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In Home Assessment of Three Anti-Snoring Devices, a cross over study

Clinical Protocol

Protocol# SRC-AI-SilentNight-10090

Version 3.0
11/14/2017

Sponsored by

Respironics, Inc., a Philips company ("Philips Respironics")
1740 Golden Mile Highway
Monroeville, PA 15146
USA

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I. DOCUMENT CONTROL PAGE

Protocol Title: In Home Assessment of Three Anti-Snoring Devices, a cross over study

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Investigator Agreement.

As Investigator of the study entitled “In Home Assessment of Three Anti-Snoring Devices, a cross over study”, Protocol # SRC-AI-SilentNight-10090, I agree to:

(i) conduct the Study in accordance with: this Investigator Agreement; the Study’s Protocol as approved by the IRB (the “Protocol”); Good Clinical Practices, the Declaration of Helsinki; all other applicable laws and regulations; and any IRB or FDA conditions of approval;

(ii) await IRB approval for the Protocol before obtaining informed consents;

(iii) ensure that all requirements for informed consent are met and not let any subject participate in the Study before obtaining that subject’s informed consent;

(iv) not make modifications to the Protocol as supplied to me by Philips Respironics (the “Sponsor”), without first obtaining the written approval of the Sponsor;

(v) provide the Sponsor with accurate financial information as required by FDA regulations;

(vi) supervise all testing of investigational devices that involves any Study subject;

(vii) maintain Study documentation for the period of time as required by FDA regulations;

(viii) will supply to the Sponsor, as part of this Investigator Agreement, my curriculum vitae.

Investigator Signature:_____

Printed Name: _____

Date:_____

PROTOCOL REVISIONS

Rev Level	Changes Made	Date	Contributors
0.0	Initial	September 6, 2017	N. Papas, B. Shelly, D. White M.D.
1.0	Addition of Appendix XIII, updated Version of myTAP device, Change in Positional trainer from Pose to SPT, increased participant compensation, updated Appendix III, updated compensation, timing of visit 2 and 3 updated to reflect IC, provided clarity on regulatory	September 22, 2017	N. Papas
2.0	Various typos, modified exclusion criteria, changed visit schedule (Visit 2 replaced with a phone call, Optional combination week removed Visit 5 removed), increase compensation	September 26, 2017	N. Papas
3.0	Administrative change, did not completely remove all references to combination of products in Version 2.0, see aims section for update	November 14, 2017	N. Papas

RESPIRONICS, INC. CONTACT INFORMATION

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Reporting of Adverse Events or Adverse Device Effects

Report the occurrence of an adverse event or adverse device effect to Philips Respironics within 24 hours of the occurrence.

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II. Glossary of Definitions and Terms

Obstructive Sleep Apnea (OSA): a disorder in which the airway collapses, either completely or partially, repeatedly during the night and is associated with oxygen desaturation, sleep fragmentation, and daytime sleepiness.

Snoring: a snorting or grunting sound in a person's breathing while asleep (Oxford Dictionary)

AHI: an index used to indicate the severity of sleep apnea. It is represented by the number of apnea and hypopnea events per hour of sleep. The hypopneas (pauses in breathing) must last for at least 10 seconds and be associated with a decrease in blood oxygenation or an arousal from sleep.

CPAP: Continuous positive airway pressure, colloquially often used to refer to a machine which uses an increase of air pressure to keep an airway open in someone who has OSA

EDC: Electronic Data Capture, a system to record clinical data in an electronic manner and which is auditable.

HIPAA: Health Insurance Portability and Accountability Act of 1996, a US legislation that provides data privacy and security requirements for safeguarding medical information.

III. BACKGROUND AND SIGNIFICANCE

A. Clinical Significance:

Snoring is defined as a coarse, harsh sound caused by the vibration of soft tissue in the upper airways involving anatomical structures such as the soft palate, uvula, and tongue base. Habitual snoring is common, but prevalence varies widely 15-54% ([1-5]). In looking at differences in sex, 44% of men snore and 28% of women snore [5]. Common correlations with snoring include age, being overweight, nasal and sinus problems, alcohol intake, smoking, certain medications, and sleep position.

Snoring is a common sign of obstructive sleep apnea (OSA); however many cases of snoring are unrelated to OSA. This is known as simple or primary snoring. If one removes those who have an Apnea Hypopnea Index (AHI) greater than five, prevalence of primary snoring is approximately 42% in both men and women [5] (calculated from Table 3 of reference). In these cases, the sleep of the primary snorer is less likely affected, thereby leaving their bed partner to contend with the loud sounds. Bed partners of snorers frequently suffer from poor sleep quality and even possible hearing loss due to the disturbance [6]. Furthermore, this poor sleep quality leads to excessive daytime sleepiness which interferes with daily life [5].

The biomechanics of snoring is interesting; from a theoretical perspective it can be modeled as “coupled oscillation of the walls of the airway with airflow through it” [1]. Specifically, snoring occurs when airflow becomes unstable over a flexible structure. Anatomically, there are a few places where the sound can originate, most notably the pharynx, and soft palate (tonsil, velar, tongue) [1, 3, 7]. These locations can have different acoustic signatures [3, 7] and may require different solutions to resolve.

Due to the multiple etiologies of a snore, many anti-snoring solutions exist. They include (but are not limited to) oropharyngeal exercises [8], pharmacologic solutions [9], nasal dilators [10-14], positional trainers [15, 16], and mandibular advancement (also

known as oral appliances) [16-20]. Even CPAP has been used to treat primary snoring [21].

Primary snoring itself is not considered a medical condition per say, thus these solutions are not always considered medical devices. Hence, concerned snorers may or may not be dealing with the condition under council of a physician and would not necessarily know what the source of the snoring is. Therefore concerned snorers often blindly use a "trial and error" approach to select an anti-snoring solution. This method is often expensive, time consuming, and unsuccessful [22].

A previous clinical study conducted at Philips, CAI-16023-SNOPIL-KD, attempted to systematically move participants through a decision tree (Philips study algorithm) and understand the sleep disturbance of bed partners who use the anti-snoring solutions recommended by the decision tree. The study algorithm would recommend one of three snoring solutions (Mute, myTAP, Pose [analogous to SPT]) based upon a three question questionnaire. Then, based upon usage and perceived snoring reduction, combinations of products would be recommended at subsequent visits. It was hypothesized that 60% of the couples in the study would see a measurable reduction in partner's sleep disturbance.

For the study, 33 couples were enrolled, 32 couples finished the study. The bed partners' average sleep disturbance due to snoring (the primary outcome from this trial) went from 7.6, on a 0-10 scale, to a 2.8 at study's end. Further, 72% of bed partners agreed that the trial reduced their partner's snoring, but only 42% felt it stopped the snoring completely. However, to achieve this outcome, the study algorithm took 5 weeks and 64% of snorers ended up on a device combination of the two most expensive snoring solutions [23]. Finally, this trial and market research rejected the business model proposed by the trial's Philips study algorithm. Consumers favor an approach that "gets its right the first time" and may be willing to pay for a personalized

recommendation on anti-snoring solution if their/bed partner's snoring is reduced by 50% [22].

Therefore, in order to help the concerned snorer find a solution, more data must be gathered. There is a need to assess the same three interventions (Mute, myTAP, and Sleep Position Trainer [SPT] [see section III.B.]) in order to understand how well each intervention works in a specific individual. Then, there is a hope to cluster the individuals based upon intervention success to understand what questions can be asked *a priori* that would predict an intervention's success. Thus, there is a hope to redesign the intake questionnaire for the SilentNight app, ensuring that the right product is recommended from the start and a "trial and error" approach (as the prior study algorithm used) is not needed.

Lastly, there is also a desire to develop an audio detection of snoring to create a "snore score," a numerical representation of how someone snored during the night. It is also in the development pipeline to use audio to more accurately phenotype an individual's problem. Prior studies have looked at audio of snoring both in a lab setting [24-26] and while patients were in drug induced sleep [7, 27]. For example, it has been shown that tongue based snoring has a frequency above 500 Hz. whereas palatial snoring is below 500 Hz. However, little "in the wild" data exists. So, while it may be theoretically possible to phenotype a snore based upon audio, it is still unknown if it is practical to phenotype a snore using audio recorded in a user's bedroom.

B. Description of Intervention Studied:

We will use three different anti-snoring devices which target different sources of snoring. All study devices are single patient use. One is currently marketed in the US while the other two are investigational. In addition, we will use an audio recording device to record room sounds for product development of a snore detection app.

1. Mute nasal device (RhinoMed, Richmond, Victoria 3121, Australia)

Mute is a pair of nasal dilators that fit snugly in the nose of the snorer dilating the nostrils to help reduce or eliminate snoring. This is an over-the-counter (OTC) product and is cleared by FDA for use in the United States. The introduction video for Mute is located at http://mutesnoring.com/how-to-use/.

Nasal dilators have been used to treat snoring and sleep apnea [10-13]. Many studies focus on external nasal dilators like Breathe Right Strips. These interventions largely were not effective in treating OSA [10]. However, there is some evidence to suggest internal to the nose dilators (like Mute) may work to reduce snoring. A small study (n=11) using Nozovent, showed that there was substantial decreasing in snoring noise in all patients studied [13]. Also a white paper from RhinoMed claims that 73% of bed partners reported a reduction in snoring severity [28].

2. myTAP™ V (Airway Management, Carrollton, TX)

For purposes of this trial, we will be using an investigational myTAP V, which is not available for commercial use. The changes from the released product are: a vertical offset (+3mm) has been added to the design of the adjustment post and mechanism to improve overall comfort.

myTAP™ is a mandibular advancement device used for snoring relief. The product requires a prescription and is cleared by FDA for use in the United States. The introduction video for myTAP™ is located at https://www.youtube.com/watch?v=ehVZf1b2wi0.

Mandibular advancement devices have shown to be effective, but not necessarily acceptable to primary snorers [16-20].

3. Sleep Positional Trainer (SPT) (NightBalance, Delft, Netherlands)

Sleep Positional Trainer (SPT) is a small device worn around the chest with an ergonomic band that continuously monitors the sleep position of the snorer. When the snorer is supine, it emits a gentle vibration to remind them to turn to the side to help reduce or eliminate their snoring. It is not available in the United States and therefore is considered investigational use as part of this study. Though this product is available in various European countries including Austria, Belgium, Denmark, France, Ireland, The Netherlands, Norway, Sweden, and Switzerland. The instruction video for NightBalance SPT is located at http://www.nightbalance.com/product-support/.

Studies have shown mixed results for positional therapy as a whole [15]. Braver and Block reported that foam wedges used to keep patients in a lateral position were not effective in reducing snoring in 20 individuals [29]. But Choi et al successfully treated 17 individuals with an inflatable vest reducing snoring rate from 36.7% to 15.7% [30]. In a far more extensive study of OSA patents, Benoist et al tested a NightBalance product specifically [16]. In a sample of 81 individuals they found that positional therapy with the NightBalance product reduced AHI in an OSA population from 13.0 to 7.0, which was just as effective as an oral appliance. Also, adherence to positional therapy was almost 90%. Therefore, it can be hypothesized that the SPT will also be effective for positional primary snoring.

4. Philips SilentNight Mobile Application

Philips SilentNight application is an audio recording application for the collection of snoring sounds. It may also be used to collect questionnaire data. The app complies with applicable privacy and security standards for clinical research activities. The app's functionality is limited and data will be contained on the phone. At each visit in the trial, data will be removed from the phone by a member of Philips staff. Wire frame of the app is shown in Appendix I.

During the trial, the snorer will be asked to use a provided Android-based device with the app installed to record themselves sleeping each night. Snorers will be instructed to use the app to collect recordings daily. Although the app is intended to collect snoring sounds, all room sounds will be recorded each night. The snoring sounds will be extracted from the recordings at a later time for further product development of a snore detection app. Permission to record all room sounds will be obtained from both the snorer and bed partner during consenting.

IV. STUDY PURPOSE AND OBJECTIVES

A. Purpose

The purpose of this trial is twofold. Firstly, while each of the interventions to be studied are known to be effective for snoring cessation, each is not fully effective in the total population. Each intervention's efficacy on a given individual is predicated by an individual's physiology and their contributing factors to their snoring. In order to improve the SilentNight recommendation algorithm, more information needs to be gathered. By asking a battery of questions of a snorer and having them trial all three snoring solutions, it may be possible to understand the comparative effectiveness of each solution, the user acceptance of each solution, and which questions should be used to discern an acceptable and effective solution for a given individual.

Secondly, it is a long-term development goal of the SilentNight program to use audio analysis of a snore in order to make product recommendations. This protocol is designed to collect "in the wild" audio of snoring. The goal of this data collection is to identify unique characteristics in the sound recording. These, paired with the answers to the intake questions and the relative effectiveness of the three anti-snoring solutions could phenotype the snore and snorer. This audio data could also be used to develop

or refine a “snore score”, a semi-objective assessment of snoring audio which can be calculated daily.

B. Primary Aim

Understand the comparative effectiveness of three different anti-snoring solutions and determine which is/are the correct solution for a given individual.

We expect there to be a different effectiveness of each of the three anti-snoring solutions over the entire population studied. However, there is no hypothesis as to which will be most effective. Rather it is a goal to understand what the best solution is for a given individual, and generalize this finding to a larger population.

C. Secondary Aims

1. Understand user acceptance of each solution.
2. Collect audio data of snoring in different individuals in a baseline setting and using various anti-snoring solutions.

All secondary aims are information gathering. There is no hypothesis to test.

V. STUDY DESIGN AND METHODS

A. Design

This is an open-label crossover, comparative effectiveness trial.

B. Study Design Rationale

This is a pilot study. As each participant will serve as their own control, our enrollment size can be kept small. Thus, this is a feasibility study utilizing a small number of patients. No previous data exist for power calculations. The results may also provide statistical justification for later studies. Also, being a pilot, there are no procedures taken to avoid bias, such as randomization or blinding. This is

a limitation of the study as we will not be able to separate the device effect from any possible order effect.

C. Study Participants

We anticipate enrolling up to 30 couples to have 25 completing the study. We will attempt to study an equal number of men and women. Participants will be enrolled in the study for up to 40 days.

Potential participants will be recruited by an external to Philips marketing firm (Campos Inc., Pittsburgh, PA), either from their existing database, word of mouth, or through media advertisements (e.g. Craigslist, local newspapers, flyers, targeted Facebook advertisements, institutional postings). These ads will be used to identify participants with a history of snoring and their troubled bedpartner. Participants at high risk for sleep apnea will be excluded from the study, as determined by the Snore Scale Score [31] and OSA50 [32] questionnaires (Appendix II) identified through a phone screening (Appendix III).

D. Inclusion Criteria (Snorer):

- Adults aged 21 to 55
- Able and willing to provide written informed consent
- Able to read and understand English
- History of snoring for more than 6 months (by self-report).
- Sleep with a bed partner for at least 4 nights per week (by self-report).
- Told by bed partner that snoring frequently disturbs his or her sleep (by self-report).
- Have seen a dentist within 12 months (by self-report).
- Willing to not use any anti-snoring aids that are not associated with the study (by self-report).

- Has purchased or used or bed partner has purchased an anti-snoring product in the past (by self-report) [These individuals may be included in the study if recruitment timeline dictates it]

E. Exclusion Criteria (Snorer):

- Scored higher than a 9 on the Modified Snore Scale Score (MSSS>9)
- Scored higher than a 6 on the OSA 50 screener (OSA50>6)
- The presence of physical or mental limitations that would limit the ability to use the anti-snoring solutions.
- Any unstable medical condition like congestive heart failure, neuromuscular disease, renal failure, or cancer (as determined by self-report and reviewed by the study PI).
- Any severe respiratory condition (like an exacerbation of Chronic Obstructive Pulmonary Disease, bronchitis, sinusitis, respiratory failure or insufficiency or patients requiring oxygen therapy).
- Known history of Obstructive Sleep Apnea (OSA) or Central Sleep Apnea Syndrome (by self-report)
- Only able to sleep in the supine (flat on one's back) position (by self-report).
- Actively suffering from an upper respiratory infection (by self-report).
- Have a planned medical or dental procedure involving the head, neck, face (eyes, ears, nose, teeth, mouth), or lungs during the trial period (by self-report).
- Under active treatment for an active dental problem by a dentist or orthodontist
- Have one or more of the following dental issues (by self-report)
    - Removable dentures or bridges.
    - Temporary crowns, loose teeth, loose crowns, loose fillings, or broken teeth
    - Less than 8 natural, healthy teeth in each dental arch (upper and lower teeth)
    - Dental braces
    - TMJ issues

F. Inclusion Criteria (Bed Partner):

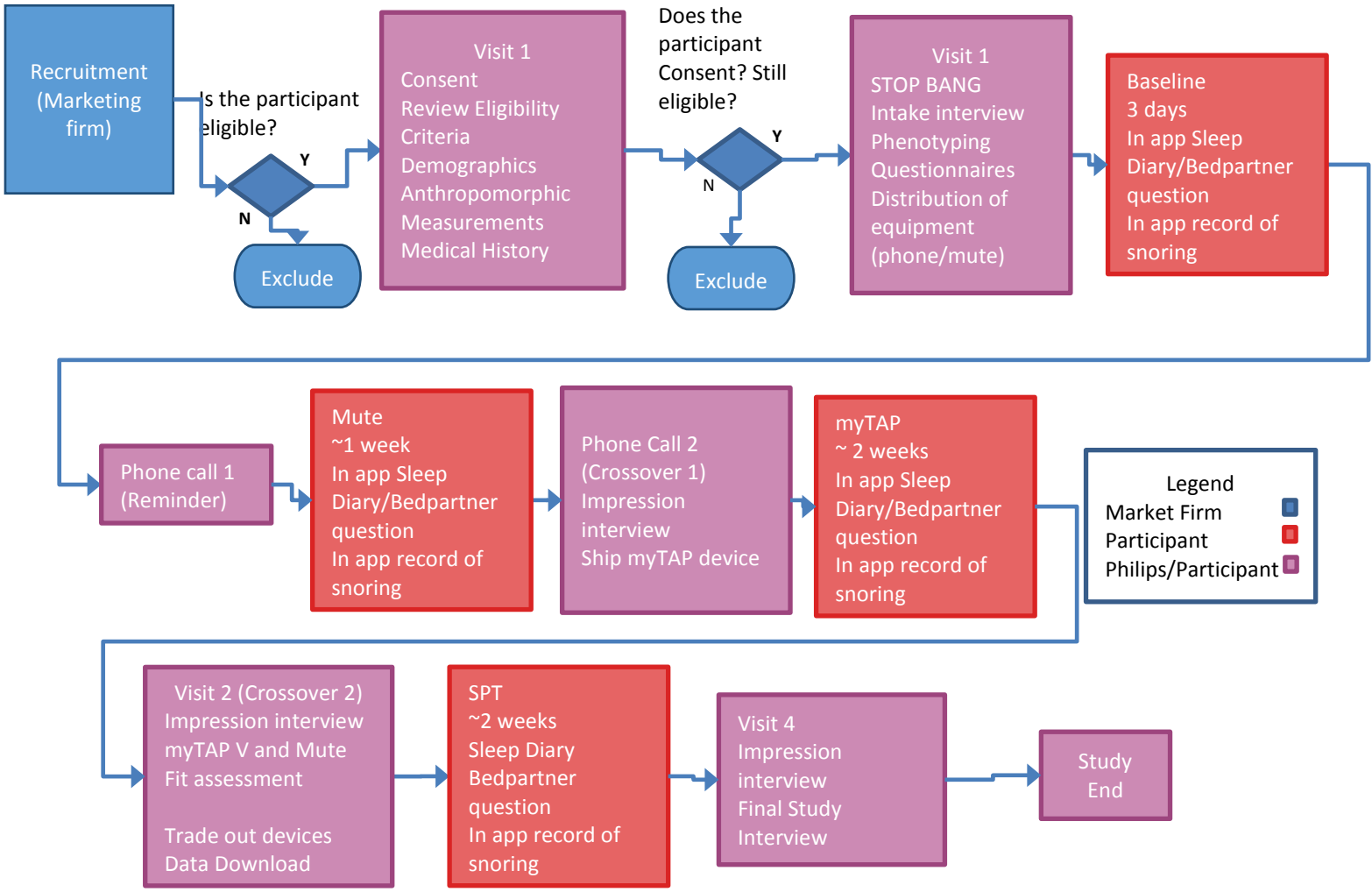
- Adults aged 21 to 70
- Able and willing to provide written informed consent
- Able to read and understand English
- Rates sleep disturbance caused by partner's snoring greater than or equal to 4 on a scale of 1-10
- Rates level of snoring volume greater than or equal to 7 on a scale of 1-10
- Willing to sleep in same room as snorer during the study period (by self –report).
- Willing to not start any new over-the-counter or prescription sleep medication including sedatives and hypnotics during the study period (by self-report).

G. Exclusion Criteria (Bed Partner):

- Told by bed partner that their snoring frequently disturbs his or her sleep (by self-report).

H. Study Procedures and Measurements:

1. Study Flowchart



2. Telephone Screening

As stated in section V. C. Study participants, an outside marketing firm will be conducting recruitment and doing an initial phone screening. The script of the phone screen is attached as Appendix III, and involves screening out participants for OSA. For this purpose the OSA50 and MSSS questionnaires will be used (Appendix II).

3. Visit 1, Intake interview, baseline questionnaires:

The recruited couple will be asked to come to the Philips facility, or other 3rd party location (Campos, or nearby hotel meeting room). After both participants are consented to the study procedure, eligibility will be reviewed, including an OSA screening questionnaire (snorer only). Demographic data will be collected. The snorer will have a baseline assessment including, STOP-BANG (Appendix XIV), medical history, a review of current medications, anthropometric measurements (height, weight, neck circumference), and BMI. A phenotyping questionnaire about snoring and sleep will be completed by the snorer (Appendix IV). The couple will be interviewed by the Philips researchers using a semi structured interview style (Appendix V and Appendix VI). These interviews may be audio recorded (with participant consent), and stored for up to 6 months on a secure server. These interviews will be in person.

Next, participants will be given a phone with the SilentNight app preloaded. They will be shown how to use the application and reminded to record their snoring every night and answer the questionnaire every morning. During the trial period, the bed partner is instructed to sleep in the same room with the snorer in order to provide feedback about their sleep.

Finally, they will be given a "trial pack" of the Mute devices. Instructions for use for the Mute device will be reviewed, and study procedures will be reiterated (app usage, nightly recording and morning questions). The entire visit will take approximately 1 hour.

4. Baseline Nights (3 nights)

Participants will record three nights of baseline snoring. No intervention will be used on these nights. In the morning, both the snorer and bed partner will fill out the daily questionnaire (Appendix VII) in the app on the mobile device.

5. **Phone Call 1**

On day three of the study, participants will be contacted by Philips, reminding them to start using the Mute. The Philips team will check in to see if there are any issues with the app, and they will also remind them of the upcoming visits to the Philips designated facility.

6. **Intervention Nights Set 1 (Mute) ~ 1 week**

Snorers will be asked to wear the Mute device for one week.

If they have any concern over the use of the Mute device, or note any significant discomfort they are to stop its use and call Philips.

During this week, the bed partner will be instructed to sleep in the same room as the snorer. Participants will record room noise during the night. In the morning both the snorer and bed partner will fill out the daily questionnaire on the phone.

7. **Phone Call 2 1st cross over**

Approximately 1-2 weeks after the initial visit participants will be called 30 min interview.

The snorer and bedpartner will be interviewed separately again using the guided interview technique. They will be asked questions regarding the use of the Mute device, their perception of snoring, and sleep quality. The interviews will follow a script attached as appendices VIII and IX. These interviews may be audio recorded (with participant consent), and stored for up to 6 months.

Finally, they will be sent the myTAP V product, and a set of instructions. They will be asked to view the video on how to fit the myTAP which is included in the consent form. They will also be sent a questionnaire specific to the myTAP V fitting, which they will

need to complete partly just after fitting, and partly after the approximately 2 weeks of use.

8. Intervention Nights Set 2 (myTAP V) ~ 2 weeks

Prior to the set of intervention nights, the snorer will follow the instructions and fit the myTAP V device themselves using the "boil and bite" technique (See Appendix X for more information). After fitting they will need to complete Q1 of the myTAP V questionnaire (Appendix XIII). They will utilize the device at night. They will have the opportunity to titrate the mandibular advancement per the study instructions for use (Appendix X), in order to gradually get used to the device, and potentially improve effectiveness. At the end of their myTAP V use, they will complete the remainder of Appendix XIII.

If they have any concern over use of the myTAP V device, or note any discomfort they are to stop its use and call Philips. They may be instructed to discontinue the use of myTAP V all together, or make some adjustments. All will be at discretion of the PI.

Regardless of device usage, the bed partner will be instructed to sleep in the same room as the snorer. Participants will record room noise during the night. In the morning both the snorer and bed partner will fill out the daily questionnaire on the phone.

9. Visit 2 2nd cross over

Approximately 2-3 weeks after Phone Call 2 (1st crossover) and 3-4 weeks after the initial visit 1, participants will return for an approximately 30 min visit. They will bring both the myTAP V device and mobile device with the SilentNight application. Data from the mobile device will be downloaded off of the phone. A grouping standardized picture of the myTAP V device will be taken and the investigational device returned to Philips.

Participants will report what size of Mute device they used for the week of use. They then will be assessed using the Mute online snoring guide (https://mutesnoring.com/wp-content/uploads/2016/11/Mute_online_sizing_guide2.pdf), in order to confirm they used the proper size.

Next, the snorer and bedpartner will be interviewed separately, again using the guided interview technique. They will be asked questions regarding the use of the myTAP V device, their perception of snoring, and sleep quality. The interviews will follow a script attached as appendices VIII and IX. These interviews may be audio recorded (with participant consent), and stored for up to 6 months. The bed partner interview may be conducted over the phone.

Finally, they will be given sizing information for the SPT device and will choose a size. Instructions for use for the SPT device will be reviewed, and study procedures will be reiterated (app usage, nightly recording and morning questions).

10. Intervention Nights Set 3 (SPT)

Snorers will be asked to wear the SPT device for two weeks. The first few nights will be the normal calibration period with the device, and the second week will be full sleep training mode. The titration of the device will be as follows:

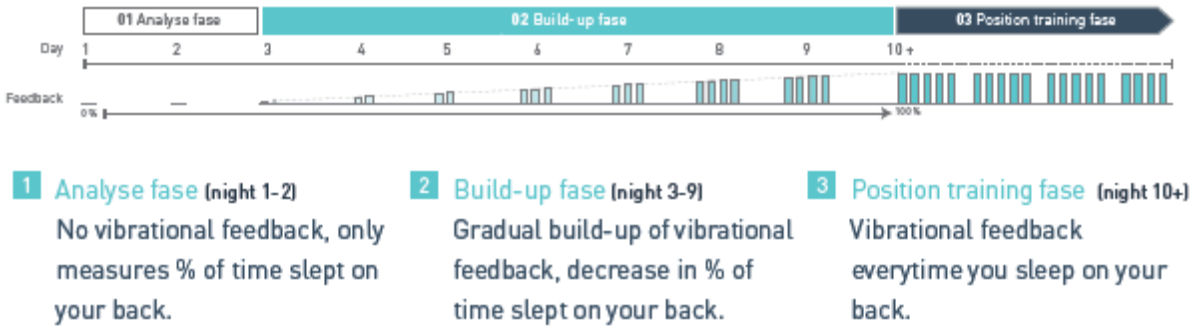


Figure 2: SPT Titration program, taken from the SPT Device Manual

If they have any concern over the use of the SPT device, or note any discomfort they are to stop its use and call Philips.

During these two weeks, the bed partner will be instructed to sleep in the same room as the snorer. Participants will record room noise during the night. In the morning both the snorer and bed partner will fill out the daily questionnaire on the phone.

11. Visit 3 Exit interview

Approximately 5-6 weeks after the initial visit (~2 weeks after visit 3) participants will return for an approximately 1 hour visit. They will bring the mobile device with the SilentNight application. Data from the mobile device will be downloaded off of the phone.

Next, the snorer and bedpartner will be interviewed separately again using the guided interview technique. They will be asked questions regarding the use of the SPT device, their perception of snoring and sleep quality. The interviews will follow a script attached as appendices VIII and IX. These interviews may be audio recorded (with participant consent), and stored for up to 6 months. These interviews will be in person.

A final exit interview will be conducted, see appendices XI and XII for details. Like all other interviews, it may be audio recorded and the recording will be kept on file for 6 months. Most of the investigational materials (mobile device and SPT) from the study will be collected. The participant may dispose of the Mute device if they desire. Data from the SPT device may be downloaded, by either Philips or NightBalance.

12. Marketing continuation

After the exit interview, we will ask participants their permission for Philips to follow up with them at any time in the 3 months following the study's end. This will be a purely marketing effort. As such, after Visit 5 participants will be considered exited, and adverse events will no longer be tracked. The follow up will be useful after the data

analysis has begun, thus questions are not known at this time. Participants that agree to be contacted will initial an acknowledgement of participation at the time of consent, and will be entered into a drawing to win an additional $50 gift card.

13. Table 1: Study Procedures

Procedures	Visit 1	Phone Call 1	Phone Call 2	Visit 2	Visit 3
Consent	X				
OSA Screening Questionnaires	X				
History & Physical	X				
Anthropometric Measurements	X				
Medication List	X				
Baseline Questionnaire	X				
Baseline Snoring Questionnaire	X				
Distribute Audio Device/App w/Training	X				
Mute Instructions	X	X			
myTAP V instructions			X		
SPT Instructions				X	
Download Data				X	X
Guided interview			X	X	X
Bed partner may be interviewed over the phone			X	X	
Exit Interview					X
Collection of Equipment					X

I. Participant compensation

The couples will be compensated for their time in the study as well as incentivized to provide data recordings and daily survey answers. The latter incentive in no way reflects their use of any of the products in the study, participants can stop their use at any time. However, in a prior study CAI-16023-SNOPIL-KD there was issue with collection of recordings. Further couples will still be paid a base of 25 dollars a week regardless of recording etc. Couples may withdraw at any point and compensation will be prorated at that time. In total the enrolled couple could earn up to $1000 dollars. The payment schedule is as follows:

Visit 1: $125

Phone Call 2:	$50
Visit 2:	$75
Visit 3:	$100
In home study enrollment:	$90 dollars per week of (5 wks for a total of $450).
Successful audio recording	$5 (40 nights for a possibility of $200)

VI. STATISTICAL ANALYSIS

A. Determination of Sample Size

Thirty couples may be enrolled in order to ensure 25 completed the data sets. Since this is a pilot study, no sample-size calculation was performed.

B. General Considerations

Descriptive statistics will be presented for all variables of interest. Continuous data will be summarized by mean, standard deviation, median, minimum, and maximum values. Categorical data will be presented as frequencies and percentages. Endpoints will be compared between conditions to assess algorithm performance. Any formal significance testing will be performed at $p < 0.05$.

C. Subject Disposition

Subject disposition, including the total number of participant's enrolled, completed, early terminations and withdrawal will be presented in the analysis. In addition, a listing will be provided with the reasons for discontinuation.

D. Demographics and Baseline Characteristics

These data will be collected and summarized with descriptive statistics.

E. Primary Efficacy Analysis

The primary endpoint will be the daily rating of snoring severity as rated by the bed partner. The daily responses will be averaged on a weekly basis. Due to titration and acclimation during the 9 nights of use nights 10-14 of myTAP V and SPT use will be compared to the week of Mute use. If formal statistical comparisons are performed, continuous data will be compared between the three therapies using repeated-

measures ANOVA or the non-parametric Friedman Test, depending on the distributions of the endpoints. If an overall significant effect is observed, post-hoc pairwise tests will be done with a suitable adjustment for multiple comparisons. Categorical data will be compared between therapies using the Cochran's Q test.

Other analysis may be conducted looking at trends, or grouping the full gamut of nights for these longer interventions.

F. Secondary Analysis

Also studied will be endpoints such as snorer perception of their sleep and
Bed partner perception of sleep quality, subjective acceptability of the solutions, etc.

G. Phenotyping exercise (Baseline characteristics, audio file analysis)

A cluster analysis will then be performed on the baseline questionnaire data to determine if effective and acceptable snoring solutions can be recommended based on simple questionnaire data. Similarly, a cluster analysis will also be performed on the baseline audio data in order to determine if effective snoring solutions can be recommended based on audio data or audio and questionnaire data.

H. Study Termination Criteria

Due to the small sample size, there are no *a priori* criteria for the termination of the study, nor is there a need for sensitivity analysis

I. Safety Analysis

Safety evaluations will be performed by recording clinical adverse events at the time originally reported and at each visit thereafter. Adverse events will be provided in data listings.

A complete medical history will be obtained at screening, and subjects having any of the outlined exclusion criteria will be immediately discontinued.

J. Interim Analysis

As this is a pilot study, analysis will be completed as desired by the sponsor.

VII. PROTECTION FOR HUMAN PARTICIPANTS

A. Potential risks and discomforts

Overall, risks in this study are minimal. However, the potential risks are detailed below, and they will be described in informed consent and will be repeated verbally to the participants prior to use of the anti-snoring devices.

The use of positional therapy devices such as SPT may include slight discomfort of the ergonomic band that wraps around the chest to keep the trainer in place. If the participant experiences pressure from the band, it can be slightly adjusted to increase comfort. Participants can also wear the band over common sleepwear to minimize any discomfort.

Possible side effects of the myTAPV include:

- Slight tooth or gingival discomfort due to pressure from the appliance.
- Excess salivation initially. This will improve as you become accustomed to wearing the myTAP V
- Slight jaw soreness or tightness, initially and with adjustments.
- Temporary bite change. This may subside approximately 30 minutes after the myTAP V is taken out of the mouth in the morning.
- Unconsciously taking the myTAPV out of your mouth at night.
- Movement of teeth.
- Pain in the jaw joint.
- Permanent bite change.
- Mouth dryness – the mouth shield accessory can help prevent dryness.

Furthering the risk of the myTAP V product, will be its use in an in home setting, and not being fitted by a trained specialist (i.e. dental hygienist, sleep technologist, dentist etc.). The product is commonly sold as an over the counter product in other markets, and there is a desire to see if this model can work with SilentNight. Therefore, participants will be given instructions and tips and tricks prior to fitting the device themselves.

The nasal dilators like the Mute may cause nasal irritation and discomfort. Inform the participant to discontinue use and contact the study center if irritation occurs.

There are no substantial bodily risks associated with use of the SilentNight app and Android phone device. Risks in using the Android phone device is no different than those routinely encountered with using other mobile phone devices. There is a risk that the snoring app will collect data not related to the study (secondary data) which may include the potential of recording personal and sensitive data. It is recommended that this data be deleted and/or not stored with the recording and additionally removed from any retention of the recording for other research uses and purposes.

Both participants may experience difficulty sleeping and drowsiness during the study.

B. Potential Benefits

There are no direct benefits to participants in this study. It is possible that one or more of the interventions will prove to be effective at reducing the snoring disturbance. It is hoped that the results of this study will lead to new treatment strategies for snoring.

C. Confidentiality

Privacy rules and requirements according to governing regulations will be implemented. All the information collected as part of this study will be kept confidential. All information collected for this study will be kept in a secured area or stored in a password protected computer if digital. Except when required by law, participants will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in study records. For records disclosed outside Respironics, participants will be assigned a unique code number. The key to the code will be kept by the investigator. Data will be managed by study number and analyzed anonymously.

The study results will be retained in the participant's research record for five years or until the study is completed, whichever is longer. The sponsor will use and disclose participant study information only for research or regulatory purposes or to prepare research publications or presentations at meetings.

A unique source record will be available for each study participant including documentation of the informed consent form review process, HIPAA completion to ensure patient privacy (United States), medical history, and concomitant medications review

D. Provisions to Protect the Privacy Interests of Participants

Subjects will only interact with approved members of the research staff, and will have the option to decline to provide any information that they are uncomfortable revealing. Federal Privacy Regulations provide safeguards for privacy, security, and authorized access.

E. Compensation for Research-Related Injury

There is no compensation available for research-related injury.

F. Vulnerable Populations

N/A

G. Community-Based Participatory Research

N/A

H. Sharing of Results with Participants

Study results will not be shared with the subject.

I. Economic Burden to Participants

There will be no cost to the subject to participate in the study.

J. Withdrawal Criteria

The term "discontinuation "refers to the participant's premature withdrawal from the study prior to completing all procedures. Participants may be discontinued from the study for any of the following reasons:

- Noncompliance.
- At the request of the participant.
- It the discretion of the site principal investigator if he/she believes continuing with the protocol is not in the best interest of the subject.

The study coordinator will document whether or not each participant completed the study. If, for any participant, study treatment or assessments were discontinued, the reason will be recorded.

The study goal is to have 25 participants complete the entire study, and in order to complete this number we will attempt to recruit 30 couples to allow for drop out and screen fail. However, if a minimum of 15 participants are recruited we will begin the study.

VIII. MONITORING AND QUALITY ASSURANCE

All adverse events, serious and non-serious, occurring during the course of the study will be collected, fully documented, and reported to the Allendale Review Board (IRB) by the Sponsor. Serious adverse events will be reported to the Sponsor within 24 hours of the study team being aware of the event. For each adverse event, the investigator will provide the onset, duration, intensity and treatment required, outcome and action taken. We anticipate that adverse events during this study would be related to device usage. Discomfort or pain in the jaw/mouth while using the myTAP V may occur. All reasonable care will be taken to avoid these complications. All data will be kept confidential and in a locked cabinet. Only approved study personnel will have access to study related documents.

All device deficiencies, use or user errors, and equipment failures will be documented. Use or User errors will be captured as part of the source documentation. Device deficiencies and equipment failures will be kept on a separate log. The serial numbers and type of deficiency/failure will be captured.

This clinical study will be monitored by Philips Respironics Inc. (Sponsor) in compliance with the Code of Federal Regulations (CFR) for clinical research; namely, 21 CFR Parts 50, 54, 56 and 812 and others as applicable. The purpose of such monitoring is to assure that the study remains in compliance with the approved protocol, investigator agreement and regulatory requirements, to verify the completeness and accuracy of study data and to resolve any issues that arise during the conduction of the study. The Sponsor will scheduled monitoring visits periodically as specified by the monitoring plan that will be conduct by trained clinical research professionals. A unique source record will be created for each study participant. This record will include documentation of the informed consent form review process, HIPAA competition according to site policies, concomitant medications and applicable medical history. The Sponsor will have access to these source records. An electronic data capture (EDC) will be used for this trial. Only those members of the study team that have completed training and have been delegated by the Principal Investigator will be able to access the EDC to enter data or make changes to the data.

IX. REGISTRATION ON CLINICALTRIALS.GOV

Pursuant to Philips QSP 7.9.4-2017 Registration and Disclosure of Clinical Studies, this trial will be registered with clinicaltrials.gov as some of the devices used in the trial are considered investigational and there may be a desire to publish results. Therefore, participants will be consented that their de-identified data may be used in publication or teaching tools.

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XI. APPENDICES

	Title	Page(s)
Appendix I	SilentNight app v. 1.0.0 wireframe	13 pages
Appendix II	Study OSA Screening Questionnaire	1 page
Appendix III	Telephone Screening Script	5 pages
Appendix IV	Phenotyping Questionnaire	1 page
Appendix V	SNORER Intake Interview Guide	5 pages
Appendix VI	BED PARTNER Intake Interview Guide	4 pages
Appendix VII	Daily In-App questions	2 pages
Appendix VIII	SNORER Crossover Visit Interview Guide	3 pages
Appendix IX	BED PARTNER Crossover Visit Interview Guide	4 pages
Appendix X	myTAP V Study Instructions for Use	3 pages
Appendix XI	SNORER Exit Interview Guide	3 pages
Appendix XII	BED PARTNER Exit Interview Guide	4 pages
Appendix XIII	SNORER myTAP V Questionnaire	2 pages
Appendix XIV	STOP-BANG	1 page