many hours before sleep onset may mitigate the detrimental effects that increases in loop gain have on apnea severity. However, further work is required to determine if other forms of plasticity (long-term facilitation of upper airway muscles) that could mitigate apnea will be ineffective if administered many hours before sleep.

Another issue not addressed in the commentary is the need to maintain a consistent dose of mild intermittent hypoxia. The inability to maintain a consistent dose within or across days of therapy will clearly lead to inconsistent outcome measures. In our study, we tightly regulated the partial pressure of end-tidal oxygen and consequently oxygen desaturation by blending in 100% oxygen during the hypoxic exposures (average oxygen desaturation = 88.14% $\pm$ 0.69%). This consistency is not attainable if an individual inhales from an air source with a lower fractional concentration of oxygen or 100% nitrogen without the administration of supplemental oxygen. If uncontrolled, oxygen saturation will vary between episodes and often will decline beyond the intended target of mild oxygen desaturation. This is an important consideration for clinical application, as the inability to control the intensity of the hypoxic exposure will expose patients to highly varying degrees of oxygen desaturation. The uncontrolled desaturation to severe oxygen desaturation could lead to negative clinical outcomes. Thus, we caution against using a protocol with a fixed hypoxic duration when degrees of oxygen desaturation cannot be consistently maintained.

Overall, we appreciate the commentary and support from Chen and colleagues. We believe the issues the authors addressed are practical and will be solved in time. Ultimately, solving these issues will lead to larger multisite clinical trials to gauge the therapeutic effectiveness of mild intermittent hypoxia. ■

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Gino S. Panza, M.A., Ph.D.
Shipra Puri, M.P.T., Ph.D.
Ho-Sheng Lin, M.D.
M. Safwan Badr, M.D., M.B.A.
Jason H. Mateika, M.S., Ph.D.*
John D. Dingell Veterans Affairs Medical Center
Detroit, Michigan

and

Wayne State University School of Medicine
Detroit, Michigan

On behalf of all the authors

ORCID ID: 0000-0002-0228-9843 (G.S.P.).

*Corresponding author (e-mail: jmateika@med.wayne.edu).

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Clinical Implications of Obstructive Sleep Apnea Diagnostic Misclassification

To the Editor:

We have read with interest the study recently published in the *Journal* by Lechat and colleagues (1), which highlights the significant variability in the results obtained from consecutive sleep studies for OSA diagnosis and severity. According to the conclusions of this study, up to 20% of patients are misclassified in terms of their severity of OSA (on the basis of the apnea–hypopnea index [AHI]) if they only undergo a sleep study during 1 single night (the most common clinical practice). Although there are some other studies on this topic, even a recent meta-analysis (2, 3), it is really necessary to congratulate the authors for the effort made in their study to analyze an average of 170 consecutive sleep tests in more than 67,000 individuals.

However, we think it is very important to answer two additional questions to assess the extent to which these results have a relevant clinical impact and can help clinicians to better manage their patients from both a diagnostic and therapeutic viewpoint.

On the one hand, we have to assume that the cutoff points in the AHI usually used to classify the severity of OSA are, to a certain extent, arbitrary, as the impact of OSA or the need for continuous positive airway pressure (CPAP) treatment depends not only on the AHI value but also on other circumstances, such as the patient's clinical characteristics or the outcome analyzed (4). Apart from the misclassification of patients owing to sleep test variability based on

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the AHI value, the really important question from a clinical viewpoint would be this: In what percentage of cases could this variability lead physicians to change their therapeutic decision (e.g., the indication of CPAP or alternative treatments)? To make this calculation, the authors would need access to individual patients' clinical data. We do not know how many of the studied patients were treated with CPAP (or alternatives), but even without this information, the authors could make an estimate based on the indications for treatment specified in the different international guidelines (5).

On the other hand, the authors could offer additional clinically relevant information by assessing the minimum number of consecutive sleep studies needed to minimize their variability and thus reduce costs. The authors observe that the more sleep tests that are performed, the more the AHI stabilizes, according to an analysis of the different areas under the receiver operating curve (ROC) curves at different moments in time. Thus, it can be seen that, although the variability was very high in the first days, it was much lower after 1 week and even more so after 2 weeks, although the results obtained on Days 7 and 14 were very similar. The authors could calculate the relevant differences between the various areas under the ROC curves from clinical and statistical viewpoints. This information would be of enormous clinical relevance, as it would indicate the minimum number of days required for sleep tests to obtain an optimal balance between the least variability that would allow a minimum number of clinically acceptable misclassifications (and, above all, a minimum number of relevant therapeutic changes) and lower costs, less time to make an accurate diagnosis, and fewer resources.

Therefore, we believe that it would be very interesting and enriching for the study, and for clinicians who care for patients with OSA, if the authors could contribute these suggested new analyses to their already excellent study. ■

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Miguel Angel Martinez-Garcia, M.D.*
Hospital Universitario y Politécnico La Fe
Valencia, Spain

and

Instituto de Salud Carlos III
Madrid, Spain

Grace Oscullo, M.D.
Jose Daniel Gómez-Olivas, M.D.
Hospital Universitario y Politécnico La Fe
Valencia, Spain

ORCID ID: 0000-0002-7321-1891 (M.A.M.-G.).

*Corresponding author (e-mail: mianmartinezgarcia@gmail.com).

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How Many Nights Are Really Needed to Diagnose Obstructive Sleep Apnea?

To the Editor:

We read with great interest the report by Lechat and colleagues (1) on characterizing the prevalence, variability, and diagnostic misclassification of obstructive sleep apnea (OSA) using multinight testing. The authors are to be commended on leveraging observations from the largest community-based sample with home recordings to address an issue of immense clinical relevance. The amassed data are impressive given the number of people included and the volume of nocturnal data used to describe the variability and misclassification of OSA. The authors were indeed crafty in using crowdsourced data from scalable technology and have thus paved the way for future studies that can leverage the ongoing explosive growth in sensors. Without doubt, the report by Lechat and colleagues (1) adds to the accepted notion that one night of monitoring, which is common in clinical decision making, is insufficient to case identify and classify OSA severity. Because the data on OSA diagnosis were derived at home, the issues of variability and misclassification, a phenomenon that is well known with in-lab studies, has been further addressed in the home setting (2).

Despite the many valuable insights, however, their report also raises several issues. First, the terminology used to describe the prevalence, variability, and misclassification uses "OSA" without further qualification. In their methods, the authors state OSA was defined as an apnea–hypopnea index (AHI) of ⩾15 events/h. However, the qualifier, " … at least moderate severity … ", does not consistently permeate the report, particularly with regard to the global estimate of OSA prevalence. It is important to recognize that the estimate of 22.6% is for moderate to severe OSA and not just OSA. This is not a trivial issue, because the prevalence of OSA of any severity will be much higher than 22.6%. In fact, analyses presented in Figure 2 show that data on prevalent mild, moderate, and severe

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