Research Protocol

Title: “Medical Cannabis as an Opiate alternative”

NCT number: not yet assgned

Protocol ID 856134

Date of Document: October 11, 2024

Purpose:

Opioid use for pain has increased drastically over last decade with disastrous results that lead to an epidemic of overdoses and deaths in the United States. Philadelphia has been described as “ground zero” in the opiate epidemic of overdoses and deaths in the United States. Some initial clinical experience shows that medical marijuana can potentially assist patients suffering from certain serious medical conditions by alleviating pain and improving quality of life, allowing them to discontinue opiates.

Medical Cannabis is very safe and a viable option for pain relief to improve patients and their family’s quality of life. The medical marijuana law in Pennsylvania was passed in 2016 with the hope that this might alleviate the opiate crisis. The opioid death rate in Pennsylvania was 37.9 per 100,000 people. However, medical cannabis is not covered by insurance and is an out of pocket expense. This has been a barrier to some patients trying medical cannabis as an alternative. This can create a disparity in care of chronic pain patients.

Methods:

Recruitment and inclusion/exclusion criteria: Potential participants will be recruited from an outpatient chronic pain clinic. 40 patients who have agreed to attempt wean down on opioid medication and have a diagnosis which qualifies them for medical marijuana will be selected for our study. In these selected patients cost of the treatment was the main barrier for starting medical cannabis. Each participant will undergo a urine drug screen, a pain assessment using the visual analog scale and pain quality will be assessed using the SF-36 health related

quality and McGill Pain Questionnaire, which measures sensory, affective and evaluative dimensions of pain prior to receiving medical marijuana and then at 6 months.

Each patient will be evaluated by a physician who is certified to evaluate patients for Medical Cannabis. If the patient qualifies for Medical Cannabis the next step is for the patient to register on the state of Pennsylvania medical marijuana website. Medical conditions that qualify patient in the states of Pennsylvania for medical marijuana are ALS, Cancer, Crohn's MS, Neurodegenerative diseases, neuropathies, chronic or intractable pain of neuropathic origin. After the patient registers the physician will also certify them on the website. After the patients are certified they will apply for medical marijuana card. Once the patient receives a medical marijuana card the patient will start an opioid weaning plan. Each patient will have an individualized plan for weaning off their opioids which is their standard care plan. The patient will go to the select medical marijuana dispensary and will be able to choose their medical cannabis product. The Curaleaf medical cannabis dispensary will have a list of patients and they will be able to choose from the cannabis products. The patient will be followed up monthly for six months by physician and he will assess the patient's pain levels and Medical Cannabis doses and opioid doses monthly. We will also note the patient side effects, tolerance and any decrease in symptoms. At six months the physician will recheck a urine drug screen, current pain level and readminister the McGill Pain Questionnaire and SF-36 health related quality. The Medical Cannabis doses and strains will be noted.

UNIVERSITY OF PENNSYLVANIA
RESEARCH PARTICIPANT
INFORMED CONSENT AND HIPAA AUTHORIZATION FORM

Protocol Title: Medical Cannabis as an Opioid Alternative

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Research Study Summary for Potential Participants

You are being invited to participate in a research study. Your participation is voluntary, and you should only participate if you completely understand what the study requires and what the risks of participation are. You should ask the study team any questions you have related to participating before agreeing to join the study. If you have any questions about your rights as a human research participant at any time before, during or after participation, please contact the Institutional Review Board (IRB) at (215) 898-2614 for assistance.

The research study is being conducted to assess the use of medical marijuana (cannabis/cannabinoids) as an alternative to opioid based medications for chronic pain management. You have been identified as a patient who may benefit from medical cannabis for chronic pain but have been unable to access it due to the high cost or lack of availability.

If you agree to join the study, we will assist you in registering with the Pennsylvania Medical Marijuana Program and follow your treatment progress for 6 months. You will be asked to attend monthly visits where your physician will manage your pain medication and medical cannabis while the research team will collect data. At each visit we will assess your health and pain management. The majority of these assessments

would occur regardless; however the research may impact their timing or frequency. You will also be asked to complete a urine drug screen at the enrollment and at the end of the study that would normally be part of your clinical care.

The potential benefits are better pain relief with a safer medication than the opioids you are taking. The most common risks of participation are worsening pain, withdrawal symptoms from weaning of opioids, side effects from the medical cannabis which include palpitations, paranoia, increased appetite and/or altered mental state.

Alternatives to participating in this research study are to continue with your current medication, enroll in a trial of physical therapy, or other adjunct non opioid medications, holistic remedies or surgical interventions. Medical marijuana is also available outside this research study.

Please note that there are other factors to consider before agreeing to participate, such as additional procedures, use of your personal information, costs, and other possible risks not discussed here. If you are interested in participating, a member of the study team will review the full information with you. You are free to decline or stop participation at any time during or after the initial consenting process.

Why am I being asked to volunteer?

You are being invited to participate in a research study because you have suffered from chronic pain and are taking opioid medications which have high risk for side effects and medical cannabis costs have been a barrier to access.

Your doctor may be an investigator in this research study. You do not have to participate in any research study offered by your doctor. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. You may also decide to discuss the study with your family, friends, or family doctor. Being in a research study is different from being a patient. As an investigator, your doctor is interested both in your clinical welfare and in the conduct of this study.

If you decide to participate, you will be asked to sign this form.

What is the purpose of this research study?

The purpose of this study is to assess medical cannabis as an alternative to opioids in a population where cost is a barrier to access. Medical cannabis, while available for medicinal purposes in Pennsylvania, is not FDA approved for any use. Insurance does not generally cover its cost. We plan to facilitate access to medical cannabis for patients with chronic pain who would otherwise be unable to access this possible opiate alternative.

How long will I be in the study?

The study should take one year to complete but your involvement will be approximately 6 months. We plan to enroll approximately 40 participants in this study. You will continue to follow with your care provider after completion of the study.

What am I being asked to do?

You're are being asked to consult with your physician on an individualized pain management plan including medical cannabis. The research team will provide support to help you sign up for the Pennsylvania Medical Marijuana Program. Once you receive your card your name will be given to Curaleaf cannabis dispensary. This will give you access to medical cannabis product at dispensary. You will provide information on your medical history and the history of your pain. This will include information on all treatments you received for your pain in the past. You will be asked about your age, date of birth, sex, race and ethnicity. You will have your height, weight and vitals signs taken.

You will be required to complete a urine drug screen at the beginning of the study and the end. Your medical care and medication management, including medical cannabis use, will be overseen by your physician and will not be impacted by the research beyond providing access and recording your health information.

You will work with your physician on tapering, if possible, of your opioid medication in conjunction with taking the medical cannabis product. You will meet with your physician monthly to assess your health and adjust your pain management plan as necessary. At the beginning and end of study you will be given McGill Pain questionnaire and Short Form 36 Health survey to assess your pain and how it affects your daily life functions. At each visit you will be assessed for your pain and any side effects to treatment. Your medication will be adjusted accordingly with your input.

While the assessments are consistent with standard clinical care, the timing, frequency, and specific measures may be impacted by the research.

What are the possible risks or discomforts?

Breach of confidentiality is the main risk of participation. Procedures are in place to protect your identity and health information, hence we believe this risk is low.

There are risks associated with medical cannabis use and withdrawal of opiate medications. Your doctor should discuss these risks with you separate from this research consent because your medication and medical care should not be dictated or impacted by the research beyond providing access.

Side effects of medical cannabis may include (vary by strain, potency and amount used):

- dizziness
- interactions w/medication
- anxiety
- drowsiness
- altered mental state
- raised appetite

Symptoms of Opioid Withdrawal may include:

- sweating
- anxiety
- nausea
- shaking
- loss of appetite
- restlessness

Reproductive risks

If you are currently pregnant, it is important that you inform the investigator because you will not be able participate in the study.

If you do become pregnant, you must tell the investigator and consult an obstetrician or maternal-fetal specialist.

What if new information becomes available about the study?

During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?

You will be given access to medical marijuana. The possible benefits of medical cannabis may include better control of your chronic lowering doses or completely stopping your opioid narcotic dependence. Better pain control can lead to increase function in activities of daily living and better quality of life. However, there is no guarantee that you will benefit from gaining access to medical cannabis.

What other choices do I have if I do not participate?

Medical cannabis is available to you regardless of research participation. However, you must participate in the research to obtain our assistance in accessing medical cannabis.

Alternative treatment choices include continuing on your current pain regimen, discussing with your physician other non-opioid medications, physical therapy, surgical interventions. Some of these options may be covered by your insurance or have lower out of pocket costs. You should discuss these with your doctor before you decide whether to participate.

Will I be paid for being in this study?

Participants who enroll in the Program will already have a medical marijuana card prior to participating. There is no compensation for this study for participants. Participants will be charged $.01 per transaction, since state law requires that medical marijuana must be purchased even if for a nominal fee, it cannot be given away at no cost.

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Will I have to pay for anything?

You or your insurance will remain responsible for the costs of all medical care and fee for the medical marijuana card. If you elected to participate in the program, we will give your name to Curaleaf so they would know to provide you with the medical marijuana at minimal cost. We did not give them any other information about you.

You are still responsible for any deductibles or applicable co-pays for routine office visits, scans and bloodwork. Please talk to your doctor and study team about putting you in touch with a financial counselor to determine exactly what the deductible and co-pay will be for you; this is highly variable depending on your type of insurance.

When is the Study over? Can I leave the Study before it ends?

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped at any time by your physician, the study Sponsor, or the Food and Drug Administration (FDA) without your consent because:

- The Primary Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The Sponsor, the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study.

If you decide to participate, you are free to leave the study at any time. You may do this by contacting the investigator noted on page one of this form. Withdrawal will not interfere with your future care. You may need to titrated back onto your opioid medication if study is abruptly stopped. Please contact your physician if you must stop the study early.

If you decide to stop participating in the study, we encourage you to talk to your doctor first. It is important to tell the doctor if you are thinking about stopping so any risks to you can be minimized. A final study visit may be requested to ensure your safety.

How will my personal information be protected during the study?

We will do our best to make sure that the personal information obtained during the course of this research study will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. The Institutional Review Board (IRB) at the University of Pennsylvania will have access to your records. If this study is being overseen by the Food and Drug Administration (FDA), they may review your research records.

Your data will be coded so that your identity is not directly associated with your health information. The code, the key, and your health information will be stored on servers and devices that are password protected and maintained by Penn Medicine. Any papers records will be stored in a locked office or cabinet.

Future Use of Data

Your information will be de-identified prior to storage for future use. De-identified means that all identifiers have been removed. The information could be stored and shared for future research in this de-identified fashion. The information may be shared with other researchers within Penn, or other research institutions, as well as pharmaceutical, device, or biotechnology companies. It would not be possible for future researchers to identify you as we would not share any identifiable information about you with future researchers. This can be done without again seeking your consent in the future, as permitted by law. The future use of your information only applies to the information collected on this study. If you change your mind, we will not be able to destroy or withdraw your information were shared because all identifiers would have already been removed.

Will information about this study be available to the public?

A description of this clinical trial will be available on www.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 is an Electronic Medical Record?

An Electronic Medical Record (EMR) is an electronic version of your medical chart within a health system. An EMR is simply a computerized version of a paper medical record.

If you have never received care within Penn Medicine and are participating in a University of Pennsylvania research study that uses Penn Medicine healthcare related services, an EMR will be created for you for the purpose of maintaining any information produced from your participation. The creation of this EMR is a requirement of your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). If you have been a patient at Penn Medicine in the past, information from your research participation will be added to your existing medical record.

What may be placed in the EMR?

Information related to your participation in the research (e.g., laboratory tests, notes from your physician, imaging studies, and clinical procedures, etc.) will be placed in your EMR maintained by Penn Medicine.

Once placed in your EMR your information may be accessible to appropriate Penn Medicine workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by Penn Medicine to be appropriate to have access to your EMR (e.g. Health Insurance Company, disability provider, etc.).

Penn Medicine also participates in automated information sharing through Health Information Exchanges (HIEs). HIEs securely share parts of your electronic health record, including research information, with other healthcare organizations involved in your care. This information is shared to improve the quality, safety and efficiency of your healthcare. To request that your health information not be shared through HIEs, please call 215-662-4484.

Will I, as a participant, have access to research related information within the EMR?

The 21st Century Cures Act requires healthcare institutions to allow patients increased access to their electronic medical record. As part of your participation in this research, you will have access to research related information within your EMR through Penn Medicine's patient portal – called MyPennMedicine (MPM).

Will I receive the results of research testing that may be relevant to my health?

All of the testing and assessments are consistent with standard clinical care and will be entered into your medical record and made available to your healthcare providers. This includes urine drug tests and questionnaires about your health, well-being, pain management, and medication usage.

What information about me may be collected, used or shared with others?

The information collected for this study collected from you will be your name, date of birth, information in the medical record, results of physical examinations, medical history, lab tests, or PHI identifiers. In addition to the information collected during the 6 months of active participation, the study team will review your medical records to collect additional information about your health.

Why is my information being used?

Your information is used by the research team to contact you during the study. Your information and results of tests and procedures are used to:

- do the research
- oversee the research
- to see if the research was done right
- to evaluate and manage research functions.

Where may my information be stored?

Information related to your participation in clinical research will be contained in a clinical trial management system (CTMS). A clinical trial management system (CTMS) is used to register your information as a participant in a study. This allows for your research data to be entered and stored for the purposes of study operational and financial applications and other activities required as part of the conduct of the research. Once placed in the CTMS your information may be accessible to other authorized personnel at Penn Medicine that support research operations. Your information may be held in other research databases.

Who may use and share information about me?

The following individuals may use or share your information for this research study:

The investigator for the study and the study team

- Other authorized personnel at Penn Medicine and the University of Pennsylvania, including offices that support research operations
- Other research personnel with access to the databases for research and/or study coordination and as otherwise approved by the IRB

Who, outside of Penn Medicine, might receive my information?

Oversight organizations

- The U. S. Office of Human Research Protections (OHRP)

Once your personal health information is disclosed to others outside Penn Medicine, it may no longer be covered by federal privacy protection regulations.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to Penn Medicine procedures developed to protect your privacy.

How long may Penn Medicine use or disclose my personal health information?

Your authorization for use of your personal health information for this specific study does not expire.

However, Penn Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization
- The University of Pennsylvania's Institutional Review Board grants permission
- As permitted by law

Can I change my mind about giving permission for use of my information?

Yes. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the investigator for the study. If you withdraw your permission, you will not be able to stay in this study.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study.

You will be given a copy of this Research Participant HIPAA Authorization describing your confidentiality and privacy rights for this study.

By signing this document, you are permitting Penn Medicine to use and disclose personal health information collected about you for research purposes as described above.

Who can I call with questions, complaints or if I'm concerned about my rights as a research participant?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research participant, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the IRB at the number on page one of this form.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your protected health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that protected health information to outside organizations or people involved with the operations of this study.

A copy of this consent form will be given to you.

_____ _____ _____

Name of Participant **[print]** Signature of Participant Date

_____ _____ _____

Name of Person Obtaining Signature Date

Consent **[print]**