Official Title: A Depression and Opioid Pragmatic Trial in Pharmacogenetics (Chronic Pain Trial) (ADOPT PGx)

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INDIANA UNIVERSITY
INFORMED CONSENT STATEMENT FOR RESEARCH

Consent to Participate in a Research Study
CHRONIC PAIN-ADULT
A Depression and Opioid Pragmatic Trial in Pharmacogenetics (ADOPT PGx)

SUMMARY

The purpose of this study is to find out if a genetic test can help your provider better manage your chronic pain. Certain changes in our genes can affect if medicines commonly used for pain control work well or cause side effects.

Not all medicines work the same way for everyone. It can be hard to predict who will benefit from a medicine, who will have a reduced or no response, and who will experience side effects. We want to find out how inherited differences in genes affect the body's response to medicines. You will be assigned in a way similar to a toss of a coin to have your genetic information reported to your provider either at the beginning of the study, or after you finish the study. That information could lead to better control of your chronic pain.

In this study, we will ask survey questions and questions about what medicines you are taking. You will be asked to complete surveys at the start of the study, 1 month, 3 months and 6 months after enrollment. The surveys can be completed in various ways, for example in-person, over the phone, or electronically. The questions about what medicines you are taking will be completed with study staff in person or over the phone. The study team will collect a blood or saliva sample for genetic testing. You will be in the study 6 months from the time of enrollment.

Risks of the study involve pain, bruising, infection, dizziness, or fainting during or after a blood draw. Results of the genetic test may cause anxiety or distress. In research, there is always a risk of loss of private information, but we have procedures in place to reduce that risk.

If you are interested in learning more about this study, please continue to read below.

You are being asked to take part in this research study because your provider has prescribed medicine to treat your chronic pain. Research studies are voluntary and only include people who choose to take part. Please read this consent form carefully and take your time making your decision. Ask the study team to explain anything you do not understand. You can speak with your family and friends before you decide to take part.

This study is funded by a grant from the National Human Genome Research Institute, which is part of the National Institutes of Health (NIH). The NIH is a part of the US Health and Human Services that supports health research. This grant pays parts of the salaries of the researchers and their team.

WHO WILL BE MY DOCTOR ON THIS STUDY?

If you decide to participate, you will continue to see your regular doctor. Todd Skaar, PhD will oversee the study where you get your healthcare.

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WHY IS THIS STUDY BEING DONE?

We are trying to find out if information from a person's genetic makeup (DNA) can help providers better manage pain. DNA determines a person's body traits, like height and eye color. DNA is different in every person and is what you inherit from your mother and father. This is why you may have a different eye color, or are a different height than someone else. By being in this study, we want to find out if your DNA can help providers choose better medicines for managing your pain. Your provider may find out information about other genes that may tell them how you respond to other types of medicines.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

About 1,000 people will take part in this study at about 50 different hospitals and practices across the United States. About 250 people will take part where you get your care.

WHAT IS INVOLVED IN THE STUDY?

If you agree to be in this study, we will ask you to sign and date this consent form. Being in the study is voluntary.

If you agree to take part, you will be asked to do these things at the start of the study:

- Provide a genetic sample by blood or saliva. This will be at the start of the study.
- Complete study surveys and questions about what medicines you are taking when you first enroll. Questions will include things like how bad your pain is and how you take your pain medicines. You will also be asked to tell us about any side effects from your pain medicines.
- We will randomly assign you (like the flip of a coin) to one of two groups:

Group 1: Your genetic test will be done right away and results will be reported to your provider.

- Your results will go into your electronic health record and be given to your provider along with a note with medication recommendations.

Group 2: Your genetic test will be done about 6 months after your study enrollment

- Your sample will be stored at the lab. It will not be tested and no one will know the results of the test until after you finish the study.
- After completing the study, in about 6 months, your stored sample will be tested. The results will go into your electronic health record and be given to your provider.

Both Groups:

- Complete study surveys at the time below after enrollment:
  - 1 month
  - 3 months
  - 6 months
- A trained staff member from the University of Florida College of Pharmacy Call Center or your study team will call you about your medicines at 3 months and may ask you to complete the 3 month survey over the phone.

- The other study surveys can be done in-person, over the phone, or through an email or text message link.
- If you choose to complete the other study surveys over the phone, a University of Florida College of Pharmacy Call Center trained staff member or your local study team will contact you.
- After completing the study, in about 6 months, you will get your genetic test results in writing.

As part of this study, we will test for genes that affect medicines. One of the genes affects medicines used to treat pain. We will share suggestions for chronic pain medicines with you and your provider. This gene may also affect medicines people take for other health problems. These results may help guide some medicines for those problems. If you have questions about the effect on other medicines you are taking now or may take in the future, please ask your provider or pharmacist.

HOW LONG WILL I BE IN THIS STUDY?
You will be in the study until about 6 months after you enroll. We will look at your medical record for events related to the study (like emergency room visits and hospitalizations) that happened up to 1 year after you enroll.

WHAT ARE THE RISKS OF THE STUDY?
Taking part in a research study can include risks. These can include:

Blood Draw: If you give a blood sample, you may have some pain or bruising. Rarely, some people get an infection, bleed a lot, or faint due to a blood draw.

Survey: Some questions may make you feel uncomfortable. You don't have to answer them and can always take a break if you need to.

Genetic information: There is a Federal law called the Genetic Information Nondiscrimination Act (GINA). This law makes it illegal for health insurance companies, group health plans, and most employers with over 15 people to show bias against you based on your genetic information. However, it does not protect you against bias by companies who sell life insurance, disability insurance, or long-term care insurance.

When your genetic information is given to your provider, your provider will receive recommendations of medicines that the genetic tests suggest should be best for you. However, there is a chance that the recommended medicines may not work as well or have more side effects than the medicines your provider would have otherwise prescribed.

ARE THERE BENEFITS TO BEING A PART OF THIS STUDY?
You may not benefit from being a part of this study. If you are in Group 1, your provider will have your genetic information and you may have better pain management during the study period. Whichever group you are in, your provider will have your genetic information and this may be helpful with

selecting medications or doses in the future. We hope that the information learned from this study will benefit other people in the future.

WHAT ARE MY OTHER CHOICES THAN TAKING PART IN THIS STUDY?
Your provider can order the genetic test as part of your regular care without being in the study. You can do this at any time. Just ask your provider. You are responsible for the test cost if ordered outside of this study.

WILL MY INFORMATION BE KEPT CONFIDENTIAL?
Being in research involves some loss of privacy. We will do our best to keep your information private but we cannot guarantee total confidentiality We will do everything we can to reduce the risk. We will share only the smallest amount needed to conduct the research.

We have to connect your information to your samples because your provider will get your test results and put them in your electronic medical record.

Researchers involved in this study, including those funding, and overseeing the study may see your personal healthcare information. We will share only the minimum necessary information in order to conduct the research.

To protect your privacy, a part of the government, the Department of Health and Human Services (HHS) issued a Certificate of Confidentiality. Study members may not share research information that may identify you to any other person or group unless you have written down that you approve for them to do this. If you decide to share private information with anyone not involved in the study, the law made to protect your privacy may not apply to the things you have shared.

If you need medical help, or we learn that you could harm yourself or harm others, we will share your information to connect you with needed care.

HOW LONG DO YOU KEEP MY DATA?
Your results will be in our records for at least 6 years after the study is done. Within 6 years after the end of the study, we will take out all information about you from the study results. Your medical record will keep your genetic results indefinitely.

Some information, like your genetic information, age, sex, ethnic background, diagnosis and disease history may be entered into one or more NIH-designated scientific databases. These databases store medical research information from many studies done at many different places and are available with proper approvals to other researchers. Researchers can then study the combined information to learn even more about health and many different diseases. Your data will only be in databases for which researchers must apply for permission to use the data, and will not have any information that can

identify you such as your name, address and telephone number. Because your genetic information is unique to you, there is a chance that someone could trace it back to you. The risk of this happening is very small. Researchers will always have a duty to protect your privacy and to keep your information confidential.

If you have Medicare or Medicaid Insurance, or if at any point during your participation in the study you have Medicare or Medicaid Insurance, this section applies to you.

The study also wants to see if having genetic information in your health record helps improve health outcomes without additional costs. We will do this by getting details on the costs and types of related healthcare services that were covered by your insurance if Medicare or Medicaid insures you at any point during the study. The study will collect this information through claims data. Claims are filed to your insurance to cover the costs of your healthcare. We will request claims data for:

- up to 12 months before starting the study
- up to 12 months after you finish the study

The study team will give your health care system your name, medical record number, date of birth and your unique study ID. Your healthcare system will use this information to retrieve your social security number (SSN) and/or Medicaid or Medicare insurance identification number and securely send an electronic file with this to your insurance provider (Medicare and/or Medicaid). Your insurance provider will use this information to retrieve records about your healthcare visits and cost of care and return this information to the study team. The information returned to the study team will not include your SSN or insurance identification numbers.

Your insurance provider will then link the file sent by your health care system to their records using the provided identifiers and provide all detail on healthcare claims that are submitted for you. The linked data will be de-identified. The de-identified data will be securely sent to the University of Florida with only the unique study ID as the identifier. The claims data of participants in Group 1 will be compared to the claims data of participants in Group 2. This will show us if there were more or less claims and/or healthcare costs for the participants in one group.

A description of this clinical trial will be available on https://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.

WHAT ARE THE COSTS TO YOU?
The research team and study sponsor will pay for the DNA sample collection and genetic test. Neither you, nor your insurer will be charged or billed for the sample collection or test. They are free for you. You or your insurance provider will be billed for all costs related to your routine medical care including copayments and deductibles as normal, just as they would if you had not been part of the study.

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WILL I BE PAID TO BE IN THIS STUDY?

If you agree to take part in this study and finish all the surveys, we will pay you up to $75 for your time and effort (gift card). You will be given a $25 gift card after you complete the first study survey, and then again after you complete the 3 and 6 months study surveys. If you take part in the study and do not complete all the surveys, we will pay you a smaller amount of the $75, based on how many surveys you finish.

If you are seen at the University Hospital study site, your parking may be paid. Transportation services may be available, please talk to a study team member for more information.

WHAT ABOUT RESEARCH RELATED INJURIES OR OTHER PROBLEMS OR QUESTIONS I MIGHT HAVE?

In the event of physical injury resulting from your participation in this study, necessary medical treatment will be provided to you and billed as part of your medical expenses. Costs not covered by your health care insurer will be your responsibility. Also, it is your responsibility to determine the extent of your health care coverage. There is no program in place for other monetary compensation for such injuries. However, you are not giving up any legal rights or benefits to which you are otherwise entitled.

If you have any questions about the study or research-related injury, contact Todd Skaar, PhD at 317-274-2821.

For questions about your rights as a research participant, or to discuss problems, concerns or suggestions related to the research, or to get information or offer input about the research, contact the Duke University Health System Institutional Review Board (IRB) Office at (919) 668-5111.

For questions about your rights as a research participant at Indiana University, to discuss problems, complaints, or concerns about a research study, or to obtain information or to offer input, please contact the IU Human Subjects Office at 800-696-2949 or at irb@iu.edu.

CAN I REFUSE TO TAKE PART OR WITHDRAW?

You do not have to take part at all. You can stop taking part at any time without losing any benefits. Your decision not to take part or to withdraw will not affect your access to health care at your institution. If you decide to stop taking part in the study, we ask that you tell a study staff member.

If you withdraw from the study, we will not take any new data about you other than data needed to keep track of your withdrawal. All data that has already been taken for the study will be sent to the study sponsor.

If our team feels it is best for your health and safety, we may withdraw you from the study. Another reason that our team could withdraw you from the study would be if you are in Group 2, where your genetic test is delayed until about 6 months after your study enrollment, and you or your study provider want your genetic test results prior to your study completion.

The agencies or institutions funding and overseeing this study may stop this study at any time without your consent. This could happen if there are problems with the way the study is being done, if the investigator believes it is in your best interest, or for any other reason. If this happens, we will notify you and discuss other options with you.

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STATEMENT OF CONSENT

"A study member has explained the purpose of this study, what will be done, the risks and benefits. I have been allowed to ask questions, and all my questions have been answered in a way I understand. I was told who to contact if I have questions, problems, concerns, or suggestions about the research. I have read, or someone read me this consent form and I agree to be in this study. I understand I may withdraw at any time. I have been told that I will be given a signed and dated copy of this consent form."

_____ _____ _____
Signature of Subject Date Time

_____
Printed Name of Subject

_____ _____ _____
Signature of Person Obtaining Consent Date Time

_____
Printed Name of Person Obtaining Consent

(Optional)

_____
Name of Witness (Print)

_____ _____ _____
Signature of Witness Date Time