# Ketamine Tolerated Dose to Prevent Postpartum Depression and Pain after Cesarean Delivery (PREPARE 1)

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| Principal Investigator: | Grace Lim, MD, MSc |
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*Department of Anesthesiology & Perioperative Medicine*

University of Pittsburgh

*INFORMED CONSENT STATEMENT AND AUTHORIZATION FOR RESEARCH*

**Ketamine Maximum Tolerated Dose to Prevent Postpartum Depression and Pain after Cesarean Delivery (PREPARE-1)**

**Principal Investigator:**
Grace Lim, MD MSc
**412-641-2179**

**Funding source: National Institutes of Mental Health R01MH134538**

**ABOUT THIS RESEARCH**

You are being asked to participate in a research study. Scientists do research to answer important questions which might help change or improve the way we do things in the future.

This consent and authorization form will give you information about this study to help you decide whether you want to participate. It is your choice whether you want to be in this research study. Please read this form, and ask any questions you have, before agreeing to be in this study.

**KEY INFORMATION**

Research studies include only people who choose to take part. The study team will explain the study to you and will answer any questions you might have. You should take your time to make your decision. The purpose of this research study is to examine the acceptability and tolerability of ketamine infusions for pain relief after cesarean delivery. Ketamine is a medication that is commonly used for surgical anesthesia. Ketamine is approved for use by the

United States Food and Drug Administration (FDA) as an anesthesia (pain control) drug. Its use in the study is considered experimental because there is not enough data to confirm it is safe for use for pregnancy. However, the study medication will be started after you deliver your infant and the dose you will receive in this study is very low. In low doses, ketamine has been used to treat pain and/or depression. We are measuring how tolerable ketamine infusions are after cesarean delivery. Ketamine may be processed differently in women's bodies who are in the late stages of pregnancy, or who recently delivered than women who are not pregnant or who have not just delivered a baby. Our goal in conducting this study is to ensure that the doses of ketamine provided to women after cesarean delivery not only control post-surgical pain, but also has few enough side effects so that mothers can adequately care for their newborns.

**OVERVIEW OF PARTICIPANT ACTIVITIES**

If you are eligible and interested in participating, you will complete a series of questionnaires prior to your surgery, receive an infusion of ketamine for pain management after your cesarean delivery, and complete weekly questionnaires about your mood and pain throughout the first 3 months postpartum.

Prior to the delivery of your baby, you will be asked to complete a series of questionnaires about your mood and current pain levels. The study team will collect some information from your hospital records, and your infant's hospital records. This information will include your medical history and your surgeon's report of your cesarean surgery as well as your baby's health and gestational age at delivery.

After your cesarean delivery, you will receive a ketamine infusion for pain management. This infusion will be given for 12-hours after your cesarean delivery. Your clinical team and the study team will monitor how you are feeling throughout the duration of the ketamine infusion and for 12-hours after the ketamine infusion ends. We will ask you to identify any side effects experienced for 24-hours, beginning when the infusion starts. You will be observed several times during the first hour of the infusion and at minimum every four hours for the next 24-hours. To measure how you metabolize the ketamine following your delivery, blood samples will be taken 1, 6, 10, and 12 hours after the initiation of the ketamine treatment and any time you experience any adverse side effects.

After you are discharged from the hospital, you will complete a series of questionnaires about any persisting pain as well as changes in mood once per week for 12 weeks after delivery.

These questionnaires will assess mood, stress levels, pain, experiences breastfeeding and with your infant in general, as well as use of medications for pain management. These questionnaires will typically be administered electronically and require less than 25 minutes to complete.

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by US 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.

**OVERVIEW OF RISKS**

Risks associated with this study include those that are:

- **Likely**: inconvenience/discomfort associated with answering study related questions and completing blood draws.
- **Likely**: Side effects of ketamine include sedation, dizziness, lightheadedness, bad dreams, hallucinations, excessive happiness, unhappiness or frustration, nausea, or vomiting. These risks are minimized by using doses below the doses that we typically see these side effects.
- **Less likely**: Uncommon effects of ketamine include high blood pressure or low blood pressure, rapid heart rate, or slow heart rate. These risks are minimized as much as possible by using doses below the doses that we typically see these effects. If these effects are noted, the drug will be stopped until the effects dissipate.
- **Less likely**: potential breach of confidentiality; discomfort, inconvenience, bruising or infection from blood sample collection.
- **Less likely**: When we share your data and biospecimens, there is a small risk that people may get access to it who are not supposed to. We will protect your data and biospecimens as much as possible during storage and when they are shared. However, there is a small chance your identity could be discovered.

Steps have been taken to minimize these risks as much as possible.

**OVERVIEW OF BENEFITS**

As a result of your participation in this study, you will receive increased monitoring of postpartum pain, mood, and depressive symptoms. On a larger scale, we hope that the information obtained in this research study will allow for the development of more effective and safe treatment options for mothers who undergo cesarean deliveries in the future. You will not receive any direct benefit from sharing your data and biospecimens. However, sharing

your data and biospecimens may contribute to research that helps others in the future. Whether you decide to participate in this research or not will have no influence on the care that you and your baby receive during and after your delivery.
*Please review the rest of this document for more details about this study and the things you should know before deciding whether to participate in this study.*

**WHY IS THIS STUDY BEING DONE?**
The purpose of this study is to identify ketamine doses that will be tolerated well in women post-cesarean delivery. The study will investigate the relationship between the delivery of ketamine after cesarean delivery with pain associated with cesarean surgery, and any side effects that result from the ketamine infusion. The goal is to identify the best ketamine dosing level to maximize pain relief and minimize side effects that may alter a new mom's ability to care for their neonate. We hope that the information obtained in this research study will help us to develop effective, safer, and tailored identification and treatment options for pain management and possibly postpartum depression.
**We are asking you if you want to be in this study because you:**

- Are having or may have a cesarean delivery at Magee-Women's Hospital
- Are NOT planning to breastfeed
- OR Are receiving a ketamine infusion as pain management following cesarean delivery

**HOW MANY PEOPLE WILL TAKE PART?**
You will be one of up to 24 participants taking part in this study.

**WHAT WILL HAPPEN DURING THE STUDY?**
***Prior to surgery***, you will complete a series of surveys via a link sent to your email regarding your current pain, stress, and mood. Information will be collected from you, your clinical care team, and/or your medical records. This information may include but is not limited to your medical history, the medications that you are currently taking, and your baby's gestational age. If you are presenting for vaginal delivery and are considering participation, you will be asked to complete baseline questionnaires while you are laboring, and it is understood that some surveys may not be completed depending on their labor course. If you do not require a surgical delivery, your data will not be used.
***After your surgery,*** information will be gathered about your surgery, your baby's health at the time of birth from their medical record, and any complications that arose during the surgery. While in the operating room, you will begin the 12-hour infusion of ketamine through your IV after you deliver your baby and your baby's umbilical cord has been clamped to stop the

exchange of blood flow from mom to baby. At several points during the infusion (0, 4, 8, 10, and 12 hours after the infusion begins), a member of the research team will ask you a few survey questions regarding any side effects that you may be experiencing, your pain level, and your mood. Several tubes of blood will be drawn at 1, 6, 10, and 12 hours after the start of the infusion. Additional blood samples may be taken if you experience side effects during or after the ketamine infusion. At the end of the 12-hour infusion, as well as at 4-, 8-, and 12-hours post-infusion and at the time of onset of any side effects, the study team will ask you to respond to some questions about how you are feeling (pain and mood) and if you are experiencing any side effects of your pain management.

***After hospital discharge***, questionnaires will be sent weekly for 12-weeks after surgery. These questionnaires will take less than 15 minutes to complete and will help us assess your pain, mood, and recovery progress. You can complete these surveys via computer, smartphone, or tablet by following the link sent to you by the study team through the Mosio system. Each week you will be prompted by text message to complete a set of questionnaires. The Mosio-interface will link those surveys to your phone so that you can complete them easily. If you would prefer, the study team will call you and verbally ask you the survey questions over the phone.

***End of procedures.*** Your participation will end 12-weeks following your surgery.
***Recontact.*** We may contact you in the future to ask if you would like to take part in other research studies.

**ALTERNATIVE TREATMENTS**
You may choose to have your pain managed according to your doctor's plan and this sometimes includes the use of ketamine, but not typically.

**WHAT ARE THE RISKS OF TAKING PART IN THE STUDY (in addition to those listed on page 2)?**
You may be uncomfortable while answering the survey questions. While completing the study surveys, you can skip any questions that make you uncomfortable or that you do not want to answer.

You may be uncomfortable during the blood draws. To minimize this discomfort, we will try to use existing IV catheters to collect your blood samples during the study. The risks of drawing blood include pain, bruising, and, rarely, infection. Blood will be collected by

qualified staff members. All attempts will be made to have your blood samples taken at the same time as your regular medical care.

There is a risk someone outside the study team could get access to your or your baby's research or medical information from this study (breach of confidentiality). Emails used in the communication during this study may not be encrypted during transmission or storage, and may be intercepted and used by others not associated with this study. More information about how we will protect your information to reduce this risk is below.

**WHAT ARE THE BENEFITS OF TAKING PART IN THE STUDY?**

As a direct benefit of your participation in this study, you will receive closer monitoring and closer support than is standard, for postpartum depressive symptoms. If depression is identified during the surveys, the study team will contact you and offer various methods of support. On a larger scale, we hope that the information obtained from this research study will allow for the development of more effective treatment options for mothers who undergo cesarean deliveries in the future. If you decide not to participate in this research, you will receive your standard obstetric and pain management care. Whether you decide to participate in this research or not, will have no influence on the care for you and your baby during and after your delivery.

**WILL I BE PAID FOR PARTICIPATION?**

You will be paid up to $1,050 for participating and completing this study. You will be paid on a reloadable debit card. Your name, address, and social security number are needed to create or load the card and this information will be released to the Accounting Office. All compensation is taxable income to the participant. If you receive $600 or more in a calendar year from one organization, that organization is required by law to file a Form 1099 – Miscellaneous with the IRS and provide a copy to the taxpayer. Individuals who do not provide a social security number may still participate in the research, but the IRS requires that 24% of the payment be sent by the institution to the IRS for 'backup withholding;' thus you would only receive 76% of the expected payment.

Upon completion of the baseline inventories and the ketamine infusion and blood collection, you will receive a payment of $750. Upon completion of the postpartum diaries and the weekly surveys, a final payment of up to $300 will be made ($25 per weekly completed surveys) in two installments at 6- and 12-

weeks post-delivery.

**Payment Schedule**

***In-Hospital Encounter***

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| Baseline inventories | |
| Complete infusion and all blood draws | $ 750.00 |

***Postpartum Encounters***

*Complete all daily diaries and weekly surveys (postpartum) @ $25.00/week*

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| Complete weekly surveys for 6 weeks | $ 150.00 |
| Complete weekly surveys for weeks 7-12 | $ 150.00 |
| **Grand Total** | **$ 1,050.00** |

Your data and specimens used in this research study may contribute to a new discovery or treatment. In some instances, these discoveries or treatments may be of commercial value and may be sold, patented, or licensed by the investigators and the University of Pittsburgh for use in other research or the development of new products. You will not retain any property rights, nor will you share in any money that the investigators, the University of Pittsburgh, or their agents may realize.

**WILL IT COST ME ANYTHING TO PARTICIPATE?**

There is no direct cost to you for participating in this study.

**WHO WILL PAY FOR MY TREATMENT IF I AM INJURED?**

If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. Currently, there is no plan for any additional financial compensation. You do not waive any rights by signing this form.

**HOW WILL MY INFORMATION AND SPECIMENS BE USED?**

The study team is asking your permission to collect information from your and your infant's medical records to do this study. This may include:

1. Collecting information to make sure you meet the criteria to be in this study, including that you do not have any serious illness.
2. Gathering information about your medical history, details of your delivery, and your infant's health as described on page 2.
3. Checking on your health in the future to help answer our research question.
4. To inspect and/or copy your research records for quality assurance and data analysis.

The information released and used for this research will include your medical records. Those records may contain information related to mental health, alcohol or substance abuse, HIV/AIDS, sexually transmitted diseases. This information will be available for an indefinite period and your authorization does not expire. If researchers suspect that you are at risk of hurting yourself or others, they are required to inform the appropriate legal authorities.

The following individuals and organizations may access or use your identifiable health information:

- The researchers and research staff conducting the study
- Representatives of the Office of Research Protections of the University of Pittsburgh for the purpose of monitoring the conduct of the research
- Regulatory agencies as required by law such as the FDA (Food and Drug Administration).
- State or Federal agencies with research oversight responsibilities, including but not limited to:
    - Office for Human Research Protections (OHRP)
    - National Institutes of Health (NIH) or National Institute of Mental Health (NIMH)

This study is funded by the National Institutes of Mental Health (NIMH). As such data and biospecimens collected from you will be deidentified. We would like to make your data and biospecimens available for other research studies that may be done in the future as part of the collaborations with the NIMH. The research may be about similar diseases or conditions to this study. However, research could also be about unrelated diseases, conditions, or other aspects of health. These studies may be done by researchers at other institutions, including commercial entities. Our goal is to make more research possible to learn about health and disease.

1. Your data and biospecimens and future genetic analysis data will be stored at the University of Pittsburgh. We plan to keep your data and biospecimens until completely used**.** Your data, biospecimens and genetic data may be shared with investigators around the world or federal repositories. However, access to the data and biospecimens is controlled by the principal investigator of the study. Your name and identifying information will not be on any data and biospecimens you provide. Investigators cannot link your identifying information to the data and biospecimens.

2. There is no plan currently, but your stored research samples could undergo genetic analysis for future research. This might include whole genome sequencing (WGS). WGS identifies your entire unique genetic code from your biological parents. The risk of doing genetic studies includes the potential for a breach of confidentiality, which means someone could see your genetic testing results who is not authorized. The information could be used to affect what insurance or jobs you may be able to get. Or it could affect your decision to have children. It could also cause stress and conflict in your family relationships, as it can confirm who is a child's father, identify a risk for a certain disease, or cause you or other people to have negative feelings if the results show you may be more likely to get certain diseases.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), helps to reduce the risk of discrimination by health insurers and most employers based on your genetic information. This law will protect you in the following ways:

Health insurance companies and group health plans may not request your genetic information that we get from this research. Health insurance companies and group health plans may not use your genetic information that we get from this research when making decisions regarding your eligibility or premiums. Employers with 15 or more employees may not use your genetic information from this research when deciding to hire, promote, or fire you or when setting the terms of your employment. Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance disability insurance, or long-term care insurance, nor does it protect you against genetic discrimination by all employers. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease."

Participating in this study means you agree to share your data and biospecimens. You can change your mind later, but researchers may still use your data and biospecimens that have

already been shared. If you do not want your data and biospecimens used for other projects, you should not participate in this study.

**HOW WILL MY INFORMATION BE PROTECTED?**

Every effort will be made to keep your personal information confidential, but we cannot guarantee absolute confidentiality. No information which could identify you will be shared in publications about this study.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use any information, documents, or specimens that could identify you in any legal action or lawsuit unless you say it is okay. However, there are some types of sharing the Certificate does not apply to. The Certificate does not stop reporting required by federal, state, or local laws, such as reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate does not stop a government agency who is funding research from checking records or evaluating programs. The Certificate also does not prevent your information from being used for other research when allowed by federal regulations.

Researchers may release information about you when you say it is okay. For example, you may still give them permission to release information to insurers, medical providers, or others not connected with the research.

**WHO SHOULD I CALL WITH QUESTIONS OR PROBLEMS?**

For questions about the study please contact Alex Anderson, primary study coordinator, at 412-641-4154. For emergencies, the PI be contacted at 412-641-1000.

**WHAT IF I DO NOT PARTICIPATE OR CHANGE MY MIND?**

After reviewing this form and having your questions answered, you may decide to sign this form and participate in the study. Or you may choose not to participate in the study. This decision is up to you. If you choose not to participate in this study or change your mind after signing this document, it will not affect your usual medical care or treatment or relationship with UPMC or the University of Pittsburgh.

If you change your mind and decide to leave the study in the future, you may contact one of the study coordinators.

If you choose to withdraw your authorization for use and disclosure of your protected health information from your medical record, you must do so in writing by notifying Dr. Lim at:

Dr Grace Lim
Department of Anesthesiology & Perioperative Medicine
300 Halket Street, Suite 3510
Pittsburgh, PA 15213

If you withdraw your authorization, you will not be able to continue in this study. However, even if you cancel this authorization, the research team, research sponsor(s), and/or the research organizations may still use information about you that was collected as part of the research project between the date you signed this document and the date you cancelled this authorization. This is to protect the quality of the research results. Otherwise, this authorization remains valid until the research ends and required monitoring of the study has been completed.

You can change your mind about sharing your data and biospecimens at any time. If you change your mind, please contact the study team to let us know. We will not share your data and biospecimens going forward. We will do our best to retrieve all your data and biospecimens that have already been shared, but it may not be possible. For example, if some research with your data and biospecimens has already been done, the information from that research may still be used. We will not know which data and biospecimens are yours if the identifying information was removed. Also, if the data and biospecimens have been shared already with other researchers, it might not be possible to get them back.

Per University of Pittsburgh policy, all research records must be maintained for at least 7 years following final reporting or publication of a project.
The researchers may stop your participation in the study even if you do not want to stop if the study doctor determines that it is in your interest.

**PARTICIPANT'S CONSENT AND AUTHORIZATION**

The above information has been explained to me and all my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any part of this research study during this study. Any future questions, concerns or complaints will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the telephone number(s) given. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator. I understand that I may contact the Human Subjects Protection Advocate of the Human Research Protection office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations that occurred during my participation. By signing this form, I consent to participate in this research study and provide authorization to use and share my medical records. A copy of this consent form will be given to me.

_____

**Participant's Printed Name** **Date & Time**

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**Participant's Signature**

I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and we will always be available to address future questions, concerns or complaints as they arise. I further certify that no research component of this protocol was started until after this consent form was signed.

_____

**Investigator Printed Name** **Date & Time**

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**Investigator Signature**