Standardized List Evaluating Apnea (SLEAP): A comprehensive survey to define quality of life in OSA

AUTHORS:

Mohamed Abdelwahab MD PhD,[1-2] Mikhail Saltychev PhD,[3] Matt Lechner MD PhD,[4] Elahe Adibi MD,[1] Elizabeth Walker Wadsworth MD MSCR,[2] Thomaz Fleury MD PhD, [1] Abdelwahab Rakha MD PhD,[5] Yasser Khafagy MD PhD,[5] Ahmed Abdelfattah MD,[5] Ahmed A. Al-Sayed MD FRCSC, [1,6] Courtney Chou MD, [7] Ban Ali BDS MPH, [8] Stanley Liu MD DDS,[1] Clete Kushida MD FAASM, [9] Robson Capasso MD FAASM [1]

AFFILIATION

[1]Division of Sleep Surgery, Department of Otolaryngology–Head & Neck Surgery, Stanford University School of Medicine, Stanford, California.

[2] Division of Sleep Surgery, Department of Otolaryngology–Head & Neck Surgery, Medical University of South Carolina, Charleston, South Carolina.

[3] Department of Physical and Rehabilitation Medicine, Turku University Hospital and University of Turku, Turku, Finland

[4] UCL Cancer Institute and Academic Head and Neck Centre, UCL Division of Surgery and Interventional Science, University College London, London, UK

[5] Department of Otolaryngology, Mansoura University School of Medicine, Mansoura, Egypt.

[6] Department of Otolaryngology – Head & Neck Surgery, College of Medicine, King Saud University, Riyadh, Saudi Arabia

[7] Division of Sleep Surgery, Department of Otolaryngology–Head & Neck Surgery, Icahn School of Medicine at Mount Sinai, New York

[8]A.T Still University, Department of Public Health, Kirksville, Missouri

[9] Division of Sleep Medicine, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, California

KEYWORDS:

obstructive sleep apnea; sleep surgery; quality of life; patient-reported outcome measure; world health organization

WORD COUNT: 3000

CORRESPONDING AUTHOR:

Mohamed Abdelwahab, MD, PhD

Assistant Professor, Sleep and Facial Skeletal Surgery, Director

Department of Otolaryngology – Head & Neck Surgery (O-HNS)

Department of Oral and Maxillofacial Surgery

Medical University of South Carolina

Address: 135 Rutledge Avenue, MSC 550, Charleston, South Carolina, 29425, USA

E-mail: wahabm@musc.edu

CONFLICT OF INTEREST: None

FINANCIAL DISCLOSURE STATEMENT: None to disclose.

SHORT RUNNING HEAD: Standardized List Evaluating APneas (SLEAP)

CONTRIBUTIONS: Mohamed Abdelwahab: contributed to the design, conduct, analysis, and critical editing of the manuscript, original conception, Mikhail Saltychev: contributed to the design, conduct, analysis, and critical editing of the manuscript, Matt Lechner: contributed to the design, conduct, analysis, and critical editing of the manuscript, Elahe Adibi MD: contributed to the design, conduct, editing of the manuscript, Thomaz Fleury: contributed to the design, conduct, analysis, and critical editing of the manuscript, Abdelwahab Rakha MD: contributed to the design, conduct, analysis, and critical editing of the manuscript, Yasser Khafagy, Ahmed Abdelfattah: contributed to the design, conduct, editing of the manuscript, Ahmed A. Al-Sayed: contributed to the design, conduct, analysis, and critical editing of the manuscript, Courtney Chou: contributed to the design, conduct, analysis, and critical editing of the manuscript, Ban Ali: contributed to the design, conduct, analysis, and critical editing of the manuscript, Clete Kushida MD FAASM,[9] Stanley Liu MD DDS,[1] Robson Capasso MD FAASM [1] contributed to the design, conduct, analysis, and drafting of the manuscript.

Abstract

Objective:

To develop and validate a patient-reported outcome measure to evaluate the quality of life among patients with obstructive sleep apnea (OSA).

Study Design: prospective cohort study

Settings: tertiary referral center

Methods:

We developed a 15-item English questionnaire that was administered to 176 adults with OSA and 22 adult controls without symptoms of OSA in a tertiary sleep surgery clinic between June 2021 and December 2021. The internal consistency and test-retest reliability were measured using the Cronbach's alpha and the intraclass correlation coefficient, respectively. The two-sample Wilcoxon rank-sum (Mann-Whitney) test was applied to compare the two groups. Convergent validity of the test scores of the questionnaire were compared to previously validated outcome measures and objective sleep study outcomes using the Spearman correlation coefficient.

Results:

Of the 198 respondents (176 cases and 22 controls), 198/198 answered the questionnaire; 71% were men and 29% were women. The internal consistency was excellent with alpha of 0.92 (lower 95% CL 0.90). All the test-retest correlations were positive, significant, and strong ranging from 0.50 to 0.90. The differences between cases and controls were statistically significant for all the items and for the total score. The total score of the questionnaire with the Epworth Sleepiness scale and objective OSA measures was moderate to strong.

Conclusions and Relevance:

The new tool provides a validated patient-reported outcome measure to evaluate the quality of life among OSA patients specifically.

Level of Evidence: 4

INTRODUCTION:

Obstructive sleep apnea (OSA) is a common form of sleep-disordered breathing observed in about 1/7th of the adult population[1] affecting around a billion subjects over the age of 30 years.[2] Studies on the prevalence of OSA (defined based on an apnea-hypopnea index [AHI] ≥5 events/hour) have estimated 9 to 61% in women and 31 to 84% in men in the US.[3-6] Moderate OSA (AHI > 15 events/hour) affects around 23% of women and 50% of men.[6] Women develop a later onset of the disease compared to men.[7]

The associated intermittent desaturation is linked to chronic inflammation and oxidative stress,[8-11] that is correlated with impaired global cognitive function, memory, executive function, attention, verbal fluency, and intelligence.[12,13] This also impacts different systems including cardiovascular,[14-18] endocrinal,[19] and neurovascular systems due to overstimulation of the sympathetic nervous system.[20-22]

From a patient's perspective, OSA presents with nocturnal and diurnal symptoms affecting one's physical well-being. From a social standpoint, OSA has shown to impact partner's lives via snoring, reduced libido, and depression with lost interest in daily activities.[23,24] The impact of OSA extends to reduced productivity, road traffic and work accidents resulting in an overall economic burden of nearing $150 billion dollars.[25] Given the prevalence of this underdiagnosed disease,[26] and its impact on a multitude of aspects in our community, it is not surprising that there is an increased body of literature addressing the quality of life (QoL) among OSA subjects.[23,27]

Home sleep studies and polysomnography (PSG) report the apnea-hypopnea index (AHI). However, OSA is a complex multi-dimensional condition affecting individuals, families, the economy, and society at large, hence, although these studies are objective, they do not adequately account for all OSA burdens. Given the weak correlation between patients' perception and objective sleep studies, relevant patient-reported outcome measures (PROMs) were developed to evaluate outcomes in everyday clinical practice and research. PROMS in OSA can be generic or specific instruments, global overall well-being, or preference-based instruments focusing on particular domains that assess different activities of daily living.[23,27]

The constitution of the World health organization (WHO) in agreement with the Charter of the United Nations has defined health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity."[28,29] Similarly, Schipper et al mentioned that "Quality of life in clinical medicine represents the functional effect of an illness and its consequent therapy upon a patient, as perceived by the patient."[30] They suggested that primary domains for QoL measurement should entail physical (including occupational), psychological wellbeing, social interaction, and somatic sensation.

Considering the previous statements and the prior results of two systematic reviews evaluating twenty-two PROMs for OSA,[23,27] the objective of this study was to develop and validate a novel comprehensive yet concise PROM to measure QoL of patients with OSA. Current OSA PROMs are not fully validated.[23] Moreover, many of these PROMs were developed as an adaptation of OSA non-specific QoL tools and thus did not incorporate OSA patients. Only 9 existing PROMs are OSA specific. Although the Maugeri Obstructive Sleep Apnea Syndrome (MOSAS)[24] questionnaire, the Obstructive Sleep Apnea Patient-Oriented Severity Index (OSAPOSI),[31] the Quebec Sleep Questionnaire (QSQ),[32] the Sleep Apnea Quality of Life Index (SAQLI),[33] and the Patient-Reported Apnea Questionnaire (PRAQ) are content validated, they are cumbersome to administer with the possibility of questionnaire fatigue.[34] Therefore, to our knowledge no comprehensive yet concise OSA-specific PROM exist and we aimed to fulfil the clinical-need for such a tool.

MATERIALS AND METHODS:

With the approval of the Stanford Institutional Review Board, we followed the internationally accepted guidelines for developing the Standardized List Evaluating Apneas (SLEAP) survey using a stepwise approach.[35-38] Adult subjects (≥18 years old) with OSA confirmed using a polysomnography (PSG) or a Food and Drug Administration (FDA) approved home sleep test were included. FDA-approved home sleep tests were included given the limitations imposed on the study due to the coronavirus disease of 2019 (COVID-19) pandemic. In PSGs, apneic episodes were defined as the occurrence of chest/abdominal wall motion in absence of airflow for ≥10 seconds. Hypopneas were defined as events with a ≥30% reduction in nasal pressure signal outings from baseline and an associated ≥3% or 4% desaturation from pre-event baseline for ≥10 seconds.[39] Subjects who displayed an AHI <5 event/hour were excluded.

Phase 1: Defining a conceptual framework and relevant items (20 OSA respondents)

The three main domains suggested by the constitution of the WHO and the United Nations,[28,29] were utilized to develop the preliminary scale to comprehensively evaluate factors potentially affecting quality of life in OSA. The three main concepts/domains considered relevant for the task were: 1) physical well-being (perceived by patients during daytime and nighttime) 2) mental well-being; and 3) social well-being (**Figure 1**). At a tertiary sleep apnea surgery center, 20 patients diagnosed with OSA and evaluated for different management options for their OSA were interviewed face-to-face between February 2021 and May 2021. Each 10-minute interview consisted of open-ended questions concerning 1) the most bothersome complaints related to OSA and 2) the expected outcome of adequate management. Next, employing the WHO conceptual framework as a guideline, the items were established under each domain, and a preliminary set of items was developed. A Likert-like scale from 0 to 5 was used with 0 representing no effect of OSA on QoL and 5 representing the worst possible effect.

Phase 2: Eliminating redundancy (34 OSA respondents)

To eliminate potential ambiguity and minimize potential redundancy, the preliminary questionnaire was administered to a new sample of subjects with an OSA diagnosis in the form of interviews during June and July 2021. This sample was presented to the sleep surgery clinic for exploring different options for OSA management. Patients were not using any form of treatment and were CPAP/oral appliance non-compliant/intolerant. Non-adherence was defined as no CPAP use after 1 month. Patients were asked to provide their feedback as respondents to reduce or clarify the questions.

Based on their comments, a panel reduced the number of items using the Delphi technique. The panel of experts consisted of 5 fellowship-trained sleep surgeons with more than 2 years of practice experience. Each of the items was evaluated separately by the panel. Items that were thought to be superfluous and did not provide any unique information were omitted. The breakdown of the included 15 items is as follows: the first 6 items together with the last 2 (sleepiness) describe the respondent's physical well-being, the following 2 describe the respondent's mental health, and the following 3 describe their psychosocial health, followed by 1 item assessing the impact of OSA on their occupation.

Phase 3: Field testing and psychometric measurement (176 OSA + 22 non-OSA respondents)

After development of the final 15-item questionnaire, we performed preliminary field testing to an additional group (142 subjects) bringing the total sample size to 176 English-speaking patients between June 2021 and December 2021. Administration of the questions and scoring were performed on the patient population at the sleep medicine and surgery clinic. All OSA patients either did not receive CPAP/oral appliance or were non-compliant, to capture the impact of OSA on their QoL. Another group of healthy subjects (control group) without OSA diagnosis was also incorporated into the analysis (n=22). This group was volunteers who were thought not to have OSA, with an Epworth Sleepiness Scale (ESS) <10, a low risk for OSA using the STOP BANG, and most importantly did not seek any medical advice regarding their sleep or airway. They were selected through convenience and were excluded if they reported any trouble with their sleep. A summary of the phases is illustrated in figure 2.

Statistical analysis

The estimates were reported as means and standard deviations (SDs), or as absolute numbers and percentages, when appropriate. The estimates were accompanied by 95% confidence intervals (95% CIs).

Internal consistency

To test internal consistency, the Cronbach's alpha was calculated along with a one-sided (lower) 95% confidence limit (95% CL). The alpha ≥ 0.9 was considered excellent, ≥ 0.8 good, ≥0.7 acceptable, ≥0.6 questionable, ≥0.5 poor, and <0.5 unacceptable. Several additional alpha-related estimates were reported: item-test correlations, item-rest correlations, average interitem covariances, and alphas with one item removed at a time.

Test-retest reliability

To investigate the correlations between the responses given at an interval of two to four weeks, the intraclass correlation coefficient was calculated along with its 95% confidence interval (95 CI).

Difference between cases and controls (discriminant validity)

The two-sample Wilcoxon rank-sum (Mann-Whitney) test was applied to investigate if the first responses given by cases were significantly different from the first responses given by healthy controls. The significance level of all the two-tailed *p*-values was set at ≤0.05.

Exploratory factor analysis

To evaluate the factor structure of a new scale, an exploratory factor analysis (EFA) was conducted on the estimates obtained from all the respondents (cases and controls). This included both quantitative (unrotated principal factors and parallel analysis) and graphical analyses (scree plot along with a parallel analysis line). The cut-off for retaining was set at eigenvalue ≥1.0 (Kaiser rule).

Convergent Validity

To evaluate the convergent validity of the SLEAP survey, the estimated scores were compared with previously validated PROMs and sleep study outcomes. To validate the SLEAP for OSA specifically, we used the FOSQ-10 as an OSA-specific PROM,[40] as well as Epworth Sleepiness Scale (ESS),[41] Fatigue Severity Scale (FSS),[42] Respiratory Disturbance Index (RDI), Apnea-Hypopnea Index (AHI), Oxygen Desaturation Index (ODI 3% and 4%), and Nasal Obstruction Symptom Evaluation (NOSE)[43] scores using a Spearman correlation coefficient. A Spearman correlation of ≥0.70 was considered very strong, 0.40 to 0.69 strong, 0.30 to 0.39 moderate, 0.20 to 0.29 weak, and 0.01 to 0.19 as none or a negligible correlation Based on the 95% confident interval of the intraclass correlation coefficient (ICC) estimate, values less than 0.5, between 0.5 and 0.75, between 0.75 and 0.9, and greater than 0.90 were indicative of poor, moderate, good, and excellent reliability, respectively.[44] All the analyses were carried out using Stata/IC Statistical Software: Release 16, College Station (StataCorp LP, TX, USA).

RESULTS:

In the conceptual framework phase, 20 patients (17 men) were interviewed to evaluate the most bothersome aspects experienced by their OSA. Of the 198 respondents (176 cases and 22 controls) in phase 2 and 3, 198/198 answered the questionnaire; 71% were men and 29% were women (table 1). These ratios were different in the control group, 59% being women and lower age (37). Twenty-five cases were retested to evaluate a test-retest validity. The average age of the 176 OSA respondents (including the initial 34 patients) from field testing phase was 44.9 (SD 14.3) years. After interviewing the 34 patients (in the redundancy reduction phase) followed by the Delphi panel of five experts, 15 items were retained (Figure 3). For OSA-specific PROM validation, 62 subjects were enrolled to validate the SLEAP against FOSQ-10.

Reliability

The internal consistency of the SLEAP was excellent with alpha of 0.92 (lower 95% CL 0.90) (Table 2). All the items demonstrated at least moderate item-test and item-retest correlations. Excluding one item at a time did not improve the alpha.

All the test-retest correlations were positive, significant, and strong ranging from 0.50 to 0.90 (Supplement-table 1). The differences between cases and controls (two-sample Wilcoxon rank-sum [Mann-Whitney] test) were statistically significant for all the items and for the total score – all the *p*-values were <0.05.

Validity and Readability

There were two factors with eigenvalues above the cut-off of 1.0 (supplement-table 2 and 3, and Figure 4). However, the first one had an eigenvalue of 6.8 while the next one had an eigenvalue of 1.1, which is very close to a cut-off of 1.0. In such a situation, only the first factor was retained. While there were three factors above the parallel analysis line, factors #2 and #3 had eigenvalues of 1.1 and 0.56, close to or below the pre-agreed cut-off for retaining >1.0. The loadings of items on the retained factor varied from 0.44 to 0.81.

As shown in Table 3, the total score of the SLEAP strongly correlated with the ESS, the FSS and the FOS-Q scores, 0.57, 0.67 and -0.72, respectively. Respective correlations with the NOSE and the RDI scores were moderate, 0.40 and 0.32, respectively. Correlations with other scales were weak or negligible/insignificant. Readability assessment is shown in supplement 4.

DISCUSSION:

A novel PROM (SLEAP) was introduced to measure the quality of life in OSA patients. It was developed based on interviews to enroll relevant items using patients' own input. The SLEAP was found to be an internally consistent, test-retest reliable and unidimensional scale covering the recommended QoL features. The SLEAP scale showed strong convergent validity when compared with ESS, FSS, and moderate validity with RDI and NOSE scores. Factor analysis validated the construct validity of the new scale.

In developing the SLEAP scale, we evaluated subjects presenting with an OSA diagnosis including those who were not treated and failed CPAP. To our knowledge, this is the first scale to incorporate this population. Additionally, the scale has been streamlined for efficiency yet maintained relative comprehensiveness. The scale was contrasted with objective measures of sleep studies and showed a significant correlation with the RDI. This supports the construct validity of this scale and provides for the first time a scale that can bridge the gap between patients' perception and objective outcomes.

However, limitations include the use of a relatively small sample size and the selection of control subjects, where OSA is unlikely but could not be excluded. However, control subjects with negative sleep studies carry the risk of sleep/airway complaints that may influence the control group, therefore, were selected based on their ESS and STOP BANG scores, and their history (not seeking medical advice for sleep). This could have potentially compromised the analysis and biased the results towards the lack of difference between the groups. There was a difference in age and gender included in the study and control group. While unclear whether gender or age could play a factor in differences in developing a validated OSA-specific PROM, it must be highlighted.

Moreover, assessing libido is a missing domain that has been omitted as this may make patients uncomfortable answering the survey and thus limiting reliability. However, item#10 includes relationships with family that can cover the prior concern. The Likert-type ordinal data used for the factor analysis were considered interval data. While common, such an approach is always an approximation. The ordinal data obtained from the SLEAP scale can be further analyzed using an item response theory requiring big samples. However, the SLEAP scale was developed based on a conceptual framework for QOL suggested by the WHO and was tested using the commonly recommended psychometric methodologies for initial evaluation of a new instrument. We also did not outline comorbidities, yet all subjects were considered for surgical interventions indicating they are by proxy healthier candidates. However, other OSA PROMs (SNORE-25 and others) did not highlight comorbidities as well. This study did not investigate the potential role of the SLEAP scale in assessing therapeutic success, however this is a future step. Another limitation is that some questions were left unanswered like snoring, that is challenging for subjects living by themselves (these were excluded).

The new scale has certain similarities with previous scales as the Symptoms of Nocturnal Obstruction and Related events (SNORE-25),[45] and OSAPOSI,[31] in quantifying daytime, nighttime symptoms, medical, emotional and occupational problems. However, although the SNORE-25 questionnaire showed good reliability with a Cronbach's alpha of 0.91, it entails 25 questions which could be cumbersome to fill out leading to questionnaire fatigue. Moreover, the SNORE-25 study did not report reliability and included subjects that were not formally diagnosed with OSA objectively. Similarly, the OSAPOSI is a complicated scale utilizing a 2-point system for 32 questions with a total score out of 640 that is time consuming to administer despite good content validity.

Other instruments as the MOSAS,[24] Quebec sleep questionnaire (QSQ)[32] and SAQLI,[33] had good content validity but showed limited convergent validity. Moreover, the QSQ had poor reliability. Therefore, convergent validity and reliability were integral to the design of the current study. Convergent validity was compared to the previously validated ESS, FSS, and NOSE as well as objective sleep study parameters. Test-retest reliability was assessed based on 25 subjects showing strong correlation with an interval of 2 to 4 weeks.

Convergent validity of the PRAQ with ESS ranged from 0.56 to 0.83 according to the domain, however the authors did not comment on the other 2 domains as they are not related: "symptoms at night" and "social interaction". Convergent validity with fatigue was 0.52 -0.86, while SLEAP showed an overall correlation of 0.67, and showed strong validity with the FOSQ (OSA-specific QOL) of 0.72. The internal consistency of the PRAQ domains was 0.81 to 0.86, which is comparable (slightly lower) to our results (0.91-0.92).

The SAQLI and MOSAS questionnaires additionally include domains for treatment-related outcomes. However, the SAQLI requires an intensive interview format to score the 56 + 28 treatment-related outcomes questions and the MOSAS part B only focuses on CPAP therapy and thus is ineffective to measure surgical outcomes. Meanwhile, the SLEAP scale can be used to track surgical outcomes due to its convergent validity and ease of use.

More recently, the Patient-Reported Apnea Questionnaire (PRAQ)[34] was developed as a practical tool for the clinician to track the success of treatment outcomes and measures the changes in a patient's condition over time. It allows patients to complete the PROM without the need for an interviewer unlike the PROMs previously discussed. The SLEAP scale is similar to the PRAQ in that regard, however, it is much more streamlined than the 10 domain, 43 items PRAQ that requires 15 minutes on average to fill out.

Amongst OSA-related specific symptom scales, none of the PROMs were fully validated, yet the Beck anxiety inventory (BAI) has the most evidence of validation.[23] That being said, the ESS is the most heavily used in both academic and clinical practice for measuring one OSA-specific symptom "*sleepiness*", with more than 20 studies validating this tool.[46] The SLEAP score showed strong correlation with the ESS as well as with the FSS. Moreover, it shows very strong correlation with OSA-specific PROMs (FOSQ). Previous studies evaluating fatigue showed a correlation between OSA severity and fatigue using various fatigue scales.[47] Self-perceived QoL, particularly sleep quality, is independently associated with fatigue among OSA patients rather than the severity of the apnea itself, highlighting the value of PROMs.[48] Very little evidence was found regarding the quality of generic outcome measures for subjects with OSA.[23,27] These are mainly used to compare health status between OSA and other diseases.

Evaluating different QoL features in OSA is of paramount importance. Our proposed tool is a short, validated questionnaire for use in all OSA severities. There are no specific instructions other than handing the questionnaire to the patient and asking him or her to complete it. By tracking the individual patient's progress, the clinician can identify problems that may not be evident during routine clinical interaction.

Our next step is to conduct larger studies to assess therapeutic success using the SLEAP scale, establish the minimal clinically important difference, and estimate its suitability for quality assessment at an aggregate level beyond its use at the individual patient level. We'll also develop a digital tool to enhance the data collection process and ease of administration.

Conclusion:

A new PROM for OSA was developed based on a comprehensive framework; suggested by different systematic reviews and the WHO guidelines. The SLEAP score has excellent internal consistency, reasonable test-retest reliability, discriminant validity, and construct validity as compared to other PROMs and objective measures. Future directions include establishing levels of meaningful change, minimal clinically important difference, and investigate its utility in assessing therapeutic success.

References

1. Benjafield AV, Ayas NT, Eastwood PRet al. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. Lancet Respir Med 2019; 7:687-698.
2. Benjafield A VK AN, Eastwood PR, Heinzer RC, Ip MS. Global prevalence of obstructive sleep apnea in adults: estimation using currently available data. San Diego, CA, 2018.
3. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993; 328:1230-1235.
4. Quan SF, Howard BV, Iber Cet al. The Sleep Heart Health Study: design, rationale, and methods. Sleep 1997; 20:1077-1085.
5. Bixler EO, Vgontzas AN, Lin HMet al. Prevalence of sleep-disordered breathing in women: effects of gender. Am J Respir Crit Care Med 2001; 163:608-613.
6. Heinzer R, Vat S, Marques-Vidal Pet al. Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study. Lancet Respir Med 2015; 3:310-318.
7. Fietze I, Laharnar N, Obst Aet al. Prevalence and association analysis of obstructive sleep apnea with gender and age differences - Results of SHIP-Trend. J Sleep Res 2019; 28:e12770.
8. Kontogianni K, Messini-Nikolaki N, Christou K, Gourgoulianis K, Tsilimigaki S, Piperakis SM. DNA damage and repair capacity in lymphocytes from obstructive sleep apnea patients. Environ Mol Mutagen 2007; 48:722-727.
9. Tempaku PF, Mazzotti DR, Tufik S. Telomere length as a marker of sleep loss and sleep disturbances: a potential link between sleep and cellular senescence. Sleep Med 2015; 16:559-563.
10. Yamauchi M, Nakano H, Maekawa Jet al. Oxidative stress in obstructive sleep apnea. Chest 2005; 127:1674-1679.
11. Noguchi T, Chin K, Ohi Met al. Heat shock protein 72 level decreases during sleep in patients with obstructive sleep apnea syndrome. Am J Respir Crit Care Med 1997; 155:1316-1322.
12. Morley JE, Sanford A, Bourey R. Sleep Apnea: A Geriatric Syndrome. J Am Med Dir Assoc 2017; 18:899-904.
13. Cohen-Zion M, Stepnowsky C, Johnson S, Marler M, Dimsdale JE, Ancoli-Israel S. Cognitive changes and sleep disordered breathing in elderly: differences in race. J Psychosom Res 2004; 56:549-553.
14. Lyons OD, Bradley TD. Heart Failure and Sleep Apnea. Can J Cardiol 2015; 31:898-908.
15. Ibrahim B, de Freitas Mendonca MI, Gombar S, Callahan A, Jung K, Capasso R. Association of Systemic Diseases With Surgical Treatment for Obstructive Sleep Apnea Compared With Continuous Positive Airway Pressure. JAMA Otolaryngol Head Neck Surg 2021; 147:329-335.
16. Sapina E, Torres G, Barbe F, Sanchez-de-la-Torre M. The Use of Precision Medicine to Manage Obstructive Sleep Apnea Treatment in Patients with Resistant Hypertension: Current Evidence and Future Directions. Curr Hypertens Rep 2018; 20:60.
17. Gami AS, Howard DE, Olson EJ, Somers VK. Day-night pattern of sudden death in obstructive sleep apnea. N Engl J Med 2005; 352:1206-1214.
18. Punjabi NM, Caffo BS, Goodwin JLet al. Sleep-disordered breathing and mortality: a prospective cohort study. PLoS Med 2009; 6:e1000132.
19. Ip MS, Lam B, Ng MM, Lam WK, Tsang KW, Lam KS. Obstructive sleep apnea is independently associated with insulin resistance. Am J Respir Crit Care Med 2002; 165:670-676.
20. Chopra S, Rathore A, Younas Het al. Obstructive Sleep Apnea Dynamically Increases Nocturnal Plasma Free Fatty Acids, Glucose, and Cortisol During Sleep. J Clin Endocrinol Metab 2017; 102:3172-3181.
21. Ke X, Guo W, Peng Het al. Association of aldosterone excess and apnea-hypopnea index in patients with resistant hypertension. Sci Rep 2017; 7:45241.

22. Follenius M, Krieger J, Krauth MO, Sforza F, Brandenberger G. Obstructive sleep apnea treatment: peripheral and central effects on plasma renin activity and aldosterone. Sleep 1991; 14:211-217.
23. Abma IL, van der Wees PJ, Veer V, Westert GP, Rovers M. Measurement properties of patient-reported outcome measures (PROMs) in adults with obstructive sleep apnea (OSA): A systematic review. Sleep Med Rev 2016; 28:18-31.
24. Moroni L, Neri M, Lucioni AM, Filipponi L, Bertolotti G. A new means of assessing the quality of life of patients with obstructive sleep apnea: the MOSAS questionnaire. Sleep Med 2011; 12:959-965.
25. Frost S. Hidden health crisis costing America billions. Underdiagnosing and undertreating obstructive sleep apnea draining healthcare system. American Academy of Sleep Medicine 2016.
26. Abdelwahab M, Marques S, Previdelli I, Capasso R. Peri-operative antibiotic use in sleep surgery: clinical relevance. Otolaryngology - Head and Neck Surgery 2021.
27. Moyer CA, Sonnad SS, Garetz SL, Helman JI, Chervin RD. Quality of life in obstructive sleep apnea: a systematic review of the literature. Sleep Med 2001; 2:477-491.
28. CONSTITUTION of the World Health Organization. Public Health Rep 1946; 61:1268-1279.
29. International Health C. Constitution of the World Health Organization. 1946. Bull World Health Organ 2002; 80:983-984.
30. Schipper H CJ, Olweny CLM. Quality of life studies: definitions and conceptual issues. In: B S, ed. *Quality of life and pharmacoeconomics in clinical trials*. Philadelphia, PA: Lippincott-Raven, 1996:11–23.
31. Piccirillo JF, Gates GA, White DL, Schectman KB. Obstructive sleep apnea treatment outcomes pilot study. Otolaryngol Head Neck Surg 1998; 118:833-844.
32. Lacasse Y, Bureau MP, Series F. A new standardised and self-administered quality of life questionnaire specific to obstructive sleep apnoea. Thorax 2004; 59:494-499.
33. Flemons WW, Reimer MA. Development of a disease-specific health-related quality of life questionnaire for sleep apnea. Am J Respir Crit Care Med 1998; 158:494-503.
34. Abma IL, Rovers M, M IJ, Hol B, Westert GP, van der Wees PJ. The development of a patient-reported outcome measure for patients with obstructive sleep apnea: the Patient-Reported Apnea Questionnaire (PRAQ). J Patient Rep Outcomes 2017; 1:14.
35. Acaster S, Cimms T, Lloyd A. The design and selection of patient-reported outcomes measures (PROMs) for use in patient centered outcomes research. Patient Centered Outcomes Research Institute (PCORI) 2012:1-82.
36. Health UDo, Evaluation HSFCfD, Researchet al. Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims: draft guidance. Health and Quality of Life Outcomes 2006; 4:1-20.
37. Lohr KN. Assessing health status and quality-of-life instruments: attributes and review criteria. Quality of Life Research 2002; 11:193-205.
38. Mokkink LB, Terwee CB, Patrick DLet al. The COSMIN checklist for assessing the methodological quality of studies on measurement properties of health status measurement instruments: an international Delphi study. Quality of Life Research 2010; 19:539-549.
39. Berry RB, Budhiraja R, Gottlieb DJet al. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. J Clin Sleep Med 2012; 8:597-619.
40. Chasens ER, Ratcliffe SJ, Weaver TE. Development of the FOSQ-10: a short version of the Functional Outcomes of Sleep Questionnaire. Sleep 2009; 32:915-919.
41. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 1991; 14:540-545.

42. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol 1989; 46:1121-1123.
43. Stewart MG, Witsell DL, Smith TL, Weaver EM, Yueh B, Hannley MT. Development and validation of the Nasal Obstruction Symptom Evaluation (NOSE) scale. Otolaryngol Head Neck Surg 2004; 130:157-163.
44. Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. J Chiropr Med 2016; 15:155-163.
45. Skirko JR, James KT, Garrison LP, Weaver EM. Development of a Sleep Apnea-Specific Health State Utility Algorithm. JAMA Otolaryngol Head Neck Surg 2020; 146:270-277.
46. Kendzerska TB, Smith PM, Brignardello-Petersen R, Leung RS, Tomlinson GA. Evaluation of the measurement properties of the Epworth sleepiness scale: a systematic review. Sleep Med Rev 2014; 18:321-331.
47. Bercea RM, Mihaescu T, Cojocaru C, Bjorvatn B. Fatigue and serum testosterone in obstructive sleep apnea patients. Clin Respir J 2015; 9:342-349.
48. Stepnowsky CJ, Palau JJ, Zamora T, Ancoli-Israel S, Loredo JS. Fatigue in sleep apnea: the role of depressive symptoms and self-reported sleep quality. Sleep Med 2011; 12:832-837.

Figure Legends:

1. The conceptual framework for building the SLEAP (Standardized List Evaluating APneas).
2. The four phases used to build the SLEAP (Standardized List Evaluating APneas).
3. The individual items of the SLEAP (Standardized List Evaluating APneas).
4. Scree plot of exploratory factor analysis

Table 1. Sample characteristics of the enrolled patients.

Variable	Total		Cases		Controls	
	Mean	SD	Mean	SD	Mean	SD
SLEAP, points	34.7	17.6	37.8	15.8	9.3	7.9
ESS, points	9.2	5.6	9.3	5.7	7.0	1.7
FSS, points	36.7	15.5	37.9	15	16.3	6.8
NOSE, points	8.6	5	9	4.9	2.9	2.7
RDI	25.5	21.7	25.5	21.7	-	-
AHI 3%	25.3	21.6	25.3	21.6	-	-
AHI 4%	15.9	18.7	15.9	18.7	-	-
AI	9.6	14.6	9.6	14.6	-	-
ODI 3%	16	17.5	16	17.5	-	-
ODI 4%	13.1	19.4	13.1	19.4	-	-
LSAT	84.3	9.8	84.3	9.8	-	-
Age, years	44.1	13.9	44.9	14.3	37.3	6.8
Gender, n and %						
Women	58	29%	45	26%	13	59%
Men	140	71%	131	74%	9	41%

SLEAP: Standardized List Evaluating APnea, ESS: Epworth sleepiness scale, FSS: Fatigue severity scale, NOSE: nasal obstruction symptom evaluation, RDI: Respiratory disturbance index, AHI: Apnea hypopnea index, AI: Apnea Index, ODI: oxygen desaturation index, LSAT: lowest oxygen saturation. AHI3%: defining 3% reduction in O2 level with hypopnea, AHI4%: defining 4% reduction in O2 level with hypopnea.

Table 2. Internal consistency of the SLEAP items

Item	n	Sign	Item-test correlation	Item-rest correlation	Average interitem covariance	Alpha
Item 1	198	+	0.59	0.52	1.29	0.92
Item 2	198	+	0.66	0.59	1.26	0.92
Item 3	198	+	0.63	0.57	1.28	0.92
Item 4	198	+	0.81	0.77	1.24	0.91
Item 5	198	+	0.57	0.50	1.31	0.92
Item 6	198	+	0.65	0.58	1.27	0.92
Item 7	198	+	0.80	0.77	1.24	0.91
Item 8	198	+	0.75	0.70	1.25	0.91
Item 9	198	+	0.81	0.77	1.21	0.91
Item 10	198	+	0.75	0.70	1.24	0.91
Item 11	198	+	0.75	0.70	1.24	0.91
Item 12	198	+	0.78	0.73	1.23	0.91
Item 13	198	+	0.65	0.58	1.27	0.92
Item 14	197	+	0.57	0.50	1.31	0.92
Item 15	197	+	0.48	0.43	1.37	0.92
Total score					1.27	0.92

Table 3. Convergent validity – correlations between SLEAP total score and other measures (all 198 respondents included)

Measure	Spearman correlation	95% CI		n
ESS	0.57	0.46	0.66	187
FSS	0.67	0.59	0.75	187
FOSQ	-0.72	-0.82	-0.57	62
NOSE	0.40	0.27	0.51	187
RDI	0.32	0.09	0.52	71
AHI 3%	0.18	0.03	0.32	172
AHI 4%	0.27	0.01	0.50	56
AI	0.21	-0.07	0.46	51
ODI 3%	0.14	-0.05	0.33	100
ODI 4%	0.33	0.13	0.51	89
LSAT	-0.07	-0.22	0.08	171

SLEAP: standardized list evaluating apnea, ESS: Epworth sleepiness scale, FSS: Fatigue severity scale, NOSE: nasal obstruction symptom evaluation, FOSQ: functional Outcomes of Sleep Questionnaire, RDI: Respiratory disturbance index, AHI: Apnea hypopnea index, AI: Apnea Index, ODI: oxygen desaturation index, LSAT: lowest oxygen saturation. AHI3%: defining 3% reduction in O2 level with hypopnea, AHI4%: defining 4% reduction in O2 level with hypopnea.