PROTOCOL TITLE: Oxytocin to Enhance Alcohol Behavioral Couple Therapy

PRINCIPAL INVESTIGATOR: Julianne Flanagan, Ph.D.

ClinicalTrials.gov ID: Pro00082233

Document Date: August 16, 2022

Medical University of South Carolina
CONSENT TO BE A RESEARCH SUBJECT

TITLE OF RESEARCH: Oxytocin to Enhance Alcohol Behavioral Couple Therapy

Concise Summary

Your consent is being sought for a research study. Participation is voluntary. The purpose of the study is to examine if an investigational medication called oxytocin, which comes in the form of a nasal spray, is able to improve the outcomes of a talk therapy called Alcohol Behavioral Couples Therapy. If you and your partner are eligible and you decide to enroll in the study, your participation will last approximately 17 weeks, or 9 months.

The study will involve a screening phase which will include 1-2 appointments. You will complete questionnaires and interviews in a private room apart from your partner and some tests to measure alcohol use and pregnancy. The treatment phase of the study will involve 12 weekly therapy visits, which can be performed in person or via home based teleheath. Before each therapy session, you and your partner will take the study medication or placebo (saline) in the form of a nasal spray. You will also complete follow-up visits three months and six months after the treatment phase is complete. There are risks of participating in the study that are described in this document. The most significant risks include risks for pregnant women and loss of confidentiality. If you are a woman, you will complete a pregnancy test each week before the medication is taken to be sure that you are not pregnant.

Everyone who participates will be provided with 12 weeks of an evidence-supported talk therapy to help couples reduce problems associated with alcohol use and improve their relationship functioning. Your alternative is not to participate in the study.

A. PURPOSE OF THE RESEARCH

You are being asked to volunteer for a research study. Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making you decision. As the study staff discuss this consent form with you, please ask him/her to explain any words or information that you do not clearly understand.

The purpose of this study is to examine the ability of a medication called oxytocin to reduce alcohol consumption and improve relationship functioning during couple's therapy. Oxytocin is currently approved by the Food and Drug Administration (FDA) to induce labor in pregnant women. However, oxytocin is considered "investigational use"

in this study, meaning that the FDA has not approved it for the purpose of improving outcomes in couple's therapy for alcohol use disorder. This is a Phase II study of oxytocin, meaning that it has established use for other purposes and researchers are now testing this medication in larger populations. You are being asked to participate because you are over 18 years of age, you are in a romantic relationship, and either you or your partner has an alcohol use disorder. The investigator in charge of the study is Dr. Julianne Flanagan at the Medical University of South Carolina (MUSC). This study is being conducted with funding from a grant from the National Institute on Alcohol Abuse and Alcoholism (NIAAA). Portions of Dr. Flanagan's and her research team's salaries will be paid by this grant. This study is being conducted in Charleston, SC and will involve approximately 100 couples, or 200 participants total.

B. PROCEDURES

If you agree to be in this study, the following will happen:

1. Screening visit
    a. In total, this study will include approximately 17 visits. The first visit is includes screening for study eligibility and will take approximately 3 hours. You have the option to complete this in 1 or 2 visits. During that time, you will be asked to answer some questions about yourself such as your age, health, relationship with your partner, and your use of alcohol and drugs to determine if you are eligible to participate.
    b. If you have recently started taking a prescription medication, you may be asked to wait 4 weeks until you participate in the study so that the effects of the medication will be stable and won't affect the study results.
    c. If you meet initial eligibility criteria and you choose to participate, you and your partner will begin the assessment portion of the screening visit. If you are a woman, you will be asked to complete a urine pregnancy test. The urine pregnancy test must be negative in order to participate. If your pregnancy test is negative, or if you are male, you will be asked to provide a urine sample to test for drug use and a marker of recent alcohol use called Ethyl Glucuronide, or EtG. You will complete a breathalyzer test and will undergo a short physical exam.
    d. You will also be asked questions and given questionnaires to complete about your use of alcohol, drugs, and tobacco, mood, behaviors, sleep, and thinking abilities.
    e. Trained personnel will take a blood sample to measure levels of a marker of alcohol drinking called phosphatidyl ethanol, or PEth. Five total blood samples will be taken during the study. Each time, 4mL of blood will be drawn (about a teaspoonful amount).
2. Weekly visits- Treatment Phase
    a. There will be 12 weekly study visits that will last approximately 2-2.5 hours. You and your partner will complete weekly visits together and in person or via telehealth.

During each visit, you will be asked to complete a pregnancy test prior to administration of study medication. If your pregnancy test is negative or if you are a man, your urine will may be tested for drug use and EtG. A breathalyzer or saliva alcohol tests will also be done to determine current levels of alcohol in your system. After, you will self-administer nasal spray containing either oxytocin or placebo (saline). You will also complete a brief check in visit will study staff. Approximately 30 minutes after the medication is administered, you and your partner will meet with the study therapist for your weekly session. A blood draw will be conducted at Weeks 6 and 12 in order to test again for PEth. If you are completing this study via telehealth, you and your partner will administer the medication at the same time. Similar to in-person appointments, study staff will watch the administration of the medication.

b. Each weekly ABCT session will be conducted with a trained therapist, either in person or via telehealth. You and your partner will discuss different topics each week such as learning about how alcohol use has influenced your relationship, managing alcohol cravings, learning how to increase positive interactions with your partner, and how to communicate more effectively about alcohol related problems and other problems in your relationship. Your therapist will work with you to develop practice exercises, or 'homework,' that will allow you and your partner to practice skills outside of the therapy session.

3. Follow-up phase

a. You will also be asked to complete 3 and 6 month follow up appointments – either in person or via telehealth. At these visits, you will be asked to complete questionnaires and interviews similar to those you completed at the screening visit. Much like previous visits, you will answer questions about your overall health and wellbeing. Your urine may also be tested for pregnancy, drug use, and EtG. If you are completing this appointment in person, a blood draw will be conducted in order to test again for PEth. No additional counseling will be provided at these appointments. These appointments will last about 1-1.5 hours.

b. If there is anything that makes it difficult for you to come to MUSC, you may choose to do your study appointments via home-based telehealth (HBT). HBT allows a study team member and participant who are not in the same room together to communicate. This is usually done over the computer using MUSC approved teleconferencing applications. In order to complete sessions via HBT, you will need to have internet or cellular access in your home and a computer, tablet, or smartphone capable of accessing the internet. Barriers to being unable to come to MUSC for face to face treatment varies, but typically involves transportation, financial, or child care issues. Biological samples will not be collected for telehealth visits. All required study materials will be shipped to you if you complete appointments via telehealth (study medication, saliva alcohol test strips, pregnancy tests).

TELEHEALTH

If there is anything that makes it difficult for you to come to the MUSC, home-based telehealth (HBT) is available for this study. In order to complete sessions via HBT, you will need to have internet or cellular access in your home and a computer, tablet, or smartphone capable of accessing the internet. If you complete this study via telehealth, biological measures and specimens will not be collected. Pregnancy tests, alcohol saliva tests, and study medication will be shipped to you monthly via trackable overnight UPS shipment. Females will be required to provide verbal and photo (of dipstick) confirmation of a negative pregnancy test at each appointment.

You will be asked to find a private room, away from your partner for portions of the baseline visit and for weekly appointments. The study team can also work with you and your partner to schedule these portions individually and separately in order to maintain protection of your privacy.

If you and your partner do not live together, medication and study supplies will be shipped to one (agreed upon) residence.

In the event you are unable to make it to the office for your study visit, the study team may send you study medication via United Parcel Service (UPS). We would like your consent to ship study medication to the address provided on your contact information form.

Please indicate your choice below, or scroll down to the bottom of the screen and select your choice electronically:

____Yes, I would like study medication shipped to my residence if I am unable to make my appointment, or in the event MUSC is closed.

____No, I would *not* like study medication shipped to my residence if I am unable to make my appointment, or in the event MUSC is closed.

C. DURATION

Participation in the study will take about 17 visits over a period of 9 months.

D. RISKS AND DISCOMFORTS

Oxytocin: The FDA has approved oxytocin for use among women during labor. When used intravenously to start labor, adverse effects associated with oxytocin have included seizures, mental disturbances, nausea, vomiting, irregular heartbeat, high blood pressure, and unexpected bleeding or contraction of the uterus in a small number of women. These side effects have not been observed when oxytocin is used as a nasal spray. However, other side effects may include nasal irritation, runny nose, and tearing of the eyes. Several studies have been conducted in humans with intranasal doses similar to what will be used in this study, and no adverse side effects have been reported.

A recent review of the safety and side effects of intranasal oxytocin demonstrate that it has been used in over 40 completed randomized controlled trials, with over 1,500 human participants. No adverse side effects or outcomes have been reliably observed in children, women, or men using a dose of 18-40 IU. Dr. Flanagan's research team has used a 40 IU dose of intranasal oxytocin in over 300 research participants to date with no adverse side effects.

Risks of Pregnancy: Because this study involves a 50% chance of a study participant receiving the investigational medication (e.g., oxytocin) and it is well known that intranasal oxytocin is likely to have negative effects on pregnancy and fetal health, pregnant and breastfeeding women will be excluded from the trial. We will instruct women participants to use appropriate forms of contraception, and you will be asked to complete urine pregnancy tests at baseline and weekly during treatment. For telehealth participants, study staff will require a verbal confirmation of the negative pregnancy test prior to allowing medication administration. If you become pregnant during the trial (despite the requirement to use an approved method of contraception), you will be given the opportunity to continue to participate in the therapy portion of the study. However, due to safety risks, you will no longer be allowed to administer the medication. Additionally, you will not be asked questions or administered surveys regarding illegal substance use, and you will no longer complete urine drug screens.

Potential Risks of Blood Draw: Risks associated with drawing blood from your arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting is possible, although unlikely.

Randomization Risk: You will be assigned to the study medication by chance. The study medication you receive may prove to be less effective or to have more side effects than the other study medication or other available treatments.

Placebo Risk: If you are in the group that receives placebo (saline), your or your partner's condition will go without active medication treatment for 12 weeks. However, everyone who participates in the study will receive weekly couple's therapy with a trained therapist.

Interviews and Surveys: The questions that will be asked may be sensitive in nature and may make you feel uncomfortable. You may be asked personal questions that you find distressing. You may refuse to answer any question(s) that you do not wish to answer.

Risk of Loss of Confidentiality
There is a chance that your personal information may inadvertently not be kept confidential. Some answers you give during the research visits (like whether you use illegal drugs) may put you at risk if other people find out. To keep what you say private, your study records will use a code number instead of your name. We will protect your records to the extent allowed by law by keeping all your materials in locked file cabinets only accessible by research staff and all computer files will be secure password-protected

files only accessed by research staff. Your research records are kept separate from your clinic records and will not be shared with your clinical counselor. Only research staff will have access to your private information.

Limits of Confidentiality:

Suspected or known abuse or neglect of a child, disabled or elder abuse, or threatened violence to self or others may be reported to appropriate authorities.

If you are or become pregnant and test positive for illegal drugs, it is a law that the South Carolina Department of Social Services (DSS) must be notified. You and your family will be evaluated by the agency. You could be ordered to mandatory drug treatment, lose custody of your children, or possibly be jailed.

Unknown Risks: The experimental treatments may have unknown side effects. The researchers will let you know if they learn anything during the course of the study that might make you change your mind about participating in the study.

E. MEDICAL RECORDS AND CERITFICATE OF CONFIDENTIALITY

This research is covered by a Certificate of Confidentiality from the Federal government. This means that the researchers may not disclose information or biospecimens that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, nor can the information or biospecimens be used as evidence, unless you have consented to this disclosure. Information or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research unless you have consented to the disclosure. More specifically, identifiable information or biospecimens will not be shared with your medical providers who are not involved in this research unless you authorize the study to disclose information to them, or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

Information about your study participation will not be in your MUSC medical record. This means that neither your research participation nor any of your research results will be included in any MUSC medical record. A Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must authorize the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law. Examples of required disclosure include: child abuse and neglect, or harm to self and others, but there could be others.

Finally, a Certificate may not be used to withhold information from the Federal government needed for auditing or evaluating federally funded projects or information needed by the FDA.

F. BENEFITS

No specific benefit can be guaranteed or promised from participation in this study. Information gained from this study may help other researchers have a better understanding of the treatment of alcohol use disorder and relationship behaviors.

G. COSTS

There will be no cost to you as a result of participation in this study.

H. PAYMENT TO PARTICIPANTS

Each participant will each receive up to $125 for completion of the baseline assessment visit, up to $75 for completion of weekly ABCT sessions (on an escalating scale), and $100 for each follow-up visit. Thus, participants who complete all study components may receive $895 total.

You will receive payment in the form of a ClinCard, a pre-paid debit card. It works like a bank debit card, and you may use the card to purchase goods or services everywhere Debit MasterCard is accepted. Should you choose this payment option, you will be given a ClinCard at the beginning of the study. Each time you receive payment for participation in this study, the money will be added to the card, as outlined in the payment schedule above. Compensation may also be provided in the formof cash or check. If you receive compensation in the form of check, you will be asked to fill out a W9. Payment can also be made via cash, check, or direct deposit.

Finally, if there are obstacles to participation due to transportation, taxi, bus pass, or mileage compensation may be available. Mileage reimbursement is available for individuals who travel more than 50 miles to Charleston. Reimbursement will be provided at the state-approved rate and will be capped at 100 miles.

You are invited to participate in the recruitment of other subjects for this study. If you choose to participate, we will provide you with cards that you may give to other people (e.g., friends, acquaintances) who you think would be eligible and interested in this study. You may choose to tell people to whom you give these cards to call the study office if they are interested in participating in the study. These individuals will not be identified unless they contact the study office themselves. If any of the cards you are given result in successful study recruitment, you will receive $10 for each referred individual who consents to participate in the study. Participation in the recruitment process is completely voluntary and if you elect not to participate, your participation in this study will not be affected in any way.

Payments that you receive from MUSC for participating in a research study are considered taxable income per IRS regulations. Payment types may include, but are not limited to: checks, cash, gift certificates/cards, personal property, and other items of value. If the total amount of payment you receive from MUSC reaches or exceeds $600.00 in a calendar year, you will be issued a Form 1099.

I. ALTERNATIVES

This study involves an investigational medication and couples counseling. You have the option of declining to participate in this study. Alternative treatments for alcohol use disorder and couples counseling are available.

Withdrawal from the Study

Your participation in this study is voluntary. You may refuse to take part in or stop taking part in this study at any time. You should talk with the investigator in charge of this study if you decide to do this. Your decision not to take part in the study will not affect your current or future medical care or any benefits to which you are entitled. The investigators and/or the sponsor may stop your participation in this study at any time if they decide it is in your best interest. They may also do this if you do not follow the investigator's instructions. If your participation is ended for medical reasons, you will be referred to a doctor or other health professional for care. You will be responsible for the cost of these services.

J. DATA SHARING

Information about you (including your identifiable private information and/or any identifiable biospecimens) may have all of your identifiers removed and used for future research studies or distributed to other researchers for future research without additional informed consent from you or your legally authorized representative.

K. DISCLOSURE OF RESULTS

Study data will not be shared with participants to maintain confidentiality.

L. SIGNIFICANT NEW FINDINGS

If there are significant new findings during the course of the study, you will be notified.

M. STUDENT PARTICIPATION

Your participation or discontinuance will not constitute an element of your academic performance, nor will it be a part of your academic record at this Institution.

N. EMPLOYEE PARTICIPATION

Your participation or discontinuance will not constitute an element of your job performance or evaluation, nor will it be a part of your personnel record at this Institution.

O.CLINICAL TRIALS.GOV

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.

P. COLLECTION OF SPECIMENS

Blood and urine specimens will be collected in this study. We will collect specimens in order to measure two biomarkers of alcohol use: urine for Ethyl Glucuronide, or EtG, and blood for phosphatidyl ethanol, or PEth. If you are a woman, you will provide a urine sample at the screening visit and at each weekly visit during the treatment phase for pregnancy tests. If you are not pregnant, all participants will provide a urine sample during the screening phase and at each weekly visit in order to conduct a urine drug screen. Blood will be drawn by a trained member of the research staff. These specimens will be used solely as part of this research study and will not be shared with other investigators. All specimens will be coded with your numeric study code to protect your confidentiality.

Q.PERMISSION TO RECORD SESSIONS

We would like to record the therapy sessions to assure treatment quality and adherence to the treatment manual. Recording the sessions is not required for participation, but is very useful to us. This could pose a risk to confidentiality and although we will take every step possible to ensure that all recordings are stored securely and any risks minimized, there is a risk is that you could be identified, including information regarding alcohol and drug use, or other criminal behavior. To minimize any risk, all recordings will be kept in a locked file cabinet or on a secure and encrypted server and only the project staff and supervisors will have access to the recordings. They will be destroyed after the study has been completed. Would that be acceptable to you?

Please indicate you choice below, or scroll to the bottom of the screen to select your choice electronically:

_____ Yes, I permit audio or visual recording of my therapy sessions.

_____ No, I do not permit audio or visual recording of my therapy sessions.

R. FUTURE CONTACT

The researcher in charge of this study might like to contact you in the future about other research opportunities. Please indicate your choice below, or scroll down to the bottom of the screen and select your choice electronically::

____Yes, I agree to be contacted

____No, I do not agree to be contacted

You have the option of receiving appointment reminders and link to study surveys through text messages. Should you elect to receive text messages, normal cellular data usage and rates will apply. Please indicate your choice below, or scroll down to the bottom of the screen and select your choice electronically:*:*

____Yes, I agree to be contacted via text message

____No, I do not agree to be contacted via text message

S. RELEASE OF MEDICAL RECORDS TO ANYONE OTHER THAN THE INVESTIGATORS

If for any reason you would like your study records released to anyone other than the investigators, you will be asked to sign an additional release of information form. You will also be asked to sign a Health Insurance Portability and Accountability Act (HIPAA) Authorization to use or disclose your protected health information for research purposes.

CONSENT

Results of this research will be used for the purposes described in this study. This information may be published, but you will not be identified. Information that is obtained concerning this research that can be identified with you will remain confidential to the extent possible within State and Federal law. The sponsor and the Food and Drug Administration (FDA) will receive copies of the research records. The investigators associated with this study, the FDA, and the MUSC Institutional Review Board for Human Research will have access to identifying information. All records in South Carolina are subject to subpoena by a court of law.

In the event of a study related injury, you should immediately go to the emergency room of the Medical University Hospital, or in case of an emergency go to the nearest hospital, and tell the physician on call that you are in a research study. They will call your study doctor who will make arrangements for your treatment. If the study sponsor does not pay for your treatment, the Medical University Hospital and the physicians who render

treatment to you will bill your insurance company. If your insurance company denies coverage or insurance is not available, you will be responsible for payment for all services rendered to you.

Your participation in this study is voluntary. You may refuse to take part in or stop taking part in this study at any time. You should call the investigator in charge of this study if you decide to do this. Your decision not to take part in the study will not affect your current or future medical care or any benefits to which you are entitled.

The investigators and/or the sponsor may stop your participation in this study at any time if they decide it is in your best interest. They may also do this if you do not follow the investigator's instructions.

Volunteer's Statement

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. If I have any more questions about my participation in this study or study related injury, I may contact Dr. Julianne Flanagan at (843) 792-5569. I may contact the Medical University of SC Hospital Medical Director (843) 792-9537 concerning medical treatment.

If I have any questions, problems, or concerns, desire further information, or wish to offer input, I may contact the Medical University of SC Institutional Review Board for Human Research IRB Manager or the Office of Research Integrity Director at (843) 792-4148. This includes any questions about my rights as a research subject in this study.

I agree to participate in this study. I have been given a copy of this form for my own records. Please sign below for paper consents or scroll to the bottom of the screen to provide an electronic signature.

_____

Signature of Participant Date

_____

Signature of Person Obtaining Consent Date