG; 1/10 had < 5/h, and 5/10 had < 15/h. The PLM index may not correlate with the severity of RLS symptoms/ movements.
Walters et al. 1991 (309)	ClS/lab	20 11 RLS patients and 9 NIA patients	SS CR Bilateral EMG_2	≥5 consecutive LMs	Patient-selection bias	Compared to the mean for age and sex, RLS patients showed significant increases in number of awakenings ($p < 0.05$), decreases in sleep efficiency ($p < 0.01$), prolongations in sleep onset latencies ($p < 0.05$) and REM sleep onset latencies ($p < 0.05$), and decreased percent REM sleep ($p < 0.01$). All 11 RLS patients had PLMs.

CCS, case control study; RLS, restless legs syndrome; NM, nocturnal myoclonus; SS, sleep staging includes EEG (electroencephalogram), EOG (electrooculogram), and EMG_1 (chin electromyogram); EMG_2, anterior tibialis electromyogram; CR, cardiorespiratory sleep study includes AF (airflow), RE (respiratory effort), and heart rate or ECG (electrocardiogram); PLMs, periodic limb movements during sleep; TST, total sleep time; IEI, intermittent event interval; PSG, polysomnography; ClS, clinical series; NIA, neuroleptic-induced akathisia; LMs, limb movements; REM, rapid eye movement.

were compared to similar patients who did not have PLMs; the authors found that the presence of PLMs was associated with a higher percentage of stage 1 sleep and a lower percentage of REM sleep (322).

Several studies report the difficulty of recognizing PLMD without a polysomnogram (112,317,323–325). Jacobs et al. (324) found PLMD in 15 of 123 patients (12%) evaluated for chronic insomnia; the PLMD diagnosis was not suspected until found on PSG in 10 of these 15 patients (67%) with PLMD. Edinger et al. (323) found 25 of 100 consecutive patients with chronic refractory insomnia had PLMD, but the diagnosis was predicted before PSG in only 14 of 25 patients (56%). Douglass et al. (112) reported the difficulty of recognizing PLMD based solely upon patients' responses to a sleep questionnaire. The PLMD scale on the patients' responses to a sleep questionnaire showed the poorest sensitivity and specificity and lowest positive predictive value and negative predictive value. A final PSG-based diagnosis of PLMD correlated best with frequent awakenings at night and disturbing restless legs symptoms during the night and while trying to fall asleep.

Periodic limb movement disorder was the primary diagnosis and sole sleep diagnosis in 67 of 1,171 patients (6%) who had a polysomnogram at one sleep disorders center (325) and 68 of 456 (16%) at another (111). In order to qualify as having primary PLMD in the study by Mendelson (326), patients were required to have a PLM-associated arousal index [(PLM-Ar-I) or the number of periodic limb movement events that were associated with arousals per hour of sleep] of at least five per hour and no other sleep or medical disorders that would account for the patient's sleep–wake complaint. The authors found that 73% of the patients with PLMD complained of difficulty sleeping and noted that the patients, as a group, had disturbed sleep during a mean of 4 nights per week for a mean of 7 years. Daytime sleepiness was reported by 60% of the cohort. These patients with PLMD had reduced sleep efficiencies (mean 53%), relatively long sleep latencies (mean 28 minutes), and a significant positive association between the PLM-Ar-I and the amount of wake after sleep onset.

Identification of PLMD is important because PLMD has been shown to respond to pharmacologic treatment (283,327,328). Recently, Allen and Earley (327) compared the number of PLMs and the PLM-Ar-I of 40 patients with RLS and 16 patients with PLMD. The authors found no significant differences between these indexes in patients with RLS compared to those with PLMD (mean 73/h vs. 66/h), but a significantly higher percentage of PLMs were associated with arousals in patients with RLS than in patients with PLMD (58% vs. 28%). Patients with PLMD, as it is currently defined, may actually represent a heterogeneous group. They are often difficult to recognize prior to obtaining the findings from PSG.

Night-to-night variability can be seen in PSG studies of patients with PLMs and PLMD. Edinger et al. (323,329) looked at this issue and, in one study with 15 patients (329), recorded three consecutive nights of in-home PSG. Group data showed no significant differences in the PLM-Ar-I across the nights, but marked night-to-night intraindividual variability was observed between worst and best nights in a number of subjects. For most patients, however, this variability had little effect on clinical decision.

A large study of 46 elderly volunteer subjects (not selected because of a sleep disorder) used three nights of in-laboratory PSG (319); 28 subjects had PLMs on one or more nights. The recording of PLMs did not show a significant first-night effect but did show night-to-night variability, which was higher for PLMs than for RDI. The authors' various analysis techniques and predictive formulae failed to show a predictable magnitude or direction of the night-to-night variability.

8.3.3 Polysomnographic techniques

The Atlas Task Force (331) recommends that the polysomnographic technique for studying patients with suspected RLS or PLMD should include EEG (central, occipital), bilateral EOG, chin EMG, and surface EMG recorded independently from the left and right anterior tibialis muscles. Additionally, recording respiration (oral–nasal airflow, thoracic and abdominal respiratory effort, finger or ear oximetry, or snoring sounds by microphone) is necessary to permit distinction of PLMs from limb movements related to respiratory events (332).

Applying additional EMG electrodes (e.g. gastrocnemius, quadriceps, biceps, triceps, wrist flexors, or sternomastoid) has been used in some research studies (331). However, there are no studies to suggest that the ability to identify PLMD increases when muscles other than the anterior tibialis are recorded.

8.3.4 Alternative tools

Clinicians should question patients about similarly affected relatives because more than one-third of patients with idiopathic RLS will have affected relatives, a pattern suggestive of autosomal-dominant inheritance (280,285–287,308–310,332,333). The neurologic examination in patients with idiopathic RLS typically is normal. Only those patients whose complaints or neurologic findings suggest neuropathy, radiculopathy, or motor neuron disease should undergo EMG and nerve conduction studies (286,334).

TABLE 17. *Evidence for periodic limb movement during sleep*

Reference	Study design/ location	# of patients	Monitoring channels	PLMs/RLS scoring criteria	Bias	Diagnostic value of testing procedure
Allen and Earley 1996 (327)	CCS/lab	46 30 RLS, 16 PLMD	SS AF Thoracic and abdominal RE Bilateral EMG_2	≥4 consecutive LMs lasting 0.5–5 seconds with IEIs 5–120 seconds. Clinical and PSG diagnosis of PLMD = clinically significant complaints of both sleep disruption and daytime consequences associated with the sleep disturbance and PSG with a PLM-index of ≥15/h of sleep and ≥10% associated with arousal.	Patient-selection bias	There were no significant differences between the mean PLM rate (PLMs/h of NREM) between the patients with RLS and those with idiopathic PLMD (mean 72.5 vs. 65.8/h, NM). However, the patients with RLS had higher percentages of their PLMs associated with arousal than did the PLMD patients (58% vs. 28% m, $p < 0.001$).
Ancoli-Israel et al. 1981 (315)	NCT	26 (of 50 seniors)	SS CR Thermocouple legs linked SaO_2	NM diagnosed when ≥three separate episodes of 30 LMs each and the arousal index was > 5/h. Arousal = subject awoke ≥20 seconds.	Patient-selection bias, errors of measurement of outcomes	25% (6/24) had NM (≥three epochs of ≥30 LMs) and >five arousal/h of sleep; additionally, two had sleep apnea and NM. The patients with NM had 145–621 LMs/night but ArI 5.3–11.9/h. NM group had significantly more awakenings per hour of sleep than elderly patients without sleep apnea or NM (mean 7.6 vs. 5.0, $p < 0.05$), more stage 1 sleep/h (mean 9.4 vs. 5.9, $p < 0.01$) and less REM sleep (mean 42 vs. 67 mins, $p < 0.05$). Only 9/24 had ≥3 episodes of ≥30 LMs as well as ArI ≥5/h with mean ArI of 8.5 ± 2.5.
Ancoli-Israel et al. 1985 (320)	Observational/ home	200 Seniors telephone interviewed, 145 had PSG	4-channel modified Oxford Medilog/Respitrace Wrist actigraphy EMG_2 bilateral RE	≥three consecutive LMs ≤120 seconds apart. NM if ≥30 LMs in reported sleep period and MI ≥5/h.	Patient-selection bias, confounding factors, errors of measurement of outcomes, population bias	Of the 145 seniors ≥65 years of age who agreed to PSG, 50 (34%) had MI ≥ 5/h of sleep. The sleep of the seniors with MI ≥ 5/h was about 100 minutes shorter than those with no sleep disturbance.
Ancoli-Israel et al. 1991 (316)	RCT/home	427 (23% of 1,865 telephone interviewed) had PSGs	Four-channel modified Oxford Medilog/ Respitrace Wrist activity Bilateral EMG_2 RE	NM data available only on 420 patients; seven lost data. ≥three consecutive LMs 0.5–5 seconds with IEIs 5–120 seconds; MI (= PLM index) ≥5/h considered abnormal. Correlation between PSGs and Medilog for determining MI was $r = 0.64$ ($p < 0.005$).	Patient-selection bias, confounding factors	189/420 (45%) of community dwelling elderly had ≥5 PLMs/h of sleep observed in 45% (n = 189/247) of elderly. Small positive correlation between age and MI. Subjects with PLMs reported being less satisfied with their sleep, sleeping alone, kicking at night, breathing problems (other than snoring, breath-holding, or shortness of breath), and a history of leg jerks ($p < 0.009$). No significant differences in TST, sleep onset latency in those with and without PLMs. 34% had MI ≥ 10; 20% had MI ≥ 20. The patient's estimate of the number of awakenings was the strongest correlate of MI (r, 0.23; $p < 0.001$).

TABLE 17. *Continued*

Reference	Study design/ location	# of patients	Monitoring channels	PLMs/RLS scoring criteria	Bias	Diagnostic value of testing procedure
Bixler et al. 1982 (313)	CIS/lab	100	Grass model 78C SS Bilateral EMG_2	0.5 to <5 seconds with IEI of > 5 but <120 seconds. NMA = 1–2 epochs of ≥30 LMs/night. NM = ≥3 epochs of ≥30 LMs/night.	Patient-selection bias, errors of measurement of outcomes	6/100 (6%) subjects had NM with ≥3 epochs of ≥30 LMs in a night. None of the subjects who had NM or NMA complained of disturbed sleep. The six subjects with NM spent 9.2 ± 2.7 minutes of PSG night with NM activity; <10 percent of episodes during REM sleep; 79.8 ± 4.5 percent during stage 2 sleep. Only 12.1 ± 4.1% of PLMs were associated with arousals. PLMs were strongly related to NREM sleep; approximately 80% occurred during stage 2 sleep, least common during REM sleep. PLMs usually did not cause arousals.
Bliwise et al. 1985 (317)	CIS/lab	63 elderly patients with insomnia	SS EMG_2	≥four consecutive LMs lasting 0.5–5 seconds with IEIs >4 and <90 seconds. Discarded PLMs related to respiratory events.	Confounding factors	Of the 23 subjects with ≥40 PLMs, only 5/23 (22%) complained of RLS symptoms. 8/23 (35%) with ≥40 PLMs/night complained of leg twitching. Only the symptom of leg twitching could discriminate the high PLMs (≥40/night) group. RLS comeplaints among 63 elderly insomniacs were not always associated with PLMs on PSG. Found higher incidence of NM/NMA in older subjects ($p < 0.01$), during NREM sleep.
Coleman et al. 1980 (283)	CIS/lab	53 PLMD (sleep–wake complaints and > 40 PLMs/night on PSG) compared with 53 patients without PLMD but matched to the PLMD patients for age, sex, and final diagnosis	SS Bilateral EMG_2 ECG RE	LM burst 0.5–4 seconds, ≥5 consecutive L, IEI 2–60 seconds, scored 20 second epochs; PLMs defined as ≥40 PLMs in one night.	Patient-selection bias	Analysis of variance demonstrated significantly lower sleep efficiency (69% vs. 74%, $p < 0.05$). Significant negative correlation found for TST ($r = 0.31$) and minutes of REM sleep ($r = -0.25$) in relation to movement index ($p < 0.05$) suggesting patients with many PLMs have decreased TST and REM sleep and chronic sleep complaints. PLMs less disturbed the patient's sleep. Major subjective complaints among PLMs patients: nocturnal (45%) or early morning (11%) awakenings, daytime sleepiness (42%), sleep-onset difficulty (43%).

TABLE 17. *Continued*

Reference	Study design/ location	# of patients	Monitoring channels	PLMs/RLS scoring criteria	Bias	Diagnostic value of testing procedure
Dickel and Mosko 1990 (318)	CSS/lab	100	SS Bilateral EMG_2 AF (oronasal thermistor) SaO_2 RE (abdominal wall excursions)	≥four consecutive LMs lasting 0.5–5 seconds with IEIs 5–120 seconds. Respiratory related PLMs not counted. MI = average number of PLMs~h of sleep; PLMs were averaged across three nights.	Population bias	58% (58/100) elderly subjects had ≥5 PLMs/h with a mean PLM index of 30.5/h. Authors studied whether elderly with high PLM indices of ≥20/h or ≥40/h could be identified. Subjects with PLM index ≥40/h vs. <40/h reported a lower percentage of days rested on their sleep logs ($p < 0.007$). Increased number of stage shifts, higher percent stage 1 sleep, lower percent stage 2 sleep among those with PLM index ≥ 40/h. TIB, TST, sleep latency, percent of stages 3 and 4 sleep, and percent of REM sleep remained stable at all PLM index cutoffs.
Douglass et al. 1994 (112)	CCS/lab	519 435 sleep disorders patients, 84 controls	SS CR EMG_2 SaO_2 MSLT in some	≥four consecutive LMs lasting 0.5–5 seconds with IEIs 5–90 seconds used to diagnose PLMD.	Confounding factors, population bias	PLMD established by PSG in 96/435 (22%) patients; PLMD was the sole sleep disorder in 68/456 (15.6%) and a secondary diagnosis in 27/158 (17%) OSA patients and 24/39 (62%) narcoleptics. PLMD scale on the sleep questionnaire showed the poorest sensitivity, specificity, positive predictive value, and negative predictive value. PLM scale persistently showed the highest correlation with other scales. PLMD symptoms proved the least powerful scale. Low diagnostic yield of sleep questionnaire to identify PLMD.
Edinger et al. 1991 (323)	CIS/home	20 DIMS patients, 11 of 20 had PLMD	SS AF (oronasal) Bilateral EMG_2	≥four consecutive LMs lasting 0.5–5 seconds at IEIs 5–90 seconds. PLM patients with mean PLM arousal index ≥ 5/h across 3 nights.	Confounding factors, errors of measurement of outcomes	Of the 20 patients complaining of chronic insomnia, PLMs were observed in the PSG in 11/20 (55%). Four or more first night effects were observed in 6/11 PLMD patients. Many DIMS patients manifest first night effects even when studied at home with ambulatory PSG monitors.

TABLE 17. *Continued*

Reference	Study design/ location	# of patients	Monitoring channels	PLMs/RLS scoring criteria	Bias	Diagnostic value of testing procedure
Edinger et al. 1992 (329)	CIS/home	15 17 had PSGs but two lost data	SS Bilateral EMG_2 AF (oronasal thermistor)	≥four consecutive LMs lasting 0.5–5 seconds at IEIs 5–90 seconds. Arousal = increase in EEG frequency lasting ≥3 seconds within 2 seconds of PLM, could include K complex in the burst of the arousal; 10 seconds before the next arousal could be counted.	Patient-selection bias, errors of measurement of outcomes, loss to follow-up	Internight correlations conducted on group data suggested minimal differences in MIs across nights. Correlations for MIs were 0.81 night 1 versus night 3, 0.86 for night 2 versus night 3, and 0.74 night 2 versus night 3. However, for individual subjects (within subjects), night-to-night variability in MIs and selected sleep parameters were observed. Subjects had 12.4 (range 5.7–35.2) more movement-related arousals/h of sleep, slept 95.6 more mins., had 16.9% higher sleep efficiency, and had 3.3% less stage 1 sleep on their best night than on their worst night. All subjects had MI ≥ 5 on two of three nights, but two subjects had MI < 5 (false negative) on one night (one of these the first night). Clinical judgments from the first night were representative of the other nights.
Fry et al. 1989 (322)	CIS/lab	33	Expanded EEG Expanded EMG AF SaO_2	≥four LMs lasting 0.5 to <5 seconds with IEIs of 5–90 seconds. PLMs occurring within 5 seconds of termination of respiratory events were scored as PLMs. PLM arousals = appearance of alpha frequencies.	Confounding factors, errors of measurement	On baseline PSG, 9/33 (27%) patients had PLMs index of ≥5/h of sleep; during CPAP trial and repeat PSG after using CPAP 2–7 months, 14/33 (42%) had >5 PLMs/h of sleep. Patients with OSA and ≥5 PLMs/h of sleep had higher percent stage 1 sleep ($p < 0.05$) and lower percent REM sleep ($p < 0.001$) than OSA patients without PLMs. The number of PLMs increased significantly between baseline and two CPAP studies but a nonsignificant increase in number of arousing PLMs noted repeat CPAP compared with initial CPAP trial.
Jacobs et al. 1988 (324)	CIS/lab	123	EEG RE Bilateral EMG_2	NM syndrome required ≥3 periods lasting few minutes to >1 h of ≥30 LMs followed by arousal or partial awakening.	Population bias	RLS found in 4/123 (3.3%) and NM in 15/123 (2.2%) patients with chronic insomnia who had PSG as part of their evaluation. The diagnosis of DIMS associated with NM was a new, unsuspected diagnosis in 10/15 (67%) insomniacs who had NM on their PSG.

TABLE 17. *Continued*

Reference	Study design/ location	# of patients	Monitoring channels	PLMs/RLS scoring criteria	Bias	Diagnostic value of testing procedure
Mendelson 1996 (326)	ClS/lab	1,171	EMG_2	0.5–5 seconds with IEIs 4–90 seconds; PLM index ≥ 5/h considered abnormal.	Patient-selection bias	Among the 67 patients with primary PLMD, 73.1% complained of difficulty sleeping with disturbed sleep (a mean of 3.9 nights per week for a mean of 6.9 years). Daytime sleepiness was reported by 59.7%. Patients with PLMD had poor sleep efficiency (mean, 53.1%), a relatively long sleep latency (mean, 28.3 minutes), and a significant positive association between the PLM Ar Index and the amount of WASO (r, 0.32; $p < 0.05$)
Mosko et al. 1988 (319)	ClS/lab	46 seniors	SS EMG_2 AF (oronasal thermistor) RE (chest and abdominal wall strain gauges) SaO_2 in 33/46	PLMs = rhythmic trains of ≥ four LMs on either/both EMG channels each lasting 0.5–5 seconds with IEIs of 5–120 second. PLMs > 120 seconds, IEIs established separate bouts. Bouts separated by >15 minutes considered a major epoch. Total number of PLMs summed to determine the MI = average number of PLMs/h of sleep. MI ≥ 5/h considered abnormal.	Patient-selection bias, population bias	22/46 (48%) community based low-income seniors had MI ≥ 5/h. Few subjects had sleep–wake complaints. Average PLM index among complainers was 13/h compared to 20/h among the noncomplainers ($p < 0.05$). However, patients with PLM index ≥ 5/h had significantly more WASO, more stage changes, higher ratios of number of stage changes to TST, more awakenings longer than 1 minute, higher percent stage 1 sleep, and lower percent stage 2 sleep.
Pollmächer and Schulz 1993 (314)	CCS/lab	13 9 RLS, 4 PLMD	SS Bilateral EMG_2	Three consecutive LMs lasting 0.5–5 seconds at IEIs of 2–120 seconds. PLMs index = mean number of PLMs/h of time in bed (includes PLMs during wakefulness). PLM arousal index = mean number of PLMs causing partial (<15 seconds) or full (≥ 15 seconds) arousals/h of sleep.	Confounding factors	PLM occur not only during sleep but also during wakefulness. PLM during stage 1 sleep more likely to provoke an arousal than during deeper NREM sleep. PLM arousal also depends on duration of LM, and the percentage of PLM causing arousal increases with increasing PLM duration. Duration and frequency of PLMs decrease across NREM sleep stages, maximally suppressed during REM sleep.
Wittig et al. 1983 (321)	CCS/lab	77 57 consecutive narcoleptics, 20 controls.	SS ECG AF (nasal and oral) Bilateral EMG_2 MSLT	NM = at least three series of 30 PLMs each or a shorter series of PLMs but causing arousals and awakenings.	Confounding factors, loss to follow-up	Narcolepsy with PLMs in comparison to narcolepsy only had more awakenings ($p < 0.001$), increased stage 1 sleep ($p < 0.001$), and increased WASO ($p < 0.01$). Patients with narcolepsy who had PLMs had significantly more disturbed sleep architecture but were not significantly sleepier on the MSLT. Narcolepsy and PLMs compared to normal subjects had significantly more waking during sleep ($p < 0.01$) and higher percent stage 1 sleep ($p < 0.01$).

TABLE 17. *Continued*

Reference	Study design/ location	# of patients	Monitoring channels	PLMs/RLS scoring criteria	Bias	Diagnostic value of testing procedure
Yamashiro and Kryger 1994 (328)	CIS/lab	15 (8 OSA, 7 UARS)	SS CR Bilateral EMG_2 SaO_2 (ear)	≥four consecutive LMs lasting 0.5–5 seconds with an IEI of 5–90 seconds	Confounding factors	Significant decreases in PLM Ar index after nasal CPAP introduced (mean 17.8 to 9.2, $p < 0.05$). 7/15 sleep apnea patients had increase in their PLM index on nasal CPAP, but only 3/15 had an increase in their PLM Ar index, and in 2/3 the change was small. None of the patients who had increase in PLM Ar index complained of persistent EDS while using CPAP for 3 months.

CCS, case control study; RLS, restless legs syndrome; PLMD, periodic limb movements during sleep; SS, sleep staging includes EEG (electroencephalogram), EOG (electrooculogram), and EMG_1 (chin electromyogram); CR, cardiorespiratory sleep study includes AF (airflow), RE (respiratory effort), and heart rate or ECG (electrocardiogram); EMG_2, anterior tibialis electromyogram; LMs, limb movements; IEI, intermittent event interval; PSG, polysomnography; PLMs, periodic limb movements in sleep; NREM, nonrapid eye movement; NM, nocturnal myoclonus; NCT, nonrandomized controlled trial; SaO_2, arterial oxygen saturation; REM, rapid eye movement; ArI, mean number of arousals per hour of sleep; MI, myoclonus index; RCT, randomized controlled trial; TST, total sleep time; CIS, clinical series; NMA, nocturnal myoclonic activity; CSS, cross sectional study; TIB, time in bed; DIMS, disorders of difficulty initiating and maintaining sleep; CPAP, continuous positive airway pressure; OSA, obstructive sleep apnea; WASO, wake after sleep onset; MSLT, multiple sleep latency test; EDS, excessive daytime sleepiness.

Sleep questionnaires have not yet been devised that will accurately identify patients with PLMD (112). Sleep diaries and sleep logs may be helpful in evaluating the frequency and severity of sleep disorders and the patients' subjective responses to treatment. Actigraphy does not show any advantage over subjective sleep logs in studying PLMs (335,336). Simultaneous time-locked infrared videotape recording can be helpful in analyzing and interpreting leg movements, particularly those obscured by movement artifact (308). Evoked potentials (337) and blink reflexes (338) have been studied in patients with RLS and PLMD and have been found to have little or no diagnostic specificity or utility.

8.4 Future research

The identification of causative factors of RLS, PLMs, and PLMD, including specific genetic defects, will assist researchers in designing more effective treatment protocols. Further study is needed to elucidate the relationship between the arousals caused by periodic limb movements and the symptoms of insomnia or EDS. Outcomes research will assist in establishing treatment effects and associations with a quality-of-life index.

9.0 INSOMNIA

9.1 General insomnia

The indications for PSG in the general evaluation of insomnia have been covered in recent ASDA practice parameters (339) and a review paper (340), and will not be repeated here.

9.2 Depression with insomnia

Depression with insomnia is a complaint of difficulty with sleep that is associated with a psychiatric diagnosis of depression, either unipolar (major depression only) or the depressive phase of a bipolar illness (in which there are some periods of depression and others of hypomania or mania) (341). Difficulty with sleep maintenance, rather than difficulty with sleep onset, is typically the chief complaint, particularly in older patients, and the hallmark feature of disturbed sleep in depression is early-morning awakening. Daytime fatigue and exhaustion may also be presenting complaints, although true physiologic sleepiness may not be present (342). During the manic phase of a bipolar disorder, sleep may be markedly reduced in amount without the patient having a concurrent complaint of insomnia.

Interest in the relationship between sleep and de-

pression grew out of the observations in the late 1960s and 1970s that antidepressant medications had marked REM-suppressing effects and that REM sleep deprivation in depressed individuals mimicked antidepressant medication effects. These findings suggest that features of REM sleep may provide diagnostic clues to the biologic basis of depression. Decreased latency to REM sleep, increased number of eye movements during REM, and alterations in the temporal distribution of REM sleep across the sleep cycle were associated with depression. Amelioration of the depressive symptoms was associated with normalization of these characteristics of REM sleep. Whether these features of REM sleep are specific and sensitive for the diagnosis of depression is an issue that continues to generate debate.

The complaint of insomnia—difficulty in either falling or staying asleep—is the most commonly reported sleep problem in the general population; most studies report a prevalence of about 30% (212,343–346). Difficulty with sleep, particularly early morning awakenings, is an almost universal complaint in depression. A 1982 national cooperative case series study of patients evaluated in sleep disorders centers found that within the diagnostic category of insomnia, insomnia associated with psychiatric disorders was the most prevalent type of insomnia (35%) (104). A recent study reported that 20% to 40% of insomniac outpatients meet the diagnostic criteria for depression (347). Conversely, among depressed community-dwelling individuals, insomnia complaints are common in both the general population (78%) (348) and the elderly. In the group of elderly individuals, 69% had insomnia that ranged from mild to severe, with over half of this subgroup having moderate to severe insomnia (347). Indeed, the ICSD states that "at least 90% of patients with mood disorders have sleep disturbances at some time" (349). The prevalence of depression in persons who complain of insomnia is high, as is the prevalence of insomnia in persons who are depressed.

9.3 MEDLINE search terms and review of papers

The additional MEDLINE search terms for this section included *insomnia, sleep disturbance,* and *depression.* The inclusion criteria for selection of the literature included: 1) at least 10 patients with depression evaluated; 2) structured interviews used to establish a diagnosis of depression; and 3) at least sleep staging [EEG, EMG, and EOG channels scored by Rechtschaffen and Kales criteria (263)] used for evaluation criteria. One metanalysis was included because all of the studies included in the analysis required formal diagnostic criteria and scoring of sleep stages (350).

9.4 Evidence-based PSG literature

9.4.1 General insomnia

The relevant literature for the general evaluation of insomnia has recently been reviewed (340).

9.4.2 Depression with insomnia

A large body of literature describes changes in sleep that occur in patients with psychiatric disorders. Affective disorders, particularly depression, have been studied most extensively. A number of distinctive findings have been reported that are characteristic of sleep in depression, including a shortened REM latency, increased REM density, increased amounts of REM sleep early in the night, decreased amounts of delta (stage 3 and 4) sleep, and decreased sleep continuity (Table 18). These findings are not universal across all age groups (351,352), and decreased REM latencies have been shown to appear more quickly in depressed older patients than in younger depressed patients (353). Changes in PSG characteristics may be the harbingers of depression, however, and may help identify persons who are at risk for developing major depression, particularly those with a family history of depression (354). At least one study of elderly subjects demonstrates that REM latency and cumulative REM time, as well as other measures of sleep continuity, do not discriminate between community-dwelling depressed patients who have never sought treatment and normal controls (355).

A major issue that arises is whether PSG can, in fact, identify features of sleep that are specific to depression. The REM latency, for example, in individual studies is not particularly useful in discriminating between patients with depression and those with other psychiatric disorders (356,357). A recent metanalysis demonstrated that reduced REM latencies were present not only in depression, but also in a variety of other psychiatric illnesses (350). The REM density, in contrast, may be of greater utility in identifying affective states (353,357,358). The body of evidence suggests that PSG is neither sensitive nor specific enough to diagnose depression. PSG may be useful, however, in identifying early response to treatment with antidepressant medication (e.g. by demonstrating an increase in the REM latency) (359,360).

9.4.3 Alternative tools

The alternative diagnostic tools for the evaluation of the sleep characteristics in depression are those that may be used in the evaluation of other sleep disorders and include sleep diaries, ambulatory recording, and

TABLE 18. *Evidence for depression with insomnia*

Reference	Study design/ location	# of patients	Monitoring channels	Bias	Diagnostic value of testing procedure
Benca et al. 1992 (350)	Review paper	7,151 5,642 patients, 1,509 controls	SS	Errors of measurement of outcomes, ascertainment of exposure to an intervention, loss to follow-up, intensity bias, patient-selection bias	Affective disorders were significantly different from controls for the largest number of variables in comparison to other diagnostic categories. A reduction in REM latency occurred not only in affective disorders, but also in other categories of psychiatric illness. No sleep variable reliably discriminated affective disorders from other categories of psychiatric illness. This meta-analysis of PSG findings suggests that no individual sleep variable is either sensitive or specific for the diagnosis of either affective disorders or any other specific psychiatric disorder. However, some variables are helpful in distinguishing patient groups from controls.
Benson et al. 1990 (356)	CCS/lab	33 18 patients, 15 controls	SS	Patient selection, confounding factors	REM latency (both strict and lenient), REM percent, minutes of REM, and lowest REM latency (both strict and lenient) did not discriminate between borderlines with or without affective disorders or from normal controls.
Cartwright and Wood 1991 (361)	CSS/lab	70	SS	Patient-selection bias, loss to follow-up, exclusion criteria	1) Married couples have significantly longer sleep latency and higher delta percent than do divorcing subjects. 2) Depression subject had a significantly shorter REM latency than nondepressed subjects. Depressed patients have significantly higher delta percent awaiting divorce. 3) 1-year follow-up, finalized-divorce patients had significantly higher delta percent than those awaiting completion of divorce. 4) Predictive value of poor sleep for a later diagnosis of depression.
Edinger et al. 1989 (105)	CIS/home	100 DIMS patients	SS AF Limb movement (ambulatory oxford medilog)	Patient-selection bias	In 65% of subjects, sleep studies yielded important diagnostic information for PLMS/RLS, sleep apnea, and subjective insomnia. Almost half (46%) of the age 40+ subjects received one of these three diagnoses. Less than half of these three diagnoses were predicted by clinical impression alone. PSG yields important diagnostic information in elaborating causes of chronic insomnia and may be most useful in those patients who have failed initial treatment for insomnia or who are in older age groups.
Jacobs et al. 1988 (324)	Retrospective CIS/lab	123 chronic insomniacs	EEG RE EMG_2	Patient-selection bias	Prior to PSG, 63% (78/123) subjects were diagnosed as having past or present mental illness. Following PSG, 49% (60/123) received a substantial modification of the initial diagnosis. PSG can improve the specificity of diagnosis in chronic insomnia.
Kupfer et al. 1994 (359)	CSS, RCT/ lab	27 unipolar depressed patients	EEG EOG	Patient-selection bias, confounding factors	During 3 years of drug maintenance, there were no significant differences over time in sleep-continuity measures. Percentage of delta sleep declined. A reduction in number of REM periods, REM percent, and REM time, as well as an increase in REM latency and REM density, were maintained across 3 years as compared to pretreatment. PSG data show that alterations in sleep architecture during imipramine treatment are associated with sustained clinical improvement.

TABLE 18. *Continued*

Reference	Study design/ location	# of patients	Monitoring channels	Bias	Diagnostic value of testing procedure
Lauer et al. 1991 (353)	CCS/lab	125 73 depressed patients, 51 normal	SS	Population bias	Similar age-related changes in PSG-defined sleep architecture were observed in both patients and controls. A decrease in REM latency between depressed and normal subjects first occurred in the 35–44 year age group. There was a significant increase in REM density between depressed and control subjects for all age groups except the 18–24 year age group. PSG findings suggest that REM density may be a more reliable indicator for depression than REM latency.
Lauer et al. 1992 (357)	CCS/lab	46 22 panic patients, 12 depressed patients, 12 normals	EEG	Patient-selection bias	REM latencies of both panic disorder and depressed patients were similar to one another. Both were significantly shorter than REM latencies in normals. REM density index was significantly increased only in depressed patients. There were no significant PSG differences between the two categories of panic disorder patients. PSG may be of benefit in determining physiologic differences or similarities in different groups of psychiatric patients.
Lauer et al. 1995 (354)	CCS/lab	92 54 high risk proband patients, 20 control probands, 18 depressed patients	SS	Patient-selection bias, confounding factors	High risk probands of patients spent less SWS time in the first NREM period, and REM density index for the first REM period was increased. SWS latency was not prolonged, REM latency was not shortened, and mean REM density was not increased compared to control probands of patients. Eighteen percent of high risk probands of patients were classified as having depression-like sleep patterns. PSG evaluation of sleep in high risk probands of depressed patients may be of benefit in identifying vulnerability for development of future depression.
Nofzinger et al. 1991 (342)	CoS/lab	48 25 depressed bipolar patients with hypersomnia, 23 narcoleptic patients	SS MSLT	Patient-selection bias	Nocturnal REM latency was significantly longer, REM density was significantly lower, and REM percent was similar in depressed as compared to narcoleptic patients. No sleep-onset REM periods were present in the nocturnal recordings of depressed patients. PSG monitoring of daytime naps was essentially within normal limits in depressed patients. PSG nap monitoring may be of benefit in depressed patients in discriminating between physiologic and subjective sleepiness.
Reynolds et al. 1993 (358)	CCS/lab	54 27 bereaved without major depression, 27 normal	SS EMG_2 CR	Patient-selection bias, confounding factors	Phasic REM density was significantly elevated in the bereaved subjects over the 2-year study period. Grief intensity or severity of depression did not correlate with REM density. REM latency, delta sleep ratio, and sleep efficiency did not differ between the two groups. PSG reveals that REM density may be a biologic correlate of bereavement in the absence of major depression. Bereavement is not associated with other features of sleep in depression, including shortened REM latency, up to 2 years after the loss of a spouse.
Vitiello et al. 1990 (355)	CCS/ lab	48 24 depressed 24 normals	SS AF Bilateral EMG_2 SaO_2	Patient-selection bias	All sleep–wake parameters, with the exception of a significant decrease in sleep latency in depression, were similar between the two groups. REM latency, REM percent, and cumulative REM time were not significantly different between the two groups. PSG did not reveal characteristics of sleep disturbance associated with major depression in the depressed elderly who have not sought health care.

TABLE 18. *Evidence for depression with insomnia*

Reference	Study design/ location	# of patients	Monitoring channels	Bias	Diagnostic value of testing procedure
Ware et al. 1989 (360)	NCT/ lab	30 all insomniacs, 14 on trimipramine, 16 on imipramine	SS ECG CR EMG_2	Loss to follow-up, patient-selection bias	The antidepressant efficacy for patients taking trimipramine versus patients taking imipramine was similar. PSG improvement in sleep quality occurred with patients taking trimipramine but not with patients taking imipramine. REM latency increased in patients taking imipramine but not in patients taking trimipramine. PSG reveals that improvement in clinical features of depression is not necessarily associated with changes in sleep architecture.

SS, sleep staging includes EEG (electroencephalogram), EOG (electrooculogram), and EMG_1 (chin electromyogram); REM, rapid eye movement; PSG, polysomnography; CCS, case control study; CSS, cross-sectional study; ClS, clinical series; DIMS, disorders in initiating and maintaining sleep; CR, cardiorespiratory monitoring includes airflow (AF), respiratory effort (RE), and heart rate or ECG (electrocardiogram); PLMS, periodic limb movements in sleep; RLS, restless legs syndrome; EMG_2, anterior tibialis electromyogram; RCT, randomized controlled trial; SWS, slow-wave sleep; NREM, nonrapid eye movement; SaO_2, arterial oxygen saturation; CoS, cohort study; MSLT, muliple sleep latency test; NCT, nonrandomized controlled trial.

TABLE 19. *Evidence for circadian rhythms*

Reference	Study design/ location	# of patients	Monitoring channels	Bias	Diagnostic value of testing procedure
Alvarez et al. 1992 (370)	ClS/lab	14	SS	Confounding factors, errors of measurement of outcomes, errors in ascertainment of exposure to an intervention, intensity bias	No correlation of delayed sleep-phase syndrome to psychiatric illness; success of progressive delay of sleep treatment depends on motivation; melatonin results in a partial phase advance.
Rotenberg 1991 (372)	CSS/lab	45	SS Questionnaire	Population bias, intensity bias	Slow-wave sleep recovery first night, and in the day, sleep is a good adaptation to shift work; food adaptation correlates with less somatic complaints; better rest before recovery correlates with subjective reports of restful day sleep; REM recovery comes in the second recovery night.
Sasaki et al. 1986 (369)	NCT/lab	12	CR SS EMG_2 Questionnaire MSLT	Errors of measurement of outcomes, population bias	Decrease in REM after flight may be secondary to sleep at an offtime from primary time zone; daytime sleepiness increases layover sleep; subjective and objective sleepiness did not correlate; morning type had more daytime sleepiness than evening type shift workers.

ClS, clinical series; SS, sleep staging includes EEG (electroencephalogram), EOG (electrooculogram), and EMG_1 (chin electromyogram); CSS, cross-sectional study; REM, rapid eye movement; NCT, nonrandomized controlled trial; CR, cardiorespiratory monitoring includes AF (airflow), RE (respiratory effort), and heart rate or ECG (electrocardiogram); EMG_2, anterior tibialis electromyogram; MSLT, multiple sleep latency test.

wrist actigraphy. Formal diagnostic criteria based upon patient interviews are used to establish the diagnosis of depression. Although Kales et al. (101) have suggested that PSG is not necessary for the evaluation of insomnia, other studies claim that greater specificity of diagnosis and treatment is obtained with a polysomnographic evaluation of chronic insomniacs (105,324).

9.5 Future research

Survey studies suggest that complaints of insomnia are associated with the development of depression (362,363). Long-term familial studies examining the predictive value of sleep architecture changes for identifying individuals at risk of developing depression, and to determine subsequent treatment interventions for depression, may be of value. Conversely, studies could examine whether early treatment of sleep disturbance could conceivably forestall the development of depression. For example, implementation of behavior treatments and the polysomnographic evaluation of the effectiveness of these treatments in the early stages of sleep disturbance may prevent the emergence of a severe sleep disturbance and subsequent development of depression. Polysomnographic and psychologic studies that compare early versus no intervention for insomnia and the subsequent development of depression would help clarify the relationship between these disorders.

10.0 CIRCADIAN RHYTHM SLEEP DISORDERS

10.1 Overview

Circadian rhythm sleep disorders are disorders of mismatch between an individual's actual sleep pattern and the timing and amount of sleep that person desires, requires, or expects. Recognition of circadian rhythm sleep disorders originated at the time of the early studies of human circadian physiology in the 1950s. A better understanding of these disorders has developed since the identification of the suprachiasmatic nucleus as the biologic clock and the recognition of its control by light. Patients suffering from circadian rhythm sleep disorders may complain of insomnia or EDS, depending on the time of their sleep and wake periods in relationship to the societal norm and the patient's desires. This group of disorders can be precipitated or influenced by either extrinsic or intrinsic factors or by both. Distinction between intrinsic and extrinsic circadian rhythm sleep disorders is established by history, physical examination, and multiple-week sleep logs (364). Establishing the difference between intrinsic and extrinsic causes for circadian rhythm sleep disorders aids in establishing the patient's treatment and improving the prognosis.

Shift workers comprise 20% of the United States population (365), and circadian rhythm sleep disorders likely affect a substantial portion of those workers; however, the prevalence of circadian rhythm sleep disorders is unknown. Reports by Coleman et al. (104) and Coleman (366) attempted to ascertain the prevalence of circadian rhythm sleep disorders; both studies cited 2% as the frequency of circadian rhythm sleep disorders as a diagnosis. One of the studies (104) had a strong referral bias that likely influenced the data and clouds the use of this study as a current inference of the population prevalences.

There are six types of circadian rhythm sleep disorders: time zone change (jet lag) syndrome, shift-work sleep disorder, irregular sleep–wake pattern, delayed sleep-phase syndrome, advanced sleep-phase syndrome, and non–24-hour sleep–wake syndrome (367). Circadian rhythm sleep disorders may be associated with varying degrees of insomnia or EDS.

Time zone change syndrome occurs following rapid travel across multiple time zones and consists of varying degrees of difficulty in initiating or maintaining sleep, EDS, decrements in subjective daytime alertness and performance, and somatic symptoms (largely related to gastrointestinal function) (367). Shift-work sleep disorder consists of symptoms of insomnia or EDS that occur as transient phenomena in relation to work schedules (367). Individual patient tolerance to a changing work schedule is multifactorial and includes morning–evening type, age, degree of sleep loss, and the patient's sleep needs and habits (368). Irregular sleep–wake pattern consists of temporarily disorganized and variable episodes of sleep and waking behavior (367). The pattern is associated with complaints of both insomnia and EDS, and the patient's normal temperature rhythm is lost. The characteristics of irregular sleep–wake pattern are short sleep periods or prolonged naps, and the patient's major sleep period is lost. Delayed sleep-phase syndrome is a disorder in which the major sleep episode is delayed in relation to the desired clock time, resulting in symptoms of sleep-onset insomnia and difficulty awakening at the desired time (367). Advanced sleep-phase syndrome is a disorder in which the major sleep episode is advanced in relation to the desired clock time, resulting in symptoms of compelling evening sleepiness, an early sleep onset, and an awakening that is earlier than desired (367). Non–24-hour sleep–wake syndrome consists of a chronic steady pattern comprising 1- to 2-hour daily delays in sleep onset and wake times in an individual living in society (367).

10.2 MEDLINE search terms and review of papers

The additional MEDLINE search terms for this section included *circadian rhythm disruption; sleep–wake cycle; human biologic rhythms; shift work; delayed sleep-phase syndrome; 24-hour EEG recording, encephalopathy, brain tumors, drug dependency and withdrawal,* and *delirium tremens.* Because the *ICSD* (367) lists neurologic causes for circadian rhythm sleep disorders, neurologic conditions potentially affecting the function of the hypothalamus were used in an attempt to retrieve references to PSG studies that might otherwise be missed.

The inclusion criteria for the selection of the literature to be reviewed required the study of a minimum of six patients and that sleep staging be used for evaluation. Few studies of patients with circadian rhythm sleep disorders evaluated by PSG have been published. All the articles that appear in the evidence table were reports of studies conducted in a sleep laboratory.

10.3 Evidence-based PSG literature

Only three studies of circadian rhythm sleep disorders met our inclusion criteria, and all of these studies had small sample sizes, such that population biases were inherent. Studies were performed mostly on night-shift workers in research settings to determine the long- and short-term effects of circadian rhythm sleep disorders on daytime sleepiness, nighttime alertness, and job performance (Table 19). Åkerstedt et al. (368) reviewed the literature pertaining to shift-work disorder with the emphasis on EEG and EOG recording, and concluded that EEG is a good measure of sleepiness. Sasaki et al. (369) designed a study to record sleep in transpacific airline crew members before and after a scheduled flight. They made several observations: the crew members' daytime sleepiness increased during the layover period; subjective and objective sleepiness did not correlate; morning types had more daytime sleepiness than did evening types; and REM sleep was decreased, possibly secondary to the altered clock time of sleep during the layover period, as compared to the subject's primary time zone. Alvarez et al. (370) addressed delayed sleep-phase syndrome and confirmed features of chronicity and timing of the major sleep period. They found no correlation between delayed sleep-phase syndrome and psychiatric diagnoses. Kubota et al. (371) cited irregular sleep in a patient with an excised hypothalamic tumor in the absence of thyroxine-replacement therapy. Recordings performed after l-thyroxine therapy demonstrated a free-running sleep–wake rhythm. Rotenberg (372) used PSG and questionnaire responses to evaluate subjects' sleep on the first night after they worked the night shift. He subsequently assigned the subjects to one of two groups: those who were well adapted and those who were not. The maladapted subjects demonstrated more REM than NREM sleep on the day and first night of recovery. These changes were similar to those changes that occur in subjects who are studied after a single night of sleep deprivation.

The studies that have used PSG to evaluate circadian rhythm sleep disorders found PSG to be useful in identifying sleep-structure changes in subjects with circadian rhythm disorders; however, none of the studies demonstrate a value for PSG in recognizing specific circadian rhythm sleep disorders or in directing treatment. Thus, PSG is not useful in the clinical diagnosis or treatment of circadian rhythm sleep disorders.

10.4 Future research

Epidemiologic studies of prevalence, the incidence of subjects' health problems secondary to shift-work disorder, and evaluation of the relative value of PSG in the assessment of circadian rhythm sleep disorders are areas in need of further study.

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APPENDIX A. *Definition of sleep medicine terms*

Term	Definition
Ambulatory EEG:	Portable EEG recorded on computer disk or magnetic tape, that allows up to 16 channels of brain electrical activity to be recorded while the patient engages in normal activity.
Apnea index (AI)	The number of apneas per hour of sleep.
Apnea–hypopnea index (AHI)	The number of apneas plus hypopneas (obstructive, central, and mixed) per hour of sleep; also referred to as the respiratory-disturbance index.
Apnea	A cessation of breathing at least 10 seconds in duration.
Attended	The presence of a technician (at the same location) who monitors the patient's testing procedure.
Body mass index (BMI)	The body weight in kilograms divided by the square of the height in meters [wt/(ht)^2].
Electrooculogram (EOG)	A recording of voltage changes resulting from shifts in position of the eye. Along with the EEG and the EMG, EOG is one of the three basic variables used to score wake and sleep and to identify sleep stages.
Electrocardiogram (ECG)	A recording of cardiac electrical activity. In sleep testing, this channel is used for assessment of heart rate and rhythm.
Electroencephalogram (EEG)	A recording of brain electrical activity. With the EMG and EOG, the EEG is one of the three basic variables used to score wake and sleep and to identify sleep stages. The EEG is the primary variable for sleep staging.
Electromyogram (EMG)	A recording of muscle electrical activity. The chin EMG measured by surface electrodes, along with EEG and EOG, is one of the three basic variables used to score wake and sleep and to identify sleep stages.
Excessive daytime sleepiness (EDS)	Sleepiness that interferes with activities of daily living.
Hypopnea	A reduction in airflow (without complete cessation) of at least 10 seconds' duration, frequently accompanied by oxygen desaturation, arousal, or both.
Maintenance of wakefulness test (MWT)	A test of the ability to resist sleep in a sleep-inducing environment. The test consists of a series of sleep recordings under standardized conditions while the patient attempts to stay awake.
Monitoring	Recording of physiologic and behavior events with continuous data observation by trained personnel present either at the recording site or at a remote location.
Multiple sleep latency test (MSLT)	A test of the ability to fall asleep in a sleep-inducing environment. The test consists of a series of sleep recordings under standardized conditions that measure the latency of sleep onset and the occurrence of REM sleep. The test provides an objective measure of sleepiness and the propensity for REM sleep.
Non–rapid eye movement (NREM)	All sleep, except for REM sleep; is categorized further into stages 1 through 4, reflecting different patterns of brain electrical activity during sleep.
Polysomnography (PSG)	The continuous and simultaneous recording during sleep of at least EEG, EOG, EMG is necessary to stage sleep. Additional physiologic channels are usually recorded, including ECG, airflow, respiratory effort, limb movements, and other electrophysiologic variables.
Portable polysomnography	A PSG recording that uses moveable equipment that is easily transported for use outside of the sleep laboratory.
Rapid–eye movement sleep (REM)	The stage of sleep with the highest brain activity, characterized by enhanced brain metabolism and vivid hallucinations, imagery, and dreams. During stage REM, resting muscle activity is suppressed and there is a high awakening threshold to nonsignificant stimuli. REM sleep usually accounts for 20% to 25% of total sleep time.
Recording	The collection and storage of physiologic and behavior signals.
Respiratory-disturbance index (RDI)	The number of apneas plus hypopneas (obstructive, central, or mixed) per hour of sleep; also referred to as the apnea–hypopnea index.
Unattended	Trained personnel are not physically present throughout recording session (data observation via modem link is still considered unattended).

APPENDIX B. *Definition of bias and validity terms*

Term	Definition
Bias	The distortion of a study effect or outcome by a factor separate from the studied exposure or treatment.
Confounding factors	A bias that occurs when the group that is offered the intervention (treated group) and the group that is not offered the intervention (control group) differ by some factor that can affect the outcomes of interest.
Crossover bias	A bias that occurs in a controlled study when some of the subjects in either the intervention or control group receive the treatment intended for the other group.
Evidence-based approach	An approach that explicitly and systematically describes all the relevant evidence and then uses this evidence as the basis for drawing conclusions and making recommendations. This approach is opposed, for example, to those based on consensus or personal opinion.
Intensity bias	A bias that occurs if any differences exist between the circumstances of investigation and interest that could alter the intervention's effectiveness; these differences may be due to the intervention (dose, frequency), the provider (skill, training), or the setting (inpatient, outpatient, urban, rural).
Loss to follow-up	A bias caused by failure to keep track of all subjects and record their outcomes for the entire duration of the study.
Patient-selection bias	A bias that can affect the internal validity of a study if the participants are selected in such a way that those in the treated group differ from those in the control group in a way that distorts outcomes.
Population bias	A bias that occurs if differences exist between the subjects studied and the subjects of interest (i.e. age, gender, compliance to treatment) that could affect the outcomes, irrespective of the intervention.
Sensitivity	The probability that the test result will be positive if the patient actually has the disease (the true-positive rate).
Specificity	The probability that the test result for a particular disease will be negative if the patient actually does not have the disease (a high value implies few false-positive results).