Propranolol for Sleep Apnea Treatment (PROSAT)

NCT03049306

June 6, 2022

If appropriate for this study, a scanned copy of the signed consent form should be uploaded to the participant's Epic/EMR record.

Patient I.D. plate

RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title: **Propranolol for Sleep Apnea Treatment (ProSAT)**

Application No.: **IRB00113241**

Sponsor: **Johns Hopkins University, Mid-Atlantic Nutrition Obesity Research Center (NORC), American Thoracic Society Foundation , National Institutes of Health**

Principal Investigator: **Jonathan Jun, MD**
5501 Hopkins Bayview Circle
Room 5A.50A Baltimore, MD 21224
Phone: 410-550-0115
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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.

- During this study, you will not have access to certain medical information and test results collected for study purposes. If an emergency occurs while you are in the study, medical information needed for your treatment can be made available to your study physician and other physicians who treat you. When the study is completed, all the information in your medical record will be available to you.

2. Why is this research being done?

This research is being done to test whether a drug called propranolol can block the metabolic changes caused by obstructive sleep apnea (OSA). Specifically, we will study whether propranolol can prevent the increase in glucose (sugar) and free fatty acid (FFA) levels by blocking the response to stress hormones.

People with obstructive sleep apnea (OSA) have higher risks of getting diabetes and heart disease, but doctors aren't sure why. Our research has shown that OSA can increase your blood glucose (sugar) and free fatty acid (FFA) during sleep. Increased levels of glucose and FFAs can contribute to diabetes and cardiovascular disease. Thus, OSA may change your metabolism in harmful ways during sleep. We believe OSA causes release of stress hormones that lead to these high levels of glucose and FFA.

Propranolol (Inderal® LA) is a type of medication called a *beta blocker* that blocks the body's response to stress hormones. Propranolol is approved by the Food and Drug Administration (FDA) and currently prescribed for patients with high blood pressure, chest pain, and migraine headaches. It is not approved for lowering levels of glucose and FFA in people with OSA and its use in this study is considered investigational.

We are looking for participants who have OSA and are used to wearing CPAP, who are willing to stop a few days and switch to nasal dilator strips (NDS). NDS are adhesive strips applied to the nose that can reduce nasal congestion and snoring, but long-term data have not shown an effect on OSA severity. We will compare your metabolism on different nights when you are wearing CPAP or NDS, and when you take propranolol compared to a placebo (an inactive material that does not contain any active study drug). We will look at the effect of sleep apnea, CPAP, and propranolol on sleep, blood pressure, heart rate, and metabolism. To study your metabolic function we will also use stable isotopes, which are non-radioactive substances that can track how your body is using energy. Stable isotopes are naturally occurring compounds that are very similar to the regular material, except that they are a heavier form (such as "heavy water" which is just a stable isotope of water). They are already present in very small quantities in your body. In this study, on each visit, you will drink a nutrition shake that contains a stable isotope of fat, and a stable isotope of water. You will also receive tracers by IV to measure your body's fat metabolism.

As an optional part of this study, we will isolate DNA from your blood to check if sleep apnea influences your genes, or to see how your genes affect other results.

People with OSA, who are 20-65 years old, who can sleep comfortably with CPAP on, and are willing to stop CPAP for a few days to switch to NDS may join.

How many people will be in this study?

We are looking for about 30 people to complete 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:

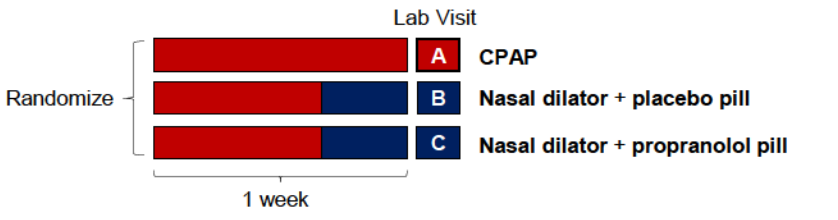
Screening

- To see if you can be in the study, you will have a brief history and physical exam with one of the study doctors. We will measure your height, weight, and neck width. You will be asked to complete a questionnaire about your health. If you are a woman who is able to become pregnant, you will have a urine pregnancy test. You will have an electrocardiogram (EKG) done. You will also have your blood count checked to make sure it is safe for you to have blood samples taken. The result of the pregnancy test must be negative, the EKG must not have certain abnormalities, and the hemoglobin level needs to be at least 10 g/dL for you to take part in the study.
- Before each of your visits we will ask you screening questions for possible Covid-19 infection (fever, headaches, sore throat, diarrhea, loss of smell/taste, sick contacts). In addition, before your visits, we will ask you to have a Covid-19 screening test (such as a nasal swab) performed. This testing requirement may change depending on the level of Covid-19 in the community and Johns Hopkins policies.

Overnight Sleep Studies

- If the results of the screening tests show that you can be in the study and you agree to continue, you will be scheduled for three overnight studies in the sleep laboratory, as shown below. One sleep study is performed wearing your CPAP. The other two sleep studies are performed wearing a NDS on your nose instead of CPAP. You are also asked to use the NDS 2 nights instead of CPAP before coming in. The studies will be scheduled about 1 week apart. On the 2 nights where you are not wearing CPAP, you will be given propranolol LA 80 mg or placebo.

To summarize:



Study visits. Participants sleep in the laboratory three nights, one week apart in random order. Red bars denote CPAP use at night, blue bars denote nasal dilator use.

- **Visit A**:
  You will sleep in the lab wearing CPAP. You will be asked to use CPAP every night before coming in. You will have blood samples taken from an IV at night. You will also have a DEXA scan and an EndoPAT test in the morning.

- **Visit B:**
  You will sleep in the lab wearing a NDS instead of CPAP. You will be asked to do the same thing at home for 2 nights before coming in. Before going to bed, you will be given propranolol LA 80 mg, or a placebo pill. You will have blood samples taken from an IV at night. You will also have an EndoPAT test in the morning.

- **Visit C**:
  You will sleep in the lab wearing a NDS instead of CPAP. You will be asked to do the same thing at home for 2 nights before coming in. Before going to bed you will be given a placebo pill (if you got

propranolol LA on Night #2) or propranolol LA 80 mg (if you got placebo on Visit B). You will have blood samples taken from an IV at night. You will also have an EndoPAT test in the morning.

Here are more details about what happens on each night:

Check-in and evening procedures:

- You will arrive to the Clinical Research Unit (CRU) at about 4:00 PM.
- IV's will be placed in your arms. One IV will be used to check blood samples. The other IV will be used to infuse stable isotopes to measure how your body handles its fat stores during sleep.
- You will be given dinner at 5:30 PM.
- You will be asked to drink a shake that contains a stable isotope of fat (palmitate), as well as a stable isotope of water, so that we can test how your body handles dietary fat.
- At about 9-10 PM we will set you up for an overnight sleep study. You will not be given drugs to help you sleep, and we prefer that you not take any drugs affecting sleep for at least seven days before coming for the test. You should not have alcohol or caffeine 24 hours before your sleep study. We will apply several sensors to your scalp, face and ears to monitor your sleep, and other sensors to your chest, abdomen, and legs to monitor your breathing and movements.
- A nurse will start taking blood samples from your IV, about once every 30-60 minutes. A few samples are drawn before your go to bed. Blood samples will continue to be drawn while you are sleeping. A total of 30 small blood samples will be taken during the night for a total of about 8 tablespoons of blood. The total amount of the blood collected during each visit is less than half of what is collected during a blood donation.

Bed time and sleep:

- Lights are turned out and sleep recording starts at 10:30 p.m.
- On the CPAP night (Visit A), a CPAP machine and mask is provided by the research lab. You may bring your own CPAP mask to sleep with if you wish. If necessary, the technician will adjust your CPAP settings to make sure you are receiving the correct level of pressure.
- During the 2 nasal dilator nights (Visit B and Visit C), you will wear the usual equipment that we use to measure sleep and breathing patterns, but no CPAP. You will be asked to stop using CPAP for 2 nights before coming in for each OSA study. At 6:30 PM after dinner, you will be given either propranolol LA 80 mg or a placebo pill. Some participants will get propranolol on Visit B, and placebo on Visit C. Other participants will get placebo on Visit B, and propranolol on Visit C.

Morning procedures:

- We will wake you up at 6:30 AM.
- We will perform an EndoPAT test to assess your vascular function.
- During one of your study visits (this test does not need to be done each time), we will perform a DEXA scan, which measures your bone density and body fat content. A DEXA scan is similar to an X-ray, but uses much less radiation than a normal chest X-ray (about 10%).
- The study finishes at about 9:00 and you will be served breakfast.
- Since it is possible that you may not sleep as restfully as usual, you should make arrangements for transportation so that you do not have to drive. If this is not possible, then you will be provided extra time to sleep before being discharged from the research facility.

Request to collect and store specimens for future research

As part of this research study, we would like to ask you to let us store your blood work and health information for future research related to sleep and metabolism.

The study doctor can provide you with additional information if you have questions. Also, further information about our use of your biospecimens can be found in this consent document under the heading, "*What happens to Data and Biospecimens that are collected in the study?"*

Will you allow us to store the biospecimens we collect for this study for use in future research?

YES ☐ _____
Signature of Participant

NO ☐ _____
Signature of Participant

Optional: Request for storage and analysis of genetic material

You are being asked for permission to store and analyze DNA in your blood. DNA is the substance that carries genetic (inherited) information. DNA can be turned on or off by modifying its structure through multiple ways, including methylation. We will analyze blood samples you provide as part of this study to examine if sleep apnea affects your DNA sequence or structure.

If you agree, we will purify DNA from the blood samples that you provide (16cc) as part of this study and store the samples in a secure space at Johns Hopkins University, Asthma and Allergy Building, 5th floor, 5501 Hopkins Bayview Circle, Baltimore, MD 21224. Your sample will be de-identified so that it cannot be linked to your personal information. When your DNA is purified, a special number, that is different from your study ID, will be assigned to your DNA material. We will maintain a separate "key" that links your study number to your DNA sample. This "key" will be stored on an encrypted server, and access to this server will be limited to only certain members of the study team. Your sample will be stored for up to 15 years for the purpose described in this consent form, unless you withdraw your consent. After 15 years, your sample will be destroyed.

The Genetic Information Nondiscrimination Act (GINA) may help protect your from health insurance or health-related employment discrimination based on genetic information. The law provides that health insurance companies and group health plans

- may not ask for genetic information from this research and
- may not use genetic information when masking decisions about eligibility or premiums.

This law will not stop insurance companies from using genetic information to decide whether to pay claims. This law does not apply to other types of insurance (such as life or disability insurance). Despite the GINA protections and the best efforts of the research team to protect your information, you may still be at risk if information about you were to become known to people outside of this study.

Genetic analysis is not necessary for your participation in the study and you can opt out.
Do you give us permission to store and analyze your genetic material?

YES ☐ _____ _____
Signature of Participant Date

NO ☐ _____ _____
Signature of Participant Date

How long will you be in the study?

There are 3 study visits each separated by about 1 to 3 weeks. After you consent, we will try to schedule you for sleep studies as soon as they are convenient for you, and when we have bed availability. If you are able to schedule your visits close to each other, then you will be done with the study after about 2-3 weeks. If your visits are 3 weeks apart, you may be in the study for about 6 weeks.

Permission to contact you for future research

Depending on the results of this study, we may be interested in asking you to participate in future studies related to sleep apnea. Are you willing to be contacted for this purpose?

YES ☐ _____
Signature of Participant

NO ☐ _____
Signature of Participant

Permission for the National Institutes of Health (NIH) to contact you for future research

We are working together with NIH (Bethesda, MD) on a study to examine metabolism during sleep. This study requires additional visits to NIH, after your participation in PROSAT is completed. The study involves sleeping in a room where your body's metabolism is measured when you are wearing CPAP or wearing NDS. No blood work is required for these visits. Are you willing to be contacted for this purpose?

YES ☐ _____
Signature of Participant

NO ☐ _____
Signature of Participant

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

- **Covid testing**: Before each study we will ask you to pass a Covid-19 screening test in the 3 days before your visit. This is usually performed by swabbing the back of the nose or throat with a small "Q-tip". You may need to commute to a testing center to have this done. Getting the sample can cause some pain or discomfort. If you test positive, you will not be able to continue in the study. You will need to follow guidelines about self-quarantine, after which you may be eligible to return to the study.
- **Nasal dilator strips:** These are adhesive stickers that are applied to the nose that widen the nasal passages. NDS do not work as well as CPAP for sleep apnea, so you may have less refreshing sleep any time you use NDS instead of CPAP, including at home before your lab visits. Your sleep quality on Visits B and C in the lab may also be less refreshing than when using CPAP. During NDS nights, you may experience symptoms such as awakenings from sleep, or a morning headache. During the daytime, you may be sleepier than usual. Severe sleepiness from sleep apnea could increase your risks of a car accident or other injury. You should not join this study if you have ever been in a car accident related to sleepiness, or if sleepiness on the job would place you and others at risk for injury (if you are a pilot, commercial driver, etc). There may be mild skin irritation when pulling off NDS.
- **Sleep in the laboratory may be less restful than at home.** Since you will sleep in an unfamiliar setting with monitoring equipment, your sleep might be affected. Poor sleep could increase your risks of a car accident or other injury.

- **Propranolol LA:** Medications like the study drug are called *beta blockers* and are used to block the effects of stress hormones in the body. For example, stress hormones can increase your blood pressure and blood sugar and propranolol may help prevent these changes. Propranolol "LA" stands for "long acting" since the pill dissolves slowly after you take it and the effects last for about 12-24 hours. Propranolol is used to treat conditions like high blood pressure or headaches.

  Common side effects of propranolol are fatigue, dizziness, vomiting and diarrhea. Some patients who take propranolol have their blood pressure or heart rate decrease too much causing dizziness (about 1%). This is not as likely in this study since we are using a low dose, 80 mg. Propranolol can trigger breathing problems if you have uncontrolled asthma or COPD. Propranolol can also cause cold hands or feet.

  Very rarely, as with any medication, you may have an allergic reaction that could cause serious swelling, breathing, skin rash, or blood pressure problems.

  Propranolol should be not be used if you have certain medical conditions such as chest pain, heart failure, heart rhythm problems, low blood pressure, and if you take other medications that could interact with propranolol.

- **Blood draws:** Putting in IV's may cause discomfort, bleeding or bruising where the needle enters the body. In rare cases, it may result in fainting. There is a small risk of infection. The total amount of blood we are collecting is less than the amount of collected during blood donation. You may feel fatigue, weakness, headache, cold hands and feet after blood draws.

- **Blood flow test:** We are using a device called EndoPAT which measures blood flow in your finger. During the test, you are seated in a chair and a blood pressure cuff is inflated for 5 minutes over your arm. You may feel discomfort in the hand and arm (similar to the way it feels when a doctor checks your blood pressure), but this feeling goes away when the test is completed.

- **DEXA scan:** This research study includes exposure to radiation from x-rays or gamma rays. This radiation exposure is for research purposes only and is not part of your medical care. X-rays and gamma rays can damage cells, but at low doses, the body is usually able to repair these cells. The radiation exposure that you will get in this research study is 0.001 rem (a rem is a unit of absorbed radiation). This is less than the 0.3 rem that the average person in the United States gets each year from natural sources like the sun, outer space, air, food, and soil. The risk from the radiation exposure in this research study is very small. The radiation exposure described here is what you will get from this research study only. It does not include any exposure you may have received or will receive from other medical tests outside of this study that are a part of your medical care. Radiation risk builds up with each exposure. You should think about your own history of radiation exposure from tests (like x-rays or CT scans) in deciding about the radiation in this study. If you have questions about the total amount of radiation you will be receiving, you should ask your doctor.

- **Stable Isotopes:** Your body stores fat in the form of two types of molecules called glycerol and fatty acids. In this study, we are using stable isotopes of glycerol, fatty acids, and water to track how your body uses your fat stores during sleep. Stable isotopes are not radioactive and occur in nature – a small percentage of your body's glycerol, fatty acids, and water already exist as stable isotopes. By giving you stable isotopes we will temporarily increase the amount of these molecules in your body. The amount of isotopes is very small – just enough to be detected with a mass spectrometer, which is why they are called "tracers". Our pharmacy prepares the tracers in a sterile facility to make sure the tracers are not contaminated by germs. As with any substance being given vein or by mouth

there is the chance for an allergic reaction. Also, a problem with the IV might cause leaking into the surrounding skin and cause pain or a bruising.

- **Questionnaires:** A risk of filling out questionnaires is the possible loss of confidentiality. You may get tired or bored when we are asking you questions or you are completing questionnaires. You do not have to answer any questions you do not want to answer.

5. Are there risks related to pregnancy?

This research may hurt an embryo or fetus in ways we do not currently know. **Pregnant women or nursing mothers may not participate**. If you are a woman who is able to become pregnant, you will have a urine pregnancy test. The result of this test must be negative for you to take part in the study. If you suspect that you have become pregnant while participating in the study, you are to contact the study doctor immediately.

6. Are there benefits to being in the study?

There is no direct benefit to you from being in this study. If you take part in this study you will help us learn about OSA, and its metabolic effects, which may help others in the future.

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

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

As an alternative to participation in this Main PROSAT study, you may have the opportunity to join the PROSAT-2 study. The PROSAT-2 study also focuses on cardiovascular outcomes, but involves only 2 conditions (wearing the NDS with placebo versus NDS with propranolol), and does not involve stable isotope administration. You will be provided with a separate consent form, which provides more information about the PROSAT-2 study if you are interested.

8. 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.

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

You will be paid up to $1000 for completing all parts of this study. The specific reimbursement is below:

- $250 for each sleep study (3 visits) = $750
- $50 for a DEXA scan (only done once)
- $25 for each EndoPAT test (3 visits) = $75
- $125 study completion bonus if you are able to keep your appointments as originally scheduled. You will forfeit this bonus if you must reschedule visit(s). We provide this additional compensation to help keep our research on schedule.
- You will also receive parking reimbursement so there is no fee to come to our laboratory
- You will receive dinner before each visit, and breakfast after each visit. If you are asked to return for any additional sleep studies (in cases where the data is insufficient), you will be paid an additional $250 for each additional night.

You may be required to provide your social security number to be paid for taking part in this study. Federal tax law requires that you report your research payments when you file your taxes. If your total payments from Johns Hopkins exceed $600 per year, Johns Hopkins will report these payments to the Internal Revenue Service and you will receive a 1099-MISC form from us.

10. 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.

11. 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 need treatment not allowed in the study.
- You fail to follow instructions.
- You become pregnant.
- The study is cancelled.
- We are not able to get the information we need on the tests
- 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.

12. 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.

13. Will the study require any of your other health care providers to share your health information with the researchers of this study?

As a part of this study, the researchers may ask to see your health care records from your other health care providers. We will limit our requests for health care records to what is needed for our study, or to check that you are eligible to take part in the study.

14. 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.

15. What is a Certificate of Confidentiality?

Your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study.

16. 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
- 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?
You can reach one of our study coordinators at 410-550-1816. Also, you can call the principal investigator, Dr. Jonathan Jun at 410-550-0115. If you wish, you may contact the principal investigator by letter or by fax. The address and fax number are 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 Principal Investigator at 410-550-0115 during regular office hours. **If you have an urgent medical problem** related to your taking part in this study, call Dr. Jun at 410-550-0115 during regular office hours and 443-838-8029 after hours and on weekends.

d. What happens to Data and Biospecimens that are collected in the study?
Johns Hopkins and our research partners work to understand and cure diseases. The biospecimens and/or data you provide are important to this effort.

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

With appropriate protections for privacy, Johns Hopkins may share your biospecimens and information with our research sponsors and partners.

17. 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

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 AND A COPY MUST BE GIVEN TO THE PARTICIPANT. IF APPROPRIATE FOR THIS STUDY, A SCANNED COPY OF THE SIGNED CONSENT FORM SHOULD BE UPLOADED TO THE PARTICIPANT'S EPIC/EMR RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

DOCUMENTATION OF PHYSICIAN/MID-LEVEL PROVIDER CONSENT PROCESS

My signature below indicates that I have discussed the risks, benefits, and alternatives, answered any questions, and believe the participant is able to make an informed choice to join the study.

Signature of Physician/Mid-Level Provider	(Print Name)	Date/Time

Signature of Participant	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR AND A COPY MUST BE GIVEN TO THE PARTICIPANT. IF APPROPRIATE FOR THIS STUDY, A SCANNED COPY OF THE SIGNED CONSENT FORM SHOULD BE UPLOADED TO THE PARTICIPANT'S EPIC/EMR RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

If appropriate for this study, a scanned copy of the signed consent form should be uploaded to the participant's Epic/EMR record.

Patient I.D. plate

RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title: **Propranolol for Sleep Apnea Treatment (ProSAT-2)**

Application No.: **IRB00113241**

Sponsor: **National Institutes of Health**

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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.
- During this study, you will not have access to certain medical information and test results collected for study purposes. If an emergency occurs while you are in the study, medical information needed for your treatment can be made available to your study physician and other physicians who treat you. When the study is completed, all the information in your medical record will be available to you.

2. Why is this research being done?

This research is being done to test whether a drug called propranolol can block cardiovascular and metabolic changes caused by obstructive sleep apnea (OSA). Specifically, we will study whether propranolol can prevent the increases heart rate, blood pressure, and vascular stiffness by blocking the response to stress hormones.

People with obstructive sleep apnea (OSA) have higher risks of cardiovascular disease, but doctors are not sure why. Our research has shown that OSA can increase your blood glucose (sugar) and free fatty acid (FFA) during sleep. Increased levels of glucose and FFAs can contribute to diabetes and cardiovascular disease. Thus, OSA may change your metabolism in harmful ways during sleep. We believe OSA causes release of stress hormones that lead to these high levels of glucose and FFA.

Propranolol (Inderal® LA) is a type of medication called a *beta blocker* that blocks the body's response to stress hormones. Propranolol is approved by the Food and Drug Administration (FDA) and currently prescribed for patients with high blood pressure, chest pain, and migraine headaches. It is not approved for lowering levels of glucose and FFA in people with OSA and its use in this study is considered investigational.

We are looking for participants who have OSA and are used to wearing CPAP, who are willing to stop a few days and switch to nasal dilator strips (NDS). NDS are adhesive strips applied to the nose that can reduce nasal congestion and snoring, but long-term data have not shown an effect on OSA severity. We will compare your metabolism on different nights when you are wearing CPAP or NDS, and when you take propranolol compared to a placebo (an inactive material that does not contain any active study drug). We will look at the effect of sleep apnea, CPAP, and propranolol on sleep, blood pressure, heart rate, and metabolism.

People with OSA, who are 20-65 years old, who can sleep comfortably with CPAP on, and are willing to stop CPAP for a few days to switch to NDS may join.

How many people will be in this study?

We are looking for about 14 people to complete 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:

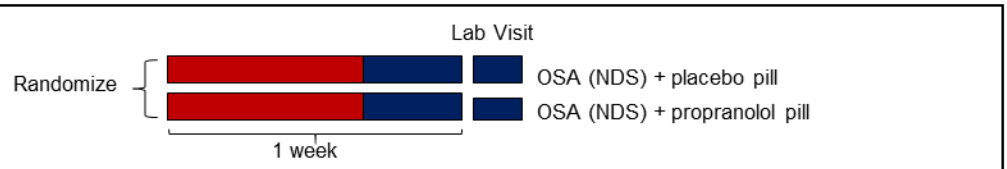
Screening

- To see if you can be in the study, you will have a brief history and physical exam with one of the study doctors. We will measure your height, weight, and neck width. You will be asked to complete a questionnaire about your health. If you are a woman who is able to become pregnant, you will have a urine pregnancy test. You will be asked to have an electrocardiogram (EKG) to measure the electrical activity of your heart. You will also have your blood count checked to make sure it is safe for you to have blood samples taken. The result of the pregnancy test must be negative, the EKG must not have certain abnormalities, and the hemoglobin level needs to be at least 10 g/dL for you to take part in the study.
- Before each of your visits we will ask you screening questions for possible Covid-19 infection (fever, headaches, sore throat, diarrhea, loss of smell/taste, sick contacts). In addition, before your visits, we will ask you to have a Covid-19 screening test (such as a nasal swab) performed. This testing requirement may change depending on the level of Covid-19 in the community and Johns Hopkins policies.

Overnight Sleep Studies

- If the results of the screening tests show that you can be in the study and you agree to continue, you will be scheduled for two overnight studies in the sleep laboratory, as shown below. Both sleep studies are performed wearing a NDS on your nose instead of CPAP. You are also asked to use the NDS 2 nights instead of CPAP before coming in. The studies will be scheduled about 1 week apart. In the evening before you sleep, you will be given propranolol LA 80 mg or placebo (a substance that looks like the study drug but contains no active drug).

To summarize:



Study schedule. Participants sleep in the laboratory 2 nights, one week apart under conditions of OSA (Nasal dilator strips, NDS) + placebo pill, or OSA (NDS) + propranolol pill. Red bars denote CPAP use, blue bars denote NDS use.

- **Visit 1:**
  You will sleep in the lab wearing a NDS instead of CPAP. You will be asked to do the same thing at home for 2 nights before coming in. Before going to bed, you will be given propranolol LA 80 mg, or a placebo pill. You will have blood samples taken from an intravenous (IV) catheter at night. You will also have an EndoPAT test (a blood flow test) in the morning.

- **Visit 2**:
  You will be asked to sleep in the lab wearing a NDS instead of CPAP. You will be asked to do the same thing at home for 2 nights before coming in. Before going to bed you will be given a placebo pill (if you got propranolol LA visit 1) or propranolol LA 80 mg (if you got placebo on Visit 1). You will have blood samples taken from an IV at night. You will also have an EndoPAT test in the morning.

Here are more details about what happens on each night:

Check-in and evening procedures:

- You will arrive to the Clinical Research Unit (CRU) at 4:00 PM. We will check an EKG if this is your first visit.
- IV's will be placed in your arms. These will be used to get blood samples without disturbing your sleep.
- You will be given dinner at 5:30 PM.
- At about 9-10 PM we will set you up for an overnight sleep study. You will not be given drugs to help you sleep, and we prefer that you not take any drugs affecting sleep for at least seven days before coming for the test. You should not have alcohol or caffeine 24 hours before your sleep study. We will apply several sensors to your scalp, face and ears to monitor your sleep, and other sensors to your chest, abdomen, and legs to monitor your breathing and movements.
- A nurse will start taking blood samples from your IV, about once every 30-60 minutes. A few samples are drawn before you go to bed. Blood samples will continue to be drawn while you are sleeping. A total of 22 small blood samples will be taken during the night for a total of about 6 tablespoons of blood. The total amount of the blood collected during each visit is less than half of what is collected during a blood donation.

Bed time and sleep:

- Lights are turned out and sleep recording starts at 10:30 PM.
- You will wear the usual equipment that we use to measure sleep and breathing patterns, but no CPAP. You will be asked to stop using CPAP for 2 nights before coming in for each OSA study. At 6:30 PM after dinner, you will be given either propranolol LA 80 mg or a placebo pill. Some participants will get propranolol on Visit 1, and placebo on Visit 2. Other participants will get placebo on Visit 1, and propranolol on Visit 2.

Morning procedures:

- We will wake you up at 6:30 AM.
- We will perform an EndoPAT test to assess your vascular function. This is similar to measuring your blood pressure but the cuff squeezes for tighter and longer.
- You will be served breakfast after the testing is complete.
- Since it is possible that you may not sleep as restfully as usual, you should make arrangements for transportation so that you do not have to drive. If this is not possible, then you will be provided extra time to sleep before being discharged from the research facility.

Request to collect and store specimens for future research

As part of this research study, we would like to ask you to let us store your blood work and health information for future research related to sleep and metabolism.

The study doctor can provide you with additional information if you have questions. Also, further information about our use of your biospecimens can be found in this consent document under the heading, "*What happens to Data and Biospecimens that are collected in the study?"*

Will you allow us to store the biospecimens we collect for this study for use in future research?

YES ☐ _____
Signature of Participant

NO ☐ _____
Signature of Participant

How long will you be in the study?

There are 2 overnight study visits separated by about 1 week. After you consent, we will try to schedule you for sleep studies as soon as they are convenient for you, and when we have bed availability. If you are able to schedule your visits close to each other, then you will be done with the study after about 2-3 weeks.

Permission to contact you for future research

Depending on the results of this study, we may be interested in asking you to participate in future studies related to sleep apnea. Are you willing to be contacted for this purpose?

YES ☐ _____
Signature of Participant

NO ☐ _____
Signature of Participant

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

- **Covid testing**: Before each study we will ask you to pass a Covid-19 screening test in the 3 days before your visit. This is usually performed by swabbing the back of the nose or throat with a small "Q-tip". You may need to commute to a testing center to have this done. Getting the sample can cause some pain or discomfort. If you test positive, you will not be able to continue in the study. You will need to follow guidelines about self-quarantine, after which you may be eligible to return to the study.
- **Nasal dilator strips:** These are adhesive stickers that are applied to the nose that widen the nasal passages. NDS do not work as well as CPAP for sleep apnea, so you may have less refreshing sleep any time you use NDS instead of CPAP, including at home before your lab visits. Your sleep quality on Visits B and C in the lab may also be less refreshing than when using CPAP. During NDS nights, you may experience symptoms such as awakenings from sleep, or a morning headache. During the daytime, you may be sleepier than usual. Severe sleepiness from sleep apnea could increase your risks of a car accident or other injury. You should not join this study if you have ever been in a car accident related to sleepiness, or if sleepiness on the job would place you and others at risk for injury (if you are a pilot, commercial driver, etc). There may be mild skin irritation when pulling off NDS.
- **Sleep in the laboratory may be less restful than at home.** Since you will sleep in an unfamiliar setting with monitoring equipment, your sleep might be affected. Poor sleep could increase your risks of a car accident or other injury.
- **Propranolol LA:** Medications like the study drug are called *beta blockers* and are used to block the effects of stress hormones in the body. For example, stress hormones can increase your blood pressure and blood sugar and propranolol may help prevent these changes. Propranolol "LA" stands for "long acting" since the pill dissolves slowly after you take it and the effects last for about 12-24 hours. Propranolol is used to treat conditions like high blood pressure or headaches.

  Common side effects of propranolol are fatigue, dizziness, vomiting and diarrhea. Some patients who take propranolol have their blood pressure or heart rate decrease too much causing dizziness (about 1%). This is not as likely in this study since we are using a low dose, 80 mg. Propranolol can trigger breathing problems if you have uncontrolled asthma or COPD. Propranolol can also cause cold hands or feet.

  Very rarely, as with any medication, you may have an allergic reaction that could cause serious swelling, breathing, skin rash, or blood pressure problems.

  Propranolol should be not be used if you have certain conditions such as chest pain, heart failure, heart rhythm problems, low blood pressure, and if you take other medications that could interact with propranolol.

- **Blood draws:** Putting in IV's may cause discomfort, bleeding or bruising where the needle enters the body. In rare cases, it may result in fainting. There is a small risk of infection. The total amount of blood we are collecting is less than the amount of collected during blood donation. You may feel fatigue, weakness, headache, cold hands and feet after blood draws.

- **Blood flow test:** We are using a device called EndoPAT which measures blood flow in your finger. During the test, you are seated in a chair and a blood pressure cuff is inflated for 5 minutes over your arm. You may feel discomfort in the hand and arm (similar to the way it feels when a doctor checks your blood pressure), but this feeling goes away when the test is completed.

- **Questionnaires:** A risk of filling out questionnaires is the possible loss of confidentiality. You may get tired or bored when we are asking you questions or you are completing questionnaires. You do not have to answer any questions you do not want to answer.

5. Are there risks related to pregnancy?

This research may hurt an embryo or fetus in ways we do not currently know. **Pregnant women or nursing mothers may not participate**. If you are a woman who is able to become pregnant, you will have a urine pregnancy test. The result of this test must be negative for you to take part in the study. If you suspect that you have become pregnant while participating in the study, you are to contact the study doctor immediately.

6. Are there benefits to being in the study?

There is no direct benefit to you from being in this study. If you take part in this study you will help us learn about OSA, and its metabolic effects, which may help others in the future.

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

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

8. 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.

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

You will be paid up to $600 for completing all parts of this study. The specific reimbursement is below:

- $250 for each sleep study (2 visits) = $500
- $25 for each EndoPAT test (2 visits) = $50
- $50 study completion bonus if you are able to keep your appointments as originally scheduled. You will forfeit this bonus if you must reschedule visit(s). We provide this additional compensation to help keep our research on schedule.
- You will also receive parking reimbursement so there is no fee to come to our laboratory
- You will receive dinner before each visit, and breakfast after each visit. If you are asked to return for any additional sleep studies (in cases where the data is insufficient), you will be paid an additional $250 for each additional night.

You may be required to provide your social security number to be paid for taking part in this study. Federal tax law requires that you report your research payments when you file your taxes. If your total payments from Johns Hopkins exceed $600 per year, Johns Hopkins will report these payments to the Internal Revenue Service and you will receive a 1099-MISC form from us.

10. 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.

11. 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 need treatment not allowed in the study.
- You fail to follow instructions.
- You become pregnant.
- The study is cancelled.
- We are not able to get the information we need on the tests
- 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.

12. 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.

13. Will the study require any of your other health care providers to share your health information with the researchers of this study?

As a part of this study, the researchers may ask to see your health care records from your other health care providers. We will limit our requests for health care records to what is needed for our study, or to check that you are eligible to take part in the study.

14. 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.

15. What is a Certificate of Confidentiality?

Your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study.

16. 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
- 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?
You can reach one of our study coordinators at 410-550-1816. Also, you can call the principal investigator, Dr. Jonathan Jun at 410-550-0115. If you wish, you may contact the principal investigator by letter or by fax. The address and fax number are 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 Principal Investigator at 410-550-0115 during regular office hours. **If you have an urgent medical problem** related to your taking part in this study, call Dr. Jun at 410-550-0115 during regular office hours and 443-838-8029 after hours and on weekends.

d. What happens to Data and Biospecimens that are collected in the study?
Johns Hopkins and our research partners work to understand and cure diseases. The biospecimens and/or data you provide are important to this effort.

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

With appropriate protections for privacy, Johns Hopkins may share your biospecimens and information with our research sponsors and partners.

17. 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

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 AND A COPY MUST BE GIVEN TO THE PARTICIPANT. IF APPROPRIATE FOR THIS STUDY, A SCANNED COPY OF THE SIGNED CONSENT FORM SHOULD BE UPLOADED TO THE PARTICIPANT'S EPIC/EMR RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

DOCUMENTATION OF PHYSICIAN/MID-LEVEL PROVIDER CONSENT PROCESS

My signature below indicates that I have discussed the risks, benefits, and alternatives, answered any questions, and believe the participant is able to make an informed choice to join the study.

Signature of Physician/Mid-Level Provider	(Print Name)	Date/Time

Signature of Participant	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR AND A COPY MUST BE GIVEN TO THE PARTICIPANT. IF APPROPRIATE FOR THIS STUDY, A SCANNED COPY OF THE SIGNED CONSENT FORM SHOULD BE UPLOADED TO THE PARTICIPANT'S EPIC/EMR RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).