COVER PAGE: protocol and statistical analysis plan

Title: A New Treatment for Mechanical Nasal Obstruction
NCT number: NCT03456115
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JHM IRB - eForm A – Protocol

- **Use the section headings to write the JHM IRB eForm A, inserting the appropriate material in each. If a section is not applicable, leave heading in and insert N/A.**
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1. Abstract

a. *Provide no more than a one page research abstract briefly stating the problem, the research hypothesis, and the importance of the research.*

Restricted nasal breathing is a common complaint among patients presenting to Otolaryngology clinics [1]. In fact, one in eight people experiences some degree of nasal obstruction, or regular difficulty breathing through the nose, which is often the result of a narrowing or collapse of the internal nasal valve [2, 3]. This condition is a daily source of discomfort that reduces productivity and quality of life [4]. Sufferers report labored breathing throughout the day, difficulty sleeping and habitual snoring, and limited stamina during sports and exercise [4].

Slight dilation of the nasal passages directly counteracts nasal obstruction and reverses symptoms in 89% of those afflicted [5]. To this end, many patients undergo functional rhinoplasty procedures to surgically widen the nasal passages [6]. However, up to 20% of patients experience unimproved or worsened symptoms postoperatively [7]. Moreover, these surgeries are invasive, requiring autologous grafts taken from the nose, ear, or ribs; and they entail a yearlong recovery period [7].

Nasal dilators such as Breathe Right strips offer a potential alternative to surgery, as they mechanically expand the nasal passages to effectively relieve obstruction. However, existing products are designed as sleep aids, and customers find them uncomfortable, difficult to use, and too visible to wear in public [8]. Although the mechanism for reversing nasal obstruction is straightforward, surgery is considered the only viable option for those who struggle to breathe during the day.

Engineers from the Johns Hopkins Biomedical Engineering Department, partnered with clinicians from the Johns Hopkins Department of Otolaryngology – Head and Neck Surgery, have developed Schnozzle, a small silicone stent to counteract nasal valve collapse and relieve restricted nasal breathing. We hypothesize that this device will improve symptoms of nasal obstruction and provide patients with a viable alternative to visible non-invasive devices or surgical management.

2. Objectives *(include all primary and secondary objectives)*

Primary objective:
Determine the effectiveness of the Schnozzle nasal dilator compared to existing nasal dilator products and a control (unaided breathing) using objective peak nasal airflow (PNIF) measurements and the Nasal Obstruction Symptom Evaluation (NOSE) instrument.

Secondary objective:
Determine the comfort, inconspicuousness, usability, overall patient satisfaction, device compliance, sizing, pricing, and other patient perception of the nasal dilator products.

3. Background *(briefly describe pre-clinical and clinical data, current experience with procedures, drug or device, and any other relevant information to justify the research)*

Mechanical nasal obstruction is one of the most common complaints heard by otolaryngologists every day [3]. In fact, over 73% of the population experiences continually elevated inspiratory resistance as a result of obstructed nasal airflow [4]. In patients seeking treatment, the primary causes of nasal obstruction are chronic inflammation due to allergies (38%) and permanent structural abnormalities (62%) [9]. While the inflammatory causes of nasal obstruction are generally well controlled with topical and systemic pharmacotherapy, the structural impedances to airflow must be treated through mechanical alteration of these flow-limiting segments [10].

The most common structural pathologies that contribute to nasal obstruction are septal deviation (54%) and internal nasal valve collapse (14%), both of which increase resistance through the internal nasal valve. The internal nasal valve is defined by the junction of the nasal septum, caudal border of the upper lateral cartilage, and head of the inferior turbinate; it contributes to two-thirds of the total nasal resistance. [3] As per Poiseuille's law, resistance increases as a factor of the radius to the fourth power. As such, small changes to the dimensions of the internal nasal valve cause an exponential change in flow. In septal-deviation, the septum- the bony and cartilaginous structure that divides the nasal cavity- is deflected, dislocated off the maxillary crest, or off-center, causing a reduction in cross-sectional area of the internal nasal valve. Valvular collapse occurs when the lateral nasal wall paradoxically moves medially on inspiration at the level of the internal valve, causing a corresponding decrease in cross-sectional area and increase in nasal resistance. The cause of which can be congenital – from weak upper lateral cartilage or lack of dilator function, develop as a result of trauma, or occur post-operatively in patients following nasal surgery [8].

There are a number of over-the-counter consumer products that attempt to relieve this mechanical nasal obstruction in an effort to avoid surgery. One of the most popular external dilators is Breathe Right, a flexible strip that is adhered to the nose and stents the lateral walls of the nose outward to prevent internal nasal valve collapse [8]. Other existing solutions take the form of nasal cones and clips that act intra-nasally to stent the collapsed nasal valve. While studies show that these products are mostly effective in increasing nasal airflow, they are typically described as uncomfortable and carry social stigma due to visibility during use, leaving their use for an extended period of time limited [11].

During the 2016 to 2017 academic year, a team of undergraduate biomedical engineering students at Johns Hopkins partnered with Dr. Patrick Byrne, MD, FACS, MBA, the Director of Facial Plastic and Reconstructive Surgery to design and prototype a discreet silicone nasal dilator device. A survey including the previously validated Nasal Obstruction Symptom Evaluation (NOSE) instrument and additional questions regarding nasal obstruction symptoms, management options, and characteristics desirable in a nasal dilator device has been developed and previously approved by the Johns Hopkins IRB (IRB00122933).

Based on this data and interviews with otolaryngologists experienced in diagnosing and treating nasal obstruction patients, the team developed design concepts for a mechanical nasal dilator intended to meet patient preferences for effectiveness, inconspicuousness, comfort, and usability. To date, the engineering team has conducted testing on prototypes to verify that upon compression dilators exert a dilation force consistent with the range that humans find effective in relieving nasal obstruction yet comfortable for extended periods of time. The team has assessed effectiveness of prototypes in improving nasal breathing using a model nose developed from de-identified patient images and informed by published medical research. The team also used this model with a compressed air device to confirm the stability of the dilator within the nose under extreme conditions, including sneezes and peak inspiratory flow.

The next step is to collect human data to assess Schnozzle's effectiveness in relieving nasal obstruction and source patient feedback to evaluate the success of these prototypes in meeting key design requirements of comfort, inconspicuousness, and usability. The team has conducted initial feasibility testing using the device and recording equipment to prepare and refine protocols for human subject testing.

4. Study Procedures

a. Study design, including the sequence and timing of study procedures (distinguish research procedures from those that are part of routine care).

Recruitment:

Participants will be recruited from patients presenting to Otolaryngology clinics with symptoms of nasal obstruction. The otolaryngologist in clinic will screen these patients for nasal valve collapse as they would in standard clinical practice. This involves visualizing the nasal cavity through nasal endoscopy and testing the nasal valve using Cottle maneuver (applying lateral force to the cheek to open the nasal valve) or the modified Cottle maneuver (using a cotton tip applicator to open the nasal valve from inside the nasal cavity) and evaluating for improvement in nasal obstruction symptoms. Improved nasal airflow during the maneuver suggests nasal valve collapse contributes to restricted nasal airflow.

The clinical Otolaryngologist will counsel patients with nasal valve collapse regarding the various treatment options as they would in routine clinical practice (management options include to doing nothing, using existing nasal dilator devices, or undergoing surgery). Patients will then be invited to participate in the study, which would involve a study session in which they are fitted with six nasal dilator devices, instructed in proper care and use, and report on their function and comfort. Additional participants will be recruited from patients who present to Otolaryngology clinics with symptoms unrelated to nasal breathing to serve as a control group. Participants will also be recruited via the clinicaltrials.gov website, as well as using recruitment flyers and social medial posts.

Study design:

If a patient expresses interest in participating they will be introduced to a member of the research team to discuss the study and complete informed consent. All participation is voluntary and participants are able to withdraw from the study at any point. The study participant will be asked to complete a questionnaire, which was adapted from the previously approved survey (IRB00122933), which includes the NOSE instrument, questions regarding the patient's current treatments, and a ranking of their preferred characteristics of an ideal nasal dilator (see Appendix A).

Patients will then be asked to inhale rapidly into an airflow transducer to measure baseline peak nasal inspiratory flow (PNIF). Following the pre-test survey participants will be fitted serially with five commercially available nasal dilator products per manufacturer recommendations (Breathe Right strips, Max Air nose cones, Sleep Right dilator, Mute dilator, and Nozovent dilator), and one experimental nasal dilator designed by the research team ("Schnozzle"). In this crossover design study participants will be blinded as to which dilators are branded and which are experimental, and the order of fitting nasal dilators will be randomized. Each subject will undergo PNIF testing for all six devices.

After each fitting and use for five minutes to adjust to the device and confirm there is no immediate discomfort or irritation, participants will undergo repeat PNIF testing with each device and then will be free to go home and trial the devices on their own. Participants will be given a schedule specifying one device to trial for at least one continuous hour per day. This schedule will specify devices in a randomized order,

and participants will continue to be blinded as to which device they will be using on a particular day (Schnozzle, Breathe Right, Max Air, Sleep Right, Mute, and Nozovent). The devices will be numbered in a random fashion, for participants to be able to identify which device via the assigned number they are scheduled to use on that day. They will similarly use the device number when performing any device evaluation.

Participants are free to wear the assigned nasal dilator at their leisure beyond one hour, but must log the hours and activities performed while wearing the device (for example, "10am-11am exercising"). Patients are not required to wear a device in public at work or during exercise unless they feel comfortable doing so. All devices should be worn overnight. When the schnozzle is utilized at night, a modified version will be used where each portion inserted into the nares will be connected by an external bridge. This is to prevent posterior displacement of the device during sleep. Each morning, the participant will complete a survey summarizing their experience using the assigned device (Appendix B). If there is any discomfort, irritation, skin breakdown, or epistaxis the participant should stop wearing the device and contract the research team immediately.

Over the course of the first six days since the initial clinic visit, the participant will trial and log their use of each of the six nasal dilators. After at least six days (one day per device) participants will return to the office for an exit interview with the study team in regards to their subjective experience with each device. At the end of each trial day they will be asked to fill out a concluding survey (see appendix C). At their exit interview they will be asked to submit both appendix B and C for each device they trialed.

Before returning to the clinic for the conclusion of the study, participants may have several days without an assigned device. Participants are free to stop wearing all devices or use any device as they please as long as it is consistent with proper care and use of the device(s).

b. Study duration and number of study visits required of research participants.

This study requires two office visits – one to begin the study with baseline PNIF measurements, device fitting, PNIF with each device in place, and a perception survey. This will be followed up with a wrap up visit end the study with a concluding survey. Each patient will participate in the study for at least six days to trial each device, and the entire duration depends on an individual patients' ability to return to the clinic, no more than two weeks.

Participants will be free to stop participating at any point during the study. Participants will have the option to be included in a list of individuals who would be interested and willing in participating in additional study sessions.

c. Blinding, including justification for blinding or not blinding the trial, if applicable.

Patients will be blinded to the names of the devices tested to limit bias when they complete the surveys. They will also be blinded as to which device was designed by members of the research team.

d. Justification of why participants will not receive routine care or will have current therapy stopped.

The standard of care is to do nothing, use existing nasal dilator devices, or surgery. This one session comparison study of nasal dilators does not prevent patients from proceeding with the standard of care after the study session, and will familiarize them more thoroughly with available treatment options.

e. Justification for inclusion of a placebo or non-treatment group.

Participants will serially wear the prototype Schnozzle device and marketed nasal dilators, all of which are treatments. We will get a baseline NOSE and PNIF score from participants without any assistive devices in place, which serves as the placebo/ non-treatment arm of the study. Following the study session participants can continue to use currently marketed nasal dilators or proceed with planning surgery.

f. Definition of treatment failure or participant removal criteria.

Participants will be removed from the study if they experience substantial discomfort with the study devices, or if they experience any adverse events, such as epistaxis, or skin breakdown or if they would like to discontinue testing for any reason.

g. Description of what happens to participants receiving therapy when study ends or if a participant's participation in the study ends prematurely.

At the end of the study session participants will be able to continue using any of the marketed nasal dilator products currently on the market, and this study will not influence their ability to proceed with scheduling surgery if indicated and desired. They will not be able to continue using the Schnozzle nasal dilators at this time as it is still in early stage development and not widely produced or available.

5. Inclusion/Exclusion Criteria

Subjects will be recruited from patients who have presented to Otolaryngology clinics with complaints of nasal obstruction. Specifically, patients who have been found to have nasal valve collapse by an Otolaryngologist based on performance of the Cottle maneuver will be invited to participate in the study. Additionally, participants will be evaluated for inclusion in the same manner if they were recruited utilizing flyers, social media, or discovered our study via the clinicaltrials.gov website. They will be excluded if after examination they are determined by their Otolaryngologist to be unsuitable or unsafe for an internal nasal dilator (e.g. history of granulomatosis with polyangiitis, extensive prior sinus or turbinate surgery altering nasal cavity anatomy, pre-existing mucosal injuries or abnormalities). Included participants will then be asked to complete the survey, NOSE questionnaire, and testing session either at the same visit or on another visit depending on patient and tester availability. Additionally we will include a control arm whom do not have evidence of nasal valve collapse, but are willing to participate in the study. Members of the control arm will also be excluded if they are deemed unsuitable based on nasal anatomy and/or the above exclusion criteria listed above.

6. Drugs/ Substances/ Devices

a. The rationale for choosing the drug and dose or for choosing the device to be used.

The control devices (Breathe Right strips, Sleep Right dilator, Mute dilator, Nozovent dilator, and Max Air nose cones) were selected from several other nasal obstruction products available on the market based on discussions with patients and opinion leaders in nasal airway obstruction due to their popularity and reported effectiveness. These are all legally marketed in the United States as Class I 510(k) exempt medical devices available over-the-counter.

The Schnozzle was developed as a non-invasive, discreet alternative to the current products available for nasal airway obstruction. Schnozzle is still in prototype form, and this testing will influence final design updates to improve the dilator before full-scale manufacturing and marketing. For this testing, Schnozzle prototypes will be produced using an FDA approved silicone.

Schnozzle is a Class I device not requiring FDA approval prior to use in humans. It fits into the existing internal nasal dilator classification as defined by Code of Federal Regulations (CFR) Title 21, Part 874 - Ear, Nose, Throat Devices, Subpart D - prosthetic devices, section 874.3900. According to this definition, a nasal dilator "provides relief from temporary causes of breathing difficulties resulting from structural abnormalities" through a mechanism that "decreases airway resistance and increases nasal airflow". More specifically, the Schnozzle device fits into the internal nasal dilator subcategory. As stated in the FDA's ruling, "the internal nasal dilator is constructed from metal or plastic and is placed inside the nostrils; it acts by pushing the nostrils open or by gently pressing on the columella". The Schnozzle nasal dilator fits this definition, being a prosthetic device placed inside the nostril with the purpose of increasing nasal airflow.

As confirmed by Greenleaf Health, a regulatory consulting firm, Schnozzle can be considered Class I device exempt from 510(K) premarket notification.

b. *Justification and safety information if FDA approved drugs will be administered for non-FDA approved indications or if doses or routes of administration or participant populations are changed.* N/A
c. *Justification and safety information if non-FDA approved drugs without an IND will be administered.* N/A

7. Study Statistics

a. Primary outcome variable.
Peak Nasal Inspiratory Flow (PNIF) and Nasal Obstruction Symptom Examination (NOSE) score for each individual before the trial and while using each tested nasal dilator.

b. Secondary outcome variables.
Comfort, appearance, ease of use, and general favorability of each device.

c. Statistical plan including sample size justification and interim data analysis.
The purpose of this pilot study is to understand patient needs and preferences regarding nasal dilators, and to use this data to refine the design before potentially marketing the product. In this pilot study we plan to test 70 individuals with nasal valve collapse. Previous studies have demonstrated an ability to detect a statistically significant difference in PNIF with a power of 80% and an alpha of 0.05 with a sample size of 30 patients with nasal valve collapse. We aim to recruit 70 individuals, 35 patients with nasal valve collapse, 35 patients without nasal valve collapse with expected attrition of 5 patients in each cohort.[12] If we proceed to pursue statistical evaluation of the data we will use ANOVA with a $p < 0.05$ predetermined as significant.

d. Early stopping rules.
After 5 and 10 participants complete testing we will evaluate the data to look for themes and determine if further testing is likely to yield additional information. If a large percentage of patients are unable to complete the study due to complaints with device comfort or due to previously defined adverse outcomes we will halt the study.

8. Risks

a. Medical risks, listing all procedures, their major and minor risks and expected frequency.
Application and wearing of any of the experimental or existing nasal dilators could conceivably lead to:
1. Discomfort, including moderate temporary pain, or irritation, including tickling that may cause sneezing. Discomfort associated with wearing the devices is expected to be uncommon, minor, and self-limited. Participants have the option to refuse or remove any or all of the nasal dilator system at any point.
2. Epistaxis (nose bleeding), is unlikely given that patient with abnormal nasal mucosa are not included in the study. Participants will be trained and assisted by study personnel to a-traumatically apply and remove the nasal dilator devices. Should a participant experience epistaxis they will be managed according to the standard of care, which would involve application of manual pressure to the cartilaginous portion of the nose for 20 minutes. Should bleeding be severe or persistent they will be seen by an Otolaryngologist for further management and treatment.
3. Migration of nasal dilator device is highly unlikely given the pre-clinical testing of nasal dilators in a nose model under extreme conditions of high airflow that could be associated with sneezing and peak inspiratory breathing. Additionally, the normal nasal anatomy, namely the inferior nasal turbinates, limit the open space in the nose and should prevent migration of nasal dilators. Individuals with markedly abnormal inferior turbinates are excluded from this study.
4. Nasal dilators may be ineffective at improving nasal airflow during the study. These subjects will not be excluded but may leave the study.

b. Steps taken to minimize the risks.

Included in each risk above.

c. *Plan for reporting unanticipated problems or study deviations.*
Any unanticipated problems, adverse events, or study deviations will be immediately discussed with the principal investigator (PI) and reported to the IRB if deemed appropriate by the PI. This will be done using RF3 and RF4 as needed.

d. *Legal risks such as the risks that would be associated with breach of confidentiality.*
All collected data will be stored on an encrypted drive password protected as per protocol. Patient data will be de-identified and not have a name or date of birth associated with it.

e. *Financial risks to the participants.*
Participants' only financial risk is the opportunity cost associated with their time spent in office at the beginning and end of the trial.

9. Benefits

a. Description of the probable benefits for the participant and for society.

By participating in this study, individuals with nasal valve collapse will have an opportunity to trial several existing nasal dilators. In typical clinical practice patients are given recommendations for several types of nasal dilators but are not fitted and trained in appropriate use. Participants may notice a marked improvement in their ability to breathe while wearing the devices and an enhancement in quality of life.

Schnozzle has the potential to improve of the quality of life for the millions of nasal obstruction sufferers who currently forgo treatment. Faced with the choice between inaction and the appointments, extensive recovery period, and uncertain outcome inherent with surgery, the majority of individuals—especially those with minor to moderate obstruction—elect to live with their symptoms, which present a constant bother, source of embarrassment, and long-term health risk.

While existing nasal dilators are effective in temporarily relieving their symptoms, sufferers agree that existing products are not an option for use in their daily lives. However, these same individuals insist that a comfortable and discreet device would present a preferred solution to surgery to aid their breathing during the day. This trial will provide the clinical evidence necessary to evaluate and inform redesigns of existing prototypes to aid in the development of a finalized product ready for the market.

10. Payment and Remuneration

a. Detail compensation for participants including possible total compensation, proposed bonus, and any proposed reductions or penalties for not completing the protocol.

Participants will not be paid, but they will be given the option to keep any of the marketed nasal dilators they trialed (Breathe Right, Max Air, Sleep Right, Mute, Nozovent).

11. Costs

a. Detail costs of study procedure(s) or drug (s) or substance(s) to participants and identify who will pay for them.

The cost of the nasal dilators for participants will be borne by the research team including the principal investigator.

References:

[1] Jenson M, Malm L. Definition, prevalence and development of nasal obstruction. Allergy. 1997; 52 (SUPP/40): 3-6

[2] Rhinomed. *Roadshow Presentation*. N.p., Mar. 2016. Web. <http://www.rhinomed.global/wp-content/uploads/2016/03/Roadshow-Presentation.pdf>.

[3] Bloching MB. Disorders of the nasal valve area. GMS Curr Top Otorhinolaryngol Head Neck Surg. 2007;6:7.

[4] Miman MC, Deliktas H, Ozturan O, et al. Internal nasal valve: revisited with objective facts. *Otolaryngol Head Neck Surg*. 2006;134:41-47.

[5] Camacho, M., Zaghi, S., Certal, V. et al., 2016, "Predictors of Nasal Obstruction: Quantification and Assessment Using Multiple Grading Scales," *Plastic Surgery International*, vol. 2016, Article ID 6945297, 9 pages: doi:10.1155/2016/6945297

[6] Khosh MM, Honrado C, Pearlman SJ. Nasal Valve Reconstruction. *Arch Facial Plast Surg*. 2004. 6:167-171.

[7] Schlosser, R.J. and Park, S. S., 1999, "Surgery for the Dysfunctional Nasal Valve." *Archives of Facial Plastic Surgery* 1, no. 2: 105. doi:10.1001/archfaci.1.2.105. http://jamanetwork.com/journals/jamafacialplasticsurgery/fullarticle/479692

[8] Kiyohara, N., 2016, "A Comparison of Over-the-Counter Mechanical Nasal Dilators." *JAMA Facial Plastic Surgery* 18, no. 5: 385. doi:10.1001/jamafacial.2016.0291.

[9] Picavet VA, Grietens J, Jorissen M, Hellings PW. Rhinoplasty from a rhinologist's perspective: need for recognition of associated sinonasal conditions. Am J Rhinol Allergy. 2012; 26: 493–496.

[10] Samaha M, Rassouli A. Spreader graft placement in endonasal rhinoplasty: technique and review of 100 cases. *Plast Surg (Oakv)*. 2015 Winter. 23 (4):252-4.

[11] Kimbell JS, Frank-Ito DO. Mechanical Nasal Dilators for the Management of Nasal Obstruction. *JAMA Facial Plast Surg*. 2016;18(5):389-390. doi:10.1001/jamafacial.2016.0656.

[12] Raudenbush, B, Stenting the nasal airway for maximizing inspiratory airflow: Internal Max-Air Nose Cones versus external Breathe Right strip. Am J Rhinol Allergy 25,249-51, 2011.

If you are using Epic for this study, fax a copy of the signed consent form to 410-367-7382.

Patient I.D. plate

RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title: **Assessing Mechanical Nasal Obstruction Experience and A Potential New Treatment Option**

Application No.: **IRB00135539**

Principal Investigator: **Nicholas Rowan, MD**
601 N. Caroline St. 6th Floor
Baltimore, MD 21287 Main: (410) 614-6243

1. What you should know about this study:

- You are being asked to join a research study. This consent form explains the research study and your part in it. Please read it carefully and take as much time as you need. Ask your study doctor or the study team to explain any words or information that you do not understand.
- You are a volunteer. If you join the study, you can change your mind later. There will be no penalty or loss of benefits if you decide to quit the study.
- During the study, we will tell you if we learn any new information that might affect whether you wish to continue to participate.
- If we think your participation in this study may affect your clinical care, information about your study participation will be included in your medical record, which is used throughout Johns Hopkins. Doctors outside of Johns Hopkins may not have access to this information. You can ask the research team to send this information to any of your doctors.
- When Johns Hopkins is used in this consent form, it includes The Johns Hopkins University, The Johns Hopkins Hospital, Johns Hopkins Bayview Medical Center, Howard County General Hospital, Johns Hopkins Community Physicians, Suburban Hospital, Sibley Memorial Hospital and All Children's Hospital.
- A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.
- If you would like to review the information for this study, or a summary of the results, ask the study team doctor for the ClinicalTrials.gov study registration number.

2. Why is this research being done?

This research is being done to determine whether nasal airway obstruction can be improved with mechanical nasal dilators.

Currently nasal airway obstruction can be managed with no intervention, the use of over the counter mechanical nasal dilators, or with surgery. We want to determine if use of these over the counter devices significantly improves patient symptoms. We also want to determine if different nasal dilator devices improve symptoms of airway obstruction to different extents.

Devices we will be examining include Breathe Right strips, Sleep Right dilator, Mute dilator, Nozovent dilator, and Max Air nose cones. These listed devices are commercially available over-the-counter mechanical nasal dilators. Breathe Right strips, Nozovent, and Max Air are approved by the Food and Drug Administration (FDA) for relief from temporary causes of breathing difficulties resulting from structural abnormalities. Mute and Sleep Right are registered with the FDA and fall under the new category that exempts nasal dilators from the FDA 510(k) approval process due to their low-risk characteristics.

Additionally, we also want to determine if our team's investigational design of an internal nasal dilator can also improve symptoms of nasal airway obstruction and if it can do so to a greater extent than the previously listed commercially available devices. As with the Mute and Sleep Right dilators, our team's investigational device is exempt from FDA approval as it fulfills the definition of a nasal dilator and is exempt from the approval process.

People both with and without mechanical nasal obstruction as diagnosed by an Otolaryngologist (Ear, Nose, & Throat doctor) may join.

How many people will be in this study?
We expect a total of 70 people to be enrolled in this study.

3. What will happen if you join this study?

If you agree to be in this study, we will ask you to do the following things:

In Office Portion

- You will complete a baseline survey in regards to your symptoms of nasal obstruction, and you will then undergo testing of your nasal airway resistance. This testing is completed by breathing in against an airflow measuring tool attached to a small mask worn over your mouth and nose. This testing will take no longer than 5-10 minutes.
- After baseline testing you will then be fit with the appropriately sized nasal dilator by our team. You will be fit with 6 total devices: 5 commercially available devices and 1 investigational device.
- You will be blinded to the name of each device and as to which device is our investigational device. This means that you will not know which device you are being fit with or using. We do this so that your evaluation of each device is not biased in any way.
- After we have fit you with the correctly sized device, we will repeat testing of your nasal airway resistance with each device in place.
- We estimate the fitting period and repeat nasal airway resistance tests with the device in place will take about 20 minutes. Therefore the total length of your clinic visit would be increased by- about 30 minutes total.

At Home Portion

- You will then be instructed to take the 6 nasal dilator devices home and begin using each device as instructed. Specifically, you will be assigned to use each device in a randomized order (like drawing numbers out of a hat that correspond to the order you should use a

device in) and asked to wear each device for at least one hour continuously while you are awake.
- You will be asked to document what activities you were doing while wearing the device and for how long.
- You will then be asked to wear the same device overnight. Following your overnight trial with the device you will be asked to fill out a survey about your experience with that device. We will then ask you to do the same for the 5 other devices over the 5 following days.
- As there are 6 devices this at home portion of the study will take 6 days: 1 daytime and 1 overnight trial period for each device.

In Office Debriefing
- After evaluating all the devices you will be asked to come back in for an additional office visit where we will ask you questions about your experience with each device and you will be asked to fill out a survey ranking the device from your most favorite to least favorite. You will also be asked to hand in your surveys and other documentation you completed at home for each device at this time.
- You will be able to keep any of the commercially available devices if you wish to continue to use them. You will not be able to keep or continue using our investigational device.

How long will you be in the study?
The entire study encompasses 2 in office visits and a 6 day at home trial period.

4. What are the risks or discomforts of the study?

Risks of joining the study
- There are minimal risks of joining the study as using these mechanical nasal dilator devices is currently an accepted standard of care for mechanical nasal obstruction. Additionally your participation will not prevent you from pursuing the other potential management option of surgery at a later date.

Risks with device use
- The risks with device use are minimal and all *unlikely*. They include the following:
  - Skin irritation or breakdown around where the device is inserted or placed on the nose
  - Nose bleeding.
  - Device becoming lodged within the nasal cavity requiring removal by your doctor.

If you have any of the above outcomes you will be asked to immediately stop using the device(s) and contact Drs. Rowan, Papel and/or Kontis for in-office evaluation. Management of each of these potential risks will be on a case-by-case basis based on that examination. Interventions required or needed may range from nothing and just discontinuation from the study, to application of topical ointment (in the case of skin breakdown), to, in the very rare and unexpected case of nose bleeds that do not stop on their own, use of topical thrombotic agents (agents that make your blood clot).

Other Risks:
You may get tired or bored when we are asking you questions or you are completing questionnaires. You do not have to answer any question you do not want to answer. You may also get tired of using the different device, and/or of documenting your use and experience with each one. If at any point

you feel this way you may stop documenting or using the devices and leave the trial without any consequence.

Risks to Confidentiality Loss:
There is the risk that information about you may become known to people outside this study. We will not be collecting any personal information from you other than the measurements of your nasal airway resistance. As such, there is very minimal risk of a loss of confidentiality of your personal information.

5. Are there benefits to being in the study?

There is no direct benefit to you from being in the study. If you take part in this study, you may help others in the future. We will be able to understand if mechanical nasal dilators are a reasonable alternative to surgery for patients with nasal airway obstruction.

6. What are your options if you do not want to be in the study?

If you decide not to join this study, other options are available. You do not have to join this study to get treatment. Other treatments include surgery to correct nasal airway obstruction or no intervention at all.

You do not have to join this study. If you do not join, your care at Johns Hopkins will not be affected.

7. Will it cost you anything to be in this study?

You will receive a separate Insurance and Research Participant Financial Responsibility Information Sheet (Sheet).

This Sheet will give you the following information:

- The procedures, tests, drugs or devices that are part of this research and that will be paid for by the study (no cost to you).

- The procedures, tests, drugs or devices that will be billed to you and/or your health insurer. If you have health insurance, you will be responsible for any co-pays or deductibles not covered by your insurance.

8. Will you be paid if you join this study?

No. However, you will be able to keep and use any of the commercially available nasal dilators.

9. Can you leave the study early?

- You can agree to be in the study now and change your mind later.
- If you wish to stop, please tell us right away.
- Leaving this study early will not stop you from getting regular medical care.

If you leave the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities

10. Why might we take you out of the study early?

You may be taken out of the study if:

- Staying in the study would be harmful.
- You fail to follow instructions.
- The study is cancelled.
- There may be other reasons to take you out of the study that we do not know at this time.

If you are taken out of the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities**.**

11. How will your privacy be protected?

We have rules to protect information about you. Federal and state laws and the federal medical Privacy Rule also protect your privacy. By signing this form you provide your permission, called your "authorization," for the use and disclosure of information protected by the Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records (which may include information about HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

The research team will know your identity and that you are in the research study. Other people at Johns Hopkins, particularly your doctors, may also see or give out your information. We make this information available to your doctors for your safety.

People outside of Johns Hopkins may need to see or receive your information for this study. Examples include government agencies (such as the Food and Drug Administration), safety monitors, other sites in the study and companies that sponsor the study.

If you are in a cancer study that receives federal funding, the National Cancer Institute (NCI) now requires that we report identifiable information (such as, zip code) about your participation. You may contact the NCI if you have questions about how this information is used.

We cannot do this study without your authorization to use and give out your information. You do not have to give us this authorization. If you do not, then you may not join this study.

We will use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside Johns Hopkins who receive your information may not be covered by this promise or by the federal Privacy Rule. We try to make sure that everyone who needs to see your information keeps it confidential – but we cannot guarantee that your information will not be re-disclosed.

The use and disclosure of your information has no time limit. You may revoke (cancel) your permission to use and disclose your information at any time by notifying the Principal Investigator of this study by phone or in writing. If you contact the Principal Investigator by phone, you must follow-up with a written request that includes the study number and your contact information. The Principal Investigator's name, address, phone and fax information are on page one of this consent form.

If you do cancel your authorization to use and disclose your information, your part in this study will end and no further information about you will be collected. Your revocation (cancellation) would

not affect information already collected in the study, or information we disclosed before you wrote to the Principal Investigator to cancel your authorization.

12. What treatment costs will be paid if you are injured in this study?

Johns Hopkins does not have a program to pay you if you are hurt or have other bad results from being in the study. However, medical care at Johns Hopkins is open to you as it is to all sick or injured people.

The costs for any treatment or hospital care you receive as the result of a study-related injury that are not covered by a health insurer will be billed to you.

By signing this form you will not give up any rights you have to seek compensation for injury.

13. What other things should you know about this research study?

a. What is the Institutional Review Board (IRB) and how does it protect you?

The Johns Hopkins Medicine IRB is made up of:

- Doctors
- Nurses
- Ethicists
- Non-scientists
- and people from the local community.

The IRB reviews human research studies. It protects the rights and welfare of the people taking part in those studies. You may contact the IRB if you have questions about your rights as a participant or if you think you have not been treated fairly. The IRB office number is 410-955-3008. You may also call this number for other questions, concerns or complaints about the research.

When the Johns Hopkins School of Medicine Institutional Review Board (IRB) reviews a study at another site, that site (institution) is solely responsible for the safe conduct of the study and for following the protocol approved by the Johns Hopkins IRB.

b. What do you do if you have questions about the study?

Call the principal investigator, Dr. Nicholas Rowan at (410)614-6243. If you wish, you may contact the principal investigator by letter. The address is on page one of this consent form. If you cannot reach the principal investigator or wish to talk to someone else, call the IRB office at 410-955-3008.

c. What should you do if you are injured or ill as a result of being in this study?

If you think you are injured or ill because of this study, call Dr. Nicholas Rowan at (410) 614-6243during regular office hours.

d. What happens to Data that are collected in the study?

Johns Hopkins and our research partners work to understand and cure diseases. The data you provide are important to this effort.

If you join this study, you should understand that you will not own your data, and should researchers use them to create a new product or idea, you will not benefit financially.

14. What does your signature on this consent form mean?

Your signature on this form means that: You understand the information given to you in this form, you accept the provisions in the form and you agree to join the study. You will not give up any legal rights by signing this consent form.

WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

_____

_____
Signature of Participant (Print Name) Date/Time

_____

_____
Signature of Person Obtaining Consent (Print Name) Date/Time

_____

_____
Signature of Witness to Consent Procedures (Print Name) Date/Time

(optional unless IRB or Sponsor required)

I have received the separate Insurance and Research Participant Financial Responsibility Information Sheet.

_____

_____
Signature of Participant, LAR or Parent/Guardian (Print Name) Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR; A COPY MUST BE GIVEN TO THE PARTICIPANT; IF YOU ARE USING EPIC FOR THIS STUDY A COPY MUST BE FAXED TO 410-367-7382; IF YOU ARE NOT USING EPIC A COPY MUST BE PLACED IN THE PARTICIPANT'S MEDICAL RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

ONLY CONSENT FORMS THAT INCLUDE THE JOHNS HOPKINS MEDICINE LOGO CAN BE USED TO OBTAIN THE CONSENT OF RESEARCH PARTICIPANTS.