OSA from the contactless sensor are available. Given that the previous validation study (3) and the supplementary data comparing the contactless sensor and polysomnography showed no difference in AHI between the two tests, reporting the prevalence of different OSA categories using AHI thresholds would be of value.

Second, the authors have opted to use the mean AHI of all available nights to calculate the reference AHI against which the reliability of a subset of the nights is compared. It could be easily argued that the median AHI may be a better estimator of central tendency than the mean AHI, particularly if a person has extreme AHI values that may result from factors such as being in the supine position only or consumption of alcohol on any particular night. A possible alternative to the median could be the mode of the AHI distribution from each person. Although we are not proponents, an argument could also be made that the "diagnosis of OSA" should be based on the highest AHI value. Did the authors examine whether the prevalence and misclassification of OSA would be different if the median or mode were used for the reference AHI instead of the mean?

Third, the data on operating characteristics of multinight testing suggest that the increase in positive predictive and the drop in negative predictive values when comparing 7 with 14 nights is relatively small. Thus, what is the minimum number of nights of monitoring necessary to reliably estimate AHI in clinical practice within a ±5% margin of error? Having such information would help change the paradigm of clinical testing in which 1 night is always used despite the capability for multinight testing. It is time that multinight testing became mainstream practice, because the body of empirical evidence on AHI variability is unquestionable (4). One night is just not enough! ■

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Reply to Martinez-Garcia *et al*. and to Abreu and Punjabi

From the Authors:

We thank Dr. Martinez-Garcia and colleagues, as well as Drs. Abreu and Punjabi, for their positive comments and thoughtful insights on our recent research on multinight prevalence and the potential impact of night-to-night variability in obstructive sleep apnea (OSA) severity on misdiagnosis (1). Some of the clinically relevant discussion points raised have been eloquently outlined in the accompanying editorial by Dr. Simonds (2). To provide further insights on this important topic as outlined in the letters to the editor, additional commentary and key analyses are provided below.

Use of Apnea–Hypopnea Index of 15 or More Events per Hour

Clinical guidelines indicate that an apnea–hypopnea index (AHI) of ⩾15 events/h even in the absence of symptoms is sufficient for the diagnosis of OSA and initiation of therapy (3). Community-based cohort studies also indicate that an AHI of ⩾ 15 events/h is associated with adverse cardiometabolic outcomes (4). Thus, the focus of our analyses was primarily on a cutoff of ⩾ 15 events/h. However, prior OSA prevalence estimates have used different AHI thresholds, including as low as 5 events/h (5). To allow for comparison with these findings, OSA prevalence estimates per country based on an AHI of ⩾ 5 events/h from our data are provided in Table 1. The estimated global prevalence of ∼55% based on this definition is higher than the estimated ∼37% in the study by Benjafield and colleagues (5). This may be, at least in part, owing to selection bias of the current consumer sample. Interestingly, however, our estimates appear more consistent across countries, which may be an advantage of the standardized, objective, and long-term data collection approach.

Mean versus Median AHI

We elected to use mean AHI as the reference value rather than median values, which could potentially yield different results. However, this was not the case, with comparable misclassification rates when mean versus median values were used. For example, 21% of OSA diagnoses were estimated to be false negatives on a single-night study based on mean AHI as the reference versus 18.4% (SD = 0.15) for median AHI. Similarly, receiver operating curves, F1-scores, and detection-error curves remained comparable when mean or median was used as the reference AHI. Ultimately, the optimal multinight OSA severity metrics will need to be determined empirically on the basis of predictive performance in relation to health outcomes and/or treatment response.

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Table 1. Obstructive Sleep Apnea (Apnea–Hypopnea Index of >5 events/h) Prevalence in Countries with More Than 300 Participants

	AHI > 5 events/h	
OSA Prevalence (%)	**Current Study (1)**	**Benjafield *et al.* Study (5)**
Japan	35.7	32.7
China	40.5	23.6
Netherlands	53.4	49.0
Australia	52.7	24.5
Canada	51.8	24.5
Norway	53.7	22.1
Finland	51.7	50.4
United States	52.5	33.2
Poland	59.2	35.1
Sweden	54.2	17.0
United Kingdom	57.8	24.5
France	57.3	72.1
Portugal	58.6	17.0
Belgium	58.5	30.4
Switzerland	56.1	72.4
Denmark	56.5	48.9
Spain	61.0	35.2
Austria	60.6	48.7
Italy	60.9	20.5
Germany	62.4	60.1
Total, mean (95% confidence interval)	54.7 (51.7–57.8)	37.1 (29.1–45.1)

Definition of abbreviations: AHI = apnea–hypopnea index; OSA = obstructive sleep apnea.

Table 2. Confusion Matrix between Obstructive Sleep Apnea Severity Categories Determined via a 1-Night Apnea–Hypopnea Index Diagnosis versus the Reference Severity Categories

		1-night AHI			
		No OSA	**Mild**	**Mod**	**Sev**
Reference	No OSA	**87**	13	0*	0*
	Mild	26	**59**	14*	1*
	Mod	2†	25†	**57**	16
	Sev	0†	2†	17	**81**

Definition of abbreviations: AHI = apnea–hypopnea index; Mod = moderate; OSA = obstructive sleep apnea; Sev = severe.
Mean AHI over 28 days of recording. Values were constrained to data collected in March 2021 (N = 32,775 participants) to imitate the clinical scenario more closely. Hence, probability values differ slightly to Figure 2 in the original manuscript. OSA severity categories were defined using standard clinical cutoffs of the mean AHI (<5 = no OSA, ⩾5 and <15 = mild, ⩾15 and <30 = moderate, and >30 events/h sleep = severe OSA).
*Upper right and †bottom left corners represent potential over- and undertreatment, respectively, if clinical decision is based solely on an AHI of >15 events/h.

How Many Nights Are Needed for Clinical Decision Making?

Attempting to address how often a clinician may change their treatment decision on the basis of multi- versus single-night diagnostic data is an important question. This is somewhat challenging to comprehensively address in the current dataset in the absence of clinical information on sleepiness and other key symptoms of OSA. Nonetheless, assuming that a decision to treat is based on an AHI of ⩾ 15 events/h regardless of symptoms, the goal would be to minimize *1*) the number of patients with moderate and severe OSA misclassified as having "mild" or "no OSA" and *2*) the number of patients with no or only mild OSA on most nights misclassified as having moderate to severe OSA from a single-night assessment (i.e., minimize the percentage of patients in the bottom left and top right squares of the confusion matrix in Table 2). Based on a 1-night diagnosis, the misclassification percentage of patients with moderate to severe OSA is ∼29%. Furthermore, ∼15% of people with no OSA or mild OSA would be incorrectly classified as having moderate to severe OSA. Thus, these results suggest that almost one-third of patients may be undertreated and 15% may be overtreated on the basis of a single-night AHI value.

Increasing the number of nights decreases misclassification probability (Figure 1A). Undertreatment probability drops to 14% and overtreatment to 6% with a 5-night diagnosis. This equates to an approximately twofold increase in overall diagnostic performance. The optimal number of nights required is therefore a tradeoff between time, the cost of recording, and the precision required. The main "inflexion" of the number of nights versus diagnostic confidence curves occurs between 5 and 10 nights, after which there is only relatively small improvement in diagnostic performance (i.e., ∼8% under- and 4% overtreatment probability with 10 nights of monitoring). Similarly, the "inflexion point" for the overall diagnostic performance tended to be around 7 nights in our originally reported findings (1) (Figure E5).

To further estimate the number of nights required to yield a reliable AHI estimate, we compared the absolute difference between an X-average AHI night and the reference AHI (mean of 28 nights) (Figure 1B). On the basis of a 1-night AHI value, a single diagnostic night for a patient with mild OSA is estimated to vary by an average of 46%. For example, for a single-night AHI value of 10 events/h, the "true" mean AHI could be anywhere between ∼5 and 15 events/h. A 5-night average AHI value reduces the absolute difference to 20%. After 10 nights of monitoring in the same patient, the average AHI would be estimated to be between 9 and 11 events/h. Interestingly, the absolute difference (in %) is smaller for moderate and severe OSA. This suggests that the optimal number of nights required is likely to be patient specific. Indeed, patients with large AHI variability in the first 5 days may benefit from additional monitoring nights.

Utility of Mean Severity Scores

The above analysis assumes that OSA severity is best characterized based on mean severity, which may not be the complete story. As echoed by Dr. Simonds (2), there are several factors that can influence night-to-night variability in OSA, including body and head position during sleep, nonanatomical OSA endotypes, nasal resistance, and behavioral and lifestyle factors (6–10). For example, more time spent supine is associated with a greater AHI and likely contributes to night-to-night variability (11). More importantly, emerging evidence indicates that the degree of night-to-night variability in OSA severity impacts cardiovascular health, including atrial fibrillation (12, 13). Therefore, it may be in the patient's interest to not only quantify the

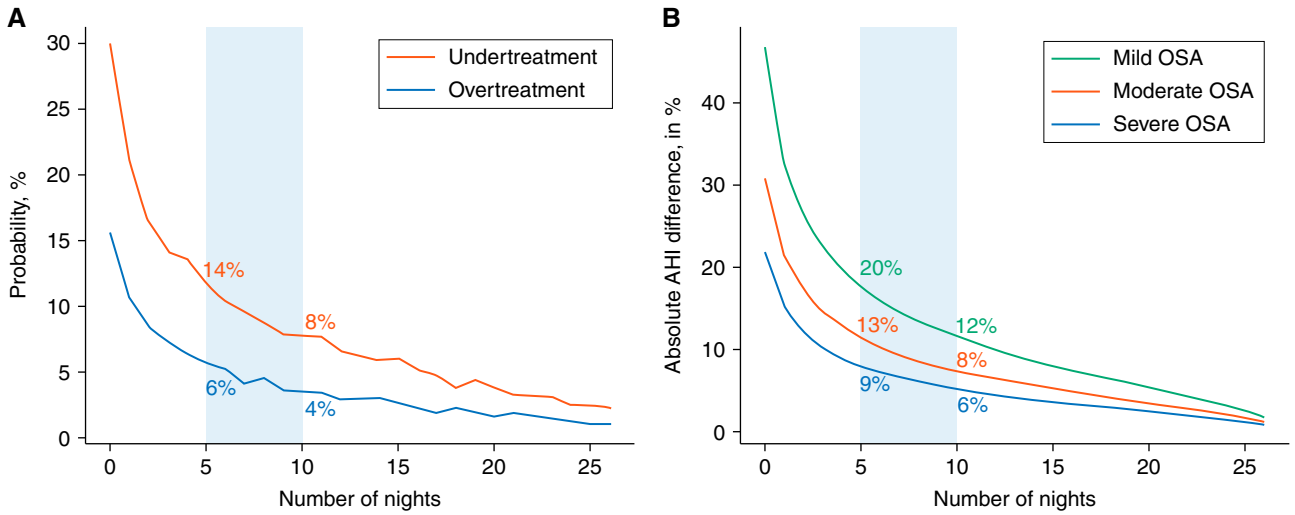

Figure 1. (*A*) Under- and overtreatment probability based on a variable number of nights monitoring. (*B*) Absolute difference (%) between the reference apnea–hypopnea index (AHI) and the average AHI value over X nights. The reference AHI was calculated as the mean AHI over 28 nights. Values were constrained to data collected in March 2021 ($N = 32{,}775$ participants) to imitate the clinical scenario more closely. OSA = obstructive sleep apnea.

"central tendency" of OSA severity but also its night-to-night variability.

Ultimately, the optimal number of nights for OSA diagnosis and management and the best technology options will need to be determined in appropriately designed randomized controlled trials in which patient benefits, cost-effectiveness, and patient acceptability are carefully considered. Initial discussions with the consumer engagement group at the Adelaide Institute for Sleep Health suggest that patients would be willing to undergo multinight noninvasive recording provided there was transparency as to why the data were being collected and appropriate privacy safeguards in place. However, patients may be unwilling to undergo full home sleep apnea tests for 7, 14, or 28 days. Patient perspectives should be carefully considered in future trials, as there may also be a financial and personal disincentive to seek treatment if the diagnostic process is too burdensome for patients. Ultimately, multinight home studies to help more effectively triage and manage OSA diagnosis, along with in-lab confirmatory studies and for complex cases where indicated, could help to improve diagnostic precision and clinical management. Noninvasive multinight assessments of sleep and OSA in the home to support current clinical diagnosis and management practices may also provide benefits via greater access to care over current routine practice and better characterization of OSA severity to inform OSA treatment trials. These new data build upon the findings of others (e.g., Reference 14) that clearly indicate that the more nights the better! ■

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