

Sponsor / Sponsor-Investigator	Dr. med. Samuel Tschopp
Study Title:	Night-to-Night Variability of Novel Physiological Parameters in Home Sleep Apnea Testing
Short Title / Study ID:	N2N-OSA
Protocol Version and Date:	Version 1, 01/02/2026
Trial registration:	This study will be registered on ClinicalTrials.gov
Study category and Rationale	<p>This research project is classified as Category A).</p> <p>The study exclusively involves non-invasive sleep measurements using validated devices also used in routine clinical practice, along with the collection of associated personal health data. No invasive procedures, biological sampling, or interventions exceeding routine clinical assessments are performed.</p>
Clinical Phase:	NA
Background and Rationale:	<p>Obstructive sleep apnea (OSA) is usually diagnosed from a single night of home sleep apnea testing using the apnea-hypopnea index (AHI). However, the AHI varies substantially from night to night, undermining diagnostic accuracy,[1–4] and shows only modest correlation with symptoms.[5, 6] This variability further limits its usefulness for predicting cardiovascular and other complications.[7] Besides the traditional AHI, more robust physiological markers are needed.</p> <p>Several emerging physiological metrics - hypoxic burden[8–11], ventilatory burden[12, 13], heart rate variability[10], autonomic arousals, and the pulse wave amplitude drop index[14] – capture the physiological impact of OSA more comprehensively and demonstrate stronger associations with cardiovascular risk. Despite this promise, their night-to-night variability has not been studied.</p> <p>A systematic evaluation of both established and novel OSA metrics across nights is essential to identify reliable, stable parameters suitable for clinical routine. This improves diagnostic precision beyond what traditional metrics can provide, enhances patient selection, reduces costs and patient harm, and may improve treatment outcomes.</p>
Objective(s):	This study aims to quantify the night-to-night variability in established and novel OSA metrics, identify factors driving this variability, and determine which measures most closely correlate with patient-reported symptoms.

Outcome(s):	<p>Primary endpoint</p> <p>The primary endpoint is to estimate the night-to-night variability of established and novel OSA metrics obtained from repeated home sleep measurements.</p> <p>Secondary endpoints</p> <p>Identification of factors contributing to and explaining variability</p> <p>Each influencing factor will be evaluated on its potential to explain the observed variability in the objective physiological parameters.</p> <p>Association between physiological parameters from sleep testing and PROMs</p> <p>Associations between physiological metrics and PROMs will be assessed.</p>
Study design:	Prospective cohort study
Inclusion / Exclusion criteria:	<p>Inclusion criteria:</p> <ul style="list-style-type: none"> - Patients with suspected or diagnosed sleep-disordered breathing, irrespective of disease severity, as defined by the indications for home sleep apnea testing in the German guidelines [15] - No active treatment during sleep recordings or within preceding two weeks (e.g., mandibular advancement devices, positive airway pressure therapy) - Written informed consent obtained <p>Exclusion criteria:</p> <ul style="list-style-type: none"> - Age <18 years - Known or suspected neurological sleep disorder (e.g., narcolepsy, parasomnia) - Known or suspected psychiatric sleep disorder - Known or suspected central and complex sleep apnea - Participants who are unable to perform sleep measurements reliably - Insufficient knowledge of the project language (German) - Inability to give consent - Shift workers (with shift work <2 weeks before testing)
Measurements and procedures:	Participants will undergo repeated sleep testing using respiratory polygraphy over 4 nights and oximetry over 10 nights, starting in parallel. Before and after the recordings they will fill out symptom questionnaires and patient-reported outcome measures.
Study Product / Intervention:	NA
Control Intervention (if applicable):	NA
Number of Participants with Rationale:	<p>In our previous study[1], the intraclass correlation coefficient for the AHI was 0.76 (95% CI 0.65-0.87). Assuming a confidence level of 95%, a confidence interval width of 0.1, and assuming similar variability for other sleep parameters, a sample size of 160 participants is required to assess variability over four nights reliably.[16]</p> <p>Assuming a 20% dropout rate, a total of 192 patients will be enrolled to achieve a sample size of 160.</p>

Study Duration:	10 days
Study Schedule:	March 2026 of First-Participant-In (planned) June 2027 of Last-Participant-Out (planned)
Investigator(s):	Dr. med. Samuel Tschopp samuel.tschopp@insel.ch, 031 632 29 41 Prof. Dr. med. Urs Borner urs.borner@insel.ch, 031 632 29 41 Prof. Dr. med. Marco Caversaccio marco.caversaccio@insel.ch, 031 632 29 41
Study Centre(s):	Inselspital University Hospital and University Bern Freiburgstrasse 20, 3010 Bern, Switzerland
Statistical Considerations:	Variability and influencing factors will mainly be analyzed using mixed-effects models, intraclass correlation coefficient, coefficient of variation and coefficient of repeatability. The statistical analysis plan is described in detail in the Project Plan. Sample Size In our previous study[1], the intraclass correlation coefficient for the AHI was 0.76 (95% CI 0.65-0.87). Assuming a confidence level of 95%, a confidence interval width of 0.1, and assuming similar variability for other sleep parameters, a sample size of 160 participants is required to assess variability over four nights reliably.[16] Assuming a 20% dropout rate, a total of 192 patients will be enrolled to achieve a sample size of 160.
GCP Statement:	This study will be conducted in compliance with the protocol, the current version of the Declaration of Helsinki, the ICH-GCP or ISO EN 14155 (as far as applicable) as well as all national legal and regulatory requirements.

Recruitment Procedure

Participants with suspected or diagnosed sleep-disordered breathing of any severity will be recruited at Inselspital University Hospital und University Bern.

No selection or stratification based on sex, gender, or any other patient characteristics is applied during recruitment. Participants are included consecutively based on the clinical indication for home sleep apnea testing, irrespective of sex or gender. Any resulting imbalance reflects the underlying clinical population and does not compromise the scientific validity of the study, as analyses will account for sex and gender as covariates and report their effects transparently.

Study Procedure/Flowchart with Timelines:

Time (days)	>-1	0	1-10	>10
Visit	Information	Screening	Home Sleep Testing	Discussion of Results
Oral and written Information	+			
Written consent		+		
Check inclusion-/exclusion criteria		+		
Medical history		+		
Participant characteristics		+		

Measurements			+	
Questionnaires		+	+	
Discussion of results <i>(if desired by the participant)</i>				(+)

Risks/ Inconveniences, which are Study specific:

This project poses minimal risks to participants. All procedures are non-invasive and based on validated home sleep apnea testing devices that are routinely used in clinical practice. Potential burdens are limited to mild, transient discomfort from wearing the devices during sleep and the time required to complete short daily questionnaires. No medical interventions, invasive procedures, or biological sampling are performed.

Coverage of Damages:

In the event of project-related damage or injuries, the liability of the institution Inselspital University Hospital and University Bern provides compensation.

Storage of Data-and Samples for Future Research Aims:

Ethical Considerations:

This project addresses a clinically relevant and **well-defined knowledge gap regarding the night-to-night variability of established and novel physiological parameters in obstructive sleep apnea**. OSA is a common disease, globally affecting an estimated 936 million people.[28] Therefore, the **results are expected to have high scientific and social value by improving diagnostic accuracy**, informing evidence-based testing strategies, and supporting more individualized patient management. The findings may benefit future patients by reducing misclassification, unnecessary treatment, and healthcare costs.

The study design is justified by the research question and relies exclusively on non-invasive, routinely used home sleep testing devices and brief questionnaires. The burden for participants is low and mainly consists of wearing validated sleep monitoring devices and completing short daily questionnaires. No interventions beyond multiple non-invasive tests using the same devices as for standard clinical practice are performed.

Participants will receive multiple nights of validated sleep measurements at no cost. This exceeds standard clinical practice and may provide a more robust assessment of their sleep-disordered breathing. While participation is not primarily intended to provide therapeutic benefit, participants gain a better insight into their disease, which better informs clinical decision-making. The primary benefit of the project lies in its expected contribution to improved understanding of night-to-night variability in established and novel OSA metrics, which may lead to more reliable diagnostics, better patient stratification, and optimized treatment decisions for future patients. Overall, the minimal risks and burdens for participants are justified by the substantial anticipated scientific and societal benefit of the project.

The most relevant References:

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