FOR CCI USE ONLY
Approved by the Beth Israel Deaconess Medical Center Committee on Clinical Investigations:

Consent Approval Date: 09/12/2022

Protocol Number: **2021P000688**

BETH ISRAEL DEACONESS MEDICAL CENTER
APPROVED BY THE COMMITTEE ON CLINICAL INVESTIGATIONS
09/11/2023
APPROVAL EXPIRATION DATE

INFORMED CONSENT FORM TO TAKE PART IN A RESEARCH STUDY

SUBJECT'S NAME:
TITLE OF RESEARCH PROTOCOL: Optimal Dose of Intrathecal Morphine for Postoperative Analgesia after Cesarean Delivery
PRINCIPAL INVESTIGATOR: Philip Hess, MD
PROTOCOL NUMBER: **2021P000688**

KEY INFORMATION

The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

Why am I being invited to take part in a research study?
We invite you to take part in a research study because you are having a cesarean for the delivery of your baby. You will need pain medication after surgery.

What should I know about a research study?
- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- Your participation is completely voluntary.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- Your refusal to participate will not result in any consequences or any loss of benefits that you are otherwise entitled to receive.
- You can ask all the questions you want before you decide.
- If you choose not to take part, or if you leave the study, your decision will in no way harm your relationship with any member of the research team or any other individuals at Beth Israel Deaconess Medical Center.

Why is this research being done?
We are trying to find the best dose of spinal morphine to use for pain relief after delivery, balancing pain control and the side effects.

How long will the research last and what will I need to do?
We expect that you will be in this research study for one day after delivery.

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You will receive a small dose of morphine with your spinal anesthesia injection. This is a standard medication. You will then have your cesarean delivery as expected. We will be evaluating the pain relief after surgery that you receive from this dose. You will be asked to rate your pain and pain control after surgery using a 10-point scale that we teach you. If at any time you feel that you need more medication for pain or to treat side effects, we will provide medicine to you. At the end of 72 hours, we will ask you to fill out a questionnaire describing how you feel and how satisfied you were with you pain control.

More detailed information about the study procedures can be found under ***"DESCRIPTION OF STUDY DETAILS".***

Is there any way being in this study could be harmful to me?
We don't believe there are any risks from participating in this research. You will receive the standard dose of morphine if you do not participate in this study.
The risks of morphine include itching and nausea/vomiting, which occur in approximately 20% of women.
Very rare risks of morphine can include difficult breathing, which occurs in <1:10,000 women in our institution.

Will being in this study help me in any way?
There are no benefits to you from your taking part in this research. We cannot promise any benefits to others from your taking part in this research. However, possible benefits to others include knowing the best dose of medication to use for pain control after surgery.

What happens if I do not want to be in this research?

Participation in research is completely voluntary. You can decide to participate or not to participate.

Your alternative to participating in this research study is to not participate.

DETAILED INFORMATION SECTION

Please read this consent form carefully and ask the investigators or study staff to explain any words or information that you do not clearly understand. Once you read this consent form and understand what your participation in this study will involve, you will be asked to sign this form if you wish to take part. You will be given a signed copy of the form to keep for your records.

DISCLOSURE OF SPECIAL INTERESTS OF BIDMC AND INVESTIGATORS

This study is being conducted by Philip Hess, MD. There is no funding agency in this study. Neither Beth Israel Deaconess Medical Center (BIDMC) nor Dr. Hess has/have any additional interests in this research project.

WHOM TO CONTACT IF YOU HAVE QUESTIONS OR PROBLEMS

If you have any questions, concerns or complaints about this research or experience any problems, you should contact Philip Hess at [617] 667-3112.

PURPOSE

We are conducting this study to determine the ideal dose of spinal morphine that will improve pain relief,

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while minimizing side effects, after cesarean delivery. This medication is considered standard of care for women undergoing cesarean delivery. Everyone in this study will receive morphine which is approved by the FDA.
Pain management following cesarean delivery now includes using multiple drugs in addition to morphine. This practice is believed to allow lower doses of morphine to be used than in the past. Within the range of doses currently being used, we would like to find out which dose provides the best combination of pain relief and minimal side effects such as itching or nausea.

STUDY PARTICIPANTS
You have been asked to be in the study because you are having a cesarean delivery.

Approximately 100 people will take part in this study at Beth Israel Deaconess Medical Center, the only site of the study.

DESCRIPTION OF STUDY DETAILS
If you agree to be in this study, you will be in this research study for about one day.

After you sign the consent form, the following things will happen:

1. Screening Procedures: Screening procedures are tests and procedures that will be done to determine if you are eligible to take part in the research study. For this research study, the screening procedures include: We will review a brief medical and obstetric history to ensure you qualify for the study, this should take no more than 10 minutes.

2. Randomization Procedures:
   You would receive morphine even if you did not participate in the study, but it is not clear at this time which of the doses of morphine used in this study would be better for you. For this reason, the study treatment plan offered to you will be picked by chance [like the flip of a coin]. You will not be able to choose which study treatment you receive. The chances of receiving either of the study treatments are approximately equal. After the randomization, you will be assigned to one of the following groups:

   A) Morphine 50 micrograms
   B) Morphine 150 micrograms
   C) Morphine 250 micrograms

   Neither you nor your physician will know which dose of morphine you are receiving. However this information can be learned in case of an emergency.

3. Research Procedures: If you qualify to take part in this research study, you will undergo these research procedures:
   You will receive spinal anesthesia for your surgery. The anesthesiologist will explain this

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procedure to you. The spinal anesthesia will include medications for your surgery, and also will include an injection of morphine. This morphine dose will be one of the three doses described earlier. After this injection, you will have your surgery.

After you arrive in the recovery room, we will ask you to rate your pain. We will instruct you on how to rate your pain and will be asking you to rate your pain at 3 time periods: arrival to recovery room, 2 hours after your surgery, and one day after your surgery. You will also receive frequent visits by your postpartum nurse, which is standard care. You will be asked to complete a short questionnaire rating the overall quality of your pain control at 72 hours. This questionnaire should take no more than 5 minutes to complete.

At some point after you have been given the spinal medication and after surgery, you may begin to experience pain from your surgical incision. You may ask for additional pain medication, as needed, for the duration of the study period. These medications will be administered as part of the standard medical care you will receive during your stay.

At some point after you have been given the spinal medication, you may experience side effects, such as itching or nausea/vomiting. You may ask for medications to treat these side effects as needed, for the duration of the study period. These medications will be administered as part of the standard medical care you will receive during your stay.

We will be analyzing the pain scores and use of additional medications for pain or side effects as part of this study.

4. Monitoring/Follow-Up Procedures. Procedures performed to evaluate the effectiveness and safety of the research procedures are called "monitoring" or "follow-up" procedures. For this research study, the monitoring/follow-up procedures include: Pain scores, side effects (if recorded in your medical chart) and a quality of pain questionnaire. This questionnaire should take no more than 5 minutes to complete.

Individual Research Results

While you should not expect to receive any results from the research testing, if we find that research results from your sample are of high medical importance, we may attempt to contact your medical provider to discuss the results.

Information

Your information will be used and shared with the BIDMC research pharmacy and the researchers involved in this study to conduct the research. The consent form provides information on who will have access to identifiable information during the study. We also want you to know that your information may be stripped of any identifiers (for example your name, medical record number or date of birth) and used for future research studies or distributed to another researcher for future research studies without additional informed consent. BIDMC researchers or other third party

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researchers may use your information in other scientific research, product testing or commercial development. It is unknown whether a product will ultimately be developed from the research described in this consent form or from any such work that may be performed by BIDMC or other third parties receiving your information. In signing this consent form, you are acknowledging and voluntarily consenting to the possibility that your information may be used for commercial purposes. For example, your information may be used to develop a new product or medical test to be sold. BIDMC and other researchers may benefit if this happens. There are no plans to pay you if your information is used for this purpose.

If your identifiers are removed, we will not be able to destroy or remove your information from distributed information. As part of this research program and as further explained in this form, information about your medical history may be provided to other researchers and/or outside collaborators.

RISKS AND DISCOMFORTS

As a result of your participation in this study, you are at risk for side effects listed in this section. These risks are associated with the use of morphine; side effects are more common with higher doses and less likely with lower doses. You should discuss these with the investigator and with your regular doctor if you choose. Please note, you would receive morphine regardless of your participation in the study.

More Common (5 to 20%)
Lightheadedness
Dizziness
sedation
sweating
Nausea and vomiting
Itchiness
Constipation
headache

Less Common (<5%)
Difficulty urinating

Rare (1 in 1,000 to 1 in 10,000)
Difficulty breathing
Allergic reaction

Loss of confidentiality
There is the potential for loss of confidentiality by participating in this study. Every effort will be made to protect the confidentiality of your identifiable information.

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CONFIDENTIALITY

Information learned about you during this research program will be maintained confidentially by the research staff as described in this form.

Information learned from your participation in this study and from your medical record may be reviewed and photocopied by the Food and Drug Administration (FDA) and/or other federal and state regulatory agencies, accreditation agencies, the Committee on Clinical Investigations, the Human Subjects Protection Office and others involved in research administration of the Beth Israel Deaconess Medical Center. Information resulting from this study and from your medical record may be used for research purposes and may be published; however, you will not be identified by name in such publications.

MEDICAL RECORD

A copy of this consent form and information collected during this research may become part of your medical record, if the information is relevant to the care you receive at Beth Israel Deaconess Medical Center. Medical records are considered permanent records; therefore, information cannot be deleted from the record. Medical records are available to health care professionals at Beth Israel Deaconess Medical Center and may be reviewed by staff when carrying out their responsibilities, as well as by external parties such as health care insurers and others in certain circumstances. If you are not currently a patient at Beth Israel Deaconess Medical Center and do not have a medical record at Beth Israel Deaconess Medical Center, one may be created for you for your participation in this research. You may also be required to register as a patient of Beth Israel Deaconess Medical Center in order to participate in this research.

POSSIBLE BENEFITS

There is no direct benefit to you from being in this study. However, your participation may help others in the future as a result of knowledge gained from the research.

OTHER AVAILABLE OPTIONS

Taking part in this study is voluntary. Instead of being in this study, you have the option to not participate. You will receive the standard dose of spinal morphine that is used at this medical center.

IF YOU DECIDE NOT TO TAKE PART IN THE STUDY

Participation in this study is voluntary. You have the right to decide not to take part in this study. If you choose to participate, you have the right to leave the study at any time. Your decision to not participate will not result in any penalties or loss of benefits to you. The investigators will tell you about new information that may affect your willingness to stay in this study.

If you decide not to participate in the study or decide to leave the study early, your decision will not affect your relationship with the research team or any other individual at Beth Israel Deaconess Medical Center.

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INVESTIGATORS RIGHT TO STOP THE STUDY

The investigators have the right to end your participation in this study if they determine that you no longer qualify to take part, or if it would be dangerous for you to continue, or if you do not follow study procedures as directed by the investigators. Beth Israel Deaconess Medical Center or the funding source may stop the study at any time.

COSTS AND/OR PAYMENTS TO YOU

COSTS COVERED BY STUDY

You will not be charged for *spinal morphine* that is part of this research study. However, you and your insurance company will be charged for other tests, procedures or medications of this study that are considered standard treatment for your medical condition.

CO-PAYMENT/DEDUCTIBLE STATEMENT

You will be responsible for any co-payments or deductibles that are standard for your insurance coverage.

PAYMENTS TO YOU:

There is no payment for participation in this study.

COST OF RESEARCH RELATED INJURY:

If you are injured as a direct result of your participation in this study you should contact the Investigator at the number provided under the section "Whom to Call if You Have Questions" in this form. You will be offered the necessary care to treat your injury. You or your insurance company will be billed for medical care and/or hospitalization related to this injury. You will be responsible for all co-payments and deductibles required under your insurance. BIDMC will consider reimbursement of injury related expenses not covered by your insurance on a case-by-case basis. At this time there is no plan to reimburse you for items such as lost wages or lost time from work. By signing this consent form you have not given up any legal rights.

A description of this clinical trial will be available on 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.

AUTHORIZATION FOR USE AND DISCLOSURE OF YOUR PROTECTED HEALTH INFORMATION

As part of this study, we will be collecting, using and sharing with others information about you. Please review this section carefully as it contains information about the federal privacy rules and the use and disclosure of your information.

DESCRIPTION OF PROTECTED HEALTH INFORMATION [PHI]

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By signing this informed consent document, you are allowing the investigators and other authorized personnel to use and disclose health information about you. This may include information about you that already exists (for example: your medical records and other sources of health information, demographic information, the results of any laboratory tests, and mental health records if applicable as well as any new information generated as part of this study. This is your Protected Health Information.

PEOPLE/GROUPS AT BIDMC WHO WILL SHARE AND USE YOUR PROTECTED HEALTH INFORMATION

Your Protected Health Information may be shared with and used by investigators working on this study, including the supporting research team (such as research assistants and coordinators, statisticians, data managers, laboratory personnel, pharmacy personnel, and administrative assistants), and may also be shared with and used by other health care providers at BIDMC who have treated you in the past and have information relevant to the research, or who provide services to you in connection with the research. Your Protected Health Information may also be shared with the members and staff of the Committee on Clinical Investigations of Beth Israel Deaconess Medical Center, which is responsible for reviewing studies for the protection of the research subjects, so that it can carry out its oversight responsibilities with respect to the study.

PEOPLE/GROUPS OUTSIDE OF BIDMC TO WHOM YOUR PROTECTED HEALTH INFORMATION WILL BE DISCLOSED (SHARED) AND WHO MAY USE YOUR PROTECTED HEALTH INFORMATION

We will take care to maintain confidentiality and privacy about you and your Protected Health Information. We may share your Protected Health Information with the following groups so that they may carry out their duties related to this research study:

- Other research collaborators and supporting research team members taking part in this study
- The members and staff of any other IRBs (beyond the BIDMC Committee on Clinical Investigations) that oversee the research
- Centralized data collectors
- Your health insurance company
- The Food and Drug Administration [FDA], the Department of Health and Human Services [DHHS], the National Institute of Health [NIH], the Office for Human Research Protections [OHRP], and other federal and state agencies that may have jurisdiction over the research
- Hospital and Clinical Research Accrediting Agencies

Those who receive your Protected Health Information during the course of the research may not be required by the federal privacy regulations to protect it, and they may make further disclosures to others and use your information without being subject to penalties under those laws.

PURPOSE: WHY WE ARE USING AND SHARING YOUR PROTECTED HEALTH INFORMATION

The reason for using and sharing your Protected Health Information is to conduct and oversee the current, secondary, and future research described in this Informed Consent Document. There are

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many other reasons beyond the research for which BIDMC may use or disclose your Protected Health Information. Not all of these reasons require your express written authorization. For example, we will use and share your Protected Health Information to ensure that the research meets legal, institutional and accreditation requirements and to conduct public health activities. The various ways in which BIDMC may use and disclose your protected health information without your authorization are explained in a document called the Notice of Privacy Practices. If you have not received a copy of BIDMC's Notice of Privacy Practices, please ask us for one and review it before signing this form. In addition to signing this document, you may also be asked to sign a BIDMC General Agreement form acknowledging that you have received the BIDMC Notice of Privacy Practices.

NO EXPIRATION DATE – RIGHT TO WITHDRAW AUTHORIZATION

Your authorization for the use and disclosure of your Protected Health Information in this Study shall never expire. However, you may withdraw your authorization for the use and disclosure of your Protected Health Information at any time provided you notify the Principal Investigator in writing. If you would like to take back your authorization so that your Protected Health Information can no longer be used in this study, please send a letter notifying the Principal Investigator of your withdrawal of your authorization to Philip Hess at 330 Brookline Ave., Boston, MA 02215. Please be aware that the investigators in this study will not be required to destroy or retrieve any of your Protected Health Information that has already been used or disclosed before the Principal Investigator receives your letter, and they are permitted to continue to use and disclose your previously collected information as necessary to complete the research.

REFUSAL TO SIGN

Your clinical treatment may not be conditioned upon whether you sign the Authorization for Research. However, if you choose not to sign this informed consent document and authorization for the use and disclosure of your Protected Health Information, you will not be allowed to take part in the research study.

RIGHT TO ACCESS AND COPY YOUR PHI

If you wish to review or copy your Protected Health Information as it is made part of your medical record, you may do so after the completion or termination of the study by sending a letter to the Principal Investigator requesting a copy of your Protected Health Information. You may not be allowed to inspect or copy your Protected Health Information until this study is completed or terminated.

ADDITIONAL CONTACT FOR QUESTIONS OR CONCERNS

You may contact the Human Subjects Protection Office at [617] 975-8500 in the event that you would like to obtain information or to offer input about the research study. This office is independent of the investigator or investigator's research staff and can also assist with questions relating to your rights as a participant in research, which may include questions, concerns or complaints about your participation in the study.

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THE FOLLOWING PARAGRAPHS CONTAIN SOME STANDARD INFORMATION WHICH GENERALLY APPLIES TO INDIVIDUALS PARTICIPATING IN A RESEARCH STUDY.

CONSENT FORM FOR CLINICAL RESEARCH

I have read the previous page[s] of the consent form and the investigator has explained the details of the study. I understand that I am free to ask additional questions.

If I wish additional information regarding this research and my rights as a research subject, or if I believe I have been harmed by this study, I may contact the Human Subjects Protection Office (HSPO).

I am aware that this is a research project and that unforeseen side effects may occur.

I understand that the Beth Israel Deaconess Medical Center has no formal program for compensating patients for medical injuries arising from this research. Medical treatment will be provided for injuries at the usual charge to me or to my insurer unless payment is otherwise provided for in this consent form.

I understand that participation in this study is voluntary and I may refuse to participate or may discontinue participation at any time without penalty, loss of benefits, or prejudice to the quality of care which I will receive.

I acknowledge that no guarantees have been made to me regarding the results of the treatment involved in this study, and I consent to participate in the study and have been given a copy of this form.

_____ _____

Signature of Subject or Legally Authorized Representative (Parent if the subject is a minor) — Date

_____

Relationship of Legally Authorized Representative to Subject

The subject has been given the opportunity to read this consent form and to ask questions before signing, and has been given a copy.

_____

SIGNATURE OF INVESTIGATOR/Co-Investigator DATE

_____

PRINT INVESTIGATOR'S/Co-Investigator's NAME

A signing co-investigator must be listed on the study's approved Research Staffing Form at the time of consent.

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THE FOLLOWING SECTIONS ARE NOT NEEDED FOR ALL STUDIES AND SHOULD BE UTILIZED AS INDICATED:

If the subject is able to speak and understand English but is not able to read or write

I was present during the entire oral presentation of the informed consent and witnessed the subject's agreement to participate in the study.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

If the subject is able to understand English but is not physically able to read or write or see

I was present during the entire oral presentation of the informed consent and witnessed the subject's agreement to participate in the study.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

If the subject is not English speaking and signed the translated Short Form in lieu of the English consent document.

As someone who understands both English and the language spoken by the subject, I interpreted, in the subject's language, the researcher's presentation of the English consent form. The subject was given the opportunity to ask questions.

Signature of Interpreter: _____

Printed name of Interpreter: _____

Date: _____