PROTOCOL TITLE: Do Anti-Snoring Appliances Reduce the Amount of Airway Manipulation in Patients Undergoing Anesthetic Sedation? A Prospective Randomized Controlled Trial

PRINCIPAL INVESTIGATOR:
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STUDY SUMMARY:

Investigational Agent(s) (Drugs or Devices)	Anti-snoring Appliances including: Zyppah
IND / IDE / HDE #	Zyppah FDA #K182312
Indicate Special Population(s)	☐Children ☐ Children who are wards of the state ☐ Adults Unable to Consent ☐ Cognitively Impaired Adults ☐ Neonates of Uncertain Viability ☐ Pregnant Women ☐ Prisoners (or other detained/paroled individuals) ☐ Students/Employees
Sample Size	28
Funding Source	TBD
Indicate the type of consent to be obtained	☒Written ☐Verbal/Waiver of Documentation of Informed Consent ☐Waiver of HIPAA Authorization ☐Waiver/Alteration of Consent Process
Site	☐ Lead Site (For A Multiple Site Research Study) ☐ Data Coordinating Center (DCC)
Research Related Radiation Exposure	☐Yes ☒ No
DSMB / DMC / IDMC	☐Yes ☒No

OBJECTIVES:
Would patients using an anti-snoring appliance intraoperatively require less airway manipulation, interventions, and rescue maneuvers during anesthetic sedation cases compared to those who do not?

Null Hypothesis:
There is no difference in the number of airway manipulations, interventions, and rescue maneuvers during anesthetic sedation procedures when an anti-snoring appliance is used.

BACKGROUND:
Surgical cases requiring sedation by an anesthesia provider, also known as monitored anesthesia care (MAC), are a popular choice for outpatient surgical procedures with benefits of “less physiologic disturbance and a more rapid recovery than general anesthesia” (Das 2015). However, MAC cases still come with risk: per the American Society of Anesthesiologists closed claim database, “the most common malpractice claim is inadequate oxygenation/ventilation, with more than 80% of claims of this nature resulting in brain damage or death” (McMurray 2020). Since 1908, anesthesia providers have been utilizing interventional airway devices that manipulate the soft tissues of the nasopharynx, oropharynx, and hypopharynx to relieve obstruction to support patient ventilation and oxygenation; however, there are few studies that directly compare the efficacy & side effect profiles between these devices (Matioc 2019). Additionally, a recent survey indicates that many anesthesia providers desire an alternative airway intervention device than the current ones most commonly used in current practice (McMurray 2020). We will examine the possibility of using at-home, over-the-counter anti-snoring devices as an intraoperative airway device.

STUDY ENDPOINTS:
PRIMARY ENDPOINT: Combined total number of airway interventions during an anesthetic sedation case – including head tilt/rotation, mandible thrust, chin lift, shoulder lift, neck extension or flexion, tongue pull.

SECONDARY ENDPOINTS:
- Satisfaction of Anesthetist via survey
- Maximum/minimum end-tidal CO2
- # of times SpO2 value < 92%
- % of time during the case SpO2 < 92%
- maximum/minimum SpO2 value
- EKG analysis that were not recorded as “Normal Sinus rhythm”:
- Heart rate maximum & minimum
- maximum/minimum Systolic, diastolic, and mean blood pressure
- Total dose and type of hypnotic & narcotic given
- Case type
- Case duration
- Baseline characteristics (Age, Gender, BMI)

- Time spent in Phase 2 PACU Recovery
- Adverse events (i.e. regurgitation and aspiration, bronchospasm, cough, case converted to GA)

STUDY INTERVENTION(S) / INVESTIGATIONAL AGENT(S):
We will use anti-snoring appliance devices (specifically the FDA approved Zyppah) to attempt to relieve tissue obstructions that cause snoring during sleep. The application of the devices to the body is less invasive than other common intraoperative rescue airway devices (e.g. nasal trumpets and oral airways) which are not designed to be patient specific.

We will be purchasing the device from the manufacturer's website. We will be purchasing the devices via funds awarded by the James E. Eckenhoff Residents' Research Award.

The device will be stored in the PI's key-locked office, until it is given to a research team member to be given to a subject after recruitment and prior to their procedure. Research personnel will bring the appliance to the preoperative holding area & will help mold it for the patient, and will insert it prior to transport to the operating suite. The device will remain in place until the completion of procedure, unless the anesthesia provider in the room feels it needs to be removed for any reason. The patient or anesthesia personnel can remove the device at their leisure after completion of the procedure.

PROCEDURES INVOLVED:
The study participants will be recruited into two groups: patients wearing an anti-snoring appliance device during an anesthetic sedation procedure; and those who do not wear an anti-snoring device. To ensure anesthetic providers have easy access to the patient's airway for standard of care manipulation (if needed), the patients eligible for this study would be those who are undergoing procedures bellow the umbilicus (e.g. gynecological, urological, orthopedic, etc.) in addition to having a STOP-BANG score of 2 or greater. This will ensure patient safety and provide a wide demographic of potential subjects to increase the generalizability of the study.

For both patient groups, the study procedure is the same. Eligible patients will be identified by chart review of various elements of the electronic medical record, as follows:

Patients will be identified and be seen by the study team in the pre-operative clinic on 17th floor Lavin and in the holding area to interview individuals who are to undergo eligible anesthetic sedation procedures as above. If the patient agrees to participate in the study, they will be randomized at that time to one of the two groups (anti-snoring appliance device to be used for procedure or not).

The groups in the prospective, randomized, controlled trial in patients undergoing anesthetic sedation procedures will be as follows:

Group #1: Anti-snoring appliance (Zyppah) that will be utilized during their procedure
Group #2: Control group, that will not utilize anti-snoring appliance

Participants will be randomized to treatment groups based on a random computer-generated (https://www.randomizer.org). Anesthesia providers will not be blinded to randomization, and research personnel will observe the procedure to collect all outcome measures in this study.

For group 1, the study team will aid them in molding and preparing the device in the pre-operative area. Anesthesia providers will be instructed on how the device works and when to place it (with aid from the research team) in addition to receiving a question and answer sheet and protocol they can follow to take with them to the operating room. Prior to the administration of anesthetic medications, the patient will be aided in inserting the device, and wear it throughout the entirety of the case. Regardless of the group, from the start of sedation until the patient leaves the procedure suite. When an anesthesia provider believes they make a clinically significant airway intervention (either via jaw lift, head turning, etc.) they will be instructed to use the “mark now” icon in the anesthetic record and utilize the free text to indicate what intervention was done and why.

All standard practices and standard monitors for anesthetic sedation cases will be utilized.

A post-survey will be administered to anesthesia providers in group 1 to gauge satisfaction.

Anesthetic record will be reviewed by research team members following the end of the case.

DATA AND SPECIMEN BANKING

We will collect data including reason for procedure, type of procedure, and patient demographics (including medical history, sex, age, and weight); in addition to data collected via electronic chart review including: Documented Obstructive Sleep Apnea (OSA), date of procedure, surgical case length, anesthesia type requested, anesthesia type documented, Provider team staff composition, documented neuraxial or nerve block procedure (if applicable), “in room” time, max/min heart rate, min/max oxygen saturation, number of instance oxygen saturation fell below 92%, % of time during case where oxygen saturation was below 92%, min/max end tidal CO2, min/max blood pressure, total dose of hypnotic & narcotic given, “out of room” time, adverse events noted in charting, free-text written by providers, and total hospital length of stay.

SHARING RESULTS WITH PARTICIPANTS

Results will not be shared with participants.

STUDY TIMELINES

Individual subjects and anesthetic providers will participate in the study for the duration of their procedure requiring anesthetic sedation. It will take approximately 3 months to enroll participants and approximately 3 months to perform data analysis.

INCLUSION AND EXCLUSION CRITERIA

Inclusion criteria

Adult patients (age 18-89 years old)

Undergoing procedures below the umbilicus requiring anesthetic sedation without an invasive airway

STOP-BANG score of 2 or greater.

English or Spanish language speaking

Exclusion criteria

Patients requiring general anesthesia.

Sleep apnea

Serious breathing or respiratory disorders such as COPD, asthma, emphysema

Poor dental health including severe gum disease, loose teeth, abscess, mouth sores, bleeding gums

Dental implant place within last 3 months

TMJ disorder

Mouth or jaw pain

Full dentures

Wear braces

Sleep with CPAP or other devices

Other special populations (individuals who are not yet adults, prisoners, vulnerable populations, pregnant) will also be excluded.

VULNERABLE POPULATIONS:

Will not be a part of study.

PARTICIPANT POPULATION(S)

Accrual Number:	Category/Group: (Adults/Children Special/Vulnerable Populations)	Consented: Maximum Number to be Consented or Reviewed/Collected/Screened	Enrolled: Number to Complete the Study or Needed to Address the Research Question
Local	Adults	28	28
Study-wide		28	24
Total:		28	24

RECRUITMENT METHODS

Patients undergoing an eligible procedure requiring anesthetic sedation will be identified by the anesthesiology team by chart review and the schedule in the pre-operative clinic on the 17th floor Lavin pavilion prior to their procedure. They may also be approached by the research team the morning of their procedure for possible enrollment into the study. If the potiental subject is interested in the study a study team member will ask for the subject's email address to send an Econsent using REDCap for their review.

The source of participants will be NMH pavilions (Galter, Feinberg, Lavin) in addition to Prentice Women's Hospital.

COMPENSATION FOR PARTICIPATION IN RESEARCH ACTIVITIES

There will be no compensation for participation; however, patients who are randomized into one of the anti-snoring device groups will be allowed to keep the device, if they wish.

WITHDRAWAL OF PARTICIPANTS

Patients can withdraw from the study at any time and their data will be deleted, and in no way will this impact their care since the study explicitly does not affect the standard of care. The study team will notify the PI by secure NM or NU email if a subject withdraws from the study.

RISKS TO PARTICIPANTS

No significant risk to the patient exists with the utilization of an anti-snoring device. The devices are non-invasive and can be easily removed by the patient or anesthesia provider, if needed. There is the potential for damage to loose teeth, gums or tongue since this is a moldable mouth guard. There is the potential for loss of confidentiality even with strict measures in place to prevent occurrence.

POTENTIAL BENEFITS TO PARTICIPANTS

If functional, the participants may benefit from utilization of an anti-snoring device by reducing snoring and airway obstruction; which would lead to improved sleep and less fatigue. It may also prevent the use of more invasive rescue airway devices that can cause patient discomfort including damage to the lips, teeth, gums, tongue, naso- and oropharynx.

DATA MANAGEMENT AND CONFIDENTIALITY

Data Statistics:
Preparation: In previous studies looking at patient satisfaction for snoring relief, 570 participants were analyzed with one of the anti-snoring devices resulting in a statistically significant benefit. However, there are currently no large published studies that analyze the use of an anti-snoring devices in the setting of MAC anesthesia. Additionally, there are no large studies comparing the efficacy of traditional invasive airway rescue devices (e.g. oral/nasal airways).

We utilized a study by Qiansong Xiao et al titled “Comparison of Nasopharyngeal Airway Device and Nasal Oxygen Tube in Obese Patients Undergoing Intravenous Anesthesia for Gastroscopy: A Prospective and Randomized Study”, which compared the oxygen saturation levels in patients who did or did not have an invasive nasopharyngeal airway at the beginning of the anesthetic sedation procedure, to perform our power analysis. 260 patients were included and randomized; with 3 patients excluded due to failure of the nasopharyngeal airway. Based on the differences in “change in SpO2” and “raising the mandible” between their test and control groups, and power analysis was completed with an alpha value of 0.05 and power value of 80%. The n per group that was calculated to provide the appropriate power to identify a statistical difference was 12 patients per study group. To compensate for patients in our study being less obese we increased the number per group to 14 subjects. We plan to approach 28 subjects and randomize 28 patients to 2 groups, allowing for patients who may not end up getting their procedure or instances where data collection is incomplete or absent.

Statistical analysis: Data will be compared between all groups using paired t-test with $p< 0.05$ required to reject the null hypothesis.

Data Security:
All collected data will be stored in REDcap using NM password protected computers for data entry. Data in REDcap is backed up nightly using NM servers which are only accessible to the NM IT administrator. Paper documents generated during the study will be stored in Arkes Pavilion 10th floor Department of Anesthesiology locked research cabinet. Data both paper and electronic will be destroyed 5 years after the completion of the study using current department policy and approved vendors.

PROVISIONS TO MONITOR THE DATA TO ENSURE THE SAFETY OF PARTICIPANTS N/A

PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF PARTICIPANTS

Patients in this study undergoing a procedure under anesthetic sedation can be stressful. If a subject does not feel comfortable with participating, they will have the option to opt out at any time and it will not impact their care if they choose to do so.

Research staff will interact with anesthesia providers on two occasions (at the beginning for ~10 minutes in the pre-operative area and end of procedure for ~5 minutes in the post-operative care area), staff will interact with participants for ~30 minutes prior to the procedure in the pre-operative area in addition to helping mold the mouthpiece.

COMPENSATION FOR RESEARCH-RELATED INJURY

n/a

ECONOMIC BURDEN TO PARTICIPANTS

There is no cost to the patient to be in this study. The device is being paid for by the Department of Anesthesiology.

CONSENT PROCESS

Introduction of the study to the potential participant and consent will take place in Northwestern Hospital's Lavin Anesthesia Pre-Operative Clinic. The potential participant will then be sent a consent document from REDcap which includes the electronic consent document for their review. If the potential participant consents one of the study team members will contact them to discuss the day of surgery planThe participant will receive instructions on acquisition and preparation of the device, in addition to instructions on bringing it to the day of their procedure. REDcap electronic consent will be utilized to decrease the number of times the paper consent would be touched. Multiple times throughout the process, the participant will be reminded that this in no way affects their standard of care and that participation can be withdrawn at any time.

NON-ENGLISH SPEAKING PARTICIPANTS

While we do not anticipate non-English speaking participants on this study, if a non-English speaking patient would benefit from enrollment in this study, the investigator will adhere to the IRB's standard requirements for non-English speaking participants.

This includes providing the IRB the following in a timely fashion:

- Certified translations of all documents the participant will be required to complete (such as surveys and questionnaires);
- A qualified translation service will be used to translate patient facing documents and consent forms

- Certified translations of the modified consent document in a language understandable to the non-English speaking participant if the English version of the approved consent document undergoes subsequent modification;

• All patient-facing documents, including consent forms, will be translated into the patient's preferred language. Any modified patient facing document or consent form will be translated by a qualified translation service, submitted to the IRB for approval, and presented to the patient with a translator present to communicate the changes to the patient and to translate any questions the patient might have, in the patient's preferred language.

• Ongoing communication with the participant will be in a language understandable to the participant

• Northwestern Medicine Interpretation services will be contacted by calling (312) 926-2521. Face to face interpretation or video remote interpreting (VRI) will be scheduled via NM. This offers remote access to an interpreter via an iPad.

• A qualified translator will be available to translate the consent and any other patient facing document in his or her preferred language. The translator will communicate all questions to the study team member who is obtaining the patient's consent.

• A translator will be available for the entire duration of their participation on the study to translate any questions/requests from the participant to the study team and from the study team to the participant.

Northwestern Medicine Interpretation services will be contacted by calling (312) 926-2521. Face to face interpretation or video remote interpreting (VRI) will be scheduled via NM. This offers remote access to an interpreter via an iPad.
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WAIVER OR ALTERATION OF CONSENT PROCESS
n/a

PROTECTED HEALTH INFORMATION (PHI AND HIPAA)
- Will a HIPAA Authorization be obtained from for all participants? Yes
- Name
- Age (years)
- Date of procedure
- Telephone numbers
- Medical Record Numbers
- Email address

QUALIFICATIONS TO CONDUCT RESEARCH AND RESOURCES AVAILABLE
The PI has 10 plus years clinical research experience. Northwestern Medical Center cares for thousands of patients who undergo anesthetic sedation procedures each year. The research team includes 2 resident physicians and a research assistant on the anesthesia care team who will assist the PI during the study period.

MULTI-SITE OR COLLABORATIVE RESEARCH:
n/a