American Academy of Sleep Medicine Response to the ACP Clinical Practice Guideline for the Diagnosis of Obstructive Sleep Apnea in Adults

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Note: The AASM submitted to the Annals of Internal Medicine an abbreviated version of this response, which conformed to the journal's word limitations. The brief comment can be viewed on the journal's website along with the ACP guideline. The following text represents the entirety of the AASM's response to the ACP.

The American College of Physicians (ACP) clinical practice guideline regarding the diagnosis of obstructive sleep apnea (OSA) in adults addresses a prevalent and serious medical illness associated with myriad adverse clinical outcomes such as cardiovascular disease, hypertension, cognitive impairment, type 2 diabetes, and postoperative cardiac and respiratory complications.\(^1\) Because of the widespread, deleterious effects of untreated OSA, the diagnosis and effective management of this chronic disease is of utmost importance to all internists. As the leading professional society representing board certified sleep medicine physicians and other health professionals in the sleep field, the American Academy of Sleep Medicine (AASM) promotes high quality, patient-centered care through the development of practice standards, including a previously published clinical guideline addressing OSA in adults.\(^2\) Although there is some similarity between the clinical guidelines published by the ACP and AASM, significant differences in the recommendations for which tests to use in the evaluation of sleep apnea are of concern to the AASM.

The ACP recommendations of polysomnography for diagnostic testing in patients suspected of OSA, and home sleep apnea testing in patients without serious comorbidities as an alternative to polysomnography, are generally consistent with current AASM standards. These two recommendations regarding use of diagnostic tests were arrived at by two different guideline development groups after similar systematic reviews, and therefore would seem to be fairly confident recommendations. However, the ACP’s recommendation to limit home sleep apnea testing to situations “when polysomnography is not available for diagnostic testing” is both overly restrictive and inconsistent with the AASM clinical guideline. In the last decade, there is increasingly solid evidence that home sleep apnea testing interpreted by a sleep specialist, in conjunction with a comprehensive sleep evaluation, may be an equally viable diagnostic option in patients...
with a high pre-test probability for moderate to severe OSA who do not have comorbid cardiopulmonary or neuromuscular disorders, or in whom other sleep disorders are not a consideration.\textsuperscript{2} Under these conditions a home sleep apnea test may be the may be the most reasonable diagnostic choice even when polysomnography is available. When these conditions are not met, yet sleep-disordered breathing is a consideration, we agree that PSG is the test of choice at this time.

Furthermore, the ACP guideline places an inordinate emphasis on sleepiness as the main reason for evaluation with sleep testing, which risks promoting both the under-diagnosis of OSA and potential overuse of sleep tests. I am concerned that the inappropriately narrow focus on sleepiness as an almost exclusive feature driving clinical investigation will reduce important health and economic benefits to patients that result from diagnosis and treatment of OSA, even when sleepiness is not readily apparent. I am also concerned that an overly superficial application of the ACP guideline recommendation focuses on testing sleepy persons for OSA, rather than carrying out a broader evaluation of sleepiness as an important symptom, considering other causes such as inadequate sleep, insomnia disorder, medication side effects, and primary central neurological causes for hypersomnia.\textsuperscript{3}

In the Wisconsin Sleep Cohort Study, only 37\% of patients with severe OSA (AHI\textgeq;30) reported daytime sleepiness. Thus, focusing diagnostic strategies around somnolence alone would exclude nearly two-thirds of patients with severe OSA, patients who have the strongest association with mortality and other important health outcomes.\textsuperscript{4} In view of these data, the ACP’s recommendation to focus on sleepiness seems counterintuitive, and appears predicated on three premises: first - that sleepiness is more predictive of outcomes than other factors; second - that there is little association between sleep apnea severity and clinical outcomes; and third - that CPAP treatment has been proven effective only at improving sleepiness. These premises are not sound.

There may be methodological reasons for the ACP arriving at a narrow focus on sleepiness. The guideline was purportedly developed using the ACP’s guideline development system, which relies on a systematic review and grading of primary evidence by an evidence review group, followed by presentation of the evidence-review paper to the Clinical Guidelines Committee for review and comments.\textsuperscript{5} According to their stated methods, “The evidence-review paper serves as a companion piece to and foundation for the ACP’s clinical practice guidelines. This paper summarizes evidence in evidence tables, analyzes the data, and synthesizes the available evidence.”\textsuperscript{5} In this case, there is no companion paper. Instead, the online supplemental materials contain the details about the review, and this material indicates that all components of the evidence review, including the search, triage, evidence extraction, and evidence quality review, were
performed by only one of the authors. This process led to an initial harvest of 2,435 potentially relevant articles, which through exclusion was reduced to 85 articles, which ostensibly make up the primary substrate for the review. It is not clear whether the online supplement was subject to the same level of peer review accorded formal review papers. Many of the conclusions stated in the main body of the ACP guideline reference articles that do not appear to be included in the updated systematic review. In the supplemental materials, only 3 articles (describing only 2 patient populations) addressed the question: “In adults being screened for OSA, what are the relationships between AHI or oxygen desaturation index (ODI), and other patient characteristics with respect to long-term clinical and functional outcomes”. These three studies involved only adults >= 40 years old, most of whom were male. Sleepiness was not assessed at all in almost 40%, and was present (as evidenced by an Epworth Sleepiness Scale > 10) in only 7% of the combined study populations. None of the studies were individually powered to detect the influence of sleepiness on outcomes. Therefore, this review alone does not seem adequate to allow valid conclusions about the importance of sleepiness and its influence on OSA-related morbidity and mortality.

Beyond all-cause mortality being linked to severe OSA, the guideline authors suggested that there was “no association” between stroke and the AHI (see Table 4 in the Guideline). They reference the study by Arzt et al (not in the systematic review group), which actually seems to endorse a significantly different conclusion. Those authors state: “These data demonstrate a strong association between moderate to severe sleep-disordered breathing and prevalent stroke, independent of confounding factors. They also provide the first prospective evidence that sleep-disordered breathing precedes stroke and may contribute to the development of stroke.” The Guideline authors conclude that there are inconsistent results linking AHI with cardiovascular mortality, but they only reference two articles. Reliance on non-systematic evidence review, and reliance on only one evidence reviewer, can lead to unwanted introduction of bias. For example, a contemporary meta-analysis specifically designed to answer whether OSA is associated with cardiovascular risk led to a very different conclusion. The pooled relative risk for total cardiovascular disease outcomes attributed to OSA was 2.45 (95%CI 1.98-3.10) and was 2.02 (95%CI 1.40-2.90) for stroke. Important conclusions in guidelines should be supported by systematic literature reviews, not limited selections.

The guideline also suggests that evidence “is lacking on the effect of CPAP on improving outcomes” other than sleep; however, this also is not a transparent statement. Contemporary meta-analyses conclude that effective CPAP therapy of patients with OSA and hypertension results in magnitudes of reductions in blood pressure approximately half of that achieved by traditional antihypertensive agents. The ACP guideline on treatment indicates that, although there were no randomized controlled trials assessing
effect of CPAP on mortality, 5 of 8 identified observational studies reported significant reductions in overall mortality rates, and that 4 out of 6 observational studies reported significant reductions in cardiovascular mortality rates associated with CPAP adherence compared with no CPAP. Furthermore, the ACP seems to be in some conflict about the merits of CPAP treatment. Statements from this current guideline, which was designed to focus on diagnosis, indicate that “evidence is lacking” for treatment, while the ACP guideline on treatment of OSA provides a strong recommendation for CPAP as initial therapy for OSA based upon moderate-quality evidence. Furthermore, the review was entirely silent on the developing evidence regarding the effective treatment of patients with OSA using oral appliances and their effect on important clinical outcomes. These examples raise questions about the methods and conclusions used in this Guideline to decide which populations ought to have sleep testing.

The authors further evaluate several clinical prediction rules in comparison to polysomnograms for OSA. The choice of the Epworth Sleepiness Scale and the Pittsburgh Sleep Quality Index (PSQI) for this purpose seems ill-advised. The ESS was never intended to be a screening test for OSA; it is a semi-quantitative scale used to quantify subjective sleepiness. The PSQI was developed to assist in psychiatric and insomnia research, and was never intended as a screening tool for sleep-disordered breathing. The STOP-BANG was intended and has been most evaluated as a pre-operative screening tool for OSA. Only the Berlin Questionnaire was developed for use in outpatient screening for OSA. It should not come as a surprise that these tools are not accurate surrogates for objective sleep testing. This highlights the potential for improvement in guideline development that might be achieved by inclusion of more than one subject matter expert in the review and interpretation of existing literature.

Sleepiness is one among many symptoms, including witnessed apneas, snoring, nocturnal gasping or choking, nonrefreshing sleep, disturbed sleep, nocturia, morning headaches, impaired concentration, memory loss, and decreased libido, that might suggest that OSA be included in the differential diagnosis. A complaint of excessive sleepiness should prompt a comprehensive review of the patient’s sleep schedule, medical history and medication usage; questioning for auxiliary symptoms of narcolepsy; and consideration for sleep specialist referral if the cause is not apparent. Concurrent risk factors, such as obesity, retrognathia on exam, hypertension, or type 2 diabetes, should prompt consideration for sleep apnea testing; however, some of the other causes of sleepiness do not require sleep apnea testing and respond to specific interventions. A key consideration to ordering testing for sleep apnea is a determination regarding the ability to follow-through with effective management of sleep apnea if diagnosed.
It is critical to advance high-value care of patients with a sleep illness such as OSA. Physicians should inquire for symptoms of sleep disturbances and specifically look for sleep apnea in patients belonging to high-risk populations, including those who do not complain of sleepiness. Appropriate testing and treatment will improve health outcomes in a cost-effective manner. The AASM would value the opportunity to review and comment on pre-publication drafts of future sleep-related clinical guidelines developed by the ACP or professional societies representing other internal medicine specialties. We recognize that internists have an important role to play in the management of patients with OSA, and we believe that collaborative relationships between sleep specialists and internists will undergird our efforts to improve public health by promoting healthy sleep.

References


