American Thoracic Society/American Sleep Disorders Association

Statement on Health Outcomes Research in Sleep Apnea

THIS OFFICIAL STATEMENT WAS APPROVED BY THE ATS BOARD OF DIRECTORS, JUNE 1997

In the fall of 1993, the Assembly of Respiratory Neurobiology and Sleep of the American Thoracic Society and Board Members of the American Sleep Disorders Association successfully petitioned their respective organizations to jointly sponsor this conference on Health Outcomes Research in Sleep Apnea. Outcomes research has as its main focus the assessment of morbidity, mortality, functional capacity, quality of life, and cost/benefit of particular diagnostic procedures and therapies for given diseases.

Both organizations had good reasons to suspect that the information gathered would be useful. First, patients, physicians, governments, insurance companies, and health care economists are interested in knowing whether diagnosing and treating sleep apnea has beneficial effects on medical, neurobehavioral, and economic outcomes for patients and society so that appropriate resources can be allocated for these purposes. Second, there are no large-scale, long-term, randomized trials of treatment in sleep apnea to assess patient-oriented outcomes such as there are, for example, in the fields of hypertension and heart failure. Third, funding agencies are interested in receiving some direction in allocating limited resources to outcomes research in sleep disorders.

Accordingly, a conference designed to examine these issues was convened on March 24-25, 1995. The main goals of the conference were to exchange information and experience among participants with expertise in sleep apnea, its epidemiology and clinical management, primary care research, outcomes assessment, and health economics in order to foster cross-disciplinary interest in sleep apnea research. Finally, the organizers felt that this conference could be used as a model for intersocietal cooperation in health outcomes assessment in other sleep disorders. While the conference focused on sleep apnea in adults, sleep apnea is also well recognized in infants and children. Because there are differences in the pathogenesis, clinical manifestations, and approach to treatment between pediatric and adult sleep apnea, specific recommendations for health outcomes research, as outlined in this report. are not applicable to the pediatric population. However, the organizers of the present conference recognize the need to address outcomes research in the pediatric population in future initiatives.

Following formal presentations, participants were divided into three working groups whose charge was to make recommendations for potentially fruitful areas for outcomes research in sleep apnea in three broad areas: medical outcomes, neurobehavioral outcomes, and medical utilization and cost outcomes. The suggestion of programs or topics for implementation was a priority as was the dissemination of this program summary and its recommendations to interested parties. The present document constitutes the formal report of the conference proceedings and its recommendations.

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PRINCIPLES OF OUTCOMES RESEARCH

The broad aims of outcomes research are the assessment of disease, its effects, and its treatment from the point of view of the patient and, to a lesser extent, society. Although an understanding of the pathophysiologic basis of disease and assessments of physiologic outcomes is critical. there is often no direct correlation between the degree of physiologic disturbance and severity of symptoms, or medical morbidity or mortality. Moreover, improvement in physiologic function due to some surgical or medical intervention does not necessarily lead to improved symptoms, quality of life, morbidity, mortality, or reduced health care utilization (1, 2). Since patients (and society) are naturally more concerned with the latter issues, outcomes research arose to address them.

There are several implications for this approach to medical research. First, it is necessary to develop reliable measures of symptoms, quality of life, morbidity, and health care utilization. Second, some knowledge of the natural history of a disease is essential in assessing symptoms and therapeutic outcomes. Studies must contrast treatment results with what would have happened without treatment. Third, wide differences occur in reported symptoms among patients with equal degrees of physiological impairment, possibly due to differences in sex, personal, cultural and economic background, lifestyle, and personal preference. Fourth, a patient's disease will also affect the lives of others, including members of his/her family and associates. Fifth, the effectiveness of therapies in actual clinical practice, as opposed to the setting of a randomized controlled clinical trial, should be the ultimate test of the effectiveness of an intervention. The matching of patients' preferences for treatment, which happens in practice but not in controlled clinical trials, can greatly affect conclusions about the value of treatments. If so, nonrandomized trials may have their place in outcomes research. The above considerations underscore the need to take into account patient preferences in medical decision making and to measure these in studies of the value of treatment. These principles have been used to assess the effectiveness of therapies in a large number of diseases and should be applicable to the study of sleep apnea as well.

Design of Clinical Trials and Alternatives

Traditionally, the clearest generally accepted outcome for a disease would be mortality, followed in the descending order by clinical events, functional status, quality of life, physiologic function, patient satisfaction, and economic costs. The most stringent means of testing the effects of diagnostic and therapeutic approaches as they relate to these outcomes would be randomized controlled clinical trials, followed in descending order by nonrandomized controlled trials, case-control studies, case series, case reports, and expert opinion. Performance of randomized trials in sleep apnea are complicated by the difficulty of finding an appropriate placebo for a prolonged pe-

riod, especially where therapy, such as continuous positive airway pressure or upper airway surgery, is readily available.

However, as described above, nonrandomized studies in the clinical setting may yield important information regarding clinical efficacy that cannot be obtained in the artificial setting of randomized trials. For example, it might be appropriate to examine costs of therapy or complications and compliance rates compared with those in the centers reporting the best results (where available). Such studies could also be used to assess adherence to well-defined standards of practice. Patient preference for treatments might also be assessed in the clinical setting.

SLEEP APNEA FROM AN OUTCOMES PERSPECTIVE

Prevalence, Natural History, and Classification of Disease Severity

Obstructive sleep apnea (OSA) is very common. In a population study of employed adults between 30 and 60 years of age, the prevalence of OSA, defined as at least five apneas and hypopneas per hour of sleep accompanied by excessive daytime sleepiness, was 4% for males and 2% for females (3). Follow-up data on the sample showed that less than 10% of the subjects who met the criteria for sleep apnea had ever sought medical care or been evaluated for a sleep problem (4). These data indicate that OSA is almost certainly being underrecognized by patients and underdiagnosed by physicians (Sleep Commission Report). OSA is also common in patients with hypertension (5) and congestive heart failure (6, 7). A relationship between OSA and idiopathic dilated cardiomyopathy has also been described (8).

Central sleep apnea (CSA) can be distinguished from OSA. It is uncommon in the general population but is commonly seen in association with Cheyne-Stokes respiration in patients with congestive heart failure (CHF). Two recent studies involving small numbers of patients with CHF described a 40–50% prevalence of CSA (6, 7). In this setting it is associated with symptoms of sleep apnea as well as paroxysmal nocturnal dyspnea and insomnia (9). In patients with CHF. CSA is a marker of increased mortality, which may be related to higher noradrenergic activity than in patients without CSA (10, 11).

Although much of the natural history of sleep apnea is unknown. clinical observations and limited data have indicated that sleep apnea has a wide spectrum of severity and is a chronic condition often without a distinct onset. Taken together, these characteristics are likely to result in clinical outcome study samples that: (I) may not be representative of the majority of people with sleep apnea, due to selection bias; (2) include people who have had sleep apnea for varying duration, from just a few years to several decades; and (3) have a broad range of severity. Study samples may also have wide variation in comorbid conditions that affect quality of life independently of sleep apnea. A major concern is that uncontrolled differences in severity or comorbidity in the study groups may mask treatment effects or cause spurious differences. Consequently, care must be taken at a design stage to overcome the methodological difficulties stemming from these natural history aspects of OSA.

There is a need to delineate diagnostic and severity criteria to define study groups and endpoints. The difficulty as well as the importance of operationally classifying OSA is underscored by the variability, subjectivity, and broad spectrum of symptoms. Operational criteria have been established for OSA and other sleep-related breathing disorders and are listed in the International Classification of Sleep Disorders manual (12). However, these criteria are not suitable for all clinical and experimental situations. For outcomes research, classification of disease severity is important for defining comparable groups of patients in clinical trials. Classification of disease severity can be based on a number of criteria, including anatomic, physiologic, genetic, symptomatic, and functional ones.

Treatment of Sleep Apnea

A number of interventions have met with varying degrees of success in alleviating OSA and relieving its symptoms. These include weight loss in the obese (13), nasal continuous positive airway pressure (CPAP) (14), bilevel positive airway pressure (BiPAP) (15), dental appliances such as an adjustable mandibular advancement device (16). surgery such as uvulopalatopharyngoplasty (UPPP) (17), laser-assisted uvulopalatopharyngoplasty (LAUP), and maxomandibular surgery (18). Each treatment, however, has limitations. For instance, although there is a good deal of evidence that CPAP consistently abolishes OSA and improves symptoms of sleep apnea, it controls the disease but does not cure it. In addition, it is an awkward apparatus to use, and there are some problems with compliance because of discomfort. It is therefore important to take into account patient preference and to consider testing the effects of the alternative therapies listed above on outcomes.

In patients with CHF, treatment of CSA should be considered if CSA persists despite optimal pharmacologic therapy for CHF. A number of therapeutic approaches can be taken including administration of nocturnal O_2 (19, 20), theophylline (21), and nocturnal CPAP at modest pressures (10–12.5 cm H_2O) (6, I I).

WORKING GROUP REPORTS

Medical Outcomes Working Group

The main medical outcome ascribed to sleep apnea is cardiovascular morbidity. However, the incidence of cardiovascular events in patients with OSA, but without known cardiovascular disease, is liable to be too low to efficiently examine the development of such events. Instead, there was a consensus among participants that a more fruitful approach would be to examine cardiovascular outcomes in patients with sleep apnea at increased risk for or with cardiovascular disease.

Hypertension. Patients with OSA have an approximate 50% prevalence of systemic hypertension (22, 23). However, while some investigators have demonstrated an independent association between OSA and daytime systemic hypertension (24, 25), others have not (26). In addition, patients with OSA develop surges in blood pressure at the termination of apneas that often exceed waking blood pressure (27). Acute abolition of OSA by CPAP attenuates these elevations in blood pressure. There is also some evidence that CPAP causes mild reductions in daytime blood pressure in patients with OSA during chronic therapy (28). However, none of these studies has been large enough or long enough to firmly establish that treatment of OSA contributes to long-term control of blood pressure.

Ischemic heart disease. Large epidemiologic population-based studies performed in the mid-1980s demonstrated an association between habitual snoring and the prevalence and incidence of hypertension, angina pectoris, and myocardial infarction (29, 30). In these studies the vast majority of subjects did not undergo sleep studies to confirm the history of habitual snoring or to determine how many of these self-reported snorers had sleep apnea.

More recent studies have demonstrated associations be-

tween OSA and ischemic electrocardiographic changes in patients without a history of coronary artery disease, as well as nocturnal angina in those with proven coronary artery disease (31). Treatment of OSA by CPAP led to acute reductions in the frequency of nocturnal ischemic electrocardiographic changes and to chronic reductions in episodes of nocturnal angina. Despite the above, however, there are no prospective data regarding the incidence of ischemic cardiac events in untreated or treated patients with OSA.

Congestive heart failure. There is only one study in which treatment of OSA in patients with CHF has been reported. In this study, treatment of OSA by nocturnal CPAP in patients with CHF of unknown etiology led to remarkable improvements, and its withdrawal resulted in deterioration in left ventricular ejection fractions (8). These data strongly suggested that OSA was contributing to or was causing left ventricular dysfunction.

There is as yet no consensus as to whether, or how, CSA should be treated in patients with CHF. Of the treatments available, only CPAP has been shown in randomized trials to improve cardiac function and quality of life in association with reductions in hospitalizations (6). Nevertheless, these trials included only small numbers of patients and lasted no longer than 3 months.

Specific Recommendations for Research Priorities in Medical Outcomes

1. ***Assessment of the effects of treating sleep apnea on blood pressure.*** Examining the effects of OSA therapy on blood pressure as a continuous physiological outcome should be conducted. Since OSA can probably cause both nocturnal and diurnal elevations in blood pressure, trials could assess either or both of these in the presence or absence of pharmacologic therapy for hypertension, depending on its severity. The rationale here is that the pathological effects of hypertension are related to the total hypertensive burden throughout the day and night. Therefore, if treatment of OSA further reduced nocturnal or daytime blood pressure in hypertensive patients already on drug therapy, it would point to the importance of treating OSA in the overall management of hypertension.

2. ***The effects of treating sleep apnea on cardiac ischemia.*** The group identified difficulties in undertaking long-term randomized trials of therapy for OSA in patients with known ischemic heart disease or serious cardiac arrhythmias. Several participants felt that there were ethical dilemmas. On the other hand, short-term randomized trials of therapy for OSA, of a few days' to weeks' duration, might practically be undertaken with assessment of physiologic outcomes such as ischemic changes on thallium scanning or cardiac arrhythmias on electrocardiograms as well as assessments of frequency of angina, quality of life, and functional status. However, large numbers of patients might be required in trials of this nature to determine clinical and physiologic responses to therapy over such short time periods. It would be more difficult to assess harder endpoints such as incidence of myocardial infarction, syncope, or death.

3. *Effects* ***of treating sleep apnea in patients with congestive heart*** *failure.* The same difficulties of undertaking long-term randomized trials of therapy and assessment of hard endpoints in the OSA patients with ischemic heart disease apply to CHF. Short- to medium-term outcomes could include physiologic endpoints such as indices of left ventricular function, and neurohumoral activity such as circulating catecholamine concentrations. In addition, symptoms of heart failure and sleep apnea as well as quality of life and functional status could be assessed. The participants felt that, since there is no generally agreed upon therapy that would be suitable for all patients with OSA, a number of different treatments, as described above, could be tested. These would include CPAP, oral mandibular advancement appliances, UPPP, LAUP, or maxillomandibular surgery. In fact, one therapy could be tested against another. One approach would be to test therapies against recommended weight loss. A stepwise approach could also be tested.

Since CSA appears to be common in patients with CHF, it was felt that long-term randomized trials of large numbers of patients examining hard, clinically relevant outcomes such as mortality, episodes of CHF, and objective measures of cardiac function, as well as assessment of functional status, quality of life, hospital admissions, and costs of treatment for CHF could be examined, albeit not without difficulty. As with OSA, the effect of one form of therapy versus another on cardiovascular outcomes could be tested.

4. ***Assessment of cardiac function in clinical studies of sleep apnea.*** The participants also recommended that investigators examining other outcomes in sleep apnea should consider designing their studies to include measurements of cardiovascular function as secondary outcomes. For example, in studies examining treatment of OSA with CPAP on neurobehavioral outcomes, echocardiography might also be easily performed and might reveal changes in cardiac function associated with therapy.

Neurobehavioral Outcomes Working Group

Quality of life and functional assessments. Quality of life is the most global, and undoubtedly the most frequently used, measure in outcomes research in general. Quality of life is defined as total well-being, encompassing both physical and psychosocial factors. Until recently, quality of life was not commonly measured in either sleep apnea research or clinic settings. Several studies of quality of life and sleep apnea are under way, as evidenced by abstracts and presentations, but there are few published studies to date.

Self-rating scales of life satisfaction are used to assess the affective components of quality of life. Tools range from those with a single item (all things considered, how happy are you with your life?) to those that rate satisfaction with specific aspects of life (family, job, social life, etc.). Items from the Danoff Scale, in which aspects of life are rated on a scale, were used in a follow-up study of a clinic population, and life satisfaction appeared to be higher among treated as compared with untreated patients with OSA, holding severity and other factors constant (32).

Functional status is an important component of quality of life, and most relevant measurement tools focus primarily on this component. Functional status is a multifaceted concept that characterizes the ability to meet needs, fulfill roles, and maintain health and well-being. Functional status measures may include basic and instrumental activities of daily living and role performance. The Nottingham Health Profile (33), the SF36 "short form" of the Medical Outcomes Study Inventory (34), and the Sickness Impact Profile (35) have been used extensively for diseases and conditions other than sleep apnea, and are not disease-specific. The advantage of using these non-disease-specific tools is that they would allow comparisons of quality of life in patients with sleep apnea to that in patients with other diseases. However, the "floor" and "ceiling" effects of the standardized general tools are well known, such that data on less relevant items will have little variance (e.g., nearly all sleep apnea patients may rate their ability to dress themselves as very high).

Disease-specific measures offer the advantage of greater

sensitivity in discriminating gradations of derangement due to larger variance in aspects of quality of life that are most affected by a particular disease. Two functional status tools specifically for sleep apnea under development and in preliminary use are the Functional Outcomes of Sleep Questionnaire (36) and the Sleep Apnea Quality of Life Index (37). Both were developed by investigators with extensive experience in sleep medicine and the latter was developed using guidelines for developing quality-of-life indices for chronic obstructive pulmonary disease (COPD), asthma, and CHF.

Declines in functional status can be a result of many factors including motivation, mood, and other medical conditions, which, if not accounted for, can be confounding factors in trying to assess the impact of sleep apnea. At present, there are few descriptions of the functional limitations associated with sleep apnea, making the development of a disease-specific instrument difficult. Furthermore, the relative contribution of the various acute consequences of the abnormal events of sleep apnea (e.g., oxygen desaturation, sleep fragmentation) to the functional limitations is unknown. If these acute conditions affect functional status differently, it may be difficult to detect a general association with sleep apnea if only a broad definition (e.g., Apnea Plus Hypopnea Index) is used.

General performance: psychomotor and cognitive functions. Performance assessments can be a critical probe of central nervous system capability, serving to identify zones of vulnerability in sleepy people, provide a common metric by which outcomes data can be calibrated against laboratory data, and give meaning to the consequences of physiologic and subjective changes. There are numerous widely used tests with known psychometrics and normative data that have been used successfully in sleep research (38). Among these general tests are reaction time or vigilance tests, finger tapping speed, speed and accuracy of canceling digits or substituting symbols, and recalling items in a word list. A taxonomy of six documented effects of sleep loss on performance of various short duration tasks has been proposed (39). Further validation may result in a sleep disorders-specific performance evaluation battery. The effects are lapsing, false responding, optimum response shifts, cognitive response shifts, short-term memory deficits, and time-on-task decrements.

Measures of driving performance may be considered a disease-specific performance tool for sleep apnea and sleepiness, since patients with OSA have an increased rate of traffic accidents (40). A few studies have related driving performance as measured by computerized laboratory-based driving simulation tests to sleepiness and sleep apnea, including the "steer clear" test (41) and a tracking and visual search test (42). Patients with OSA have impaired performance on both of these tests. Preliminary data indicate that the performance of patients with OSA on the latter test improved with CPAP treatment (C. F. P. George, personal communication, University of Western Ontario, London, Ontario, Canada).

Neuropsychological assessment. Recurrent apnea-related cerebral hypoxia and reduced cerebral perfusion as well as insufficient, fragmented sleep are very likely to have adverse effects on mood and mental performance. Standardized instruments are available to assess mood, anxiety, depression, memory, learning, integrative functions, and motor efficiency associated with various disorders (43, 44). None of these instruments is specific to sleep apnea. As in the case of quality-of-life assessments, use of standardized, general tools to investigate neuropsychological outcomes for sleep apnea would allow comparison to other diseases, but the development of sleep apnea-specific tools would probably be more useful in evaluating treatment effectiveness. A complicating factor in interpreting such tests is the undoubted effect of hypersomnolence on mental function.

Assessment of sleepiness. Pathologic sleepiness is the most prominent behavioral outcome of sleep apnea that leads patients to seek medical attention. Sleepiness may be directly or indirectly involved in other behavioral morbidity of sleep apnea, including accidents, mood problems, and social problems. Consequently, measurement of sleepiness is a disease-specific and extremely important outcome measure for sleep apnea. Sleepiness can be assessed either by self-reporting, by reports of behavior, or by objective measurements.

There are several tests of sleepiness using self-reporting, including analog rating scales for sleepiness (45), the Stanford Sleepiness Scale (46), two of the six subscales of the Profile of Mood States (POMS) (fatigue and vigor) (47), the Sleep-Wake Inventory (S-WAI) (among patients with sleep apnea, this factor normalizes after treatment) (48) and the Epworth Sleepiness Scale (49).

Reports of sleepy behavior by others or of adverse events, such as work-related accidents and injuries and motor vehicle accidents, have been used as a marker of impairment due to sleepiness. Motor vehicle accidents represent a distinct behavioral outcome, apart from being a surrogate measure for sleepiness. Proper investigation of motor vehicle accidents as a primary outcome, however, will necessitate very large study samples because the overall occurrence is relatively low.

The most commonly used physiologic measures of sleepiness are the multiple sleep latency test (MSLT) (50), which measures how quickly one falls asleep, and the Maintenance of Wakefulness Test (MWT), which measures a subject's ability to remain awake under restful conditions (51). A distinct advantage of the MSLT over the MWT is that its validity has been widely studied and reviewed, and guidelines for its use have been established (52). Other measures, including pupillometry and evoked potentials, are used less often, but technical improvements may make these types of tests more feasible in the future.

Specific Recommendations for Research Priorities in Neurobehavioral Outcomes

1. ***Assessment of standard and novel neurohehavioral measurement tools in sleep apnea.*** Progress in measuring neurobehavioral outcomes is likely to be impeded by lack of understanding and/or improper use of the existing tools, particularly the objective ones. Moreover, determination of specific contextual dependence, learning, and practice effects of both disease and non-disease-specific tools for use in sleep research is needed. Other areas worthy of attention include comparison of sleep apnea and other disease on quality of life and general health status measures, and further development of sleep apnea-specific measures of neurobehavioral outcomes.

2. ***Effects of treatment of obstructive sleep apnea on neurobehavioral outcomes.*** Assessment of self-reported, observer-reported, and objective measures of neurobehavioral outcomes, both general and sleep apnea-specific, in controlled trials of CPAP versus other treatments should be undertaken. An interesting idea to consider is the addition of a "patient-preference" assessment in studies in which patients would be allowed a choice of therapy and thus would not be randomized, or where patients are allowed to determine what dose or usage would minimize the side effects and maximize the benefits of the therapy assigned by randomization (e.g., leaving off CPAP a few nights a week). The usage of various treatments would be monitored by diaries, meters, etc., when possible. One value of such designs is that when patients' choices are driven by preferences, there is likely to be overlap in disease

severity, allowing comparisons of outcomes for patients with similar initial symptom severity.

3. ***Identification of valid tools for practical assessment of neurobehavioral consequences in the clinical practice setting.*** Once various neurobehavioral tools are validated, as discussed above, it would be useful to determine which of these could be put to practical use in the setting of clinical practice. This would facilitate decision making by practitioners and provide some practical measure of control of the quality of medical care in the future.

4. ***Compare the impact of obstructive sleep apnea and other diseases (e.g., cardiovascular diseases, clinical depression) on self-reported neurobehavioral outcomes using general rather than disease-specific tools.*** This will allow assessment of the relative burden of OSA on functional status and quality of life and would be useful in informing allocation of research and clinical funds.

Medical Utilization and Cost Outcomes Working Group

There are several features unique to sleep apnea that might complicate the analysis of medical utilization and cost. For example, there is a secondary impact of sleep apnea on coexistent diseases. In addition, there is a regulatory environment at the present time that seeks to limit new costs and often assigns values to therapies independently of their true efficacy. In this environment durable medical goods, such as CPAP, may be viewed less favorably than medicines or surgery.

Although there is a paucity of good studies on health care utilization and cost/benefit in sleep apnea, there have been estimates from the National Commission on Sleep Disorders Research of the global cost of sleep disorders and of sleep apnea. This imposes an enormous burden on society estimated at almost $18 billion per annum. However, these estimates were based upon anecdotal evidence, case reports, or case series.

Preliminary evidence from a health maintenance organization (HMO) in Seattle, Health Care Cooperative of Puget Sound, about the economic impact of assessing and treating sleep apnea in a managed care setting was presented (Robert Sandblom and James DeMaine, personal communication). From 1991 to 1994 there was a 30% increase per year in primary care recognition and referral of patients for diagnosis and management of sleep apnea. Nevertheless, the cumulative rate of identified sleep apnea remained well below that anticipated by estimates of disease prevalence from community-based sampling. The cost of diagnostic and therapeutic procedures rose twice as fast as for the overall budget for the HMO despite attempts to reduce costs through various strategies, such as the provision of home respiratory monitoring and home CPAP titration. Although this did reduce costs per case, total costs continued to rise because it increased the ability to recognize and treat sleep apnea. This experience raised the point that analysis and estimation of medical utilization is particularly appropriate to sleep apnea, since there will be increased efforts to identify and treat sleep apnea that is currently unrecognized in the general population.

Specific Recommendations for Research Priorities in Medical Utilization and Cost Outcomes

1. Case identification and costs of diagnosis. A common language and guidelines for definitions of disease and disease severity need to be developed (53-55). A stepwise approach is probably needed to achieve these goals. Sleep apnea is presently diagnosed by demonstrating apneas during sleep. Therefore, initially, objective measures of apneic activity and sleep disruption could be used as the primary criteria for diagnosis and classification of disease severity (56). Then it would be appropriate to develop questionnaire-based identification of disease and to validate this against the physiologic disturbance observed during polysomnography. These tools, along with physician-based, clinic-administered predictive models of sleep apnea, would be used to define entry criteria for studies on both utilization and cost (57, 58). Such studies are presently under way, but there is a need for larger, more broadly based multicenter studies (59) to determine the general usefulness of such tools to identify patients with clinically significant sleep apnea. One could then determine thresholds for therapy (60, 61), the relative cost and benefit of a variety of diagnostic or treatment strategies (53, 54), and risk adjustment for outcomes of treatment (62).

2. ***Patientpreferences for treatment.*** One of the major determinants of what patients and health care providers will pay for a given medical service in a free market economy is patient preference and satisfaction (53). The participants therefore felt that patient preference and satisfaction should play an important role in further research. Impediments to this approach might be the impact of sleepiness and inattention on patient preferences, as well as the need to involve family members or disinterested parties, in addition to physicians (for example, nurses and respiratory therapists) to determine care and to help patients make decisions. This line of research recognizes that certain forms of therapy might have different efficacy in different patients despite similar disease severity. If one wanted to test the effectiveness of this approach, one would have to develop and study technology that would provide a balanced presentation of the current therapy for sleep apnea syndrome, such as an interactive video. Such a balanced presentation has been employed in studies of breast cancer, prostate cancer, and coronary artery disease (1, 2). The reactions of patients and their physicians to these methods are also relevant to research in sleep apnea. This approach could then be compared with traditional methods in which the physician provides information directly to the patient and discusses the options with him or her (63). Information about patients' preferences derived from such studies appears necessary for the development and refinement of a strategy to care for sleep apnea in the general population (64).

3. ***Costs of treatment.*** Research directed at the financial aspects of sleep apnea should be undertaken, because it will help form the basis for rational utilization of scarce resources. While there is some literature beginning to articulate the costs (65-67) and benefits (32, 68, 69) of diagnosing and treating sleep apnea, a number of questions remain to be answered. What are the costs of various forms of treatment? Are there regional differences in these costs and are they related to the relative differences in the proportion of patients receiving different types of treatment? If there are regional differences, for example, in the proportion of patients treated by CPAP versus upper airway surgery, what is the cause of these differences? Does this resource utilization at the present time reflect our understanding of the epidemiology of disease in terms of sex, age, socioeconomic status, and race?

Once information relevant to these questions becomes available, it could be further examined to see how different approaches to resource allocation varied from an ideal recommended approach. Data should come from a large number of centers so that results are meaningful to physicians, government health policy decision makers, and managed care organizations. A rigorous way of determining costs would be to perform prospective randomized or unrandomized trials using different treatments and tracking medical utilization and costs, either as a primary or secondary outcome. However, such an approach would

be expensive, time-consuming, and fraught with the problems of assessing potentially outmoded methods in the face of rapidly evolving technologies for diagnosing and treating sleep apnea.

SUMMARY AND CONCLUSIONS

Clinical research in sleep apnea has focused to a large extent on pathophysiology and the effects of treatment on physiologic outcomes such as apneas, O_2 desaturation and arousals from sleep, and daytime measures of blood pressure and sleepiness. However, the advancement of outcomes research in sleep apnea will require a stronger focus on clinical and patient-oriented outcomes and preferences, not just in the setting of controlled clinical trials but in the clinic setting as well. In addition, patients and health care providers will need better information on health care utilization and the costs of diagnosing and treating sleep apnea.

The above recommendations of the working groups for studies in outcomes research are not exhaustive and would be subject to change as new technologies and information emerge. Nevertheless, such studies could provide initial results to shape broad guidelines for health care policy makers, patient organizations such as the American Sleep Apnea Association and the National Sleep Foundation, and national research agencies such as the National Center for Sleep Disorders Research of the United States and the Medical Research Councils of Canada and the United Kingdom, with the goal of creating clinical research initiatives and networks in this area.

Participants in the American Thoracic Society/American Sleep Disorders Association Conference on Health Outcomes Research in Sleep Apnea included:

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