Obstructive Sleep Apnea Syndrome: The Diagnostic Strategy Dilemma

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Abstract
Obstructive sleep apnea syndrome is a major public health hazard affecting 2–4% of the adult population; only 10% of these patients are recognized by healthcare providers. In the last decade the number of referrals for polysomnography increased threefold in Israel, compared to 12-fold worldwide, and is expected to increase even more in the coming years. This constant demand for PSG studies is beyond the current capacity of sleep laboratories, thus preventing diagnosis for most patients with suspected OSAS. In the current review, we examine problems facing decision-makers on how to treat the increasing flood of patients presenting with symptoms suggestive of sleep-disordered breathing. We evaluate the cost-effectiveness of current technologies for OSA diagnosis, i.e., laboratory versus at-home technologies. We conclude that no current alternative exists to the use of PSG for OSA diagnosis. When at-home technologies are suggested for OSAS diagnosis, data should be provided on factors influencing its cost-effectiveness, e.g., accuracy rates of diagnosis, relative cost of human resources, and case-mix of patients tested. Since PSG remains the gold standard for diagnosis, in Israel resources should be allocated to increasing the volume of beds for PSG studies in order to increase access to diagnosis and treatment, which in turn provides better quality of life, saves scarce resources of the healthcare system, prevents unnecessary accidents and increases workers' productivity.

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Obstructive sleep apnea syndrome is a common sleep-related breathing disorder affecting 2–4% of the working-age population [1,2]. This disorder is characterized by the occurrence of complete or partial repetitive upper airway obstruction during sleep. One of the main consequences of these breathing pauses is a major fragmentation of sleep, causing a marked deterioration in sleep quality. OSAS primarily affects overweight middle-aged males, but can affect men and women of all age and weight categories. The main complaint of OSAS patients is excessive daytime sleepiness, which results in a substantial deterioration in quality of life [1–3]. OSAS patients have a tenfold difficulty learning new tasks in their places of work, a reduction in mental performance, and increased risk of motor vehicle [4–6], work and domestic accidents [7]. OSAS is a risk factor for chronic conditions (cardiovascular diseases, hypertension), as well as acute conditions (stroke, myocardial infarction, cor pulmonale, congestive heart failure) and even sudden death [8–10].

Despite its impact on patients and the community, less than 10% of patients with clinically significant sleep apnea syndromes are recognized [11]. Interestingly, only 4% of the referrals to sleep laboratories are made as a result of the clinician eliciting a history of sleep-related complications. However, the growing awareness of sleep apnea among physicians and the general population has led to a steadily increasing demand for the investigation of patients suspected of having this disorder, which has resulted in unacceptably long waiting lists in many sleep laboratories [12].

The modern era of sleep apnea began in earnest in the 1980s. The seminal discovery by Sullivan and colleagues [13] of nasal continuous positive airway pressure enabled treatment of the disorder. Other treatments include surgery, weight reduction and behavioral therapy. During the 1980s, the National Heart, Lung and Blood Institute initiated research in this area that has substantially enhanced our knowledge on its pathogenesis, epidemiology, genetics, consequences, and treatment outcomes. However, in contrast to the increased reported frequency of OSAS and insomnia, the frequencies of other sleep disorder diagnoses such as parasomnias, restless legs syndrome, and narcolepsy, as a primary, secondary, or tertiary diagnosis, did not change significantly from 1990 to 1998, neither did that of common diseases such as upper respiratory tract infection, hypertension or diabetes mellitus as a primary, secondary, or tertiary diagnosis during the same period [14]. The 12-fold increase in the volume of referrals for sleep studies over the past decade has alerted healthcare policy makers to the problem [11,14]. The economic burden on the healthcare system has been estimated in billions of dollars as OSAS patients were heavy consumers of healthcare services in the years before PSG diagnosis [15]. Treatment with CPAP reduces healthcare utilization in adults [16] and improves quality-adjusted life years [17].

The flood of undiagnosed patients presenting with symptoms suggestive of sleep-disordered breathing is a major challenge to decision-makers and requires a disease management approach. Since polysomnography studies are expensive, it is not feasible to provide this test for all patients with suspected OSAS. Therefore, in order to adequately manage diagnosis in patients with sleep disorders, the following question should be addressed: Are

PSG = polysomnography
OSAS = obstructive sleep apnea syndrome
CPAP = continuous positive airway pressure
undiagnosed cases of OSAS a burden on the healthcare system? And if so, what is the cost-effective alternative for PSG diagnosis of OSAS?

**Technologies available for OSAS diagnosis**

The American Academy of Sleep Medicine and the American Thoracic Society recommend PSG as the key diagnostic test for determining OSAS severity and evaluating patients' response to CPAP treatment [18,19]. This in-laboratory study is relatively expensive and usually requires two PSGs: a diagnostic study followed, if indicated, by a second CPAP titration study. These studies involve sleeping overnight in a laboratory setting with multichannel monitoring of multiple physiologic variables under the supervision of a well-trained technologist. It should be recognized that if ASSM and ATS guidelines for PSG are followed meticulously, on the basis of incidence estimates alone, it would be necessary to perform 600 PSG studies per 100,000 population per year [12]. According to the Wisconsin Sleep Cohort study, 82% of men and 93% of women with moderate to severe sleep apnea have not been diagnosed [11]. Using these estimates, we assume that the volume of undiagnosed patients with OSAS who need PSG studies requires about 540 additional PSG studies per 100,000 subjects per year. This estimate assumes that each patient requires only one PSG study. Because of the high costs and the increased number of referrals for sleep studies, it is not possible to perform in-laboratory PSG studies for all patients suspected of having OSAS.

This financial restraint led to the development of “Split-Night” PSG studies for patients with severe OSAS (>20 or 40 events per hour) [20]. Instead of studying patients with OSAS over two nights, the night is split into two halves: in the first half, diagnosis of OSAS is made and in the second half, CPAP titration is performed. Thus, because some patients are considered to have severe OSAS, it is important to acknowledge that this “split-night” approach may contribute only slightly to reducing the staggering demand for sleep studies. Split-night PSG studies are not appropriate in OSAS patients with rapid eye movement-related obstructive sleep apnea. These studies can adequately diagnose OSAS, justify therapeutic intervention, and determine effective CPAP pressures and management strategy. Split-night PSG studies can increase sleep study efficiency, expedite treatment and lead to potential cost savings; however, they cannot be used to exclude a diagnosis of OSAS. Saving costs with split-night sleep studies need to be explored further [17].

Unattended at-home diagnostic devices have been proposed as a potential alternative low cost method for the diagnosis of OSAS [21–23]. In Europe, two-thirds of the sleep studies in the year 2000 were performed in-laboratory and the remainder used ambulatory monitoring in the patient’s home [24]. It was postulated that by the year 2001, approximately 80% of sleep studies would be performed at home and that the portable cardiorespiratory monitoring of OSAS patients at home would reduce PSG costs by 30% [25]. The average cost for in-lab studies in Europe [24] is US$390 (390 Euro/

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ASSM = American Academy of Sleep Medicine
ATS = American Thoracic Society

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study, range 180–700), while the average cost for ambulatory studies is approximately $120 (120 Euro/study, range 70–180). Unattended monitoring at home is less accurate and has a limited number of parameters, a greater susceptibility to data loss, and poor diagnostic reliability compared to PSG [18,19,21–23]. For their cost-utility analysis to decide who should be treated with CPAP, Chervin et al. [17] formulated a decision tree that evaluated the relative effectiveness of three diagnostic strategies. They compared PSG with an at-home study using one system and the possibility of no testing. Their study was based on the premise that all patients being evaluated for OSAS should undergo the same diagnostic tests regardless of the pretest probability of the disorder. The results of their study favor the use of PSG over the at-home and no-testing alternatives under all modeled conditions. We also [26] used a decision analysis to investigate aspects of OSAS diagnosis and therapies (i.e., diagnostic agreement, data loss/technical failure, and study-cost elements such as human resources, accessories and capital). At-home portable sleep monitoring did not present any cost-effective advantage with regard to diagnosis and treatment over the in-laboratory studies. This conclusion is currently supported by others [18,19].

**Managing diagnosis for patients with suspected OSAS**

Several key facts should be borne in mind when managing a flood of patients suspected of having OSAS: a) less than 10% of patients with OSAS are diagnosed, b) more than 80% had a missed diagnosis years before the PSG study [11], and c) only 4% of the referrals were made as a result of clinician-elicted history of sleep-related complications. In fact, most cases are self-referred due to patient/spouse awareness. The number of reports of sleep apneas by physicians will increase tenfold in the next few years, similar to the level of other chronic diseases such as hypertension, upper respiratory tract infection and diabetes [14]. The capacity of the healthcare system to perform the necessary PSG studies is limited and dependent on the number of beds available. About half of PSG studies are positive for sleep apnea [12]. At our Soroka Sleep-Wake Disorders Center, about 70% of PSG studies are positive for OSAS and require CPAP treatment [26]. The Berlin questionnaire [27] provides a means of identifying patients who are likely to have sleep apnea and may increase the percent of PSG tests that are positive for OSAS [14]. An average of 1.13 beds/100,000 subjects are available for suspected OSAS patients in the United Kingdom, Belgium, Australia, United States and Canada (range 0.3 beds per 100,000 people in the UK to 1.5 beds per 100,000 people in Canada) [12]. In Israel, we calculated 0.85 beds/100,000 subjects, at least 25% lower than the average number of beds in these countries and 45% lower than in Belgium, Australia and Canada. Recently, it was estimated that 2,310 PSG studies are needed annually per 100,000 people in order to adequately meet the demand for diagnosis and treatment of patients with suspected moderate to severe sleep apnea. This estimate exceeds, by a factor of at least 10, the actual capacity to perform PSG studies in most countries [12]. In many locations around the world, especially in Israel, the actual capacity to perform PSG studies is lower by far than the demand, due to the
discrepancy between the increased volume of referrals (demand) and the capacity (few beds existing in sleep laboratories) to perform PSG studies. This discrepancy prevents access to sleep diagnostic studies and results in unacceptably long waiting lists, as in North America [12]. In Israel, waiting time for PSG studies is determined mainly by scarce resources, i.e., policies regarding the waiting time are set differently by decision-makers in the various regions according to local budget constraints and demand. The demand facing decision-makers is mainly dependent on primary care physicians’ level of awareness to OSAS during a patient encounter. If the administrative barriers are relieved and knowledge levels of primary care physicians increase, a flood of patients is expected. One way to control the flood of patients who need PSG studies is to use sleep specialists as gatekeepers. In sleep centers where sleep specialists control access to PSG, their availability is likely to be more limiting than the PSG. It was estimated that in order to properly treat OSAS a full-time specialist capable of reviewing 1,500 new patients with suspected sleep apnea per year (6 patients per day) will be required [12]. Thus, a population of 100,000 would require 1.4 full-time sleep specialists. In Israel, our current estimate of the number of physicians who are sleep specialists is low, with only one full-time sleep specialist per 500,000 population, which is far less than required. Since most Israeli sleep specialists are not board-certified, a variety of professionals are practicing Sleep Medicine – pulmonologists, neurologists, otolaryngologists, psychiatrists, psychologists, physiologists.

There is no simple answer with regard to the future cost-effectiveness of new technologies to diagnose and treat OSAS. From the point of view of patients and organizations, the best result from the diagnostic process is one that improves the condition of the patient and leads to effective treatment or determines that no further therapy is needed [28]. As with other chronic illnesses, the best possible way to identify patients with OSAS is to use reliable screening methods in subjects suspected of having OSAS, however, such methodologies are not currently available.

**Diagnostic devices**

Some investigators have declared that the PSG era has ended for sleep medicine [24]. However, this statement is inconsistent with several lines of evidence suggesting that other at-home technologies provide limited and inaccurate information and have not proven to be cost-effective [26]. The main barriers to at-home use of diagnostic technologies are the nature of the study designs and analyses of data. Many studies involve simultaneous assessment by the simplified device and full PSG. This approach has been criticized because it is not the design for which the device was intended to be used [29]. The alternative design involves assessment by the simplified device on a separate night, often in the home. A recent review [18] co-sponsored by the AASM (American College of Chest Physicians) and the ATS discussed and recommended how to improve the quality of research on diagnostic methods, and compared portable monitoring to PSG for sleep apnea. Studies of individual proprietary devices are supported by individual manufacturers and have small sample sizes (because of financial constraints), thus methodologically rigorous reviewers judge them to be of poor quality. Several key areas should be addressed by investigators comparing portable monitors with a reference standard PSG when presenting new technology: a) investigators should document any perceived or actual bias that could result if the funding for the study originated with industry or if a manufacturer of a portable monitoring device paid them a consulting fee; b) recruitment should include consecutive subjects from a pool that is not subject to selection bias by the investigators; c) if common co-morbidities are included, subjects should be defined clearly and stratified into separate groups; d) the sample size should be sufficient to make the results representative of the population, and a power analysis based on a clearly stated hypothesis should be performed prior to the study; e) the study population should be described well enough to allow readers to determine whether the study subjects are similar enough to their own patient population to justify using the results in clinical practice, and f) details about the performance and scoring of the PSG and the portable monitor should be sufficient to allow a reader to replicate the study and to ensure that all important sources of bias were controlled for. Additional research questions have recently been proposed [30] for determining the value of portability in OSAS: Can portable monitoring rule OSAS out or in? Are portable monitor results reproducible? What is the cost-benefit of testing with portable monitors? What are the failure rates of testing with portable monitors? What patient populations were studied? Davies et al. [31] emphasized some prerequisites to minimize the level of uncertainty during the introduction of new technology into the healthcare system. These include: a) likely utilization rates of the new technology; b) probability that the new intervention will be proven effective or ineffective by Health Technology Assessment; c) maximum lifetime for the new technology; d) probability of additional new technologies and utilization rates; e) transition costs of adopting the new intervention; and f) cost of Health Technology Assessment.

Most surprising in the article by Flemons et al. [12] is the widespread use of ambulatory approaches to diagnosis rather than full in-laboratory PSG. Several recent reviews and policy documents [18,19,29,32], including one by an independent group (not sleep professionals) [29], indicate that this strategy cannot be recommended. Why, then, is this approach being used widely by thoughtful sleep physicians? As previous reports indicate, it is not the technology per se, indeed the technology looks promising [29], but rather the lack of compelling evidence due to poor study design [12,18]. The widespread use of this approach [12] suggests that a major focus of future research should be proper evaluation of alternative diagnostic strategies. Physicians are using non-conventional approaches for diagnosis and treatment, approaches not based on solid evidence. New screening devices (unattended at-home monitoring) for sleep apnea are emerging all the time, but only a few studies have adequately examined their cost-effectiveness compared to the gold standard approach [18,19]. Since many devices are currently lumped together into classes [19], reviews of evidence for a particular class of devices evaluate results of studies of all devices within that class [18,19]. Therefore, if one particular technology is outstanding, it may not be recommended because the
evidence can be weighed down by results from inferior devices. The results from a study of one device cannot be extrapolated to another device. This situation is unlike research using PSG, where standards have been set so that results are more generalizable and evidence can develop quickly.

The cost of human resources
Little information is available on cost elements of the overall diagnostic process. With at-home or in-laboratory technologies, 7–85% of the overall expense of any sleep study includes the cost of human resources and is constant regardless of the technology used [26]. A technician is required to handle the equipment and to analyze the initial data. A polysomnographer and physician are needed to perform a second data analysis and clinical patient evaluation before a final diagnosis is made. Total price tag per sleep study alone is not sufficient to determine whether a particular sleep study strategy should be adopted. We demonstrated that although a single at-home sleep study reduces costs by 30%, the overall cost of the diagnostic process, to meet PSG standards, is not reduced [26]. This is mainly due to the need to repeat sleep studies because of uncertain parameters such as lack of “diagnostic agreement” [21] and technical failures. Other investigators [22] have reported that unattended home PSG studies, while using proper protocols and quality controls, still require that approximately 1 out of 10 be repeated. However, those investigators relate the repeated study mainly to technical issues and not to aspects of diagnostic agreement.

Increasing OSAS diagnosis studies
The article by Flemos et al. [12] lays down a clear challenge. We need to use all available strategies to increase access to diagnosis and treatment for patients with sleep-disordered breathing. The major issue now is access. Let us commit to solving it [33]. The goal of an evaluation is not to precisely determine the apnea-hypopnea index, but rather to identify individuals who will benefit from treatment. Currently however, diagnostic sensitivity and specificity are assessed by whether the apnea-hypopnea index is above or below a fixed threshold, e.g., 15 episodes per hour. This results in the absurdity that if the apnea-hypopnea index is 16 episodes/hour for the full PSG, but 14 episodes/hour for the simplified test, this is a diagnostic failure! [33] Clearly therefore, new approaches are needed to evaluate the different sources of variance: differences between diagnostic equipment, differences between nights, and differences between in-home and in-laboratory settings. “Diagnostic agreement” [21] of partial sleep monitoring is about 70% when compared with PSG studies. Diagnostic agreement is an important variable that must be taken into account when a new technology is being evaluated, since it provides estimates of how many patients will need repeat sleep studies to reach a clinical decision regarding OSAS. For example, 70% diagnostic agreement means that 30% of the subjects obtained “non-definitive results.” This leads to an increase of approximately 40% in the number of sleep studies necessary to achieve a diagnostic confidence of 99% [26]. Since the cost of human resources is constant and relatively high, technological improvement in data loss and diagnostic agreement are insufficient to support the adoption of at-home sleep studies. Recently a Watch PAT100 device was offered [34] as an accurate, robust, and reliable ambulatory method for the detection of OSAS, with minimal patient discomfort, although its cost-effectiveness has yet to be determined.

Some investigators suggested that sleep medicine should turn its attention from technology to quality improvement protocols and issues of clinical utility [35]. It was proposed that each sleep unit should determine its own case-mix of complex and less complex OSAS patients in order to calculate the overall cost of the services. Case-mix information will help us understand the association between the number of patients and the number of required studies, especially in the subgroup of patients about whom there is poor diagnostic agreement [21]. This in turn will help us to better understand the market structure and to develop sleep diagnostic technologies [31].

Among other parameters, information on cost-effective diagnostic processes is required to define the appropriate case-mix of patients with high and low pre-test probability of OSAS. For example, in patients with a high pre-test probability, a simple monitoring device such as overnight oximetry may provide sufficient confirming evidence to begin treatment for OSAS [36]. A creative approach that reserves in-laboratory PSG for patients with a low pre-test probability of OSAS and a negative signal-monitoring test may provide more cost-efficient care than in-laboratory PSG for everyone.

There is a wealth of evidence that automated CPAP devices, continually adjusting pressure as needed to maintain airway patency [37,38], can titrate OSAS as effectively as a technologist during overnight PSG. Thus, programs that provide the patient with adequate education and support regarding CPAP treatment may further reduce the cost of diagnosis and treatment by eliminating routine in-laboratory CPAP titration for most patients [38]. Further studies on automated CPAP devices should analyze the overall process and cost-effectiveness before such a technology can be adopted. A ratio of 1.2 between PSG and attended partial monitoring in sleep laboratory settings under the supervision of nighttime technologists is another alternative strategy for cost-containment in a sleep laboratory, which can reduce diagnosis costs up to 10% annually [26] by the use of two devices. This strategy uses the same human resources, therefore saving the time needed for data analysis and patient handling [21]. We extrapolated that in a 12-bed laboratory of 1.5 PSG/partial sleep monitoring, the cost per single sleep study can be reduced by one-third as compared to the in-lab PSG cost.

The Israeli healthcare market
We estimated a threefold increase in the number of beds in Israel available for PSG over the last decade. The National Ambulatory Medical Care Survey [14] estimated that the number of PSG studies has increased more than tenfold in the last decade. From this survey, we can safely estimate an additional tenfold increase in PSG studies in the coming decade. Therefore, due to the significant lack of PSG studies in Israel, demand for OSAS diagnosis will continue to increase more than 20-fold the current volume of diagnostic
studies, in comparison with other industrial countries. In order to meet this demand and avoid reduced access to PSG, the number of beds and sleep specialists should increase accordingly. Two decades of exploring alternative technologies for at-home diagnosis of OSAS have not provided an alternative cost-effective strategy to the PSG approach. Currently, at-home monitoring technologies are not cost-effective because the cost of human resources and the level of diagnostic uncertainty do not justify the use of partial sleep monitoring at home. [26]. In contrast to the widespread use of ambulatory approaches to diagnosis, healthcare providers in Israel have not yet adopted this approach. Equipment manufacturers presenting alternative diagnostic technologies must provide information on the cost of the technology, operating costs including human resources, as well as patient-mix and the rates of accurate diagnoses, in comparison to the gold standard PSG. This information will enable decision-makers to perform a cost-benefit analysis before deciding to use low cost and low quality technology. We agree with Bahamam and Kryger [39] that until cost-effective tests are readily available and well validated, PSG remains the gold standard accepted technology for the diagnosis of OSAS. As in other industrial countries, a task force [30] is required in Israel to establish a cost-effective guideline strategy toward awareness of sleep disorders in general, and diagnosis and treatment of OSAS in particular.

References

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