Summary of Informed Consent Form

Study Title: Intravenous ketamine for emergency department treatment of suicidal ideation in a pediatric population: protocol for a double-blinded, randomized, placebo-controlled, parallel-arm pilot trial (KSI Study)

Below is a summary of information about the study. There is more information in the document called an "informed consent form" that follows this summary. Please read the informed consent form. The research team will also talk to you about the study and you can ask any questions you may have.

Participation in research is voluntary. It is your choice whether you take part in this clinical trial.

STUDY PURPOSE

This study is being done because we want to see if there are better treatments for patients who have moderate to severe suicidal thinking/ideation. Suicidal thoughts are a medical emergency and, right now, there are no fast-acting medications that are helpful to patients with suicidal thinking. Most medications used for depression and suicidal thoughts are taken by mouth and take several weeks to work.

We are studying the effects of a medication called ketamine to reduce the severity of suicidal ideation. In our study, ketamine is given by the intravenous (IV) route. Ketamine has shown to have positive effects in adults with suicidal ideation but there are no studies in patients under the age of 18 years.

DURATION

It is expected that study participation will last approximately two (2) hours today, and ten (10) minutes of your time in one week. Participants will be followed for one (1) week.

STUDY PROCEDURES

Our study is a randomized controlled trial, which means that there will be two different groups. If you decide to participate then you will be "randomized" into one of the groups described below. Randomization means that you will be put into a group by chance (like flipping a coin). There is no way to predict which group you will be assigned to. You will have an equal chance of being placed in either group.

Group 1: If you are randomized to this group you will receive ketamine by IV.

Group 2: If you are randomized to this group you will receive a normal saline placebo.

Patients will not be able to choose which group they are in or be allowed to know which group they are assigned to. We aim to enroll 10 patients in each group.

There are four phases for participants:

1) **Enrolment and Consent (Approximately 30 minutes of your time today)**
    a. During this phase a research team member will ask you questions about your current health to make sure that it would be safe for you to participate.
    b. During this phase, if you were born a female, who may be pregnant, you may be asked to provide a urine sample for pregnancy testing.
    c. If you are eligible to participate you will be asked to complete a baseline survey, this should take approximately 20 minutes.

2) **Intervention (Approximately 2 hours of your time today)**
    a. During this phase a nurse will insert an IV so that medicine can be given. If you would like, you can have freezing cream or spray before the needle poke to reduce pain.
    b. You will be hooked up to an IV pump and receive a medicine over 40 minutes, during this time, you will be supervised by your parent, guardian or a patient sitter. This will happen in a private room where you will be closely monitored.
    c. You will be asked to rate your suicidal ideation severity 3 times. Once after the infusion is complete at 40 minutes, then again at the 80 minute, and 2 hours.
    d. After you receive the study medicine, the IV will be removed.

3) **Follow up (Approximately 10 minutes of your time in the future)**
    a. A study team member will contact you by phone twice after today to ask the same questions about the severity of your suicidal thinking. Once in 24 hours, and once in 7 days. If they are unable to reach you, they will follow up a maximum of 3 times.

4) **Chart Review (No time required from you)**
    a. In one month from now, a research team member will electronically access your medical record to see if you need any further visits to the emergency department for mental health concerns or admissions to psychiatry.

RISKS.
Participation in this study may involve risks to you. These risks are described in detail in the informed consent form.

The risks you are most likely to experience are:
- Pain with intravenous (IV) insertion, or multiple attempts at IV insertion.
- If you are randomized to the ketamine group you may experience alterations in your thinking (slight confusion, floating feeling and relaxation) or a slight and temporary increase in your heart rate or blood pressure.
- Delay in your routine ED care. Participating in this study may delay your care today, however, your participation may not result in any delay at all. Most patients wait 3-4 hours, sometimes up to 7 hours, to see a doctor. It is possible that you will be able to complete your part while you wait to be seen

The most serious risks are:
- If you are randomized to receive ketamine, there are rare side effects that include respiratory depression, laryngospasm, increase salivation, vomiting, dissociated mental state, hallucinations, agitation.

BENEFITS.
If you decide to participate, you may or may not benefit from participating in this study. We expect that patients who are randomized to the ketamine group will have an improvement in their suicidal symptoms. It is possible that you are not randomized to the ketamine group, or that you do not experience a change in your suicidal symptoms.

By participating in this study, patients will help others similar to them who are struggling with suicidal

thinking.

ALTERNATIVES.
You do not have to participate in this study to receive medical care.

Informed Consent Form for Participation in a Research Study

Study Title: A phase three, double blinded, randomized, placebo controlled, parallel arm pilot trial of intravenous ketamine for emergency department treatment of suicidal ideation in a pediatric population.

Version date of this form: 5 – April -2024

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Sponsor: CHEO Research Institute

Emergency Contact Number: Dr. Michael Schlegelmilch, XXX-XXX-XXXX

INTRODUCTION

As a Substitute Decision Maker, you are being asked to provide informed consent on behalf of a person who is unable to provide consent for him/herself. If the participant gains the capacity to consent for him/herself, your consent for them will end. Throughout this form, "you" means the person you are representing.

You are being invited to participate in a clinical trial (a type of study that involves research). You are invited to participate in this trial because you are an adolescent who has suicidal thinking (suicidal ideation). This consent form provides you with information to help you make an informed choice. Please read this document carefully and ask any questions you may have. All your questions should be answered to your satisfaction before you decide whether to participate in this research study.

The study staff will tell you about the study timelines for making your decision.

Taking part in this study is voluntary. You have the option to not participate at all or you may choose to leave the study at any time. Whatever you choose, it will not affect the usual medical care that you receive outside the study. Your emergency department care may or may not be delayed by up to three hours today if you decide to participate. This will be discussed with you.

IS THERE A CONFLICT OF INTEREST?
There are no conflicts of interest to declare related to this study.

WHAT IS THE BACKGROUND INFORMATION FOR THIS STUDY?
Suicidal ideation (SI), defined as having thoughts of suicide, is a common and often severe problem for adolescents. Patients with SI often present to the emergency department (ED) with severe and distressing thoughts of self-harm or suicide, and yet, there is currently no fast-acting treatment to offer them. The standard of care for patients who do not require admission is to be discharged home with close parental supervision, family doctor follow up and resources for websites, apps, or telephone help lines. This current standard of care places immense pressure on caregivers, fails to treat the underlying suicidal thoughts and leaves patients undertreated, unsafe and vulnerable. In our experience, patients, families, and doctors feel very dissatisfied with this standard of care. Medications are nearly never initiated in the ED and patients who are already taking anti-depressants experience a very slow improvement, often with side effects, making it very difficult, and sometimes impossible to continue to take these medications.

For nearly ten years, intravenous (IV) ketamine has proved to be an effective and fast treatment in adult patients with suicidal ideation. A single dose of IV ketamine can rapidly reduce the severity of SI during an ED visit. Ketamine is widely used in pediatric emergency medicine for procedural sedation and pain control, and has a well-established safety profile. However, it has never been studied for use in children or youth with suicidal ideation. A pilot study is needed to assess the feasibility of a definitive trial, the validity of outcome measurement tools and to generate preliminary data on safety and estimated effect sizes of IV ketamine for emergency treatment of SI in a pediatric population.

Health Canada, the regulatory body that oversees the use of drugs in Canada, has not approved the sale or use of intravenous ketamine for emergency treatment of suicidal ideation in adolescents. Health Canada has allowed intravenous ketamine to be used in this study.

WHY IS THIS STUDY BEING DONE?

This study is being done because we want to see if there are better treatments for adolescents who have moderate to severe suicidal thinking/ideation. Suicidal thoughts are a medical emergency and, right now, there are no fast-acting medications that are helpful to patients with suicidal thinking. Most medications used for depression and suicidal thoughts are taken orally and take several weeks to work.

We are studying the effects of a medication called ketamine to reduce the severity of suicidal ideation. In our study, ketamine is given by intravenous (IV). Ketamine has shown to have positive effects in adults with suicidal ideation but there are no studies in patients under the age of 18 years.

The purpose of this study, called a pilot study or a feasibility study, is to test the study plan and to find out whether enough participants will join a larger study and accept the study procedures. This type of study involves a small number of participants and so it is not expected to prove safety or effectiveness. The results may be used as a guide for larger studies, although there is no guarantee that they will be conducted. Participation in a pilot study does not mean that you will be eligible to participate in a future larger study.

WHAT OTHER CHOICES ARE THERE?

You do not have to take part in this study in order to receive treatment or care. Other options (in addition to the standard or usual treatment described above) may include, but are not limited to:

- no therapy at this time

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

It is anticipated that about 20 people will take part in this study, from CHEO.
This study should take 10 months to complete and the results should be known in about two years.

WHAT WILL HAPPEN DURING THIS STUDY?

ASSIGNMENT TO A GROUP

If you decide to participate then you will be "randomized" into one of the groups described below. Randomization means that you are put into a group by chance (like flipping a coin). There is no way to predict which group you will be assigned to. You will have equal chance of being placed in either group.

Neither you, the study staff, nor the study doctors can choose what group you will be in.

This is a double-blind study, which means that neither you, the study doctors, the study staff, nor your usual health care providers will know which group you are in. Your group assignment can be identified if medically necessary. Requests to reveal your assignment for your information or participation in other research studies will not be considered until this study has been completed and the results are known.

WHAT IS THE STUDY INTERVENTION?

Group 1 (Experimental intervention): IV ketamine infusion over 40 minutes

If you are randomized to this group you will be given a low dose of ketamine by an intravenous (placed by using a needle into your vein), over 40 minutes today while in the emergency department. After this the IV will be removed and no further medications will be given during this study.

Group 2 (Non-Experimental Intervention): IV normal saline infusion over 40 minutes

If you are randomized to this group you will be given normal saline (salt water) by an intravenous (placed by using a needle into your vein), over 40 minutes today while in the emergency department. After this the IV will be removed and no further medications will be given during this study.

WHAT ELSE DO I NEED TO KNOW ABOUT THE STUDY INTERVENTION?
If you have side effects while you are on this study, the study doctor may make changes to the intervention.

Normally, you would receive an ED mental health assessment. If you decide to take part in this study, you may receive this usual treatment approximately three hours later than usual. However, your participation may not result in any delay at all depending on how long the ED wait times are.

WHAT ARE THE STUDY PROCEDURES?

Non-Experimental Procedures

The following tests will be done as part of this study. Some of these tests may be done as part of your standard care, in which case the results may be used. Some of these tests may be done more frequently than if you were not taking part in this study and some may be done only for the purpose of the study. If the results show that you are not able to continue participating, the study doctor(s) will let you know.

- Urine pregnancy testing
- Intravenous insertion

Questionnaires

You will be provided with a questionnaire 4 times today. This will be given to you, before you begin and

then at 40 minutes, 80 minutes and 2 hours after the start of the IV infusion. The same questionnaire will be given over the phone in 24 hours and 7 days from today. A member of the research team will call you on these two days.

The purpose of the questionnaire is to measure the severity of your suicidal ideation over time. The questionnaire before you start will take about 20 minutes, and the following questionnaires will take approximately 2-3 minutes to complete.

The information you provide is for research purposes only. Some of the questions are personal. You can choose not to answer questions if you wish. If you find the questions distressing or upsetting, please let the research team member know and they will ensure you receive the help you need. They will be able to connect you with a doctor to help you.

MANDATORY SAMPLE COLLECTION

If you have internal reproductive organs, are sexually active and not currently menstruating we will need to do a urine test to exclude pregnancy prior to participating. Urine will be collected in the ED and a rapid urine pregnancy test will be done by your nurse. If you are pregnant, you will be informed of this result and you will not be able to participate in the study. Your doctor will be informed of the result so that you get the medical care you need.

The collection of these samples is a necessary part of this study to ensure the safety of all participants. Once the pregnancy test has been completed, any leftover samples will be destroyed.

WHAT ARE THE RESPONSIBILITIES OF STUDY PARTICIPANTS?

If you choose to participate in this study, you will be expected to:

- Tell the study doctor about your current medical conditions;
- Tell the study doctor about all prescription and non-prescription medications and supplements, including vitamins and herbals, and check with the study doctor before starting, stopping or changing any of these. This is for your safety as these may interact with the intervention you receive on this study.
- Tell the study doctor if you are thinking about participating in another research study
- Be available for 2 telephone calls to complete the follow up surveys in 24 hours and 7 days from starting the study

HOW LONG WILL PARTICIPANTS BE IN THE STUDY?

The study has four phases, but your time is only required for the first three.

1) **Enrolment and Consent (Approximately 30 minutes of your time today)**
    a. During this phase a research team member will ask you questions about your current health to make sure that it would be safe for you to participate.
    b. During this phase, if you were born a female, who may be pregnant, you may be asked to provide a urine sample for pregnancy testing.

c. If you are eligible to participate you will be asked to complete a baseline survey, this should take approximately 20 minutes.

2) Intervention (Approximately 2 hours of your time today)

a. During this phase a nurse will insert an IV so that medicine can be given. If you would like, you can have freezing cream or spray before the needle poke to reduce pain.
b. You will be hooked up to an IV pump and receive a medicine over 40 minutes, during this time, you will be supervised by your parent, guardian or a patient sitter. This will happen in a private room where you will be closely monitored.
c. You will be asked to rate your suicidal ideation severity 3 times. Once after the infusion is complete at 40 minutes, then again at the 80 minute, and 2 hours.
d. After you receive the study medicine, the IV will be removed.

3) Follow up (Approximately 10 minutes of your time in the future)

a. A study team member will contact you by phone twice after today to ask the same questions about the severity of your suicidal thinking. Once in 24 hours, and once in 7 days. If they are unable to reach you, they will follow up a maximum of 3 times.

4) Chart Review (No time required from you)

a. In one month from now, a research team member will electronically access your medical record to see if you need any further visits to the emergency department for mental health concerns or admissions to psychiatry.

CAN PARTICIPANTS CHOOSE TO LEAVE THE STUDY?

You can choose to end your participation in this research (called withdrawal) at any time without having to provide a reason. If you choose to withdraw from the study, you are encouraged to contact the study doctor or study staff.

You may withdraw your permission to use information that was collected about you for this study at any time by letting the study doctor know. However, this would also mean that you withdraw from the study.

If you decide to leave the study, you can ask that the information that was collected about you not be used for the study. Let the study doctor know if you choose this.

CAN PARTICIPATION IN THIS STUDY END EARLY?

The study doctor may stop your participation in the study early, and without your consent, for reasons such as:

- You are unable to tolerate the study intervention
- You are unable to complete all required study procedures
- New information shows that the study intervention is no longer in your best interest
- The study doctor no longer feels this is the best option for you

- The Sponsor decides to stop the study
- The Regulatory Authority/ies (for example, Health Canada) or research ethics board withdraw permission for this study to continue
- Your group assignment becomes known to you or others (like the study doctor or study staff)

If this happens, it may mean that you would not receive the study intervention for the full period described in this consent form.

If you are removed from this study, the study doctor will discuss the reasons with you and plans will be made for your continued care outside of the study.

WHAT ARE THE RISKS OR HARMS OF PARTICIPATING IN THIS STUDY?

You may experience side effects from participating in this study. Some side effects are known and are listed below, but there may be other side effects that are not expected. You should discuss these with the study doctor if you are concerned.

The study doctor will watch you closely to see if you have side effects. Many side effects go away shortly after the study intervention is stopped, but in some cases side effects can be serious and life threatening, resulting in life saving procedures like CPR, intubation (putting a breathing tube in your throat), or death.

Risks and side effects related to the experimental intervention of IV ketamine we are studying are listed below. Ketamine is commonly used in the ED and is very safe with very low rates of side effects. The rates of side effects are highest when ketamine is giving rapidly (in less than 1 minute) at high doses. For this study, if you are randomized to receive ketamine, it will be given at half the traditional dose and over a longer 40 minute period. This way of giving ketamine dramatically decreases the risk of side effects. None of the side effects below are permanent.

Likely (20-50%)
- Pain with IV insertion, multiple attempts to insert or re-insert IV

Unlikely (5 – 10%):
- Sedation, depersonalization, floating feeling, nausea, pleasant dreams, confusion, insomnia

Rarely (1 – 4%):
- Elevated heart rate, elevated blood pressure, sweating, tremor, dizziness, unpleasant dreams, hallucinations, excitement or irrational behavior, psychic abnormalities
- Respiratory depression requiring extra oxygen, artificial breathing with a mask or a tube in your throat (intubation).

WHAT ARE THE REPRODUCTIVE RISKS?

The effects that ketamine may have on an unborn baby (fetus) are unknown. You must not be pregnant or breastfeeding to participate in this study. However, after you receive the single dose of the study medication today, there is no risk to a fetus if you become pregnant later.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?

If you decide to participate, you may or may not benefit from participating in this study. We expect that patients who are randomized (assigned) to the ketamine group will have an improvement in their suicidal symptoms. It is possible that you are not randomized to the ketamine group, or that you do not experience a change in your suicidal symptoms.

By participating in this study, patients will help others similar to them who are struggling with suicidal thinking.

HOW WILL PARTICIPANT INFORMATION BE KEPT CONFIDENTIAL?

If you decide to participate in this study, the study doctors and study staff will only collect the information they need for this study.

Records identifying you at this centre will be kept confidential and, to the extent permitted by the applicable laws, will not be disclosed or made publicly available, except as described in this consent document.

Authorized representatives of the following organizations may look at your original (identifiable) medical/clinical study records at the site where these records are held, to check that the information collected for the study is correct and follows proper laws and guidelines.

- CHEO Research Institute, the Sponsor of this study
- The research ethics board who oversees the ethical conduct of this study
- Health Canada (because they oversee the use of ketamine in Canada)

Information that is collected about you for the study (called study data) may also be sent to representatives of the organizations listed above. Your name, telephone number, or other information that may directly identify you will not be used. The records received by these organizations may contain your participant code, initials, sex, and date of birth.

If the results of this study are published, your identity will remain confidential. It is expected that the information collected during this study will be used in analyses and will be published/ presented to the scientific community at meetings and in journals.

Even though the likelihood that someone may identify you from the study data is very small, it can never be completely eliminated.

A copy of the consent form that you sign to enter the study may be included in your health record/hospital chart.

Other future research

Your coded study data and/or coded samples may be used or shared with other researchers (inside and outside of Canada) for future studies. "Coded" means that directly identifying information (such as your name and date of birth) will be replaced by a randomly generated number, which will be applied to the

study data and/or samples. This may include storing the coded study data and/or samples in controlled-access databases, for which access is limited to researcher(s) who submit a study plan and who sign an agreement to use the coded study data and/or coded samples only for that research. Very limited coded study data may also be placed in an open access, publicly accessible database. The goal of sharing is to make more research possible. However, the code matching your study data and samples with your name and other directly identifying study data will not be shared.

You will not be asked if you agree to take part in future research studies using your study data. You or your study doctor will not be told what type of research will be done. You will not be given reports or other information about any research that is done with your study data.

WILL FAMILY DOCTORS/HEALTH CARE PROVIDERS KNOW WHO IS PARTICIPATING IN THIS STUDY?

Your family doctor/health care provider will not be informed by the study team that you are taking part in the study. You can choose to let your family doctor/health care provider know, if you like.

WILL INFORMATION ABOUT THIS STUDY BE AVAILABLE ONLINE?

A description of this clinical trial will be available on www.clinicaltrials.gov. This website will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this website at any time.

WHAT IS THE COST TO PARTICIPANTS?

If you are randomized (assigned) to the group who receives, ketamine, this will be supplied at no charge while you take part in this study.

You may not be able to receive the study intervention after your participation in the study is completed. There are several possible reasons for this, some of which are:

- The intervention may not turn out to be effective or safe.
- The intervention may not be approved for use in Canada.
- Your caregivers may not feel it is the best option for you.
- The intervention, even if approved in Canada, may not be available free of charge.

Participation in this study will not involve any additional costs to you or your private health care insurance.

ARE STUDY PARTICIPANTS PAID TO BE IN THIS STUDY?

You will not be paid for taking part in this study.

In the case of research-related side effects or injury, your doctor will refer you to appropriate medical care.

WHAT ARE THE RIGHTS OF PARTICIPANTS IN A RESEARCH STUDY?

You will be told, in a timely manner, about new information that may be relevant to your willingness to stay in this study.

You have the right to be informed of the results of this study once the entire study is complete. The results of this study will be available on the clinical trial registry (see the "Will information about this study be available online" section for more details).

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected.

By signing this form you do not give up any of your legal rights against the study doctor, CHEO Research Institute or involved institutions for compensation, nor does this form relieve the study doctor, CHEO Research Institute or their agents of their legal and professional responsibilities.

You will be given a copy of this signed and dated consent form prior to participating in this study.

WHAT IF RESEARCHERS DISCOVER SOMETHING ABOUT A RESEARCH PARTICIPANT?

During the study, the researchers may learn something about you that they didn't expect. For example, the researchers may find out that you are pregnant. If this is case you will be informed of this result and appropriate medical care will be arranged for you.

WHOM DO PARTICIPANTS CONTACT FOR QUESTIONS?

If you have questions about taking part in this study, or if you suffer a research-related injury, you can talk to your study doctor, or the doctor who is in charge of the study at this institution. That person is:

__Dr. Michael Schlegelmilch_____	___XXX-XXX-XXXX____
Name	Telephone

If you have questions about your rights as a participant or about ethical issues related to this study, you can talk to someone who is not involved in the study at all. That person is:

CHEO Research Ethics Board	*613-737-7600 ext. 3272*
_____	_____
Name	Telephone

Version date of this form: 5 – April -2024

SIGNATURES

- All of my questions have been answered,
- I understand the information within this informed consent form,
- I allow access to medical records and related personal health information as explained in this consent form,
- I do not give up any legal rights by signing this consent form,
- I agree, or agree to allow the person I am responsible for, to take part in this study.
- If you have internal reproductive organs and not currently menstruating, you agree to do a urine pregnancy test prior to participating.

_____	_____	_____
Signature of Participant/ Substitute Decision-Maker	PRINTED NAME	Date

If consent is provided by Substitute Decision Maker: _____ PRINTED NAME of PARTICIPANT

_____	_____	_____
Signature of Person Conducting the Consent Discussion	PRINTED NAME & ROLE	Date

The following attestation must be provided if the participant is unable to read or requires an oral translation:

If the participant is assisted during the consent process, please check the relevant box and complete the signature space below:

☐ The person signing below acted as an interpreter, and attests that the study as set out in the consent form was accurately sight translated and/or interpreted, and that interpretation was provided on questions, responses and additional discussion arising from this process.

_____	_____	_____
PRINT NAME	Signature	Date

Version date of this form: 5 – April -2024

of Interpreter

_____
Language

☐ The consent form was read to the participant. The person signing below attests that the study as set out in this form was accurately explained to the participant, and any questions have been answered.

_____	_____	_____
PRINT NAME of witness	Signature	Date

_____
Relationship to Participant

Version date of this form: 5 – April -2024