

Pragmatic Validation of Home Portable Sleep Monitor for diagnosing Obstructive Sleep Apnea in a non-referred population: *The ELSA-Brasil study*

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ABSTRACT

Objective: Polygraphy (PG) is an attractive alternative for diagnosing obstructive sleep apnea (OSA) in patients with high pre-test probability. However, several patients may not present typical symptoms. In this scenario, it is unclear the performance of PG for diagnosing OSA in non-referred populations to sleep laboratories. **Methods:** Data from participants of the ELSA-Brasil cohort were used for this analysis. We performed an overnight home PG (Embletta Gold™) synchronized with a wrist actigraphy (Actiwatch model 2™). The validation strategy comprised three scorings from each participant: 1) Original scoring (PG): Routine scoring using data from the exclamation button mark to define “analysis start” and “analysis stop”; 2) Scoring using actigraphy data (PG+actigraphy): total sleep time defined by the actigraphy data; 3) Scoring using diaries (PG+diary): “analysis start” and “analysis stop” based on the diaries. Bland-Altman plots were generated to assess the agreements (Kappa) between each scoring strategy. **Results:** A total of 300 participants were included in the final analysis (45% males, mean age: 48±8 years). The frequency of OSA using the PG score was 27.3%. Despite small differences in the OSA severity index, we obtained a high concordance of AHI comparing the PG vs. PG+actigraphy (Kappa: 0.95) as well as PG+diary vs. PG+actigraphy (Kappa: 0.96). No significant changes in the OSA classification (mild, moderate and severe) were observed in the 3 protocols. **Conclusion:** Using a pragmatic approach to address OSA at home, our results suggest that PG is a useful tool for OSA diagnosis even in subjects not referred to sleep studies.

Keywords: Sleep Apnea; Diagnosis; Polysomnography; Wrist.

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INTRODUCTION

Obstructive Sleep Apnea (OSA) is a clinical condition characterized by repetitive upper-airway obstructions during sleep promoting sleep fragmentation, intermittent hypoxia and intrathoracic pressure reduction¹. OSA is common in the general population²⁻⁴, reaching one third of adults in a recent population study using contemporaneous definitions of apnea and hypopnea⁴. Consistent evidence from the literature pointed that OSA is associated with increased risk for metabolic and cardiovascular consequences⁵⁻⁸.

In clinical practice, however, OSA is still underdiagnosed⁹. The reasons for this unrecognition are multiple and include: 1) lack of medical background in sleep medicine; 2) lack of typical symptoms in a significant proportion of patients; 3) the gold standard method for diagnosing OSA, namely polysomnography, has limited access, long waitlists¹⁰ and significant costs¹¹. In this scenario, portable sleep monitors, also called polygraphy (PG) have gained growing interest to be used as an attractive alternative to surpass the main above limitations. PGs have been extensively validated against polysomnography in patients with high clinical probability of OSA¹²⁻¹⁵. However, whether PGs can be used for diagnosing OSA in non-referred populations is unclear. From an epidemiologic perspective, it is important to understand if cohorts evaluating the consequences of OSA may have benefits in using pragmatic and feasible forms of OSA diagnosis in the home environment¹⁶. In addition, there is a growing interest for wide spreading sleep evaluation using simplified tools¹⁷.

In the present study, we selected non-referred participants derived from the ELSA-Brasil cohort to compare the OSA diagnosis agreement using PGs and wrist actigraphy simultaneously. This approach is approved by the AASM as a validated method for estimating the total sleep time when polysomnography is not available¹⁸. We hypothesized that home PG scoring or PG scoring using diary data had good agreement in diagnosing OSA (and the related severity classifications) compared to the PG coupled with actigraphy (the reference group) in a non-referred population.

METHODS

The local ethical committee approved the study and all participants provided an informed consent.

This is an ancillary to the ELSA-Brasil study, which cohort profile and routines were previously reported¹⁹⁻²¹. Briefly, all active or retired employees (aged 35–74 years) of the six institutions (Federal Universities of Bahia, Espírito Santo, Minas Gerais and Rio Grande do Sul; University of São Paulo, and Oswaldo Cruz Foundation) were eligible for the study. Exclusion criteria were current or recent (<4 months) pregnancy, intention to quit working at the institution in the near future, severe cognitive or communication impairment, and, if retired, residence outside of a study center's corresponding metropolitan area. As previously described¹⁶, the sleep approach in ELSA-Brasil was conducted in the participants of the Sao Paulo site, and the only pre-defined exclusion criterion is the refuse to perform sleep studies.

Overnight Home Sleep Study

Sleep studies were performed using the Embletta Gold (Natus Medical Inc., Ontario, Canada) a standardized level-3 portable diagnostic device including the following outputs: nasal airflow (nasal pressure transducer), thoraco-abdominal movements (inductive respiratory bands), arterial oxygen saturation (pulse oximetry), snoring episodes (derived from the integrated pressure transducer), and body position¹⁶. This device has an exclamation point button to report events. The participants were actively instructed to push the button when they turn out the lights to sleep and wake-up to help physicians to report total recording time. The Embletta system has been validated in patients with high suspicion of OSA¹². All studies are being manually scored by an expert in sleep medicine. The respiratory events are being scored according to the American Academy of Sleep Medicine (AASM) 2012 criteria²² as follows: An apnea was defined as a $\geq 90\%$ decrease in airflow from the baseline value for ≥ 10 seconds. Hypopnea was defined as $\geq 30\%$ drop of airflow lasting at least 10 seconds with a $\geq 3\%$ O₂ drop. Apneas were further classified as obstructive or central based on the presence or absence, respectively, of respiratory-related chest-wall movement. The sum of apnea and hypopneas per hour determined the apnea-hypopnea index (AHI). We excluded participants with predominantly (>50%) central apnea events. Considering that growing evidence suggesting that mild OSA is not associated with increased cardiovascular risk²³, we decided for classifying OSA using a more conservative AHI cut-off of ≥ 15 events/hour. However, we performed a sub-analysis using the standard classification of mild (AHI 5-14.9), moderate (AHI 15-29.9) and severe OSA (AHI ≥ 30 events/h).

Wrist actigraphy

Participants were instructed to wear the actigraphy (Actiwatch model 2,™ Philips Respironics) in the same night of the sleep monitor recording. As previously described¹⁶, participants were asked to press the event marker button on the actigraph each night when they began trying to fall asleep and again when they got out of bed each morning. A validated algorithm was used to calculate sleep duration (calculated as the total time of the epochs classified as sleep between sleep start and sleep end), fragmentation index (the number of interruptions of sleep by physical movement calculated as $100 \times$ the number of groups of consecutive mobile 30-s epochs by the total number of immobile epochs) and sleep efficiency ($100\% \times$ sleep duration/the time between bedtime and rise-time).

Diary

We instructed all participants for filling diaries reporting routine events, including subjective sleep time.

Validation strategy

The time of portable sleep study and wrist actigraphy were synchronized in the respective softwares. The validation strategy comprised three scorings from each participant: 1) Original scoring (PG): Routine scoring using data from the exclamation button

mark to define “analysis start” and “analysis stop”. If the participant did not press the button, we defined “analysis start” when all traces were working properly and the body position sensor suggested the participant is lying in the bed; for the “analysis stop”, we defined the first period of the standing up position and lack of traces suggesting that the device was removed as recommended in the instructions; 2) Scoring using diaries (PG+diary): In this case, “analysis start” and “analysis stop” were based on the related events reported in the diaries; 3) Scoring using actigraphy data (PG+actigraphy): the “analysis start” and “analysis stop” were defined by the timing suggested by the actigraphy as sleep start and stop, respectively. A same trained researcher performed the original (PG) scorings of all participants while another researcher performed two new reports using diary data (PG+diary) or actigraphy data (PG+actigraphy) to recalculate the AHI and the related hypoxemia variables. There two new reports used the same respiratory events but the second researcher did not check the sleep report provided by the original score.

Statistical analysis

Continuous variables with normal distribution were presented as mean±SD. For skewed variables, medians and interquartile ranges were reported and Kruskal–Wallis tests were performed. Categorical variables were presented as frequencies and analyzed using chi-square tests. Bland–Altman plots and Pearson tests were generated to assess agreement (Kappa) and correlations, respectively, of PG alone and PG+diary as compared to the PG+actigraphy results. In addition, we compared the proportion of participants with no, mild, moderate and severe OSA using these three strategies.

Finally, we performed a comparison of participants that did press or not the button mark to define “analysis start” and “analysis stop” (not only for mimicking the real practice but also to extrapolate our findings to PGs that do not have available button mark to define “analysis start” and “analysis stop”). A p value of <0.05 was considered statistically significant (2-sided).

RESULTS

For this study, we initially recruited consecutive 440 participants from the ELSA-Brasil who performed the portable sleep monitor and the wrist actigraphy in a synchronized way. After exclusions, a total sample of 300 participants were included in the final analysis (please see Figure 1 for details).

Characteristics of participants were reported on Table 1. Overall, our sample comprised middle-age and overweight participants. Almost half of them were men and two thirds of them were white. Twenty-seven percent of them had OSA. Compared to no OSA, participants with OSA were older, had higher frequency of men, presented higher levels of adiposity parameters as well as higher frequencies of hypertension, diabetes and current smoking. The wrist actigraphy data showed that OSA participants had higher sleep latency, higher time in minutes of wake after sleep onset (WASO), higher frequency of number of awakenings (AWAKE), and lower sleep efficiency than no OSA group.

Table 2 describes the comparisons of sleep data using the PG, PG+diary and PG+actigraphy scores. The total time for analysis was lower in the PG+actigraphy as compared to the remaining groups. There was a trend for lower AHI in the PG+actigraphy

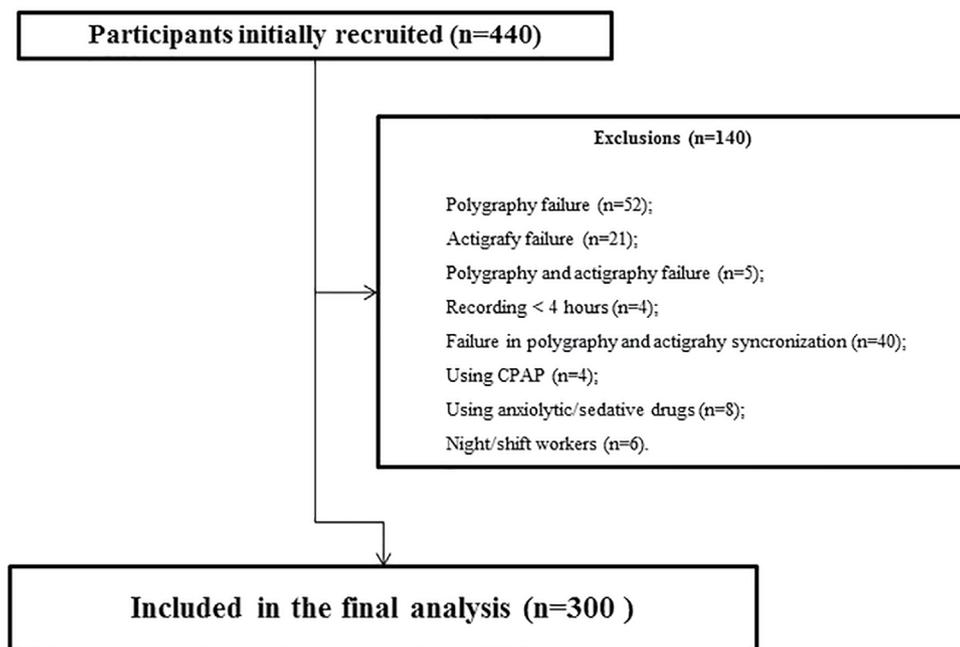


Figure 1. Flow chart.

Table 1. Characteristics of the participants.

Characteristics	Total N=300	No OSA N= 218 (72.7%)	OSA N= 82 (27.3%)	p value
Demographic and anthropometric data				
Male sex, n (%)	135 (45)	82 (37.6)	53 (64.6)	<0.001
Age, years, mean (SD)	48 (8.3)	47 (7.8)	50 (8.9)	0.001
White (self-reported race), n (%)	206 (68.7)	154 (71)	52 (63.4)	0.511
Body-mass index, kg/m ² , mean (SD)	26.8 (4.6)	26 (4.5)	28.9 (4.5)	<0.001
Classification of BMI, n (%)				
Normal	62 (20.7)	96 (44.1)	13 (15.9)	
Overweight	129 (43)	85 (39)	44 (53.7)	<0.001
Obesity	109 (36.3)	37 (17)	25 (30.5)	
Neck circumference, cm, mean (SD)	35.9 (3.7)	35.1 (3.4)	37.9 (3.6)	<0.001
Waist circumference, cm, mean (SD)	88.8 (11.9)	85.8 (11)	96.6 (10.8)	<0.001
Hypertension, n (%)	65 (21.7)	37 (17)	28 (34.1)	0.001
Diabetes, n (%)	48 (16)	24 (11)	24 (29.3)	<0.001
Current Smoking, n (%)	35 (11.7)	22 (10.1)	13 (16)	0.159
Depression, n (%)	16 (5.3)	14 (6.5)	2 (2.5)	0.175
Excessive daytime sleepiness, n (%)	105 (35)	83 (38.1)	22 (26.8)	0.069
Sleep data (Wrist actigraphy)				
Sleep time, min, mean (SD)	396.5 (57.7)	396.9 (58.1)	395.5 (55.3)	0.839
Sleep time <6 hours, n (%)	74 (24.7)	55 (25.2)	19 (23.2)	0.712
Sleep latency, min, mean (SD)	21 (14.6)	19.7 (14)	24.4 (15.7)	0.013
Sleep efficiency, min, mean (SD)	82.8 (6.4)	83.6 (6.2)	80.7 (6.5)	<0.001
WASO, min, mean (SD)	44 (18.9)	41.1 (17.2)	51.8 (21.1)	<0.001
AWAKE, n, mean (SD)	32.7 (11.2)	31.3 (10.2)	36.3 (12.9)	<0.001

OSA: Obstructive Sleep Apnea

BMI: Body-mass index

WASO: Wake after sleep onset

AWAKE: Number of awakenings

Table 2. Comparisons of sleep data using the original scoring, combined with actigraphy data and using the diary.

Sleep study characteristics	PG	PG + diary	PG + actigraphy	p value*
Record duration, median (IQR)	436(383-483)	430(386-480)	413(359-459) *	<0.001
AHI, events/hours, median (IQR)	8.9 (4.1-16.2)	8.9 (4.1-16.7)	8.8 (4.1 -16.5)	0.058
Baseline SpO ₂ %, median (IQR)	94.4 (93.2-95.5)	94.4 (93.2-95.5) *	94.4 (93.2-95.5)	<0.001
Lowest SpO ₂ %, median (IQR)	87 (83-90)	87 (82-90)	87 (83-90)	0.004
Time SpO ₂ <90%, median (IQR)	0.2 (0-2.1) &	0.2 (0-2.3)	0.2 (0-2.2) #	<0.001
Supine AHI (events/hours), median (IQR)	14.6 (4.9-29.5)	14 (5-29.8)	14.3 (4.5-29.8) *	<0.001
Supine events, median (IQR)	28 (10-61)	28 (10-60)	26 (8-55)	<0.001

IQR: Interquartile range. Some variables presented identical median and IQR but have significant variabilities among the groups.

* p<0.05 vs. remains groups

p<0.05 vs. PG

& p<0.05 vs. PS + actigraphy

group but all of them were in the mild OSA range. Significant differences were observed in the hypoxemic parameters, but all absolute values were very similar, suggesting no clinical relevance. Supporting this concept, the percentages of no OSA, mild, moderate and severe OSA were similar in the three scores analysis (Figure 2).

Figures 3 and 4 reported the agreement and correlation of AHI in each method. Using PG+actigraphy as the reference group, a high agreement (Figure 3A) and correlation (Figure 3B) were observed for the comparisons of AHI derived from PG

vs. PG+actigraphy as well as in the comparisons of AHI derived from PG+diary vs. PG+actigraphy (Figures 4A and 4B).

Finally, we also compared the AHI in patients that did (n=241, 80%) and did not (n=59, 20%) press the Embletta Gold™ button to sign the sleep onset and sleep end. We found no differences in the performance and OSA severity classification among those who used versus not used this particular Embletta Gold™ function, suggesting that our result may be applied for all type 3 monitors (please see supplemental file).

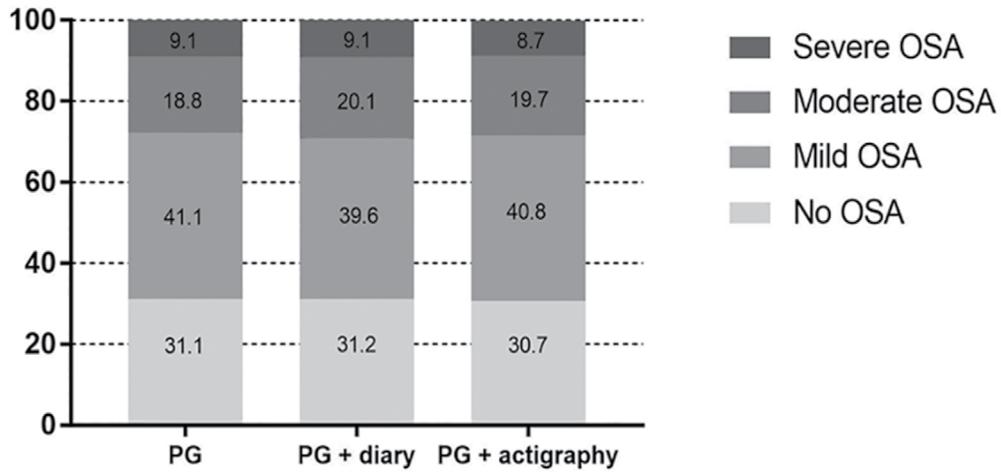


Figure 2. Frequency of normal, mild, moderate and severe obstructive sleep apnea (OSA) using the PG, PG + diary and PG + actigraphy analysis.

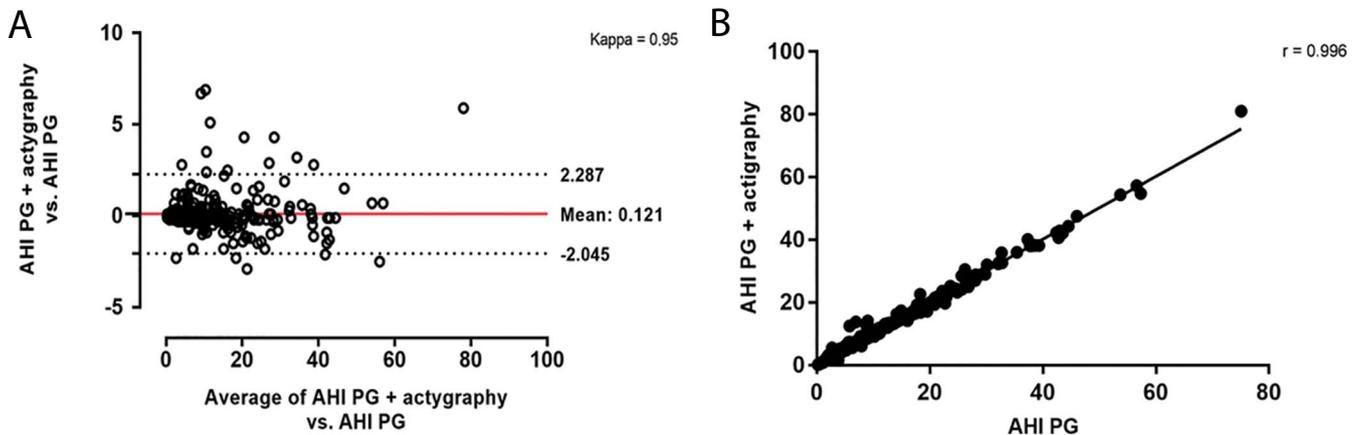


Figure 3. Bland-Altman (A) and correlation (B) between the apnea-hypopnea index (AHI) using the PG versus PG + actigraphy data.

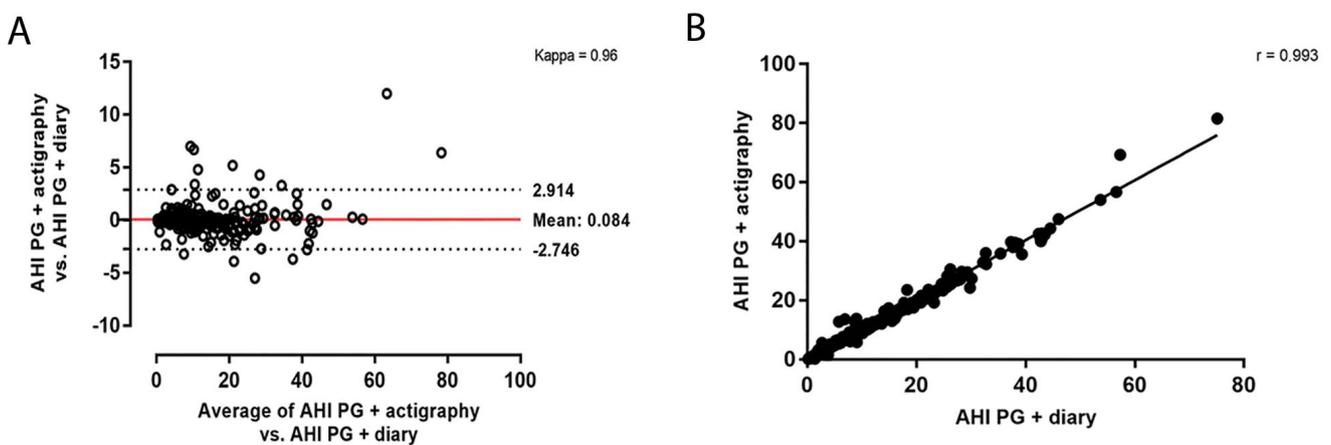


Figure 4. Bland-Altman (A) and correlation (B) between the apnea-hypopnea index (AHI) using the PG + diary versus PG + actigraphy data.

DISCUSSION

This is one of the largest studies devoted to validating portable sleep monitors. The novelty here is the validation of this simplified method for diagnosing OSA in a non-referred population using a pragmatic approach (home PG coupled with actigraphy as a reference group). We found an excellent AHI agreement and correlation after performing three different scoring strategies. Despite significant differences in some sleep parameters related to the OSA severity, these findings seem to be not clinically relevant as suggested by the lack of differences in the proportion of each OSA severity classification. Taken together, our results pointed the home PG as a feasible strategy to diagnose OSA even in those participants not referred to sleep studies.

In patients with high clinical suspicion for OSA, several portable sleep monitors have been extensively validated against polysomnography¹²⁻¹⁴. The correlation values varied from 0.890 to 0.997. This variation may be partially explained by differences in the protocols, including simultaneous versus no simultaneous polysomnography recording. It is important to mention that validation studies in the sleep laboratory as well as excessive monitoring using two methods (including two nasal cannulas) in the same night may compromise the original sleep quality and quantity. For our knowledge, a single study used only one nasal cannula with a connector for sending the signal for both sleep monitor and polysomnography¹⁴. In our study, we decided for using a simple strategy trying to resemble the normal sleep pattern using a wrist actigraphy coupled to the sleep monitor. The high agreement and correlation between the three strategies may contribute to expand the indications for using sleep monitors even in a non-referred population. The potential utility of our findings relies on the fact that several patients may not present typical symptoms of OSA. In addition, the most used questionnaires have only modest accuracy in screening OSA^{24,25}.

Therefore, pragmatic and feasible forms of OSA diagnosis ideally in the home environment may increase the awareness and treatment of this sleep-disordered breathing. In the same direction, we have observed a tremendous development of technology for monitoring vital parameters using smartphones, including sleep^{26,27}. The development and validation of apps for diagnosing OSA may be useful for OSA diagnosis in patients with no complex and comorbid conditions. Further studies in this research area are warranted.

Two interesting strategies of our study include: 1) the evaluation of having an available diary helping to define sleep start and ending in a subjective way; 2) the evaluation of having an actigraphy coupled with the PG. In clinical practice, it is not unusual to come across with patients that did not fill the diary. In our study, the rate of participants that did not have the diary report was low (partially explained by the fact that a significant proportion of them filled the diary at the time they dropped off the sleep monitor).

However, the performance of PG was similar in participants who filled or not the diary. Therefore, our results

underscore that the utility of the sleep monitor remains even in the lack of the diary data. The second interesting finding was the high agreement of the PG+actigraphy score compared to PG+diary. Our results also pointed to a no specific need of an actigraphy (already included in some devices) to validate the sleep monitor data. These findings may have clinical implications for simplifying the sources of several trademarks available for OSA diagnosis.

The present study has strengths and limitations to be discussed. The study used a large sample of consecutive participants performing sleep monitoring at home, since the sleep environment during polysomnography may not mimic real life. We carefully performed a detailed analysis of different scenarios (PG alone and combined with actigraphy and diary) as well as analysis of OSA severity classification in a blinded way. The following limitations deserve comments: 1) we did not use home polysomnography as the gold standard comparator. However, as previously mentioned, the actigraphy is an acceptable alternative for detecting sleep duration¹⁸; 2) due to our stringent protocol, we excluded almost 10% of patients that we were not confident about the time synchronization; 3) these results should be extrapolated with cautions for patients with significant comorbidities such as heart failure or chronic obstructive pulmonary disease.

In conclusion, home PG is useful for diagnosing OSA even in a non-referred population. Considering contemporary trends for using portable devices and wearable technologies to surpass the aforementioned obstacles of a formal polysomnography, this study may have implications not only for the ELSA-Brasil cohort but also for future portable and wearable device validations.

Abbreviations list

AASM: American Academy of Sleep Medicine
 AHI: Apnea-hypopnea index
 AWAKE: number of awakenings
 BMI: Body mass index
 ELSA: Longitudinal Study of Adult Health
 IQR: Interquartile range
 OSA: Obstructive Sleep Apnea
 PG: Polygraphy
 WASO: wake after sleep onset

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