Opioid Analgesic Reduction Study **(OARS)**

OARS Informed Consent for NCT04452344

This attachment pertains to:

- Informed consent for Pro2020002299 – initially approved by the IRB on 09/14/2020

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CONSENT TO TAKE PART IN A RESEARCH STUDY

Title of Study: Opioid Analgesic Reduction Study (OARS) Protocol Pilot

STUDY SUMMARY: This consent form is part of an informed consent process for a research study and it will provide information that will help you decide whether you want to take part in this study. It is your choice to take part or not.

The **purpose of the research** is to determine whether a combination of non-opioid containing pain medications are just as, if not more effective, then opioid containing pain medications. If you take part in the research, you will be asked to complete several questionnaires, to take a pain medication which you will be given and you will be asked to wear an activity monitor for 72 hours. It will take about 15 minutes during your surgery visit and post-operative visit to complete questionnaires. During the post-operative period you will receive electronic messages, via text or email, in the morning, and evening asking you to complete a an eDiary on your smartphone to record pain levels, which will take about 2-3 minutes for each entry.

Possible harms or burdens of taking part in the study may be experiencing medication side effects such as upset stomach, light-headedness, drowsiness, dizziness, constipation; and possible benefits of taking part may be obtaining pain medication free of charge and receiving compensation for taking part in this study. Study participants should be aware that opioids can be addictive.

An alternative to taking part in the research study is to follow normal post-operative care procedures which may include being given a prescription for pain medication. Your alternative to taking part in the research study is not to take part in it.

The information in this consent form will provide more details about the research study and what will be asked of you if you choose to take part in it. If you have any questions now or during the study, if you choose to take part, you should feel free to ask the study staff and should expect to be given answers you completely understand. After your questions have been answered and you wish to take part in the research study, you will be asked to sign this consent form. You are not giving up any of your legal rights by agreeing to take part in this research or by signing this consent form.

Who is conducting this study?
Dr. Cecile A. Feldman is the Principal Investigator of this research study. A Principal Investigator has the overall responsibility for the conduct of the research. However, there are often other individuals who are part of the research team.

Cecile A. Feldman, DMD may be reached (973) 972-4634 or at 110 Bergen Street, Newark, NJ, 07103.

The Principal investigator or another member of the study team will also be asked to sign this informed consent. You will be given a copy of the signed consent form to keep.

Sponsor of the Study: The Rutgers School of Dental Medicine and the National Institutes of Health, Institute for Dental and Craniofacial Research are the sponsors of this study.

Why is this study being done?
This study will determine if a combination of non-opioid containing pain medications are just as, if not more effective, then opioid containing pain medications.

Who may take part in this study and who may not?
Any adult male or non-pregnant female individual, age 18 years or older, who is able to refrain from driving or operating heavy machinery while taking the study medication will be able to participate. Participants who are English speaking and are able to provide consent will be considered. Participants must be in generally good health and able to take ibuprofen (Advil, Motrin), acetaminophen (Tylenol), and hydrocodone.

Participants who report the following history will be excluded from participating:

- Individual under the age of 18
- History of gastrointestinal bleeding and/or peptic ulcer
- History of kidney disease (excluding Kidney stones)
- History of liver disease
- History of bleeding disorder
- History of respiratory depression
- Any prior respiratory effect of an opioid or other anesthetic drug that required respiratory support postoperatively
- Active or untreated asthma
- History of known allergic reaction to ibuprofen, acetaminophen, hydrocodone, and/or anesthesia
- Currently taking any of the following medications:
    - CYP3A4 inhibitor, such as macrolide antibiotics (e.g., erythromycin), azole-antifungal agents (e.g., ketoconazole), and protease inhibitors (e.g., ritonavir), which may increase plasma concentrations of hydrocodone bitartrate and acetaminophen and prolong opioid adverse reactions, and which may cause potentially fatal respiratory depression
    - CNS depressants.
- Consumes 3 or more alcoholic drinks every day and/or has a history of alcoholism
- History of drug or alcohol abuse
- Family history of drug or alcohol abuse in a first degree relative
- Has had one or more opioid prescription filled within the past 6 months
- Currently pregnant or lactating
- Any other reason as determined by clinician

Participants will also be excluded due to any additional criteria that would place the individual at increased risk or preclude the individual's full compliance with or completion of the study which includes:

- Prior participation in this study
- Inability or refusal to provide informed consent

A urine pregnancy test will be administered to all female participants prior to surgery to reconfirm eligibility.

Why have I been asked to take part in this study?
You have been asked to participate in this study because you are having at least one impacted lower 3rd molar (wisdom tooth) extracted.

How long will the study take and how many participants will take part?
You will be asked to actively participate in this study over a 10 day period. In addition, researchers will query the state's prescription drug database 6 months later to determine if you filled an opioid containing prescription within 6 months after your surgical visit. Eighteen hundred (1800) participants will be participating in this study. It is anticipated that it will take 3 years to recruit 1800 participants.

What will I be asked to do if I take part in this study?
You will be asked to be present for two to three appointments: a Screening, Surgery, and Post-operative Visit. Screening and Surgery may take place during the same appointment. You will be asked to do the following:

- Screening Visit
  - Complete an informed consent survey
  - Complete an eligibility form
- Surgery Visit
  - Complete a pregnancy test if female
  - Complete a pre-op questionnaire using your smart phone
  - Review study protocols prior to surgery
- Between the Surgery and post-Op visit
  - Take study medication if needed for post-operative pain
  - Complete morning and evening eDiary questionnaires on your smart phone
  - Wear the Actigraph watch which monitors your sleep and activity
- Post-Operative Visit
  - Complete 2 post-operative questionnaires
  - Return study materials, including medication bottles, Actigraph watch, and unused study medication

What are the risks of harm or discomforts I might experience if I take part in this study?
All medications have the potential for side effects. Short term side effects include, but are not limited to:

- upset stomach, nausea, vomiting, loss of appetite, stomach pain;
- bloating, gas, diarrhea, constipation;
- light-headedness, drowsiness, dizziness, feeling tired;
- headache, nervousness;
- mild heartburn;
- mild itching, rash;
- ringing in your ears.
- fainting, weakness
- trouble passing urine, change in the amount of urine.
- sweating;
- bruising, bleeding.
- yellowing of the skin or whites of your eyes.
- tremors, muscle spasms, back pain;
- cold symptoms such as stuffy nose, sneezing, sore throat;
- swelling in your hands or feet.

If you are feeling drowsy, dizzy, tired or light-headed you need to refrain from driving. If the side effects become significantly bothersome, you will be asked to call an emergency surgeon who will be on-call. You will be able to stop taking the provided medication. The provided medication also may not adequately address your pain. If that is the case, you can call the on-call oral surgeon who will decide what further post-operative care is needed and whether an alternative pain medication will be prescribed.

Study participants should be aware that the study medication contains acetaminophen. There are risks associated with taking acetaminophen in large quantities (over 4,000mg per day). A number of over-the-counter (OTC) medications contain acetaminophen and participants should be aware of the additive effect of taking other acetaminophen-containing medications along with the study medication. Severe liver damage may occur if you take more than 4,000 mg of acetaminophen in 24 hours, take with other drugs containing acetaminophen, or consume 3 or more alcoholic drinks every day while using this product. Symptoms of acetaminophen overdose may include: abdominal pain, upset stomach, appetite loss, coma, seizures, diarrhea, irritability, Jaundice (yellow skin and whites of eyes), nausea, vomiting, and extreme sweating. If you are experiencing any serious or life-threatening sign or symptoms, stop taking your study medication at once, and seek medical care immediately.

Study participants should be aware that the study medication may contain an opioid and there are risks associated with taking opioid medication:

- The potential of misuse, abuse, diversion, and addiction with opioid medication.
- Side effects including: feeling drowsy, constipation, sweating, itching, cloudy thinking, withdrawal upon discontinuation of use, mood changes (including worsening depression), sleep pattern changes (including worsening sleep apnea), and effects on hormones.
- Building up a tolerance – meaning having to take more medication to get the same pain relief effect.
- Life-threatening respiratory depression – meaning you can stop breathing.
- Accidental exposure can lead to potentially fatal overdose, especially in children. You must safely store your drugs to avoid accidental exposure or theft.
- Use while pregnant may cause neonatal opioid withdrawal syndrome in a newborn.
- Combining opioids with alcohol and/or other psychoactive medication can cause a fatal overdose.

If you are experiencing any serious or life-threatening sign or symptoms, stop taking your study medication at once, and seek medical care immediately.

Study participants should be aware that opioids can be addictive. In addition, unused medications maintained in your household could be improperly used by other members of your family. To minimize these risks, all study medications will be provided in small quantities, you will be instructed to take the minimal amount required to control your pain, and you will be asked to return any unused pills. If the state's Prescription Drug Monitoring Database query reflects an opioid being prescribed after your surgical visit, you will be offered the ability to talk to an addiction counselor.

You should also tell the study doctor about all medicines that other doctors may have prescribed for you to take. You should not take any over-the-counter medicines, herbal products, vitamins or food supplements while taking part in this study, unless you tell the study doctor and get permission from the study doctor to go on taking these medicines. You will follow the instructions of the study doctor about the use of any of these products.

For Women: The drug under study is known to cause birth defects in some animals. It is likely that it may also cause birth defects in people. For this reason, no one can be in this study who is pregnant or who could get pregnant while taking the study drugs. If you are a woman of childbearing age you will be asked to take a rapid detection pregnancy test. If you are sexually active, you are asked to use one of the following methods of contraception while taking the study drugs:

- contraceptive pill
- intra-uterine device
- condoms
- abstinence:

If you are unwilling to use adequate birth control measures, you should not sign up for this study and are asked not to sign this consent form.

Are there any benefits to me if I choose to take part in this study?
The benefits of taking part in this study may be free pain medication and/or an opportunity for a free addiction counseling session. However, it is possible that you may not receive any direct benefit from taking part in this study.

If you request or fill an additional opioid containing pain prescription during the period between the surgical visit and the query of state's prescription database (if permissible by the state PDMP) which will be done 6 months later, an opioid addiction counseling session will be provided at no cost to you.

What are my alternatives if I do not want to take part in this study?
Your alternative is not to take part in this study. If you do not participate you will receive your normal treatment but will not receive free pain medication. Instead, if needed, you will receive a prescription for pain medication.

How will I know if new information is learned that may affect whether I am willing to stay in the study?
During the study, you will be updated about any new information that may affect whether you are willing to continue taking part in the study. If new information is learned that may affect you after the study or your follow-up is completed, you will be contacted.

Will I receive the results of the research?
No. You will not receive the results of this research.

Will there be any cost to me to take part in this study?
There will be no cost to you to take part in this study. You will be charged for your extractions whether you participate in the study or not.

Will I be paid to take part in this study?
Yes. You will be given a $125 Visa gift card for your participation in this study as long as you complete the pre-operative survey, at least the first three morning e-diary entries and 3 evening e-diary entries, and complete the post-operative survey during your post-operative visit scheduled within 2 weeks of your surgery. At the post-operative visit, you must also return all study materials (medication bottle with remaining tablets and activity tracker),

How will information about me be kept private or confidential?
All efforts will be made to keep your personal information in your research record confidential, but total confidentiality cannot be guaranteed. All study information will be maintained on encrypted Rutgers University servers which are password protected. Only study personnel will have access to passwords and study files.

A Certificate of Confidentiality will be issued automatically by NIH as the study utilizes identifiable, sensitive information. This certification means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena.

There are some important things that you need to know. The Certificate DOES NOT stop reporting that federal, state or local laws require, such as laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate CANNOT BE USED to stop a sponsoring United States federal or state government agency from checking records or evaluating

programs. The Certificate DOES NOT stop disclosures required by the federal Food and Drug Administration (FDA). The Certificate also DOES NOT prevent your information from being used for other research if allowed by federal regulations.

Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

A description of this clinical trial will be available on 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 will happen to my information collected for this research after the study is over?
After information that could identify you has been removed, de-identified information collected for this research may be used by or distributed to investigators for other research without obtaining additional informed consent from you as required by the National Institutes of Health policies.

What will happen if I do not wish to take part in the study or if I later decide not to stay in the study?
It is your choice whether to take part in the research. You may choose to take part, not to take part or you may change your mind and withdraw from the study at any time.

If you do not want to enter the study or decide to stop taking part, your relationship with the study staff will not change, and you may do so without penalty and without loss of benefits to which you are otherwise entitled.

You may also withdraw your consent for the use of data already collected about you, but you must do this in writing to Cecile A. Feldman at Rutgers School of Dental Medicine, 110 Bergen Street, Newark, NJ. 07103.

At any time, the study doctor can take you out of this study because it would not be in your best interest to stay in it. Your study doctor can ask you to stop taking the study medication even if you are willing to stay in the study.

If you decide to withdraw from the study for any reason, you will still be asked to return for your post-operative visit as part of the normal standard of care.

Who can I contact if I have questions?
If you have questions about taking part in this study or if you feel you may have suffered a research related injury, you can contact the Principal Investigator: Cecile A. Feldman, Rutgers School of Dental Medicine at (973) 972-4634.

If you have questions about your rights as a research subject, you can contact the Rutgers IRB Director at: Newark HealthSci IRB, 65 Bergen St., SSB 511, Newark, NJ 07107, (973)-972-3608];

PERMISSION (AUTHORIZATION) TO USE OR SHARE HEALTH INFORMATION THAT IDENTIFIES YOU FOR A RESEARCH STUDY

The next few paragraphs tell you about how investigators want to use and share identifiable health information from your medical record in this research. Your information will only be used as described here or as allowed or required by law. If you sign this consent form, you agree to let the investigators use your identifiable health information in the research and share it with others as described below. Ask questions if there is something you do not understand.

What Is The Purpose Of The Research And How Will My Information Be Used?
You are being invited to take part in this research study which is described at the beginning of this form. The purpose of collecting and using your health information for this study is to help investigators answer the questions that are being asked in the research.

What Information About Me Will Be Used?
- Gender, race, ethnicity, age
- Eligibility criteria
- Pain levels, ability to sleep, ability to perform daily functions, overall satisfaction
- Treatment procedures and treatment notes
- Medications taken
- Any opioid prescriptions filled after surgery

Who May Use, Share or Receive My Information?
The research team may use or share your information collected or created for this study with the following people and institutions:
- Rutgers University Investigators Involved In The Study
- The Rutgers University Institutional Review Board and Compliance Boards
- The Office for Human Research Protections in the U.S. Dept. of Health and Human Services
- Federal Drug Administration
- National Institutes of Health (NIH) - National Institute of Dental and Craniofacial Research (NIDCR)

Those persons or organizations that receive your information may not be required by Federal privacy laws to protect it and may share your information with others without your permission, if permitted by the laws governing them.

Will I Be Able To Review My Research Record While The Research Is Ongoing?
No. We are not able to share information in the research records with you until the study is over. To ask for this information, please contact the Principal Investigator, the person in charge of this research study.

Do I Have To Give My Permission?
No. You do not have to permit use of your information. But, if you do not give permission, you cannot take part in this study. (Saying no does not stop you from getting medical care or other benefits you are eligible for outside of this study.)

If I Say Yes Now, Can I Change My Mind And Take Away My Permission Later?
Yes. You may change your mind and not allow the continued use of your information (and to stop taking part in the study) at any time. If you take away permission, your information will no longer be used or shared in the study, but we will not be able to take back information that has already been used or shared with others. If you say yes now but change your mind later for use of your information in the research, you must write to the researcher and tell him or her of your decision: Dr. Cecile A, Feldman, Rutgers School of Dental Medicine, 110 Bergen Street, Newark, NJ. 07103.

How Long Will My Permission Last?
There is no set date when your permission will end. Your health information may be studied for many years.

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AGREEMENT TO PARTICIPATE

Subject Consent:

I have read this entire consent form, or it has been read to me, and I believe that I understand what has been discussed. All of my questions about this form and this study have been answered. I agree to take part in this study.

Subject Name (Print):_____

Subject Signature:_____ Date:_____

Signature of Investigator/Individual Obtaining Consent:

To the best of my ability, I have explained and discussed all the important details about the study including all of the information contained in this consent form.

Investigator/Person Obtaining Consent (Print):_____

Signature:_____ Date: _____