Official Title: The effects of sedatives on tobacco use disorder

NCT05505630

IRB Approval Date: 01/23/2025

Wake Forest®
School of Medicine

Department of Physiology and Pharmacology

THE EFFECTS OF SEDATIVES ON TOBACCO USE DISORDER (SED-TUD)

Informed Consent Form to Participate in Research
Merideth Addicott, PhD, Principal Investigator

SUMMARY

You are invited to participate in a research study. The purpose of this research is to learn more about the effects of medication on mood, behavior, and brains of smokers using magnetic resonance imaging (MRI) and a smartphone app. You are invited to be in this study because you are a cigarette smoker who is not interested in quitting right now. Your participation in this research will involve 5 visits and last about 5 weeks.

If you join the study, you will be asked to provide information about yourself, provide urine, and breath samples, undergo a physical exam, and receive some instructions on how to use the smartphone app. You will use the smartphone app to answer questions about your mood and smoking for four, 7-day time periods.

Half way through each of the smartphone app time periods, you will receive an infusion of medication (that is, medication given through a small tube attached to a needle inserted into a vein) and answer questions about how you are feeling. You will be asked to not smoke for about 24 hours after the medication. Then, you will return to the hospital the day after the medication for a follow-up visit, undergo MRI for about one hour, and fill out some questionnaires. A second infusion and another follow-up visit will be scheduled 2 to 4 weeks later. These visits are identical to the first two, except you may receive a different medication. Each visit will last about 3 hours.

All research studies involve some risks. The medications may cause sedation. The MRI scan is loud and may cause discomfort. There is also a risk of experiencing claustrophobia (fear of closed spaces) during the MRI scan. Not smoking for 24 hours may cause withdrawal symptoms. The smartphone app may interfere with your daily activities and may be somewhat time consuming.

You will not directly benefit from participation in this study. Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions if you need help deciding whether to join the study. The person in charge of this study is Merideth Addicott. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study, her contact information is: [redacted].

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at [redacted] or the Research Subject Advocate at Wake Forest at [redacted].

INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you are a cigarette smoker who is not interested in quitting right now. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

The purpose of this research is to learn more about the effects of sedative medication on mood, behavior, and brains of smokers using magnetic resonance imaging (MRI) and a smartphone app. We are not testing a treatment for quitting smoking, but we are interested in how the medication affects tobacco craving and withdrawal symptoms.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

We will ask up to 52 people ages 18 to 65 years old to sign up for the study so we have at least 25 people finish the study.

WHAT IS INVOLVED IN THE STUDY?

We first will see if you qualify to be in the study. We will do this by collecting the following information and performing the following tests and procedures…

- *General information about you.* We will need to know your name, age, date of birth, sex, race, address, medical history, education history, and phone number. We will also need to know about your smoking history.
- *Urine Sample Collection*: You will provide a urine sample that will be used to test for drugs of abuse and nicotine metabolites. Some prescription drugs can also be detected by this urine drug test. If you test positive for any of the drugs measured by the drug test, you may not be allowed to participate in this study.
- *Physical Exam:* You will have your vital signs, height and weight measured.
- *Women of Child-Bearing Potential:* A urine pregnancy test will be done for women. Pregnant women will not be allowed to participate.
- *Drug Use History:* You will provide information about your current and past use of prescription and non-prescription drugs. You will also answer questions about your use of tobacco.
- *Expired Breath*: You will blow into a tube to measure alcohol and carbon monoxide in your exhaled breath.

- *Psychiatric Screen:* You will undergo an interview for symptoms of psychological disorders.
- *MRI Safety Checklist:* You will provide information about your eligibility to undergo magnetic resonance imaging.
- *Eye Exam:* A standard eye chart will be used to measure your visual acuity.
- These procedures will take place in Biotech Place.

If you qualify, we will do these things:

- We will ask you to not use any nicotine or other tobacco products (other than cigarettes) while you are enrolled in the study.
- We will show you how to use the smartphone app. If you own a smartphone, we will install this app on your phone. If you do not own a smartphone, or prefer not use your own phone, a phone will be provided to you with the app installed. You may keep the phone at the end of the study. You will practice using the app in the lab, and continue using it at home. You will complete assessments of your mood and smoking behavior using the smartphone app for 28 days.

Medication Day:

- You will be scheduled for 2 medication days, these will be scheduled between 2 and 4 weeks apart.
- On each medication day, you will be given a study medication through a tube inserted in your arm (infusion). You will be asked to not eat or drink anything besides water for about 7 hours before the medication. You will have the option of being given Zofran (Ondansetron) before your infusion, which may help with nausea. You will be provided a snack when the medication infusion is complete.
- A doctor will first examine you to make sure you can safely have the medication. Your blood pressure and your body's ability to take in oxygen from the air you breathe will be taken. Your heart rate will be monitored. We will measure alcohol and carbon monoxide on your breath. Women who can bear children will receive a urine pregnancy test. If the doctor decides you can have the medication, salt water (saline) and the medication will be delivered into your arm over a 50-minute period. The medication will be one of these:

Name of study medication	**What the FDA has approved the medication to do**
placebo	no active medication
ketamine	reduce pain, help you sleep, anesthesia for surgery, block memory

midazolam	help you sleep, decrease anxiety, anesthesia for surgery, block memory
dexmedetomidine	help you sleep, decrease anxiety

- You will be given two medications on the list, separately across the 2 medication days. We cannot tell you which drug you will receive now, because it may affect the way you answer questions during the study sessions. If you wish to know the actual drugs you received, we can give you that information after all participants have finished the study using the contact information you provide us.
- After the medication, the doctor and nurse will watch you for about 2 hours and will measure your vital signs (such as pulse and blood pressure) every 15 to 60 minutes. The entire medication visit will last about 3 to 4 hours.
- Someone else must drive you home. If no one can drive you to and from the visit, a ride service will be provided at no cost to you.
- We ask that you stop smoking at the start of the medication visit and do not smoke for about 24 hours, until after the MRI scan the following day.
- These procedures will take place at the Wake Forest Brookstown Pain Center.

Follow-up Study Visit:

- You will be scheduled for a follow-up study visit about 24 hours after each medication visit. During this visit, you will be in the MRI scanner for 1 hour. You will also answer questions about your mood, your desire for cigarettes, the medication you received previously, and we will measure alcohol and carbon monoxide on your breath.
- During the follow-up visit, you will be asked to play a task in which you will move a mouse cursor around the shape of a star shown onscreen. This task makes loud noises when you perform the task incorrectly. You may stop performing this task at any time.
- For the MRI procedure, you will lie on your back on a bed that slides into the MRI scanner. A coil will be placed around your head so that we can take pictures of your brain. The MRI technician will make sure your head is in the proper place to take pictures of brain activity. The scanner is open on both ends and there will always be constant airflow through the scanner.
- During the scan you will, at times, hear loud noises from the MRI. You will wear sound-cancelling, non-metal earphones with a microphone to further reduce noise and allow us to communicate with you at all times.
- A mirror will be placed on the head coil so that you can see images projected on the screen behind you. If you have poor vision, we will offer non-metal eyeglasses. You will hold a response box with buttons to press while you do the tasks in the MRI. A call

button will be placed next to you so that you can signal the coordinator if you are uncomfortable.

- While in the MRI, we will take a picture of your brain. No contrast agents or dyes will be used during the MRI session.
- Then, you will be asked to watch some pictures of cigarettes and other items on a computer screen you can see in the MRI. These images will last about 10 minutes during the MRI scan.
- These procedures will take place in the Wake Forest MRI Center.

SHARING OF NEUROIMAGING DATA

If you agree, Dr. Addicott may share your de-identified neuroimaging data (no names) with other investigators or with large, public neuroimaging databases that allow scientists to share their data and methods. These neuroimaging databases store uploaded data indefinitely and have no provisions for individual participants to withdraw their data. However, all data will be de-identified prior to sharing with individual scientists or neuroimaging databases. This means that all identifying information (such as names, dates, addresses, etc.) will be removed from data prior to sharing.

HOW LONG WILL I BE IN THE STUDY?

You will participate in this study for about 5 weeks. The screening session today will take about 3 hours, and each medication and follow-up study visit will take about 2-4 hours. Answering questions on the smartphone app may take about 2-4 minutes during the day, and up to 5 minutes at night.

You can stop participating at any time. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to let them know.

WHAT ARE THE RISKS OF THE STUDY?

- Someone could find out that you were in the study and learn something about you that you did not want others to know. We will do our best to protect your privacy. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.
- The smartphone app that will collect data about your mood and smoking is provided by LifeData (lifedatacorp.com). This data is stored on their password-protected server and can only be accessed by the Principal Investigator. There is a risk of this data being accessed by other people. We do our best to protect your privacy by only identifying you in this dataset by your study number.
- As part of this study, you will be asked questions about your mental health and daily activities. If we learn that you or someone else is in danger of harm, the study team is

required to report that information to the proper authorities.

- The questions could make you sad or upset. Answering questions about your mood and cigarette craving on the smartphone app may increase the chances of smoking.
- The drug test and drug use history could indicate that you have used an illegal drug. Research funded by the National Institutes of Health protects participants' privacy by limiting the disclosure of this kind of information.
- The MRI scan is considered minor risk because no harmful radiation is involved. The strong magnetic field is dangerous to people with metallic implants, shrapnel, and/or pacemakers. It is important that you answer all screening questions honestly. The MRI is loud and you will be provided hearing protection. There is a risk of experiencing claustrophobia (fear of closed spaces). If this occurs, you can speak with the MRI technician. If you are experiencing discomfort, you can quit the MRI scan at any time.
- The MRI scan may reveal a brain abnormality. If so, we will ask a neuroradiologist to look at the scan and if s/he determines that medical follow-up is recommended, we will inform you and recommend that you follow-up with your healthcare provider, who might suggest a diagnostic or clinical MRI be scheduled. If you decide to follow this recommendation, you and your insurance provider will be responsible for the cost of the clinical MRI and any medical care associated with the findings. This is a research MRI scan and it is not a substitute for medical testing, it will not provide reliable information about any health issue.
- The medications can cause side effects and can affect your ability to drive. These medications may make tobacco withdrawal worse, or increase the desire to use more of the same drug. These medications may increase the strength of other sedatives (like prescription painkillers or alcohol) for a short while.
    - Midazolam can cause changes in breathing, sleepiness, difficulty remembering, hiccups, nausea, vomiting, coughing, headache, anxiousness, involuntary movements.
    - Ketamine can cause changes in breathing, problems seeing, changes in blood pressure and heart rate, muscle jerks, difficulty remembering, nausea, vomiting, uneasiness, pleasant or unpleasant dream-like states, vivid imagery, hallucinations, confusion, excitement, irrational behavior.
    - Dexmedetomidine can cause drowsiness, changes in blood pressure and heart rate, dry mouth, agitation, nausea, and vomiting.
    - (optional) Zofran can cause drowsiness, headache, constipation, tiredness, chills, and weakness.
- Quitting smoking can cause symptoms of nicotine withdrawal. These include cravings, urges to smoke, irritability, difficulty concentrating, restlessness, increased appetite, anxiety, and depressed mood.

- Due to unknown risks and potential harm to the unborn fetus, sexually active women of childbearing potential must use a reliable method of birth control while participating in this study. Reliable methods of birth control are: abstinence (not having sex), oral contraceptives, OrthoEvra patch, NuvaRing, intrauterine devices (IUD), Nexplanon implant, DepoProvera, tubal ligation, or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable, method involves the careful use of condoms and spermicidal foam or gel and/or a diaphragm with spermicide with Plan B used for any noticed condom or diaphragm failures. We encourage you to discuss this issue further with your physicians if you have any questions.

There also may be other risks that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

You may or may not receive benefit from participating in this study. The information we collect may help people with tobacco addiction in the future by finding better ways of helping people quit.

WHAT OTHER CHOICES ARE THERE?

This is not a treatment study. Your alternative is to not participate in this study. You may seek help with your smoking through your primary care physician at any time. Quitting smoking may benefit your health over time. Risks of tobacco treatment include experiencing tobacco withdrawal symptoms.

WHAT ARE THE COSTS?

All study costs, including any study medications and procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

WILL YOUR RESEARCH RECORDS BE CONFIDENTIAL?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

Participant information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative,

legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

WILL YOU BE PAID FOR PARTICIPATING?

You will not receive money for the phone screen or the first hour of the screening session today. If we decide you do not qualify for the study in the first hour, you will not receive money.

If you are here longer than an hour during the screening visit, we will give you $40. Each 7 days you complete smartphone app questions, we will give you up to $60 per week for completing 81-100% of all entries, $45 per week if you complete 61-80% of entries, $30 per week if you complete 41-60% of entries, and $15 per week if you complete up to 40% of entries (maximum of $240 for 28 days). We will give you $100 for each medication visit ($200 total). We will give you $100 for each MRI follow-up study visit and up to a $4 bonus each visit based on your computer task performance (maximum of $208 for both study visits). If you need a smartphone provided to you, you may keep the phone at the end of the study. If you used your own phone, we will give you $10 to compensate for data charges. We will give you an additional $102 bonus for completing all aspects of the study.

This money is to thank you for your time. The maximum compensation is up to $800. We will divide this into four payments received after every 7 days of using the smartphone app. This money will be credited to a ClinCard. If you change your mind and decide not to be in the study, or we decide you do not qualify for the study after the first hour of your visit, you will be paid $20/hour for the time you participated.

To receive payment, you must provide your social security number, name and address so that we can comply with IRS (Internal Revenue Service) reporting requirements. When payments are reported to the IRS we do not let them know what the payment is for, only that you have been paid. If you do not wish to provide this information you can still take part in this study but you will not be paid.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by the National Institutes of Health. The sponsor is providing money or other support to Wake Forest University Health Sciences to help conduct this study. The researchers do not, however, hold a direct financial interest in the sponsor or the research.

WHERE CAN I FIND MORE INFORMATION ABOUT THIS CLINICAL TRIAL?

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the

website will include a summary of the results. You can search this website at any time.

What Happens if You Experience an Injury or Illness as a Result of Participating in this Study?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call Merideth Addicott at [redacted].

What About My Health Information?

In this research study, any new information we collect from you about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:** your responses to questionnaires, images of your brain, visual acuity, mood, tobacco and other drug use, medical and psychiatric history, urine nicotine metabolites, pregnancy status, height, weight, vital signs.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis

centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA) or the Office of Human Research Protections (OHRP), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable. Life Data is a business that will receive health data. Data is collected and stored in WFUHS approved documentation system.

Monitors, auditors, IRB or other regulatory agencies will be granted direct access to the participant's original medical record for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for at least six years after the study is finished. At that time any research information will either be destroyed or it will be de-identified.

You can tell Dr. Addicott that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Merideth Addicott
[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or

safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because you failed to follow instructions, or because the entire study has been stopped. Information that identifies you may be removed from the data or specimens that are collected as part of this study and could be used for future research or shared with others without additional consent.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study. Clinically relevant research results will not be disclosed to you.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, Merideth Addicott at [redacted].

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted] or the Research Subject Advocate at [redacted].

You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

My de-identified neuroimaging data collected in this study may be used in future research.

___ YES ___ NO

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent (Printed):_____

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm