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The USPSTF and screening for obstructive sleep apnea: Dispelling misconceptions

R ECENT guidelines from the United States Preventive Services Task Force (USPSTF) say that there is insufficient evidence to recommend screening for obstructive sleep apnea in people who have no symptoms of it.¹⁻³

The USPSTF committee systematically reviewed the evidence, sifting through 1,315 articles,³ and found no randomized controlled trials that compared screening with no screening in adults who have no symptoms (or no recognized symptoms) of obstructive sleep apnea. Conclusion: "The current evidence is insufficient to assess the balance of benefits and harms of screening for [obstructive sleep apnea] in asymptomatic adults."

This is logical, rigorous, and evidencebased. However, the conclusions might be misinterpreted and need to be put into context.

SCREENING IS WARRANTED IF PATIENTS HAVE SYMPTOMS

First, note that the USPSTF is referring to people who have no symptoms. The American Academy of Sleep Medicine has issued recommendations about screening and diagnostic testing in people who *do* have symptoms,⁴ in whom it is important to pursue screening and diagnostic testing.

Symptoms of obstructive sleep apnea include excessive daytime sleepiness, fatigue, drowsy driving, disrupted or fragmented sleep, nocturia, witnessed apnea, snoring, restless sleep, neurocognitive deficits, and depressed mood. Treating it improves these symptoms,

as clinical trials have shown unequivocally and consistently.⁵

Moreover, the third edition of the *International Classification of Sleep Disorders* defines obstructive sleep apnea as an obstructive apnea-hypopnea index of 15 or more events per hour even in the absence of symptoms. This threshold recognizes the risk of adverse health outcomes observed in population-based studies (ie, in participants recruited irrespective of symptoms).⁶

ABSENCE OF EVIDENCE, NOT EVIDENCE OF ABSENCE

Second, the absence of sufficient evidence cited by the USPSTF does not necessarily mean that screening for obstructive sleep apnea in asymptomatic people is not beneficial—it has just not been systematically studied. There was insufficient evidence available to make a recommendation to allocate resources to screen all patients irrespective of symptoms.

The Sleep Heart Health Study suggested that few people with obstructive sleep apnea were diagnosed with it and that even fewer were treated for it.⁷ More recent data indicate that this underdiagnosis persists and is more pervasive in underserved minority groups.^{8,9}

SCREENING VS CASE-FINDING

Moreover, screening is not the same as case-finding. The purpose of screening, as defined 50 years ago by Wilson and Jungner in a report for the World Health Organization, is "to discover those among the apparently well

The finding of absence of evidence of benefit could be misinterpreted

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who are in fact suffering from disease."10

Case-finding, on the other hand, focuses on those suspected of being at risk of the disease. In the case of obstructive sleep apnea, this is a lot of people. The overall prevalence of obstructive sleep apnea is about 26% by one estimate,11 and many more people have risk factors for it. For example, in one study, 69% of patients presenting to a primary care clinic were overweight or obese, 12 and many primary care patients have diseases that obstructive sleep apnea can exacerbate. One can therefore argue that in clinical practice, testing for obstructive sleep apnea is more like case-finding than screening—most patients that you see have unrecognized symptoms of it or risk factors for it.

CRITERIA FOR A GOOD SCREENING TEST

Principles for screening outlined by Wilson and Jungner¹⁰ were:

- The condition we are trying to detect should be important
- There should be an accepted treatment for it
- Facilities for diagnosis and treatment should be available
- Testing should be acceptable to the population
- There should be cost benefit to the expense of case-finding
- There should be an agreed-upon policy on whom to treat as patients.

Screening for obstructive sleep apnea meets many of these criteria.

Obstructive sleep apnea is important

Solid evidence exists that obstructive sleep apnea exerts a bad effect on health and quality of life. Population-based studies that enrolled participants irrespective of symptoms indicate that the risk of death is about twice as high in those with severe obstructive sleep apnea as in those without, and treatment exerts benefit especially in those with cardiovascular risk.^{13,14} Therefore, the criterion for screening that says the disease must be important is met.

Pathophysiologic pathways by which obstructive sleep apnea causes harm include intermittent hypoxia, hypercapnia, intrathoracic pressure swings, and autonomic nervous system fluctuations.

Treatment is beneficial

The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure recognized obstructive sleep apnea as a cause of hypertension.¹⁵

Treating obstructive sleep apnea lowers blood pressure, which in turn improves cardiovascular outcomes. Effects are most pronounced in those with resistant hypertension. The reduction in blood pressure is only about 2 to 3 mm Hg, but this translates to a 4% to 8% reduction in future risk of stroke and coronary heart disease. ^{16,17}

The Continuous Positive Airway Pressure Treatment of Obstructive Sleep Apnea to Prevent Cardiovascular Disease multicenter randomized clinical trial investigated the impact of treating obstructive sleep apnea with continuous positive airway pressure (CPAP) compared with usual care. ¹⁸ Although no statistically significant difference was seen in the composite cardiovascular outcome, propensity-score analysis in the subgroup adherent to CPAP demonstrated a lower composite of cerebral events in those who used CPAP for at least 4 hours a day.

The findings from this trial are difficult to interpret for several reasons. Adherence to CPAP was suboptimal, the severity of obstructive sleep apnea might not have been bad enough to permit observation of a significant treatment effect, and the generalizability of the findings is unclear, given that many of the participants were from underresourced regions.¹⁹

In a meta-analysis of cohort studies comprising more than 3 million participants, Fu et al found that the cardiovascular mortality rate was 63% lower in those with obstructive sleep apnea using CPAP than in untreated patients.²⁰

APPLY CLINICAL JUDGMENT

Overall, the USPSTF report is intended to guide healthcare decision-makers. However, it includes a caveat to not substitute the findings for clinical judgment and to interpret the findings in the context of collateral pertinent information.²

Although no high-quality data exist to support or refute global screening for obstructive sleep apnea in the primary care setting,

The USPSTF findings should not substitute for clinical judgment the high prevalence of this disease and its detrimental effects on health and quality of life if left untreated should not be dismissed.

Arguably, most patients who present to primary care clinics are not healthy, are not free of symptoms, and are at risk of obstructive sleep apnea because they are obese. Testing for it is therefore more like case-finding than screening.

In view of the serious consequences of obstructive sleep apnea, we should view the situation as an opportunity to examine the impact of screening. Perhaps using electronic medical records, we could collect sleep-specific measures, implement case-finding strategies, and perform pragmatic clinical trials to inform and guide optimal and cost-effective screening approaches.

Patients with common disorders such as obstructive sleep apnea are often considered asymptomatic until asked about symptoms. Therefore, careful review of systems incorporating sleep health is important, particularly as patients do not typically volunteer this information. Obtaining this history does not necessarily fall under the USPSTF's recommendation not to screen.

Future efforts should focus on leveraging the electronic medical record platform to collect sleep-specific measures, implementing case-finding strategies, and performing pragmatic clinical trials in the primary care setting to inform and guide optimal and cost-effective approaches to screening.

REFERENCES

- US Preventive Services Task Force, Bibbins-Domingo K, Grossman DC, Curry SJ, et al. Screening for obstructive sleep apnea in adults: US Preventive Services Task Force Recommendation Statement. JAMA 2017; 317:407–414.
- Jonas DE, Amick HR, Feltner C, et al. Screening for obstructive sleep apnea in adults: evidence report and systematic review for the US Preventive Services Task Force. JAMA 2017; 317:415–433.
- Jonas DE, Amick HR, Feltner C, et al. Screening for obstructive sleep apnea in adults: an evidence review for the U.S. Preventive Services Task Force. Evidence Synthesis No. 146. AHRQ Publication No. 14-05216-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; 2017. www.uspreventiveservicestaskforce.org/Page/Document/final-evidence-review152/obstructive-sleep-apnea-in-adultsscreening. Accessed May 2, 2017.
- Kapur VK, Auckley DH, Chowdhuri S, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med 2017; 13:479–504.
- Patel SR, White DP, Malhotra A, Stanchina ML, Ayas NT. Continuous positive airway pressure therapy for treating sleepiness in a diverse population with obstructive sleep apnea: results of a meta-analysis. Arch Intern Med 2003; 163:565–571.
- American Academy of Sleep Medicine. International Classification of Sleep Disorders, 3rd ed. Darien, IL: American Academy of Sleep Medicine; 2014.
- Kapur V, Strohl KP, Redline S, Iber C, O'Connor G, Nieto J. Underdiagnosis of sleep apnea syndrome in U.S. communities. Sleep Breath 2002; 6:49–54.
- Chen X, Wang R, Zee P, et al. Racial/ethnic differences in sleep disturbances: the Multi-Ethnic Study of Atherosclerosis (MESA). Sleep 2015: 38:877–888.
- Redline S, Sotres-Alvarez D, Loredo J, et al. Sleep-disordered breathing in Hispanic/Latino individuals of diverse backgrounds. The Hispanic Community Health Study/Study of Latinos. Am J Respir Crit Care Med 2014; 189:335–344.
- Wilson JMG, Jungner G. Principles and practice of screening for disease. Geneva: WHO; 1968. www.who.int/ionizing_radiation/ medical_radiation_exposure/munich-WHO-1968-Screening-Disease. pdf?ua=1. Accessed May 2, 2017.

- Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol 2013; 177:1006–1014.
- Stecker T, Sparks S. Prevalence of obese patients in a primary care setting. Obesity (Silver Spring) 2006; 14:373–376.
- 13. Zhao YY, Wang R, Gleason KJ, et al; BestAIR Investigators. Effect of continuous positive airway pressure treatment on health-related quality of life and sleepiness in high cardiovascular risk individuals with sleep apnea: Best Apnea Interventions for Research (BestAIR) Trial. Sleep 2017; Apr 17. doi: 10.1093/sleep/zsx040. [Epub ahead of print].
- Punjabi NM, Caffo BS, Goodwin JL, et al. Sleep-disordered breathing and mortality: a prospective cohort study. PLoS Med 2009 Aug;6(8) e1000132. doi: 10.1371/journal.pmed.1000132. Epub 2009 Aug 18.
- Chobanian AV, Bakris GL, Black HR, et al. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA 2003; 289:2560–2572.
- Schein AS, Kerkhoff AC, Coronel CC, Plentz RD, Sbruzzi G. Continuous positive airway pressure reduces blood pressure in patients with obstructive sleep apnea; a systematic review and meta-analysis with 1000 patients. J Hypertens 2014; 32:1762–1773.
- He J, Whelton PK. Elevated systolic blood pressure and risk of cardiovascular and renal disease: overview of evidence from observational epidemiologic studies and randomized controlled trials. Am Heart J 1999; 138:211–219.
- McEvoy RD, Antic NA, Heeley E, et al. CPAP for prevention of cardiovascular events in obstructive sleep apnea. N Engl J Med 2016; 375:919–931.
- Javaheri S, Barbe F, Campos-Rodriguez F, et al. Sleep apnea: types, mechanisms, and clinical cardiovascular consequences. J Am Coll Cardiol 2017: 69:841–858.
- Fu Y, Xia Y, Yi H, Xu H, Guan J, Yin S. Meta-analysis of all-cause and cardiovascular mortality in obstructive sleep apnea with or without continuous positive airway pressure treatment. Sleep Breath 2017; 21:181–189.

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