STU#: STU00214445

PROTOCOL TITLE: Low Burden Wearable Sensor System for Diagnosing Obstructive Sleep Apnea Over Multiple Nights: Diagnostic Agreement with Home Sleep Testing

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PROTOCOL SUMMARY

Protocol Title (Long Title)	Low Burden Wearable Sensor System for Diagnosing Obstructive Sleep Apnea
Protocol Number	v.1
Study Duration	4 to 6 months
Setting	Northwestern University and Participant's Homes
Sample Size	A total of approximately 100 subjects may be recruited to achieve at least 30 subjects to complete the study (Home Sleep Testing portion).
Main Inclusion Criteria	• Age >22 years old or older • Subjects with suspected or confirmed OSA based on history • Persons with a previous diagnosis of OSA • Subjects with self-reported symptoms of OSA • Willingness to give consent and comply with study procedures
Objectives:	Analysis of diagnostic yield from multiple nights with ANNE Sleep • Analysis of agreement for diagnosis of moderate to severe OSA by determining a patient's Apnea-Hypopnea Index (AHI) wearing the ANNE Sleep system and WatchPAT ONE over one (1) night worn concurrently • Assessment of usability compared to current HST in the intended population
Investigational Product and Planned Use	ANNE™ Sleep System
Commercial Available HST Device	WatchPAT ONE
Statistical Analysis	Three subsequent nights will be with the ANNE Sleep system alone. Patient preference will be elicited via psychometric surveys for comfort

	and usability comparing ANNE and a commercially available Home Sleep Test (HST). We expect completion of this aim in 6 months. The apnea-hypopnea index (AHI) will be calculated in ranges of 15 – 30 apnea/hypopnea events per hour for moderate OSA and ≥30 apnea/hypopnea events per hour for severe OSA. The oxygen desaturation index (ODI), the hourly average number of desaturation episodes, will also be calculated. With a sample size of at least 30, the large amount of within-person data provides high statistical power for all planned analyses, allowing this data set to answer all proposed questions while minimizing study costs and any risk to patients.

1. LIST OF ABBREVIATIONS

AASM	American Academy of Sleep Medicine
AHI	Apnea-Hypopnea Index
ECG	Electrocardiogram
EDF	European Data Format
EDW	Electronic Data Warehouse
EHR	Electronic Health Record
EMG	Electromyography
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act of 1996
HR	Heart Rate
HST	Home Sleep Test
ICF	Informed Consent Form
ICH-GCP	International Conference on Harmonization Good Clinical Practice
IRB	Institutional Review Board
MRN	Medical Record Number
NMH	Northwestern Memorial Hospital
NPV	Negative Predictive Value
OSA	Obstructive Sleep Apnea
ODI	Oxygen Desaturation Index
PAP	Positive Airway Pressure
PAT	Peripheral Arterial Tonometry
PHI	Protected Health Information
PI	Principal Investigator
PPV	Positive Predictive Value

PSG	Polysomnography
RPSGT	Registered Polysomnography Technicians
RR	Respiratory Rate
SDB	Sleep Disordered Breathing
SL	Sleep Latency
SoC	System-on-Chip
TST	Total Sleep Time

2. OBJECTIVES:

The main objective of this study are as follows:

- Analysis of diagnostic yield from multiple nights with ANNE Sleep
- Analysis of agreement of diagnosis of moderate to severe OSA by determining a patient's Apnea-Hypopnea Index (AHI) wearing the ANNE Sleep system and WatchPAT ONE over one (1) night worn concurrently
- Assessment of usability compared to current HST in the intended population

3. INTRODUCTION

Sleep disordered breathing (SDB) is an increasingly common disorder characterized by a pathological increase in upper airway resistance experienced during sleep that ranges from benign snoring to its most severe form of obstructive sleep apnea (OSA). OSA is characterized by recurrent episodes of cessation of breathing and physiological stress as a result of intermittent periods of hypoxemia, and arousals. Studies have demonstrated that OSA leads to profound sleep fragmentation, disturbance of the autonomic nervous system, insulin resistance, increased systemic inflammation, oxidative stress, and subsequent vascular endothelial dysfunction. These physiologic changes cause significant morbidity; OSA is an independent risk factor for wide ranging adverse health outcomes including cardiovascular disease (hypertension, stroke, myocardial infarction), metabolic disorders (insulin insensitivity, diabetes), neurological (dementia), motor vehicle accidents, and mood disorders.[1-5]

The ANNE™ Sleep system has been validated as a diagnostic aid for moderate to severe OSA in a multi-center, open-label clinical study with n=225 subjects. Subjects wore PSG and ANNE Sleep concurrently for one supervised night at a sleep center. Both PSG and ANNE Sleep data were manually scored by 3 blinded registered polysomnography technicians. If AHI values determined by the 3 scorers exhibited great than 15% variation, a board-certified Sleep Medicine physician reviewed the raw data independently per AASM guidelines to account for interscorer variability. The results of the study indicate that ANNE Sleep is sufficiently accurate as an aid to diagnosis of moderate to severe OSA with sensitivity and specificity of 90% and 98% respectively.

4. STUDY ENDPOINTS:

4.1 Primary Outcome Measures

- Analysis of variation between nights of AHI derived from ANNE Sleep system across multiple sleep nights at home
- Analysis of agreement for diagnosis of moderate to severe OSA by determining a patient's Apnea-Hypopnea Index (AHI) wearing the ANNE Sleep system and WatchPAT ONE over one (1) night worn concurrently
- Patient responses on psychometric surveys for comfort and usability comparing ANNE Sleep and WatchPAT ONE

5. RECRUITMENT METHODS

5.1 INCLUSION AND EXCLUSION CRITERIA

Eligible participants will be recruited using electronic medical records from Northwestern Medicine Enterprise Data Warehouse (NMEDW) using the below inclusion/exclusion criteria for search criteria. No special populations will be targeted for the enrollment in this study. Additional patient referrals will be made by the physicians who are participating as investigators on this study. The referring physicians of patients to the study will make an assessment if a potential study subject can provide informed consent and will not refer patients unlikely to understand what is being asked of them. All potential subjects will be evaluated by research staff to match them to the inclusion and exclusion criteria that has been established.

5.1.1 Inclusion Criteria

1. ≥22 years old
2. Subjects with suspected OSA based on history and physical. Subjects with self-reported symptoms of OSA based on the STOP-Bang questionnaire indicating affirmative answers to any of the following: snoring, daytime fatigue/sleepiness/tiredness, partners who have observed the subject stopping breathing or choking/gasping during sleep. Persons with a previous diagnosis of OSA are also eligible.
3. Willingness to give written consent and comply with study procedures

5.1.2 Exclusion Criteria

1) An unstable medical condition, acute or chronic, that in the opinion of the investigator puts the subject at health risks related to this trial or interferes with the clinical trial and data collection based on the opinion of the investigator, this includes but is not limited to:
   A. Significant cardiorespiratory disease: patients that are oxygen dependent, previous hospitalization for cardiorespiratory issues, or left ventricular ejection fraction ≤ to 40%
   B. Respiratory muscle weakness due to a neuromuscular condition
   C. Awake hypoventilation or suspicion of sleep related hypoventilation
   D. Chronic opioid medication use
   E. History of stroke
   F. History of severe insomnia
2) Inability to understand instructions
3) Has a skin abnormality that precludes assessment
4) Has a history of dementia
5) Patients with implanted pacemakers or defibrillators

5.2 RECRUITMENT METHODS

Identifying potential participants will be through the Electronic Data Warehouse (EDW) and through the use of study flyers and recruitment materials. The EDW at Northwestern is updated daily. An algorithm can be set up based on the eligibility criteria of the trial to identify potential participants that have met enrollment criteria. Data gathered in the EDW request will include Name, contact information (address, email and/or phone), Date of Birth, MRN, hospitalization date(s), and if applicable, date that a HST or PS~~G~~G is ordered. The EDW request may exclude people based on the exclusion criteria. The use of the EDW will be used exclusively for recruitment purposes and no data from the warehouse will be added to the study data set for research analysis. The use of study flyers or advertisements will also be shared with potential study subjects who will be given contact information to follow up with the study team.

6. STUDY INVESTIGATIONAL DEVICE:

ANNE™ Sleep system

Sibel's ANNE™ Sleep system includes two skin-mounted, bio-integrated sensors to record vital signs, a wireless charger, a wireless charger adaptor, single-use chest adhesives, single-use finger adhesives, and a mobile device with a mobile software application that enables data recording for download for further analysis.

Heart rate (HR), snore, chest movement, and body position are recorded from the ANNE™ Chest sensor. Blood oxygenation (SpO_2), peripheral arterial tonometry (PAT), and pulse rate are recorded from the ANNE™ Limb sensor. PAT is indicative of vasoconstriction, which can serve as a proxy for respiratory disturbances and accepted by the American Academy of Sleep Medicine for use as a component of home sleep testing.

The first sensor (chest unit) located on the chest contains a 3-axis gyroscope and 3-axis accelerometer, Bluetooth Low Energy System-on-Chip (SoC), a Lithium-Polymer battery, power management component, an analog front-end component, passive electrodes for electrocardiogram (ECG).

The second sensor (limb unit) located on the finger of a patient contains Bluetooth Low Energy SoC, a Lithium-Polymer battery, power management solution, low-power microcontroller, an analog front-end component, pulse oximeter (SpO2).

The chest sensor is placed on the body via a single-use chest adhesive. Both adhesives will be removed and discarded after one use. The limb sensor is held in place by a single-use finger adhesive, which is removed and discarded after one use, then replaced with a new finger adhesive.

Chest Unit **Limb Unit**

Multi-Use

Figure 1. The ANNE™ Sleep consists of 2 sensors, a chest unit worn on the thorax and a limb unit that folds over the index finger.

6. PREPARATION OF ANNE™ SLEEP SYSTEM

6.1 Standard study supply kit

The study sponsor company will ship ANNE™ Sleep system (study supply kit) to Northwestern.

Study supply kit list
● Cardboard mailer box ● Wearable study sensors ● Study devices (Tablet(s) or smart phone(s) with sensor application pre-loaded). ● Wireless charger(s), charger adaptors ● Device accessories; chest adhesives, finger adhesives ● Printed instructions or other study materials

The research coordinator from the sponsor will document tracking records of each device. All adhesives are single use with new ones provided to each new subject.

6.2 Study Kit Cleaning

Participants will return study supply kits in person by meeting a member of the research team or by mailing them back using pre-paid shipping labels. Study sensors are reusable after completion of study procedures and data collection.

The detailed sanitation instructions for the study kit are attached as **APPENDIX D.**

7. PREPARATION OF WatchPAT ONE

The WatchPAT ONE is a commercialized HST system, which received FDA 510(k) clearance (KK183559). The WatchPAT ONE will be prepared by following its operation manual.

The study coordinator will provide study participants a case with everything needed for a WatchPAT ONE. The case will include:

- An WatchPAT ONE device. This is a rectangular device that will keep track of body position (information such as whether a person is lying on their back, side, or stomach). It will also store all the information from the system.
- A pulse oximeter. This is a wire with a gray rubber sensor placed on the finger. It will measure pulse, blood flow, and the amount of oxygen in the blood. The pulse oximeter should already be attached to the device.
- A chest sensor. The Chest Sensor monitors snoring, movement, and body position. The chest sensor should already be attached to WatchPAT ONE.
- AA batteries. This will only use these if the batteries inside the HST device stop working.

8. STUDY PROCEDURES

8.1 Sleep Study Procedures

8.1.1 Consent form

To protect participant confidentiality, we will conduct all research-related discussions and informed consent procedures in a private setting. The consent process will be completed either in person or remotely by using an electronic consent document and collection of an electronic signature with REDCap or other electronic signature service like Adobe DocuSign. The study coordinator will review the Informed Consent in person, by phone or in Zoom during the remote informed consent discussion.

The study procedures, risks, and benefits will be discussed and the study team will answer all questions prior to obtaining consent. The person performing the Informed Consent process, will ask questions of the study subject to confirm understanding and comprehension of the study. All versions of the consent forms will be approved by the relevant ethics committees prior to study initiation.

Eligible participants who do not wish to participate in this study will continue to receive care according to local clinical standards.

Informed Consent will be reviewed and signed electronically using REDCap.

8.1.2 Initial Visit Day: Screening/Enrollment

The subject will have the option to discuss with the study coordinator over the phone or by a Zoom teleconference from the subject's personal device. If Zoom communication is selected a unique meeting number and password known only to the subject will be provided. The study coordinator will monitor the number of attendees in the meeting and restrict meetings to IRB approved researchers on this study, the study subject, and additional people at the subject's discretion. Researchers will host the Zoom sessions and will utilize the waiting room feature to ensure that only the appropriate participants are included on the call.

The study coordinator will cover following topics associated with the study during the Screening/Enrollment visit:

(1) Informed Consent will be reviewed and signed electronically using REDCap.
(2) The qualified subject will be asked to schedule a study date to participate at home. The nights of sensor wear do not need to be consecutive. Subjects will be instructed to set-up both devices on Night One of sleep testing and then only the ANNE device on Nights 2-4.
    One Night = HST and ANNE Sleep
    3 Additional Nights = ANNE Sleep only
    The target time frame will be to complete the sleep nights within 8 weeks of enrollment.

(3) Subjects will be advised to avoid alcohol and sleep medication use such as antihistamine (OTC) or prescribed medicines for sleep support on the testing night. Any use of these substances on the night of monitoring sleep will be asked to be recorded in the diary.

(4) Subjects will be informed how to complete the Demographic, Medical History and Sleep Survey sleep diary and usability survey (**Appendix A-C**). The surveys should be available to complete via an email link through REDCap or printed out forms.

Any subject's questions or concerns associated with the study will also be addressed.

At least 24 hours prior to the subject's sleep nights, the study coordinator will contact the participant by phone to confirm their planned sleep study nights at home.

The below sections describe the procedures for setting up the ANNE and HST devices, respectively.

8.1.3 ANNE™ Sleep procedures

The ANNE™ Sleep sensors will be applied by the study subjects themselves.

1) The PI or study coordinator will ensure the ANNE™ Sleep sensors are functional and collecting data properly prior to providing to subjects. The study coordinator will provide instructions for use of the ANNE™ Sleep system in the subject study kit.

2) Sensor placement (to be completed by the subject):

    a) Using IPA alcohol wipes, the subject will wipe down the areas of the skin where the sensors will be placed thoroughly to remove any dirt, oils, etc. IPA alcohol wipes will also be used to clean the surface of the sensors before placement. If necessary, the subject may need to shave their chest to provide better adhesion and comfort of the sensor.
    b) The subject will apply a single use adhesive to the chest sensor and place it on their chest at the suprasternal notch (see Figure 2). The subject will

attach the limb sensor to their finger using a single-use adhesive (see Figure 2).

Figure 2. Placement of the ANNE™ chest and limb sensors

3) Setting up a mobile device with an ANNE Sleep application

a) The subject will pair the ANNE™ Chest and ANNE™ Limb sensors with the ANNE Sleep mobile application by following the instructions on mobile device
b) After checking that the sensors are placed correctly and the signal quality is adequate, subjects will then proceed to sleep.

4) Data collection and storage

a) After a full night of data collection, data will be collected through the ANNE Sleep application. The subject will download the data from the sensor through Bluetooth.
b) The data will be uploaded automatically to ANNE™ Hub, a secure data repository from the application, and will be associated with the subject ID.
c) The data will be stored in an EDF data format for further analysis.

8.1.4 WatchPAT One Procedures

The device along with a user manual and quick start guide will be provided to the participant. Participants will be instructed to follow the safety instructions in the user manual.

The procedures for the WatchPAT ONE are as follows (to be completed by the subject):

1. Subject will download the WatchPAT One mobile application on their mobile device.
2. Subject will strap the WatchPAT device to their non-dominant hand.
3. Subject will place the chest sensor
   a. Subject will thread the chest sensor through the sleeve of their shirt.
   b. Subject will peel the liner from the adhesive and attach the chest sensor to the chest under the sternal notch.
4. Subject will place the finger probe
   a. Subject will insert a finger on the non-dominant hand into the Finger Probe until they feel the tip of the probe
5. Subject will press the START button on the application to begin data collection.
6. After a night of sleep, the subject will press the END RECORDING button on the application.

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8.2 COMPLETION OF THE STUDY

(1) After completing data collection, subjects will be given surveys (**Appendix C)** to complete in print material or by email link via a secure online platform managed by Northwestern University (i.e. REDCap).

(2) Once the surveys and sleep nights are complete, the study coordinator will let the subject know that their participation is complete. The study coordinator will have a phone call with the subject to confirm testing was successful and address any issues if needed.

(3) Subjects will be instructed to arrange for a time to return the study kit to the research team in person or will be provided with a pre-paid shipping label. A compensation gift card will then be mailed to the subject's home address or given to them in-person (if they return the study kits in person to the research team).

7.1.4 Checklist for scheduled events

The study coordinator should review the schedule of events, summarized below:

	Initial Visit Day: Screening/ Enrollment	ANNE™ and HST **Night One**	ANNE™ ONLY **Night Two, Three, and Four**	End of Study*
Eligibility	X			
Consent	X			
Demographics, Medical Hx, STOP-BANG Questionnaire	X			

ANNE™ Sleep		X	X	
HST Sleep		X		
Sleep Diary		X	X	
Phone follow-up (which may occur up to 1 week after the study)				X
Usability Survey				X
Adverse Events		X		X

9. SCORING

9.1 ANNE™ Sleep Scoring

The data from ANNE™ will be reviewed and scored for respiratory events by three (3) registered polysomnography technicians (RPSGT) who are blinded to the scoring of the HST, and represent scorers in clinical practice in AASM accredited sleep disorder centers. An average will be taken of the three scores. In order to minimize interscorer variability, the technicians will have >85% concordance. To ensure quality and reproducibility, a board certified sleep medicine physician who is blinded to the experimental condition will review all raw HST data. If AHI determined from ANNE™ Sleep exhibits greater than 15% difference between three RPSGTs, a board-certified sleep medicine physician will provide the final determination of the AHI for ANNE Sleep.

Scoring of ANNE™ Sleep data will follow guidelines established by the American Academy of Sleep Medicine Manual for the Scoring of Sleep and Associated Events (v2.6)[6]. Sleep scoring includes the following variables: total sleep time (TST= the total amount of sleep time scored during the total recording time in minutes). The scoring of respiratory events to evaluate for sleep disordered breathing will also follow AASM scoring rules.

The ANNE™ Sleep will be scored similarly with the system's onboard sensors as an alternative hypopnea and apnea sensor via PAT. The definition of mild, moderate, or severe obstructive sleep apnea is based on AHI.

- AHI < 5: Normal
- AHI ≥ 5 – <15: Mild
- AHI ≥15 – <30: Moderate
- AHI ≥ 30: Severe

The AHI calculated from ANNE™ Sleep will be considered an estimation of AHI, coined as AHI.

An apnea event is defined as:

- A drop in peak signal excursion by ≥ 90% of pre-event baseline for ≥ 10 seconds using an oronasal thermal signal, PAP device flow, or an alternative apnea sensor.
- No requirement for a desaturation or an arousal

Hypopnea will be defined by:

- The peak signal excursions drop by ≥30% of pre-event baseline using nasal pressure (diagnostic study), PAP device flow (titration study), or an alternative hypopnea sensor (diagnostic study)
- The duration of the ≥30% drop in signal excursion is ≥10 seconds
- There is a ≥4% oxygen desaturation from pre-event baseline and/or the event is associated with an arousal

The scoring of respiratory events to evaluate for sleep disordered breathing will also follow AASM scoring rules. Apnea-hypopnea index will be used to determine the presence and severity of sleep apnea (AHI= apneas + hypopneas *60/TRT).

The accuracy (sum of the number of true positives and true negatives divided by the sum of the number of true positives, true negatives, false positives, and false negatives), sensitivity, specificity, positive predictive value, and negative predictive value of the ANNE™ Sleep to detect moderate to severe obstructive sleep apnea will be compared to outputs from WatchPAT ONE. A Bland-Altman plot will be gerenated with 95% confidence to intervals to assess agreement.

9.2 WatchPAT ONE Scoring

The scoring method will be produced in accordance with the device operating manual.

10. STATISTICAL ANALYSIS

10.1 Sample size

With a sample size of at least 30, the large amount of within-person data provides high statistical power for all planned analyses, allowing this data set to answer all proposed questions while minimizing study costs and any risk to patients.

10.2 Apnea-hypopnea index (AHI) and oxygen desaturation index (ODI)

1. AHI will be calculated in ranges of 15 – 30 apnea/hypopnea events per hour for moderate OSA and ≥30 apnea/hypopnea events per hour for severe OSA. Continuous variables of AHIs during ~~three~~four-night study will be summarized using tables of descriptive statistics. The AHIs with variables will be summarized using counts and percentages. Descriptive statistics will be presented by diagnosis.
2. Diagnostic outcomes will be tabulated and compared for ANNE Sleep vs WatchPAT ONE.
3. Patient preference will be elicited via psychometric surveys for comfort and usability comparing ANNE and WatchPAT ONE.

4. The oxygen desaturation index (ODI), the hourly average number of desaturation episodes, will also be calculated.

10.3 Exploratory measurements for research purposes

Additional statistical analyses will be performed to compare outputs of AHI between the different systems. Specifically, these analyses include:

1. Linear regression to establish correlation between AHI determined by ANNE Sleep vs WatchPAT ONE on the same night. Bland-Altman plots will be created to establish bias and 95% confidence intervals of agreement between AHI determined by ANNE Sleep and WatchPAT ONE.
2. Summary statistics of the sensitivity, specificity and accuracy of the classification of the severity of OSA (normal, mild, moderate, and severe OSA) determined by AHI between ANNE Sleep and WatchPAT ONE.
3. Accuracy analysis between AHI determined by ANNE Sleep vs AHI determined by WatchPAT ONE on the same night.
4. Descriptive analysis of patients' characteristics and assessments (e.g. sleep diary) before and after study procedures. Patient characteristics include age, gender, ethnicity, race, height, weight, baseline vital signs, relevant medical and surgical co-morbidities will be abstracted from the medical record or by direct survey of the participants.
5. The listings, specifically adverse events and major protocol deviations, will be ordered by subject.

11. COMPENSATION FOR PARTICIPATION IN RESEARCH ACTIVITIES

Subjects who complete the at home testing will receive $100 in gift cards for their time and effort for completing all 4 nights with corresponding surveys. If subjects complete one night with the HST and ANNE and one night with ANNE only, they will receive $50 in gift cards for their time and effort for completing these 2 nights with corresponding surveys.

Compensation will be given to participants directly or mailed to the participant's home within 4-6 weeks after study completion.

12. WITHDRAWAL OF PARTICIPANTS

Participants may end their participation at any time during the study. The study investigators may choose to withdraw a study subject if he or she is unable to use the devices or complete the study procedures. The study investigators may withdraw a patient if they develop skin sensitivity or have a medical complication that precludes wearing of the sensors on the suprasternal notch.

If a subject is withdrawn from the study, they will be asked to return the study kit that is given to them at the start of the study. Unless specifically requested in writing, researchers will maintain and use data from patients that end their participation early.

13. RISKS TO PARTICIPANTS

Risk category: minimal

Potential risk: There is a risk of skin irritation, rash, possible injury upon removal of the sensor, or allergic reaction to the ANNE™ Sleep sensors adhesive. The devices will be placed on skin epidermis without conductive gel, thereby minimizing the risk of any skin irritation or allergic reaction. In addition, there will be no skin preparation except the use of a sterile alcohol pad (provided) to gently exfoliate the dead skin cells or dirt on epidermis. The adhesives are silicone based and have passed both biocompatibility, skin sensitization and cytotoxicity testing.

There is a risk of Protected Health Information (PHI) disclosure. Subject data will be de-identified and stored securely to prevent PHI disclosure.

Protection against risks: The sleep sensors can be removed if associated with significant discomfort or rash.

SURVEY/DIARY**:** Some questions may make subjects uncomfortable or upset. Subjects do not have to answer these questions if they do not want to.

14. ADVERSE EVENTS

The PI will determine whether adverse events are related to the study or unrelated to the study. The length of the study will be 4 nights. All serious adverse events – even if not deemed to be study-related – will be reported to the IRB. This includes a participant's death, life-threatening condition, hospitalization, or disability. All study-related adverse events determined by the PI as serious will be recorded and reported to the IRB and the sponsor within 1 business day. Serious study-related adverse events are defined as adverse skin effects that warrant prescription medical therapy, skin tears leading to bleeding or an open wound, or skin burns. Study-related adverse events will be recorded on the adverse event form. If participation is discontinued, the timing of this will be recorded.

15. DATA MANAGEMENT AND PARTICIPANT CONFIDENTIALITY

Subject identifiable medical information obtained as a result of this study is considered confidential and disclosure to third parties other than the PI and the study team is prohibited. All reports and communications relating to subjects in this study will refer to each subject only by their study identification number. Data generated as a result of this study are available for inspection on request by Food and Drug Administration or other government regulatory agency auditors, Sibel business partners specifically HealthCore, Inc. and the Institutional Review Board (IRB).

Subject identity will be protected through use of a coded list of identifiers which will be maintained separately from the data set. Any paper source documents, questionnaires, and CRFs are kept in a secured area (in a locked cabinet in a locked room) and all electronic data is password protected on a secure NU research server so that only authorized personnel can have access.

Only authorized research personnel listed on the IRB protocol will have direct access to this data set, although there may be collaborative exchange of de-identified data with other research institutions for assistance in the analysis of raw data.

Data will be capture using NU REDCap, a secure research database. Data stored and used for future research will be de-identified. Data will not be used for future research outside of the scope of this study.

PROTECTED HEALTH INFORMATION (PHI AND HIPAA)

The following PHI will be collected, and is also listed on the consent form for study enrollment:

- Demographic data including name, birthdate, address and phone number
- Results of physical examinations
- Medical history
- Lab tests, or certain health information indicating or relating to a condition as well diaries and questionnaires
- Records about study medication or drugs
- Records about study devices

Entry of any data into a study site clinical record during the duration of the research study is also PHI that may be collected and listed in the consent form. PHI from the above categories may be obtained from the respective study sites and affiliated entities listed as study locations.
Any research information shared with outside entities during the study will not contain the name, address, telephone or social security number or any other personal identifier unless disclosure of the identifier is necessary for review by such parties or is required by law or study site policy except that such information may be viewed by the Study sponsor and its partners or contractors at the Principal Investigator's office.

18. PROTOCOL DEVIATIONS

Any deviation from this protocol will be reported to the IRB.

19. CONSENT PROCESS

To protect participant confidentiality, we will conduct all research-related discussions and informed consent procedures in a private setting. The consent process will be completed either in person or remotely by using an electronic consent document and collection of an electronic signature with REDCap or other electronic signature service like Adobe DocuSign. The study coordinator will review the Informed Consent in person, by phone or in Zoom during the remote informed consent discussion.

The study procedures, risks, and benefits will be discussed and the study team will answer all questions prior to obtaining consent. The person performing the Informed Consent process, will ask questions of the study subject to confirm understanding and comprehension of the study. All versions of the consent forms will be approved by the relevant ethics committees prior to study initiation.

Eligible participants who do not wish to participate in this study will continue to receive care according to local clinical standards.

20. NON-ENGLISH-SPEAKING PARTICIPANTS

Non-English-speaking participants may be enrolled if the study team acquires an official translation of the approved informed consent form or performs consent with a translator and completes the accompanying short form in the participant's native language.

The research team will only enroll non-English speaking participants if a member of the study team is a fluent or native speaker of their language and assigned to them specifically. This is to ensure that continued support, clear communication and study training is possible for all study participants.

21. GOOD CLINICAL PRACTICE

The current study will be conducted in compliance with the protocol, International Conference on Harmonization Good Clinical Practice (ICH-GCP), and the applicable regulatory requirements. Study personnel involved in conducting this study will be qualified by education, training, and experience to perform their respective task(s) in accordance with GCP.

22. INSTITUTIONAL REVIEW BOARD (IRB)

All relevant documents for this study will be submitted to an appropriate Institutional Review Board (IRB) for review. A signed and dated letter documenting IRB approval must be obtained prior to entering participants at the site. IRBs must be constituted and their authority delegated through the institution's normal process of governance according to applicable regulatory requirements for each participating site. Each participating institution must provide for the review and approval of this protocol and the associated informed consent documents and relevant participant materials by an appropriate IRB. For each participating site, the protocol and associated informed consent and relevant participant materials will be submitted for approval to the local IRB, as per site local regulatory policies and procedures. The study will not commence at any site until initial approval is obtained from the designated IRB and an approval to enroll notification is released to the site.

The investigators must obtain approval from the IRB for all protocol amendments and, when warranted, changes to the informed consent document and/or participant materials. Protocol and informed consent form amendments can be made only with the prior approval from the PI. The investigator may not implement any protocol deviation except where necessary to eliminate an immediate hazard to study participants, or when change(s) involve only logistical or administrative aspects of the trial, i.e., change of monitor(s) or telephone number(s) (ICH 4.5.2). The investigator shall notify the IRB of deviations from the protocol or serious adverse events occurring at the site.

24. REFERENCES

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APPENDIX A - SLEEP DIARY

ID/NAME:

	SAMPLE	
Today's Date	2/25/2021	
1. What time did you get into bed?	10:15 p.m.	
2. What time did you try to go to sleep?	11:30 p.m.	
3. How long did it take you to fall asleep?	55 min.	
4. How many times did you wake up, not counting your final awakening?	6 times	
5. In total, how long did these awakenings last?	2 hours 5 min.	
6a. What time was your final awakening?	6:35 a.m.	
6b. After your final awakening, how long did you spend in bed trying to sleep?	45 min.	
6c. Did you wake up earlier than you planned?	☑ Yes ☐ No	☐ Yes ☐ No
6d. If yes, how much earlier	1 hour	
7. What time did you get out of bed for the day?	7:20 a.m.	
8. In total, how long did you sleep?	4 hours 10 min.	
9. How would you rate the quality of your sleep?	☐ Very poor ☑ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good
10. How rested or refreshed did you feel when you woke-up for the day?	☐ Not at all rested ☑ Slightly rested ☐ Somewhat rested ☐ Well-rested ☐ Very well-rested	☐ Not at all rested ☐ Slightly rested ☐ Somewhat rested ☐ Well-rested ☐ Very well-rested
11a. How many times did you nap or doze?	2 times	
11b. In total, how long did you nap or doze?	1 hour 10 min.	
12a. How many drinks containing alcohol did you have?	3	
12b. What time was your last drink?	9:20 p.m.	
13a. How many caffeinated drinks (coffee, tea, soda, energy drinks) did you	2 drinks	
13b. What time was your last drink?	3:00 p.m.	
14a. Did you take any over-the counter or prescription medication(s) to help you sleep?	☑ Yes ☐ No	☐ Yes ☐ No
14b. If yes, list medication(s), dose, and time taken.	**Medication(s):** Relaxo-Herb **Dose:** 50 mg **Time(s) taken:**	**Medication(s):** **Dose:** **Time(s) taken:**
15. Comments (if applicable)	I have a cold	

APPENDIX B –
APNEAS ANNE Sleep Sensor Survey
Subject #: _____ **Date: ____/_____/_____**

Thank you for participating in wearing the ANNE Sleep system. This survey helps researchers better understand your experience with wearing sensors and helps develop and improve them for future patients. Please provide one answer to each of the following questions. You can skip any questions you do not know the answer to or do not want to answer.

1. Overall, all of the the sleep study sensors were comfortable for me to sleep with:

☐ Strongly Agree	☐ Agree	☐ Neither agree or disagree	☐ Disagree	☐ Strongly Disagree

2. Overall, ANNE Sleep sensors were comfortable for me to sleep with:

☐ Strongly Agree	☐ Agree	☐ Neither agree or disagree	☐ Disagree	☐ Strongly Disagree

3. How quickly you fell asleep comparing to typical nights for you

☐ Much Slower	☐ Slower	☐ About the same	☐ Faster	☐ Much Faster

4. The ANNE Sleep Sensors would be more comfortable to other sleep sensors

☐ Strongly Agree	☐ Agree	☐ Neither agree or disagree	☐ Disagree	☐ Strongly Disagree

5. The **application** of the ANNE Sleep Sensors was easy and comfortable.

☐ Strongly Agree	☐ Agree	☐ Neither agree or disagree	☐ Disagree	☐ Strongly Disagree

6. The **removal** of the ANNE Sleep Sensors was easy and comfortable.

☐ Strongly Agree	☐ Agree	☐ Neither agree or disagree	☐ Disagree	☐ Strongly Disagree

7. Using wireless ANNE Sleep Sensors would be easy to do at home.

☐ Strongly Agree	☐ Agree	☐ Neither agree or disagree	☐ Disagree	☐ Strongly Disagree

8. Please describe how the **wireless Chest sensor** felt while sleeping.

☐ Very uncomfortable ☐ Uncomfortable ☐ No change ☐ Comfortable ☐ Very comfortable

9. Please describe how the **wireless Limb sensor** felt on your finger while sleeping.

☐ Very uncomfortable ☐ Uncomfortable ☐ No change ☐ Comfortable ☐ Very comfortable

10. Please indicate if you experienced the following while wearing the **wireless sensors**:

☐ Redness ☐ Irritation ☐ Both ☐ None

11. Having my sleep data collected at home and sent to my doctor would be more convenient for me.

☐ Strongly Agree ☐ Agree ☐ Neither agree or disagree ☐ Disagree ☐ Strongly Disagree

12. I could see myself using ANNE Sleep at home to monitor my breathing while I sleep.

☐ Strongly Agree ☐ Agree ☐ Neither agree or disagree ☐ Disagree ☐ Strongly Disagree

13. Please provide any other thoughts about the concerns or benefits of wireless monitoring:

APPENDIX C – DEMOGRAPHIC, MEDICAL HISTORY AND SLEEP DIARY

Field Label	Choices, Calculations, OR Slider Labels
In order to ensure that this research serves all people living in the U.S., we need to ask you how identify your ethnic and racial background. This information will remain confidential, and will not affect your participation in the study in any way. It will only be used for reporting general demographics or statistics. **The following questions are about your demographic background:**	
Gender	1, Male | 2, Female
Race:	1, American Indian or Alaska Native | 2, Asian | 3, Native Hawaiian or Pacific Islander | 4, Black or African American | 5, White | 6, More than once race | 7, Choose not to answer
Ethnicity:	1, Hispanic or Latino | 2, Non-Hispanic or Latino | 3, Choose not to answer
Highest Education Level completed:	1, Never attended school or only attended kindergarten | 2, Grades 1 through 8 (Elementary) | 3, Grades 9 through 11 (Some high school) | 4, Grade 12 or GED (High school graduate) | 5, College 1 year to 3 years (Some college or technical school) | 6, College 4 years of more (College graduate)
Current Marital Status:	1, Married | 2, Single | 3, Widowed | 4, Divorced/Separated | 5, Domestic partner
Current Employment Status:	1, Employed | 2, Unemployed | 3, Retired | 4, Retired due to disability
The following questions are about your Health:	
Date of last medical exam:	
Sleep Provider:	
Location:	1, Northwestern Memorial Hospital (Downtown) | 3, Central DuPage Hospital (CDH) | 4, Northwestern Medical Group (NMG)
Height:	
Weight:	
Are you currently diagnosed or do you have a history of any cardiovascular disorders?	
Please select all that apply:	1, Hypertension (high blood pressure) | 2, Congenital heart disease (malformations of heart structure existing at birth) | 3, Arrhythmia (abnormal heart rhythm) | 4, Coronary artery disease (narrowing of the arteries) | 5, Deep vein thrombosis (blood clot in lower extremities) | 6, Pulmonary embolism (blood clot in the lungs) | 7, Heart attack | 8, Heart failure | 9, Cardiomyopathy (heart muscle disease) | 10, Other
If other, please explain:	
If you selected any of the above disorders, please include dates of diagnosis and current status (ongoing or resolved). If resolved, please include end date:	

Are you currently diagnosed or do you have a history of any pulmonary or respiratory system disorders?	
Please select all that apply:	1, Asthma | 2, Chronic Obstructive Pulmonary Disease (COPD) | 3, Chronic Bronchitis | 4, Lung Cancer | 5, Pneumonia | 6, Emphysema | 7, COVID-19 | 8, Pleural Effusion (collection of fluid between the lung and chest wall) | 10, Other
If other, please explain:	
If you selected any of the above disorders, please include dates of diagnosis and current status (ongoing or resolved). If resolved, please include end date:	
Are you currently diagnosed or do you have a history of any gastrointestinal (GI) disorders?	
Please select all that apply:	1, Acid reflux | 2, Heartburn | 3, GERD | 4, Crohn's disease | 5, Ulcerative colitis | 6, Irritable Bowel Syndrome (IBS) | 7, Peritonitis | 8, Fibrosis and cirrhosis of liver | 9, Cholecystitis | 10, Other
If other, please explain:	
If you selected any of the above disorders, please include dates of diagnosis and current status (ongoing or resolved). If resolved, please include end date:	
Are you currently diagnosed or do you have a history of any endocrine system disorders?	
Please select all that apply:	1, Hyperthyroidism | 2, Hypothyroidism | 3, Thyrotoxicosis | 4, Hypoparathyroidism | 5, Type I Diabetes | 6, Type II Diabetes | 7, Adrenal disorder | 8, Cushing's syndrome | 10, Other
If other, please explain:	
If you selected any of the above disorders, please include dates of diagnosis and current status (ongoing or resolved). If resolved, please include end date:	
Are you currently diagnosed or do you have a history of any neurological disorders?	
Please select all that apply:	1, Dementia | 2, Huntington's Disease | 3, Parkinson's Disease | 4, Alzheimer's Disease | 5, Bell's Palsy | 6, Cerebral Aneurysm | 7, Epilepsy or Seizures | 8, Fibromyalgia | 9, Amyotrophic Lateral Sclerosis (ALS) | 10, Other
If other, please explain:	
If you selected any of the above disorders, please include dates of diagnosis and current status (ongoing or resolved). If resolved, please include end date:	
Are you currently diagnosed or do you have a history of any sleep disorders?	
Please select all that apply:	1, Insomnia | 2, Restless Leg Syndrome | 3, Parasomnia | 4, Sleep Apnea (confirmed diagnosis) | 5, Narcolepsy | 10, Other
If other, please explain:	
If you selected any of the above disorders, please include dates of diagnosis and current status (ongoing or resolved). If resolved, please include end date:	

Are you currently diagnosed or do you have a history of any psychiatric or psychological disorders?	
Please select all that apply:	1, Bipolar disorders | 2, Depression | 3, Anxiety | 4, Post-traumatic stress disorder (PTSD) | 5, Schizophrenia | 6, Personality disorders | 10, Other
If other, please explain:	
If you selected any of the above disorders, please include dates of diagnosis and current status (ongoing or resolved). If resolved, please include end date:	
Are you currently diagnosed or do you have a history of any lymphatic or hematologic disorders?	
Please select all that apply:	1, Lymphedema | 2, Hodgkin's Lymphoma | 3, Non-Hodgkin's Lymphoma | 4, Anemia | 5, Sickle cell | 6, Leukemia | 10, Other
If other, please explain:	
If you selected any of the above disorders, please include dates of diagnosis and current status (ongoing or resolved). If resolved, please include end date:	
Are you currently diagnosed or do you have a history of any skin or dermatological disorders?	
Please select all that apply:	1, Acne | 2, Hives | 3, Rosacea | 4, Eczema | 5, Psoriasis | 6, Melanoma | 10, Other
If other, please explain:	
If you selected any of the above disorders, please include dates of diagnosis and current status (ongoing or resolved). If resolved, please include end date:	
Are you currently diagnosed or do you have a history of any musculoskeletal disorders?	
Please select all that apply:	1, Carpal tunnel | 2, Arthritis | 3, Osteoporosis | 4, Tension Neck Syndrome | 5, Tendonitis | 6, Broken bone | 7, Tendon or Ligament Sprain | 8, Torn Rotator Cuff | 9, Ruptured or Herniated Disc | 10, Other
If other, please explain:	
If you selected any of the above disorders, please include dates of diagnosis and current status (ongoing or resolved). If resolved, please include end date:	
Do you have a history of any allergies? This can include seasonal, skin, food, or drug/medicine allergies.	
Please list allergies here, including start dates and current status (ongoing or resolved). If resolved, please include end date:	
Do you have a history of any other medical illness?	

SLEEP DIARY	
The following questions are about your sleep last night (before study visit).	
Please list all other medical illnesses here, including start dates and current status (ongoing or resolved). If resolved, please include end date:	
2. Did you wear CPAP Device last night?	
If yes, level of titration:	
3. What time did you go into bed? {time_in_bed}	
4. What time did you try to go to sleep? {time_sleep} {ampm}	
	1, AM | 2, PM
5. How long did it take you to fall asleep?	
6a. How many times did you wake up, not counting your final awakening?	
6b. In total, how long did these awakenings last?	
7a. What time was your final awakening?	
7b. After your final awakening, how long did you spend in bed trying to fall back asleep?	
7c. Did you wake up earlier than you planned?	
7d. If yes, how much earlier?	
8. What time did you get out of bed for the day? {time_up} {am_and_pm}	
9. In total, how long did you sleep?	
10. How would you rate the quality of your sleep?	1, Very poor | 2, Poor | 3, Fair | 4, Good | 5, Very good
11. How rested or refreshed did you feel when you woke up for the day?	1, Not at all rested | 2, Slightly rested | 3, Somewhat rested | 4, Well-rested | 5, Very well-rested
12a. How many times did you nap or doze?	
12b. In total, how long did you nap or doze?	
13a. How many drinks containing alcohol did you have?	
13b. What time was your last drink? {time_drink}{am_pm_2}	
14a. How many caffeinated drinks (coffee, tea, soda, energy drinks) did you have?	
14b. What time was your last drink? {time_coffee}{am_pm_3}	
15. Did you take any over-the-counter or prescription medication(s) to help you sleep?	
Type of medication:	
Dose:	
Time taken:	

Did you take any additional medications?	
Type of medication:	
Dose:	
Time taken:	
16. Comments, if applicable:	

APPENDIX D - STUDY KIT CLEANING INSTRUCTION

Study sensors are reusable after completion of study procedures and data collection. Used study kit containers will be wiped on the outside using Sani-Cloth before handling and placed in a fume hood labeled “Contaminated Study Kits” in accordance with the study protocol.

The following procedures will be conducted by a research assistant from the study sites:

1. The researcher assistant is to wear appropriate PPE including lab coat, and nitrile gloves before handling any study supplies.
2. The fume hood labeled “Contaminated Study Kits” will have all surfaces cleaned and wiped down with Sani-Cloth and/or 70% EtOH solution.
3. The outside of study kit containers will be cleaned and wiped down with Sani-Cloth and/or 70% ETOH solution.
4. Once all used study kits are cleaned on the outside they may be opened, one at a time, to have contents cleaned. All study sensors, devices, chargers, cords and accessories will be wiped with Sani-Cloth and allowed 2 minutes to air dry on a cleaned surface.
5. Sensors will be closely examined for physical breaks, holes or tears in the silicone packaging. Any sensors that have physical damage will be sealed in separate plastic containers or plastic bags and labeled for return to the manufacturer.
6. Do not reuse towelette. Dispose of used Sani-Cloth in trash.
7. Individually wrapped, sealed adhesives may be cleaned in the same process.
8. Unsealed adhesives will be discarded along with any printed materials from the study kit.
9. Once all contents of the study kit have been removed from the container, inside of study kit containers will be cleaned and wiped down with Sani-Cloth and/or 70% EtOH solution. Allow to air dry for 2 minutes.
10. Return study kit contents to the study container.
11. The fume hood with Contaminated Study Kits will have all surfaces cleaned and wiped down with Sani-Cloth and/or 70% EtOH solution.
12. Cleaned study kits may be placed in the “Clean Kits” designated area for reuse.

Materials and PPE	Study supply kit list
● 70% ETOH ● Super Sani-Cloth Germicidal Wipe*	● Cardboard mailer box. ● Wearable study sensors ● Study devices (Tablet(s) or smart

● Disposable paper towel ● Nitrile Gloves ● Lab coat ● Face mask*	phone(s) with sensor application). ● Wireless charger(s), charger cords, bricks ● Device accessories; adhesives for both sensors ● Printed instructions or study other study materials

*Super Sani-Cloth is an EPA registered hospital-grade disinfectant to accommodate the many situations and hard non-porous environmental surfaces found in healthcare settings. This wipe kills bacteria, viruses, and yeast.

* Hospital COVID precautions will be used at all times during the study. .

The study sponsor should perform an inspection of each device and ensure cleaning procedures should be conducted before shipping and after receiving the return shipment per guidance from the Center for Disease Control[8].

APPENDIX E - STOP-BANG QUESTIONNAIRE

Snoring: Do you snore? Loud enough to be heard through closed doors or loud enough to disturb your partner?

Yes	**No**

Tired: Do you often feel tired, fatigued or sleepy during the daytime?

Yes	**No**

Observed: Has anyone observed you stop breathing, choking or gasping while you were sleeping?

Yes	**No**

Pressure: Are you being treated for high blood pressure?

Yes	**No**

Body Mass: What is your Body Mass Index (BMI)?

Height (in inches):

Weight (in pounds):

Less than 25		**Greater than 25**
Greater than 30		**Greater than 35**

Age: Are you older than 50?

Yes	No

Is your shirt collar 16 inches / 40 cm or larger?

Yes	No	Unknown

Gender: Are you male?

Yes	No

OSA - Low Risk: Yes to 0 - 2 questions

OSA - Intermediate Risk: Yes to 3 - 4 questions

OSA - High Risk: Yes to 5 - 8 questions

or Yes to 2 or more of 4 STOP questions + male gender

or Yes to 2 or more of 4 STOP questions + BMI > 35kg/m2

or Yes to 2 or more of 4 STOP questions + neck circumference 17 inches / 43cm in male or 16 inches / 41cm in female

APPENDIX F: <u>Eligibility Screening Questions:</u>

Do you have significant cardiorespiratory disease including any of the following:

Chronic obstructive pulmonary disease (COPD)

Congestive Heart Failure

Atrial Fibrillation

Other (please describe)

Have you previously been hospitalized for cardiorespiratory issues?

-If yes, please describe.

Do you have an implanted pacemaker or defibrillator?

Do you use oxygen while sleeping?

Do you have respiratory muscle weakness due to neuromuscular condition?

Have you experienced awake hypoventilation or suspicion of sleep related hypoventilation (breathing at an abnormally slow rate)?

Have you used opioid medication for more than 3 months?

Have you ever had a stroke?

Do you have a history of severe insomnia?

Do you have a history of dementia?

Follow up enrollment questions:

What is the best phone number to reach you at?

What is your preferred email address?

What is the best time to contact you? (Day(s), time(s))

APPENDIX G: ANNE Sleep Scoring Manual

ANNE® Sleep Scoring Manual

Version 1.1

Sibel Inc.
6650 W. Touhy Ave
Niles, IL 60714

Table of Contents

Change Log

Revision	Effective Date	Description of Revision
A	12/1/2021	Initial Release

1.0 1.0 Introduction

ANNE Sleep is a wireless physiological recorder for use as an aid in the diagnosis of sleep-related breathing disorders by healthcare professionals. The system features two wearable sensors that pair with the ANNE Sleep application for the transmission and

storage of data. The sensors, which are placed on the chest and finger, collect peripheral arterial tonometry (PAT), chest movement, oximetry, snoring, body position, and heart rate. The device is intended for use in the clinical and home setting under the direction of a Healthcare Professional (HCP).

The purpose of the ANNE Sleep Scoring Manual is to provide guidelines and step-by-step instructions for sleep technicians and physicians to score the ANNE Sleep recordings.

2.0 2.0 Background

2.1 Indication for use of ANNE™ Sleep

ANNE Sleep is a wearable sensor system intended for use in the collection, analysis, display, and storage of physiological parameters to aid in the evaluation of sleep-related breathing disorders of adult patients suspected of sleep apnea. The device is intended for use in the clinical and home setting under the direction of a Healthcare Professional (HCP).

2.2 ANNE Sensors Description

ANNE Sleep uses the ANNE Chest and ANNE Limb sensors to detect sleep distorted breathing. The sensors are worn by the patient during a night of sleep. Both sensors wirelessly measure biosignals and transfer them to the ANNE Sleep mobile application through Bluetooth.

The ANNE Chest sensor is placed under the suprasternal notch as shown below (Figure 1) with a silicone gel adhesive. The ANNE Chest measures snoring through the accelerometer z-axis sampled at a high-frequency and chest movement through the x and y-axis.

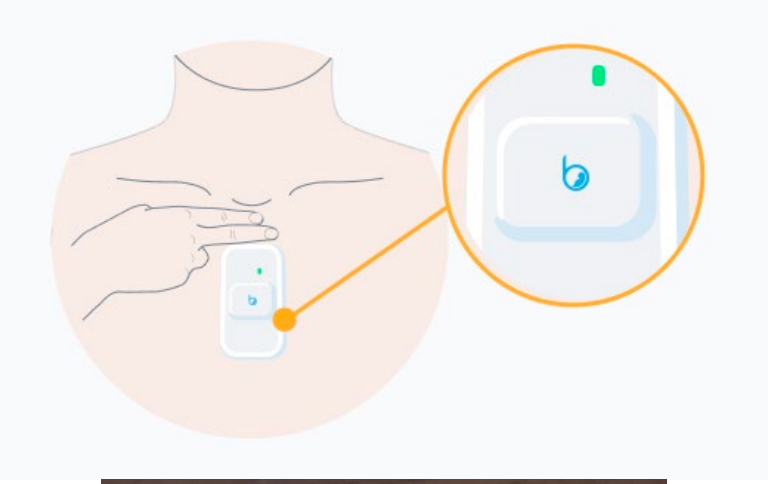

Figure 1: Placement of the ANNE Chest Sensor

The ANNE Limb sensor is worn on the finger and collects photoplethysmograph (PPG) signals for the calculation of SpO2, PAT, and pulse rate. The ANNE Limb Sensor is secured to the finger with a medical foam tape adhesive as shown below in Figure 2.

Figure 2: Limb Sensor worn

2.3 Signals Acquired by ANNE Sleep

The signals listed in Table 1 are used by ANNE Sleep to detect respiratory events. The signals will be available in the EDF file that is generated as part of the data flow. The signals are downsampled to be easily transmitted and viewed.

Table 1: Sleep Signal Generated from the ANNE Sensors

Signal	Device	Description	Sampling Rate (Hz)
PAT (A.U)	Limb	Peripheral Arterial tone	32
Pulse Amplitude (A.U)	Limb	Pulse amplitude from the PAT signal	2
Accel Vertical (g)	Chest	Chest movement picked up by ANNE Chest's vertical roll. Refer to Figure 3	32
Accel Horizontal (g)	Chest	Chest movement picked up by ANNE Chest's horizontal roll. Refer to Figure 3	32

Snore (g)	Chest	Snore signal from ANNE Chest	256
Pulse Rate (bpm)	Limb	Pulse rate derived from ANNE Limb Sensor	2
SpO2 (%)	Limb	Oxygen saturation derived from ANNE Limb Sensor	2
Body Position	Chest	Position of the Body	1

The ANNE Chest Sensor derives horizontal roll and vertical roll from the 3-axis accelerometer to measure the tilt of the sensor in both directions. Displaying the roll of the sensor instead of the acceleration allows the chest movements to be more clearly shown graphically.

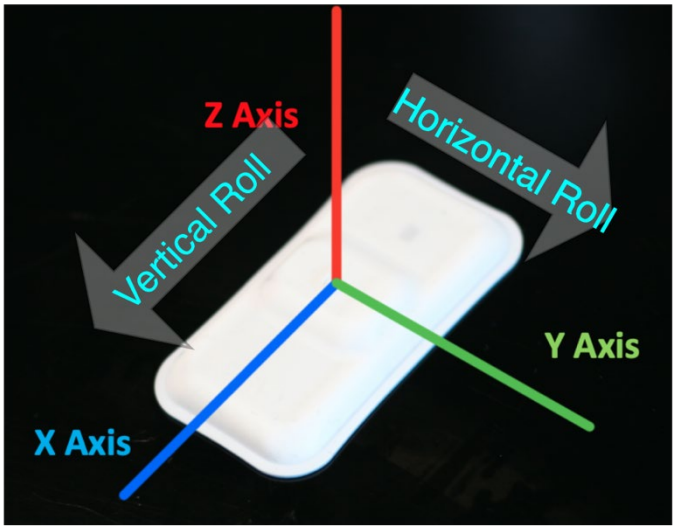

Figure 3: Accelerometer axis orientation of ANNE Chest

The body position of the patient is also derived by the 3-axis accelerometer. The system provides 5 body positions - upright, supine, prone, left, and right.

3.0 3.0 Scoring Procedure

3.1 Data Flow Overview

The high-level data flow is shown below (Figure 4). After the patient has received the ANNE Sleep system and successfully finished their sleep night data collection, the data is downloaded from the sensors and automatically uploaded to the ANNE Sleep Hub. In the ANNE Sleep Hub, the data collected from the ANNE sensors are processed and converted into an EDF format file so that it can be consumed by EDF viewers and scoring platforms such as EnsoSleep. After the dataset has been scored, the scored data is transferred back to the ANNE Sleep Hub for sleep report generation. The report generated can then be reviewed by a Healthcare Professional (HCP) to aid in the evaluation of sleep-related breathing disorders.

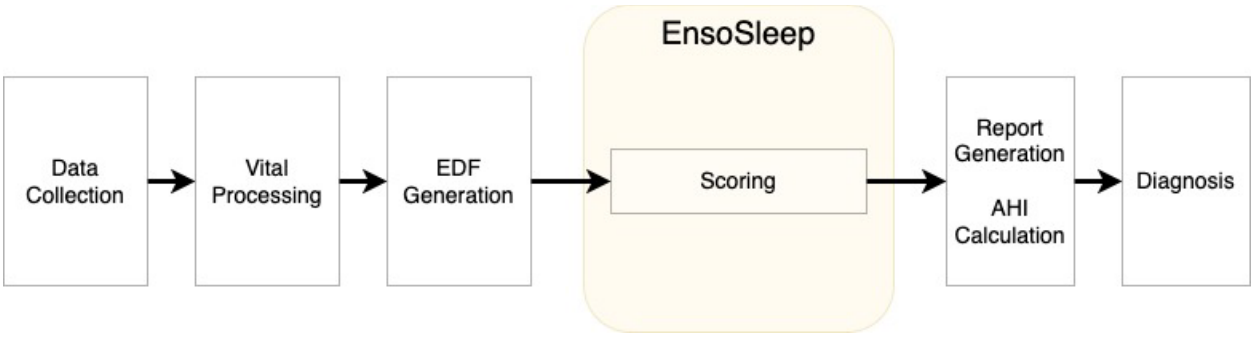

Figure 4: ANNE Sleep Data Flowchart

pAHI (peripheral arterial tonometry AHI) is calculated by counting the number of sleep-disordered breathing events for the patient divided by the TST (total sleep time). TST is automatically calculated in ANNE Sleep Hub using pulse rate.

pAHI=Total Number of Disordered Breathing EventsTotal Sleep Time (hrs)

3.2 EnsoSleep

The ANNE Sleep system uses EDF viewers or scoring platforms such as EnsoSleep for scoring the sleep recordings. This section contains the steps for scoring ANNE Sleep data with EnsoSleep.

3.1.1 Choosing a patient to Score

Select the dataset to score by identifying them through the Patient column. After selecting the patient, click the vital icon as shown below in Figure 5 to proceed to create a score set.

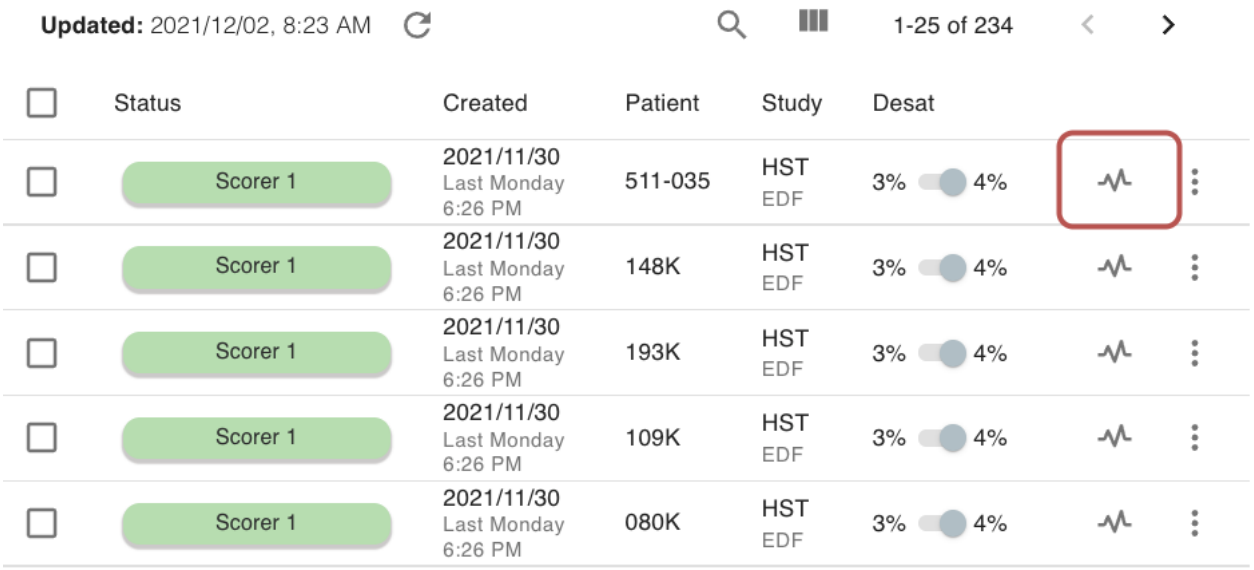

Figure 5: EnsoSleep Dashboard

3.1.2 Creating a Score Set

Create a new score set based on the "**sibel**" score set. It will contain pre-labeled sleep events from EnsoSleep. Left-click "proceed" to get to the scoring screen as shown in Figure 7.

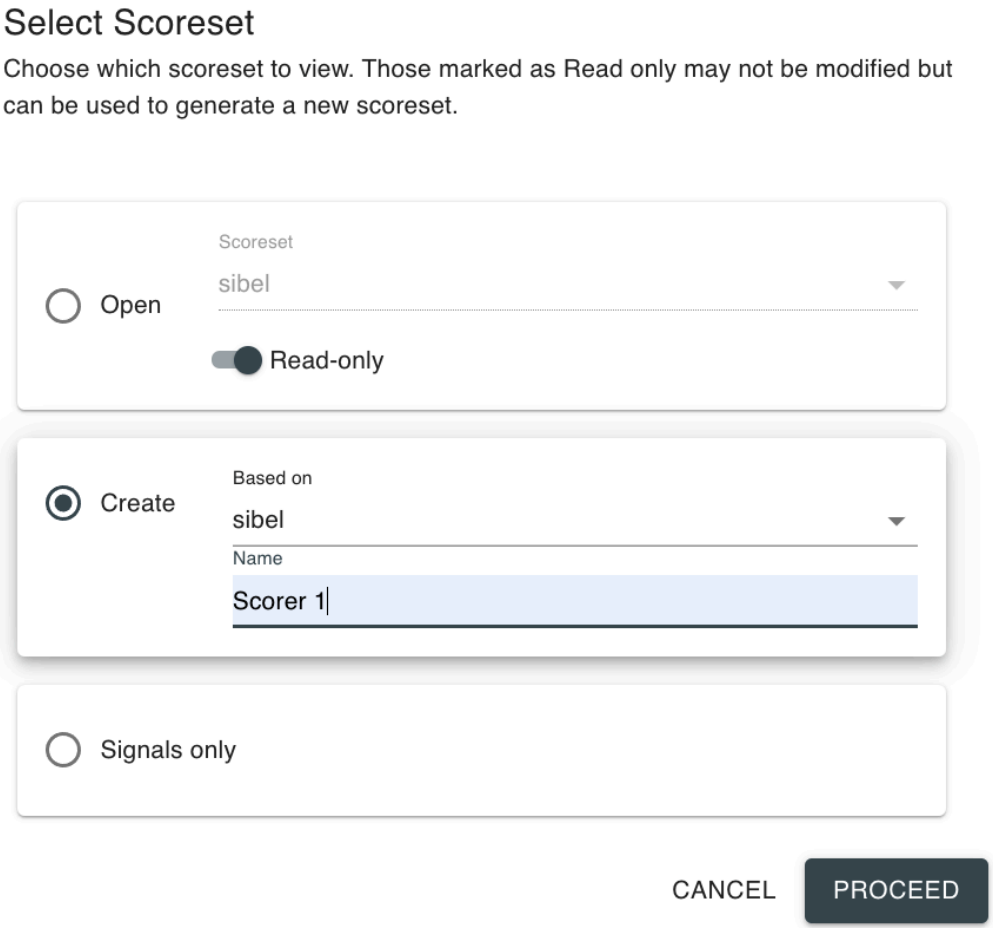

Figure 6: EnsoSleep Scoreset selection Screen

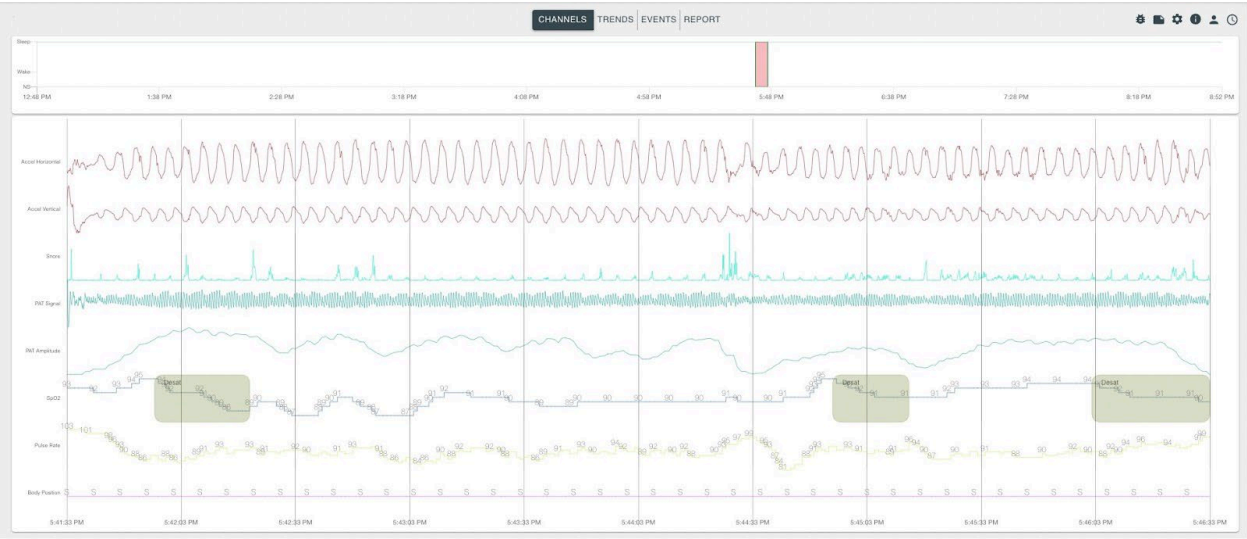

Figure 7: EnsoSleep Scoring Screen

3.1.3 Configuring the Scoring Screen

On the top right corner of the scoring screen, click the settings icon to modify the time span. A 5-minute timespan is recommended for optimal view of PAT signal changes.

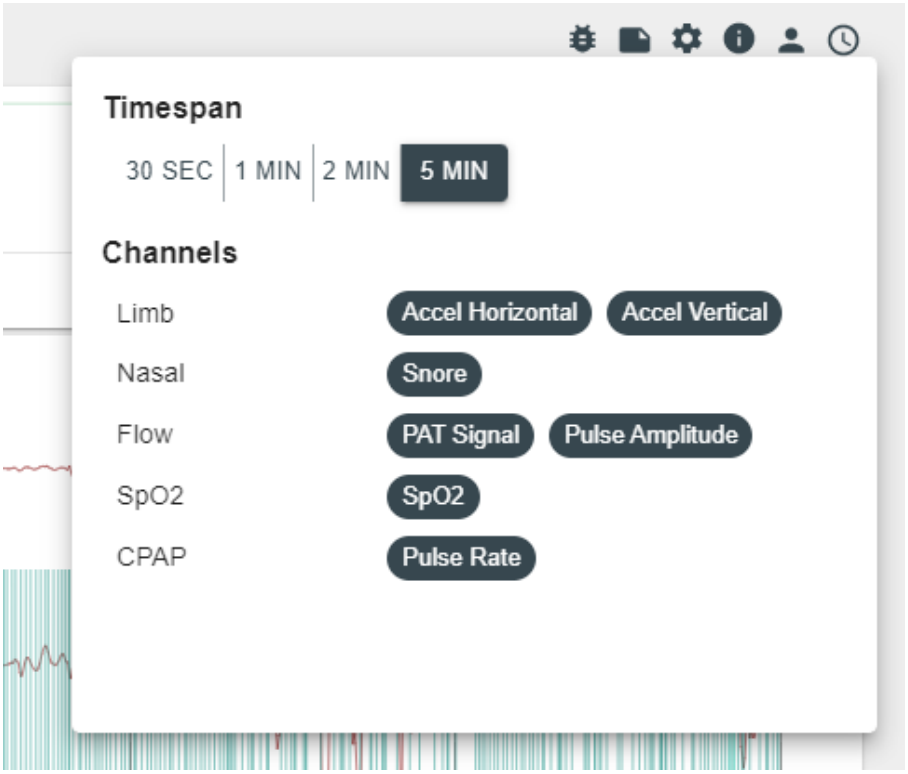

Figure 8: Enso Sleep Settings Screen

Utilize the “R” key on the keyboard to rescale all the signals throughout the scoring process.

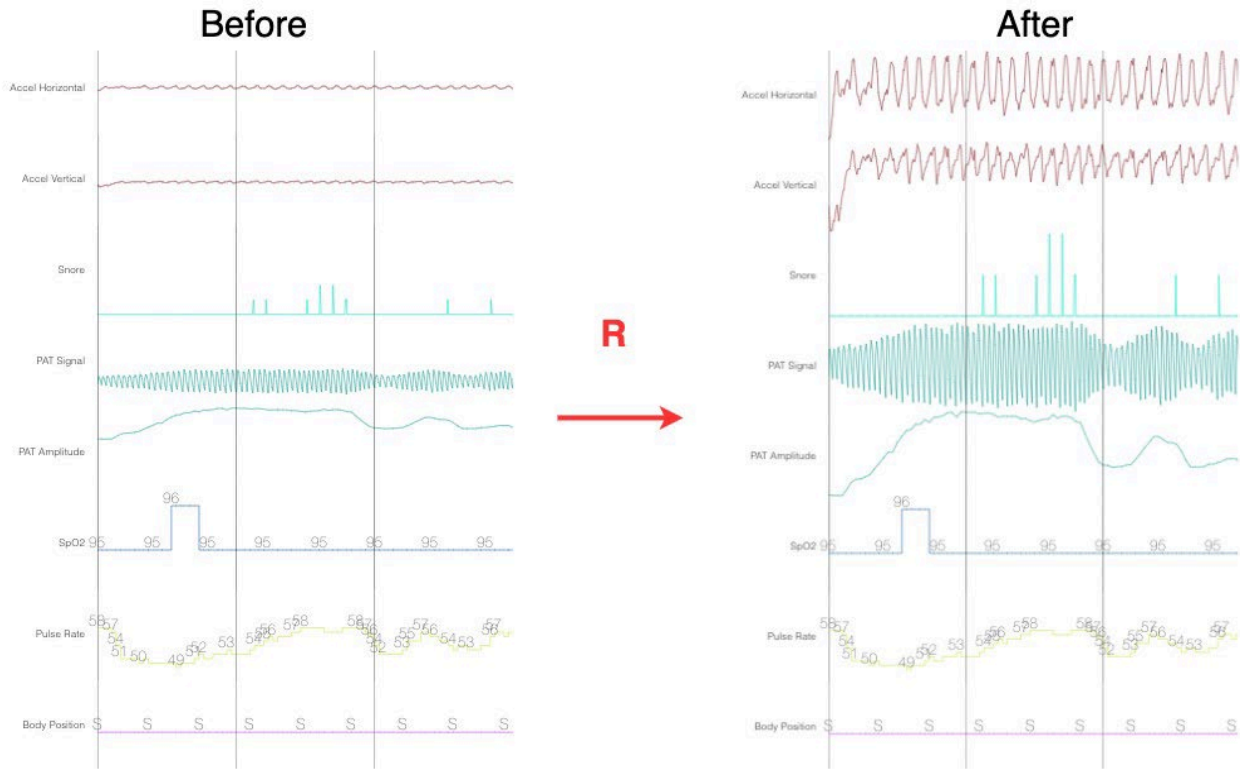

Figure 9: Before and After pressing the R key

Auto scaling obfuscates any evidence of the changes in signal due to heterogeneity in amplitude attributed to regular chest movements and motion artifacts. In order to rescale the two signals only, EnsoSleep provides features to manually adjust the desired scale for each channel. Below is an example where it might look like a chest movement reduction but is actually a zoomed-out view due to motion artifacts.

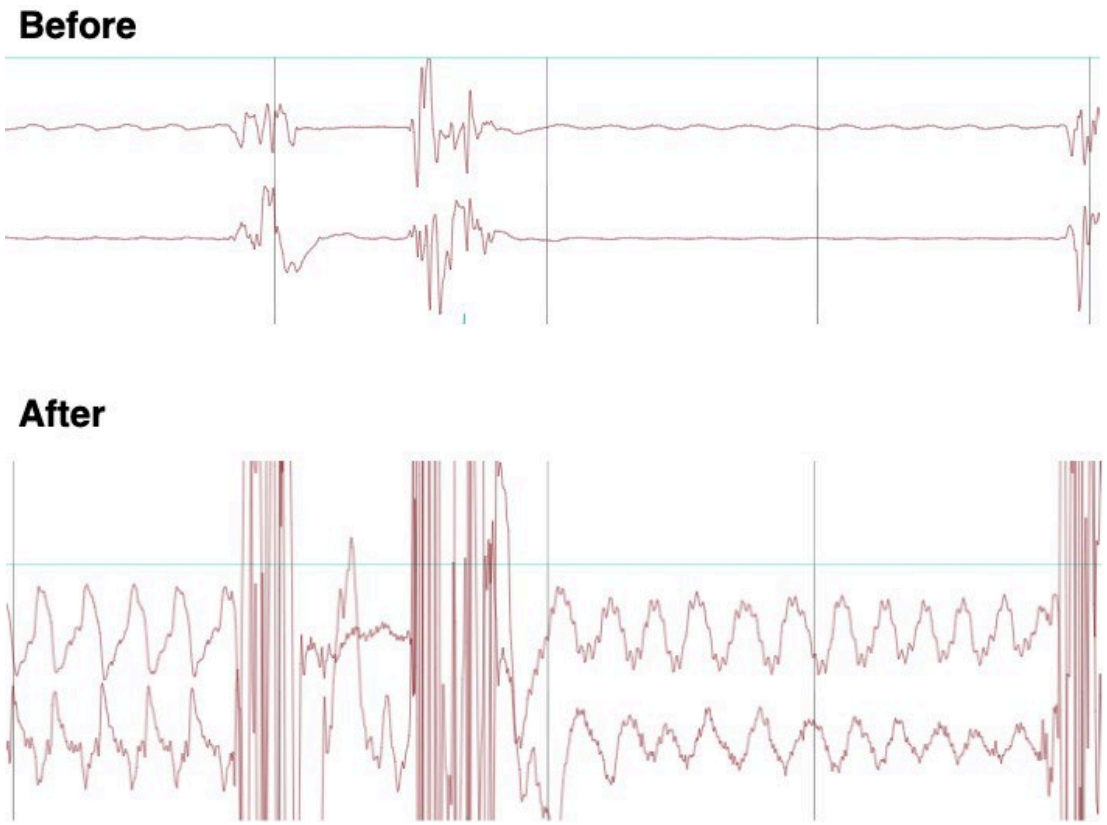

Figure 10: Signal Zoomed Out Due to Motion Artifact

When you see motion artifacts, manually rescale these two signals. You can rescale for each channel by right-clicking on the signal name on the far left side to get a pop-up screen as shown below. Click + or - to adjust the scale.

Figure 11: Rescale Feature

3.1.4 Adding Sleep Disordered Breathing Events

Drag the cursor on the **PAT signal** to label a sleep-disordered breathing event as **Obstructive Hypopnea**. Do not use other event types as the ANNE Sleep system will not distinguish differences among Obstructive Apnea, Hypopnea, and Central Apnea.

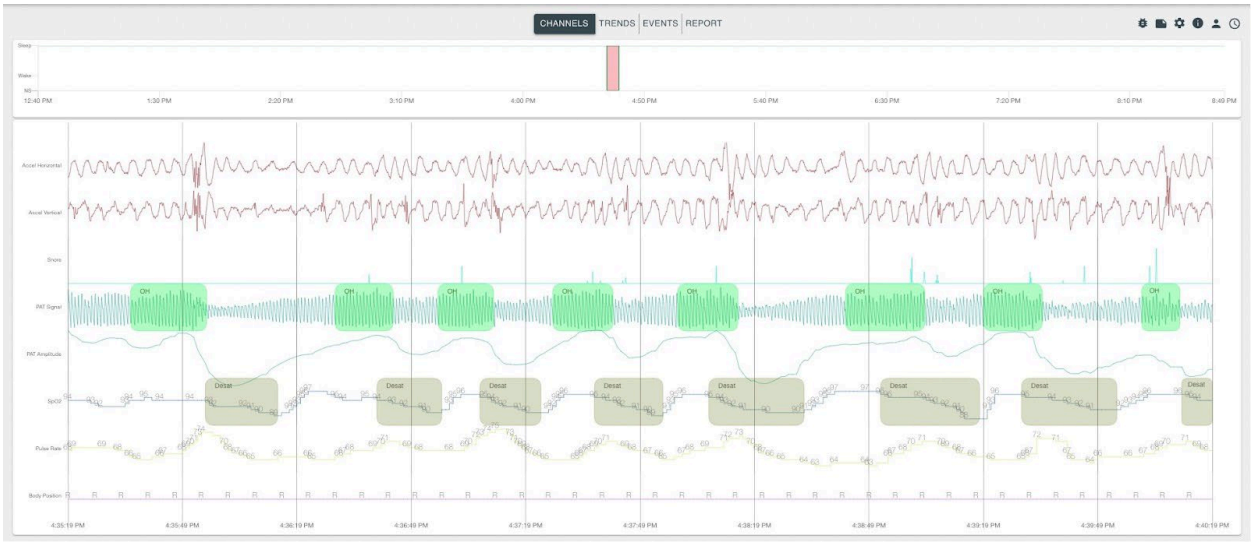

Figure 12: Enso Sleep Marked Events Scoring Screen

3.1.5 Deleting Sleep Disordered Breathing Events

To delete an event, right-click the event and click delete.

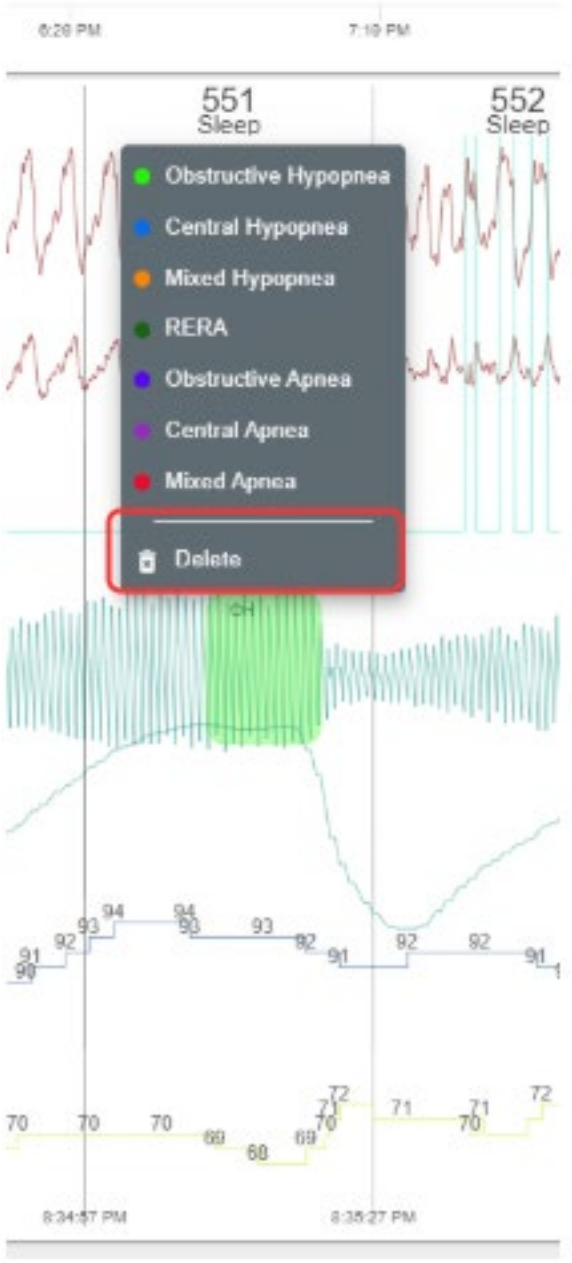

Figure 13: Deleting Events

For further instructions on how to use the platform described in this section, please refer to EnsoSleep's instruction manual.

3.2 Detecting Sleep Disordered Breathing Events with ANNE Sleep System

Respiratory events (Apnea episodes) are caused either by an upper airway obstruction following the collapse of the upper airway wall or central dysfunction in which the brain doesn't send proper signals to the muscles that control breathing. During the apnea episodes, sympathetic activation causes vasoconstriction and acceleration of the heart rate. This results in attenuation of the PAT signals. PAT amplitude may vary due to reasons other than apnea events such as periodic limb movements or spontaneous arousals. This section described the steps necessary to differentiate the true respiratory event resulting in attenuation of the PAT signal and the ones caused by events not related to it.

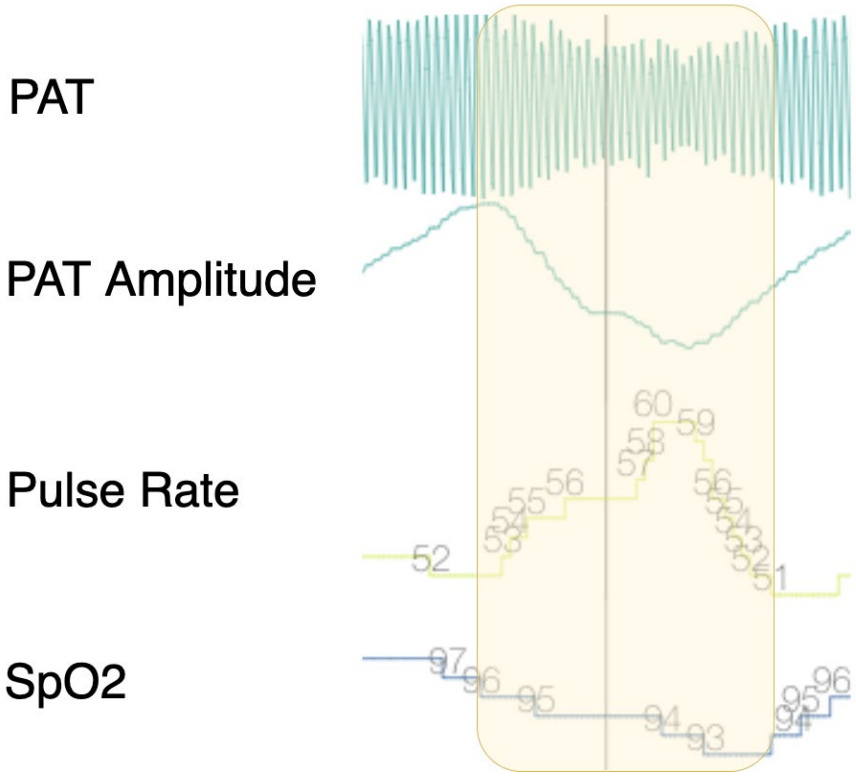

Figure 14: Typical pattern of PAT Amp attenuation and HR increase

When scoring for sleep-disordered breathing (SDB) events, the first step is to see if the area that is being analyzed has (1) motion artifact or (2) body position change. If there are any of the two signals, do not continue on to see if it is an SDB event.
Next, look at the **Accel Vertical** and **Accel Horizonta**l signal for chest movement reduction. If the amplitude of **both** signals drops by 90% or more for more than 10 seconds, it is categorized as an SDB event. If one or both signals does not look as below, move to analyze the attenuation of the PAT signal. Label the event as an SDB regardless of the limb sensor output.

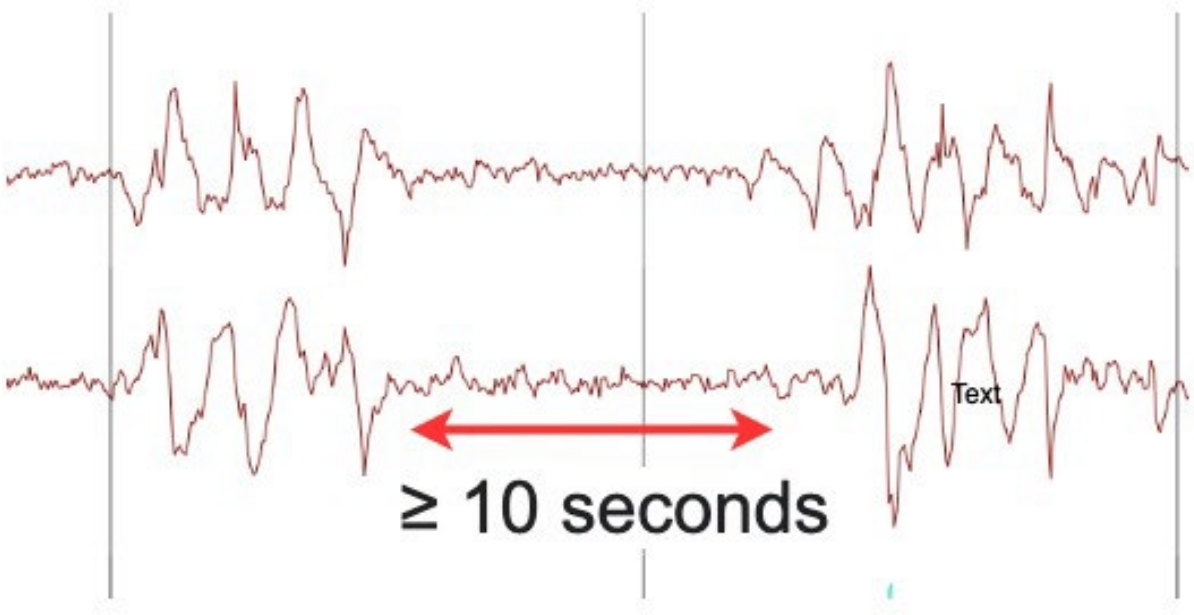

Figure 15: Chest Movement Reduction Example

If there are motion artifacts in between the chest movement reduction, do not grade the signal as SDB. An example of it is shown below. This is usually created as part of changing the body position and should be disregarded.

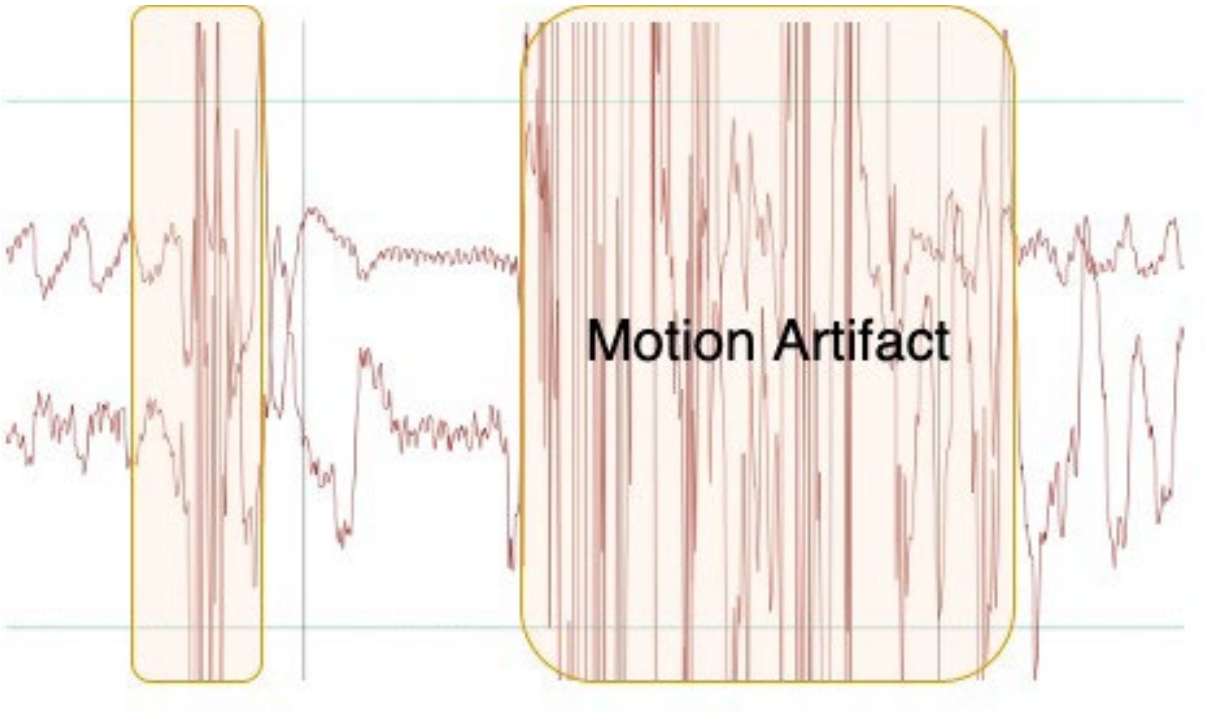

Figure 16: Motion Artifact example

After analyzing the two accelerometer signals and concluding that there is no chest movement reduction, proceed to analyze attenuation of the PAT signal, heart rate increase, and SpO2 drop. PAT attenuation can be easily identified by seeing the PAT amplitude signal drop. Also, heart rate should increase by at least 3 bpm within 15 seconds, and the SpO2 should drop by at least 3% within 60 seconds. If the conditions above are met, label the event as SDB.

If there is a reduction in PAT amplitude and an increase in heart rate but the SpO2 drop is not present, look at the snoring signal. If the area of interest has no snoring but there is snoring before that point, label the event as SDB.

A flow diagram is shown below to summarize the steps necessary to label SDB events using ANNE Sleep.

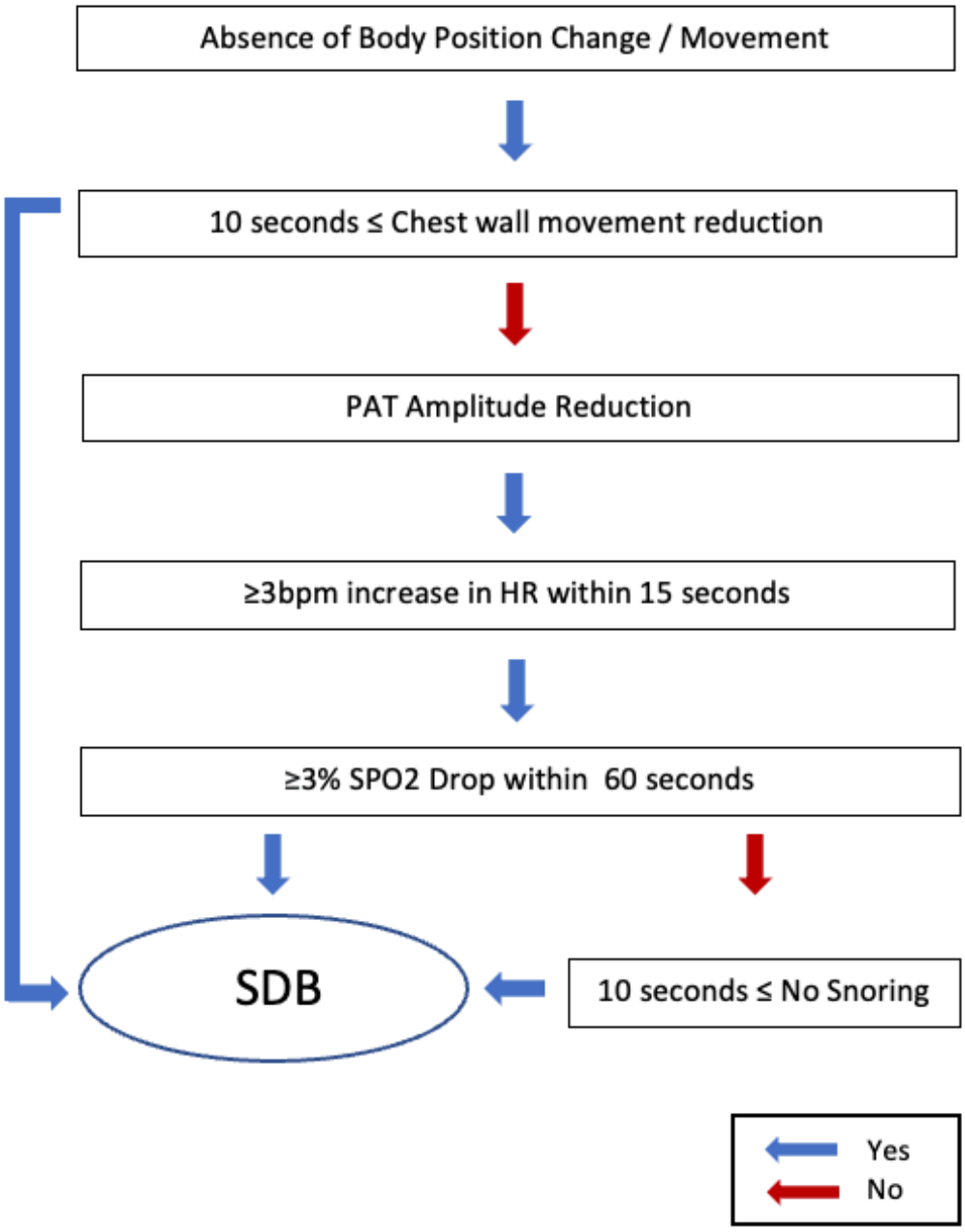

Figure 17: Flow for detection Sleep Disordered Breathing

3.3 Examples

The following are example snapshots of various SDB (Sleep Disordered Breathing) events covering the different cases in the flow diagram.

3.3.1 Example 1

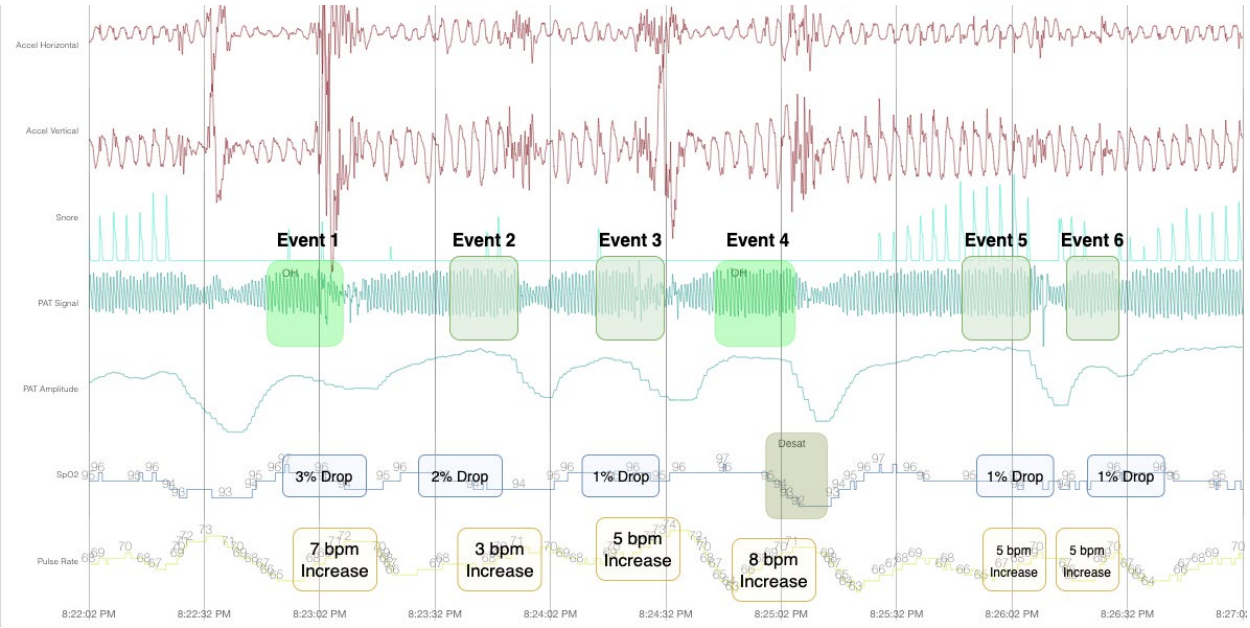

Figure 18: Example 1: Snapshot of SDB events

Event 1, 4:

- Chest movement reduction ✗
- PAT Amplitude decrease ✓
- ≥ 3% drop in SpO2 ✓
- Pulse Rate Increase ✓

Conclusion: SDB Event

Event 2:

- Chest movement reduction ✗
- PAT Amplitude decrease ✓
- ≥ 3% drop in SpO2 ✗
- Pulse Rate Increase ✗

Conclusion: Not an SDB Event

Event 3, 5, 6:

- Chest movement reduction ✗
- PAT Amplitude decrease ✓
- ≥ 3% drop in SpO2 ✗
- Pulse Rate Increase ✓

Conclusion: Not an SDB Event

3.3.2 Example 2

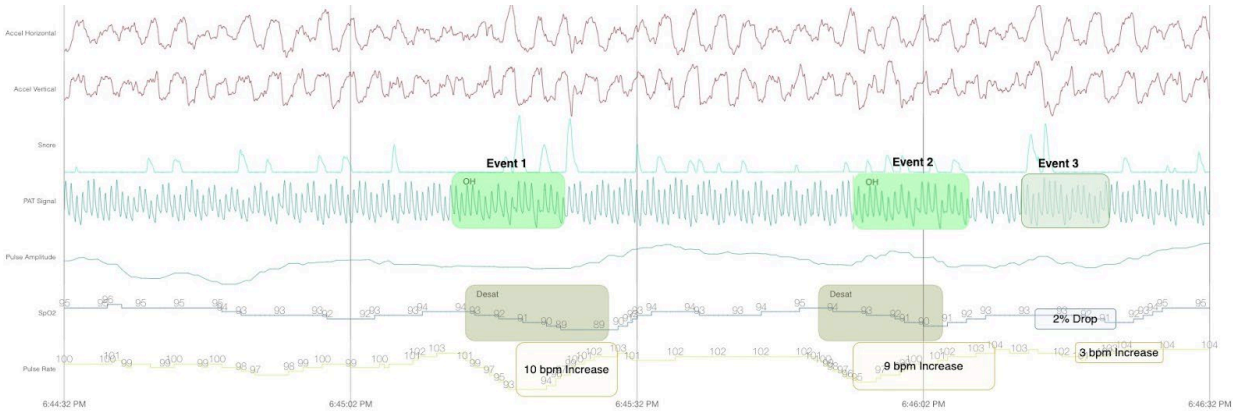

Figure 19: Example 2: Snapshot of SDB events

Event 1:

- Chest movement reduction ✗
- PAT Amplitude decrease ✗
- Pulse Rate Increase ✓
- 3% drop in SpO2 ✓

Conclusion: Not an SDB Event

Event 2:

- Chest movement reduction ✗
- PAT Amplitude decrease ✓
- Pulse Rate Increase ✓
- 3% drop in SpO2 ✓

Conclusion: SDB Event

Event 3:

- Chest movement reduction ✗
- PAT Amplitude decrease ✗
- Pulse Rate Increase ✗
- 3% drop in SpO2 ✗

Conclusion: Not an SDB Event

3.3.3 Example 3

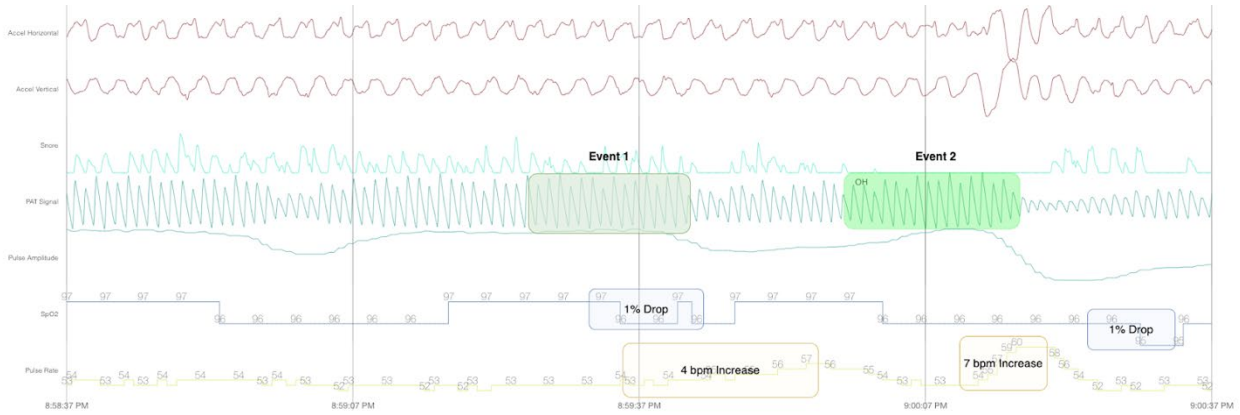

Figure 20: Example 3: Snapshot of SDB events

Event 1:

- Chest movement reduction ✗
- 3% drop in SpO2 ✗
- PAT Amplitude decrease ☑
- Pulse Rate Increase ☑
- Snoring reduction for more than 10 seconds ✗

Conclusion: Not an SDB Event

Event 2:

- Chest movement reduction for more than 10 seconds ✗
- PAT Amplitude decrease ☑
- Pulse Rate Increase ☑
- 3% drop in SpO2 ✗
- Snoring reduction for more than 10 seconds ☑

Conclusion: SDB Event

3.3.4 Example 4

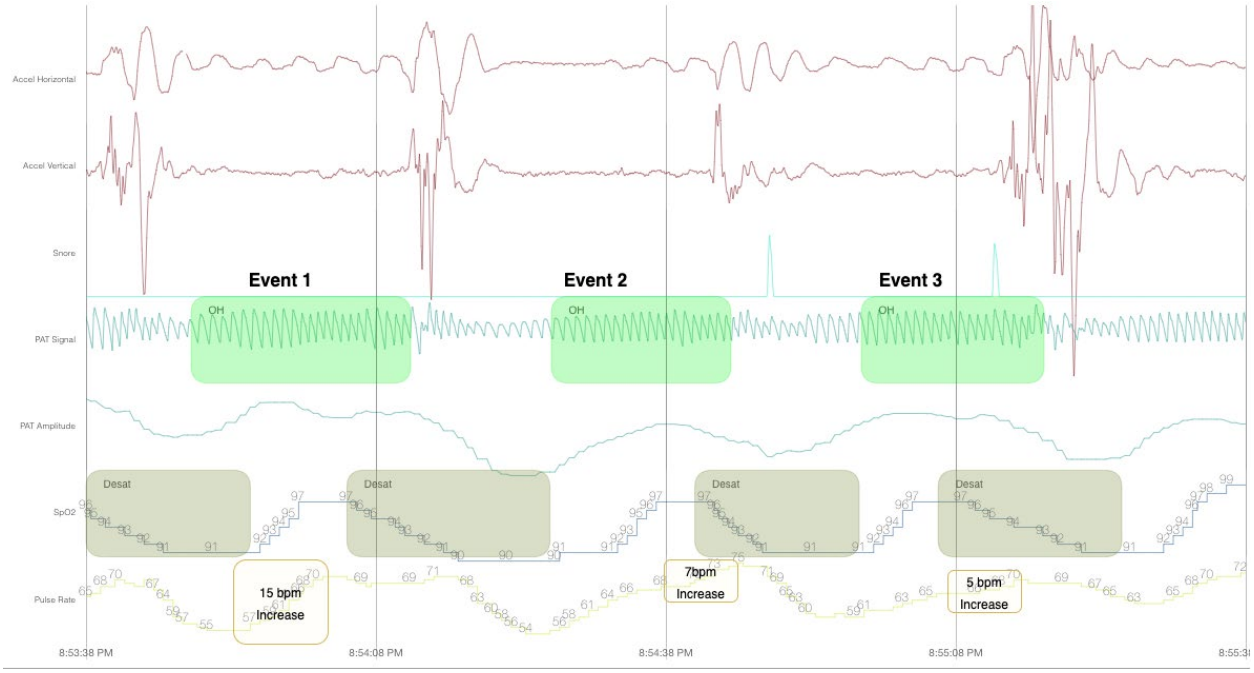

Figure 21: Example 4: Snapshot of SDB events

Event 1:

- Chest movement reduction ✗
- ≥ 3% drop in SpO2 ✓
- PAT Amplitude decrease ✓
- Pulse Rate Increase ✓

Conclusion: SDB Event

Event 2:

- Chest movement reduction ✓
- ≥ 3% drop in SpO2 ✓
- PAT Amplitude decrease ✓
- Pulse Rate Increase ✓
-

Conclusion: SDB Event

Event 3:

- Chest movement reduction ✗
- PAT Amplitude decrease ✓
- Pulse Rate Increase ✓
- 3% drop in SpO2 ✓

Conclusion: SDB Event

3.3.5 Example 5

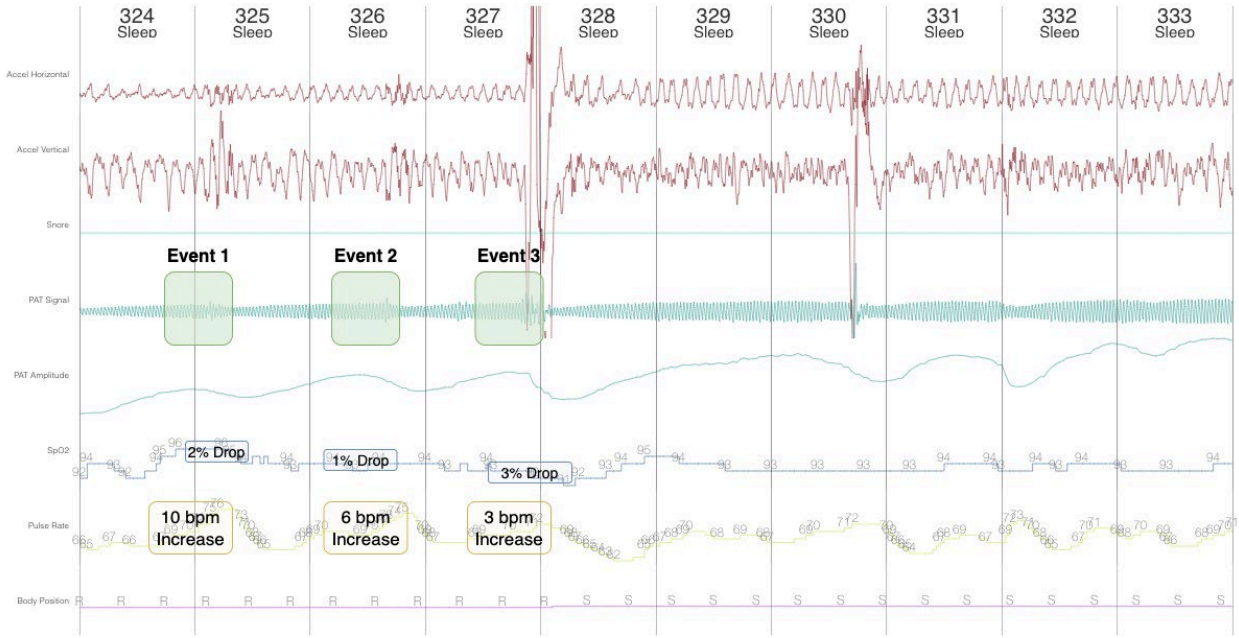

Figure 22: Example 5: Snapshot of SDB events

Event 1:

- Chest movement reduction ✗
- 3% drop in SpO2 ✗
- PAT Amplitude decrease ☑
- Pulse Rate Increase ☑
- Snoring reduction for more than 10 seconds ✗

Conclusion: Not an SDB Event

Event 2:

- Chest movement reduction ✗
- 3% drop in SpO2 ✗
- PAT Amplitude decrease ☑
- Pulse Rate Increase ☑
- Snoring reduction for more than 10 seconds ✗

Conclusion: Not an SDB Event

Event 3:

- Body Position Change ✗

Conclusion: Not an SDB Event

3.3.6 Motional Artifact Example

The following is an example of a snapshot that contains large movements. Any events under or between big motion artifacts should not be labeled as SDB. Continuous motion artifacts often relate to the patient being awake or switching body position. With large motion affecting signal quality, the associating vital signs may be invalid.

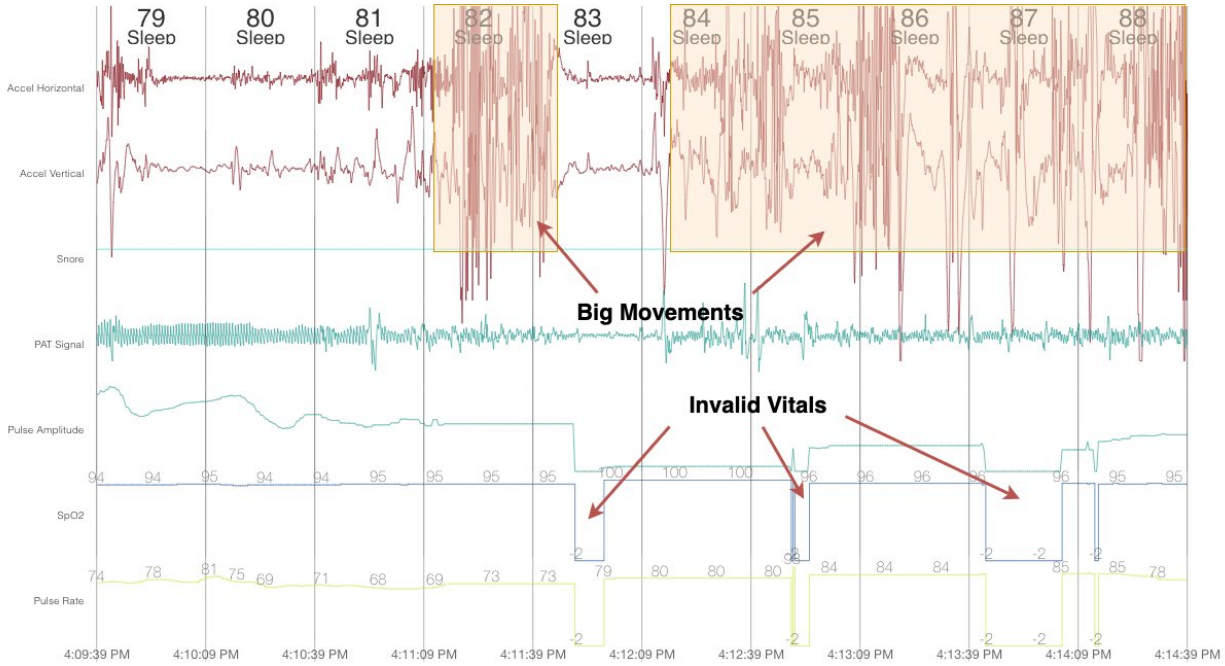

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Figure 23: Snapshot of motion artifacts