

January 20, 2021

Alex H. Crist, MD, MPH  
Chair  
US Preventive Services Task Force  
5600 Fishers Lane  
Rockville, MD 20852

Dear Dr. Crist:

On behalf of the American Thoracic Society (ATS), thank you for the opportunity to comment on the U.S. Preventive Services Task Force's (USPSTF) Draft Research Plan on Screening for Obstructive Sleep Apnea in Adults. The ATS is a multi-disciplinary society of 17,000 pulmonary, critical care, and sleep specialists researching, diagnosing, treating, and preventing respiratory illnesses such as COVID-19 and COPD and sleep disorders such as obstructive sleep apnea (OSA).

The ATS appreciates that the USPSTF is updating their 2017 recommendations on Obstructive Sleep Apnea (OSA) Screening in Adults to account for data that has accumulated since that recommendation was first published. We believe that there have been substantial improvements in the proposed analytic framework for this updated review compared to the previous recommendations. We have the following recommendations to enhance the analytic framework, key questions (KQ)'s and draft research plan and provide the basis for Task Force recommendations that will ensure the best care for individuals with OSA.

### Proposed Analytic Framework

The ATS is concerned that the proposed framework does not clearly differentiate patients with OSA who are asymptomatic from those who have unrecognized symptoms. The figure outlining the proposed framework suggests that screening of only asymptomatic patients is being evaluated, while the proposed questions place both patients who are asymptomatic and those with unrecognized symptoms into a single category. We are concerned that this lack of clarity may lead to confusion about what studies are reviewed and greater confusion in how the resulting recommendations are interpreted by clinicians. The ATS recommends that the analytic framework includes both symptomatic and asymptomatic patients, and that the research plan and KQ's address these groups separately. Additionally, an important concern is that OSA symptoms, such as excessive daytime sleepiness (EDS) and others, are often not discussed or

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prioritized during patient visits with healthcare providers, therefore there is a particular need to specify and clarify the term “unrecognized” symptoms.

### **Apnea Hypopnea Index (AHI)**

We are concerned that, as currently drafted, the analytic framework appears to equate OSA with solely having an elevated apnea hypopnea index (AHI). In fact, the most common definition of OSA in current use today, as defined by the International Classification of Sleep Disorders III (ICSD-3), which is also used by the Centers for Medicare and Medicaid Services (CMS), defines OSA as an AHI 5-15 events/hour associated with referable symptoms, or an AHI >15 events/hour. This definition of disease means that for mild OSA (AHI 5-15), the presence of symptoms is required to designate an OSA diagnosis (i.e., there is no such thing as asymptomatic mild OSA). Furthermore, a current American Academy of Sleep Medicine (AASM) Working Group that is evaluating an updated definition of OSA as part of its work to update the ICSD-3, is considering making the requirement of symptoms applicable even to those with AHI >15. The rationale behind this change is the growing evidence that the natural history and impact of treatment are divergent in patients with elevated AHI who do or do not have symptoms. This includes evidence from the multiple randomized trials which have failed to demonstrate a cardiovascular benefit in asymptomatic patients with elevated AHI in contrast to non-randomized data suggesting cardiovascular benefit in symptomatic patients. Non-interventional longitudinal data also suggest the excess cardiovascular risk attributed to OSA only exists in the subgroup of patients with elevated AHI who also report referable symptoms.<sup>i</sup>  
<sup>ii</sup> <sup>iii</sup> <sup>iv</sup> Thus, there is a strong body of scientific evidence indicating that OSA, as a disease entity, requires the presence of referable symptoms and that this should be considered a distinct entity from an asymptomatic patient incidentally found to have an elevated AHI.

The ATS strongly recommends that the USPSTF clearly distinguish an elevated AHI in the absence of symptoms from unrecognized OSA where a patient has an elevated AHI and referable symptoms, but the primary care provider has failed to recognize the symptoms, due to a failure to ask questions or take a history focused on sleep with the patient. Research suggests that this patient group (OSA with unrecognized symptoms) is highly prevalent due to low rates of sleep history-taking by primary care providers.<sup>v</sup> It is in this specific group where there is most likely potential value in universal screening and treatment. We urge the USPSTF to clarify how OSA is defined (requiring symptoms or not) so that the recommendations can be appropriately implemented by clinicians.

### **Proposed Key Questions to be Systematically Reviewed**

Consistent with our recommendation for clarification in the proposed analytic framework, the ATS strongly recommends that the KQ's should be revised to consider patients with symptoms vs. those without symptoms separately. Although commonly referenced in the literature, these populations are differentiated on the basis of presence or absence of EDS and patients may present with other symptoms instead of EDS as their main complaint, such as fatigue, tiredness, lack of energy, mood (depressive) problems, unrefreshed sleep, sleep fragmentation from nocturia, bed partner sleep disruption, etc.<sup>vi</sup> <sup>vii</sup> We recommend that the Task Force include these symptoms in their methods and not limit their searches exclusively to EDS.

### **Key Question 2 - Clarify Standard Definition of OSA**

We firmly believe that KQ2 should be revised to explicitly state the gold standard definition for OSA. The ATS recommends that the ICSD-3 definition of OSA be used as the gold standard (AHI 5-15 events/hour with referable symptoms or AHI > 15 events/hour), recognizing that this definition is currently being re-evaluated on whether to include symptoms as a requirement even in those with AHI>15 events/hour. Without clarity on the definition of OSA, the metrics calculated (sensitivity, specificity, etc.) are not meaningful. We believe the optimal definition when assessing a screening instrument is to identify patients who are likely to benefit from treatment. As such, the definition should include an elevated AHI with referable symptoms. If the point of screening is to identify patients who will benefit from treatment, then the goal should be to identify disease, not simply physiologic markers, such as an elevated AHI.

### **Key Questions 1 and 5 – Include Other Measures of Sleep Health and Comorbidities**

Regarding relevant health outcomes, we strongly recommend that measures of sleep quality, mood, vitality, and fatigue be included as relevant patient-centric health outcomes. Sleep quality could include measures such as the [Pittsburgh Sleep Quality Index](#) or the [PROMIS Sleep Disturbance metric](#). Sleep quality is an outcome highly valued by patients and so should not be ignored. Similarly, mood (i.e., depressive symptoms), vitality, and fatigue are all valued patient-centered outcomes that should be included in the proposed assessment. While each of these domains impact the patient quality of life, the sensitivity of global quality of life instruments to capture clinically important improvements in each of these components often is limited.

We agree that all KQs should include analyses by specific subgroups. Apart from the planned demographics and disease severity, we recommend addition of comorbidities and medications known to pathophysiologically interact with OSA. Comorbidities that should be included are congestive heart failure, atrial fibrillation, stroke, chronic obstructive pulmonary disease, asthma, respiratory muscle weakness, hypoventilation, chronic insomnia and post-traumatic stress disorder and opioid use.

### **Proposed Contextual Questions**

In assessing the barriers to sleep apnea diagnosis, the current contextual question 1 focuses on barriers to completion of polysomnography. However, in clinical practice, it is now clear based on nearly a dozen RCTs that home sleep testing is just as accurate as polysomnography and should be the preferred modality for routine OSA diagnosis. Thus, the relevant contextual question should be revised to refer to barriers to completion of sleep testing (home sleep testing with type IV monitors or polysomnography). Evidence suggests that the barriers to home sleep testing are much lower than polysomnography, costs are lower, and patients prefer home testing. Additionally, there are other, more prevalent barriers to sleep apnea diagnosis including its poor recognition in primary care settings due to clinician failure to ask questions about patient sleep.<sup>viii</sup> We recommend that in their KQ's, the Task Force address this specific barrier to OSA diagnosis, which holds the most benefit for expediting access to OSA care.

### Proposed Research Approach

In the treatment section of the proposed research approach, the approach describes PAP therapies in a manner not consistent with current clinical practice by listing fixed oral CPAP as the default modality. CPAP was originally intended to be delivered nasally and numerous studies have since suggested outcomes are worse using oral vs. nasal delivery.<sup>ix</sup> Both the ATS and AASM have published recommendations for the use of nasal CPAP over oral CPAP.<sup>x xi</sup> The ATS recommends that the research approach be revised to state that fixed nasal CPAP is the standard treatment modality. Additionally, the proposed research approach's inclusion of bilevel CPAP is inappropriate. Because the pressure is bilevel, it is, by definition, not continuous. The ATS recommends that the research approach be revised to refer to bilevel PAP.

Thank you for your consideration. Please contact Nuala S. Moore, ATS Director of Government Relations, at [Nmoore@thoracic.org](mailto:Nmoore@thoracic.org) with any questions.

Sincerely,



Juan C. Celedón, M.D., Dr.P.H., ATSF  
President  
American Thoracic Society

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<sup>i</sup> Yu J, Zhou Z, McEvoy RD, et al. Association of Positive Airway Pressure With Cardiovascular Events and Death in Adults With Sleep Apnea: A Systematic Review and Meta-analysis. *JAMA*. 2017;318(2):156–166. doi:10.1001/jama.2017.7967.

<sup>ii</sup> Patil SP, Ayappa IA, Caples SM, Kimoff RJ, Patel SR, Harrod CG. Treatment of Adult Obstructive Sleep Apnea with Positive Airway Pressure: An American Academy of Sleep Medicine Clinical Practice Guideline. *J Clin Sleep Med*. 2019 Feb 15;15(2):335-343. doi: 10.5664/jcsm.7640.

<sup>iii</sup> Mazzotti DR, Keenan BT, Lim DC, Gottlieb DJ, Kim J, Pack AI. Symptom Subtypes of Obstructive Sleep Apnea Predict Incidence of Cardiovascular Outcomes. *Am J Respir Crit Care Med*. 2019 Aug 15;200(4):493-506. doi: 10.1164/rccm.201808-1509OC.

<sup>iv</sup> Allan I Pack, Ulysses J Magalang, Bhajan Singh, Samuel T Kuna, Brendan T Keenan, Greg Maislin, Randomized clinical trials of cardiovascular disease in obstructive sleep apnea: understanding and overcoming bias, *Sleep*, zsa229.

<sup>v</sup> Mold JW, Quattlebaum C, Schinnerer E, Boeckman L, Orr W, Hollabaugh K. Identification by primary care clinicians of patients with obstructive sleep apnea: a practice-based research network (PBRN) study. *J Am Board Fam Med*. 2011 Mar-Apr;24(2):138-45. doi: 10.3122/jabfm.2011.02.100095.

<sup>vi</sup> Vi Chervin RD. Sleepiness, fatigue, tiredness, and lack of energy in obstructive sleep apnea. *Chest* 2000;118:372.

<sup>vii</sup> Wattanachai C, O'Brien, L, Fan, L, Chervin, R Fatigue, tiredness, and lack of energy improve with treatment for OSA. *J Clin Sleep Med* 2009 Jun 15;5(3):222.

<sup>viii</sup> Ibid. doi: 10.3122/jabfm.2011.02.100095.

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xi Ibid. doi: 10.5664/jcsm.7640.