NextGen
Understanding the impact of genome sequencing for reproductive decisions

Kaiser Permanente Northwest Institutional Review Board
Study ID: Pro00003263
Consent Form Approved: 12/9/2014

Research Consent and Authorization Form

Female Participants

NextGen: Clinical Implementation of Carrier Testing Using Genome Sequencing

Purpose of the Study

We are asking you to be in this research study because you asked for carrier testing to find out if you are a genetic carrier of an inherited condition or disease such as cystic fibrosis. You asked for this testing before getting pregnant or during pregnancy. Genetic testing involves looking at genes, which are made up of DNA and are the "instruction book" for the cells that make up our body.

Genetic research involves looking at genes, which are made up of DNA and are the "instruction book" for the cells that make up our body.

The purpose of this study is to compare a new type of genetic testing against the standard genetic test that you requested. Standard carrier tests look at one gene or a small number of genes. The new test is called Genome Sequencing. This new technology is different from standard carrier tests because:

1) It looks at more genes
2) For each gene, it looks at many more changes than just the most common ones
3) It also looks at genes that may be important for your health, not only the one for which you requested testing.

Carrier testing looks for changes called mutations in your genetic material (DNA), which can cause the condition you are being tested for. **Everybody has mutations,** but only some mutations cause disease. **Genetic carriers** of recessive conditions do not show symptoms, but can pass the mutation(s) on to their children. Children only develop the condition if they also get a second mutation in the same gene from their other parent. It is **very unlikely** that a mother and father would have mutations in the same genes that can cause a disease.

Women can also be carriers of x-linked recessive conditions. If the mother passes on the x-linked mutation to her sons, they will have the condition even if the father does not carry a mutation in this gene. Daughters must receive an x-linked mutation from both parents in order to have the condition. Parts of a cell, called mitochondria, are passed onto children from their mothers. You could be found to carry a change in your mitochondrial DNA. You may pass along the change to your child, which could cause disease.

Kaiser Permanente Northwest (KPNW) Region

Clinical Trials Required by Law to Be Registered at www.ClinicalTrials.gov

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

What if I have questions?

You can talk to the study staff about any questions or concerns you have about this study. You can call:

Mari Gilmore at 503-331-6325

Pat Himes at 503-331-6328 or

Katrina Goddard at 503-528-6361

If you have questions about your rights as a research subject, or about research-related injuries, contact the

Human Subjects Institutional Review Board (IRB): Caroline Miner, the Director of Research Subjects Protection, at 503-335-6725.

NextGen
Understanding the impact of genome sequencing for reproductive decisions

CONSENT SIGNATURES

My signature below means that:

- I have read this consent form,
- I agree to take part in this study,
- This consent form has been explained to me,
- All of my questions have been answered,
- I understand the benefits, risks, and alternatives to being in this study, and
- I understand that I will receive a copy of this consent form after I sign it.

PARTICIPANT SIGNATURE

YOUR NAME | PRINT

✗ YOUR SIGNATURE _____ DATE

NAME OF STUDY STAFF OBTAINING CONSENT | PRINT

✗ SIGNATURE OF STUDY STAFF OBTAINING CONSENT _____ DATE

THANK YOU!

51446a 12/14 CHR

You could get your information on about 700 conditions that could affect your future children, and about 150 conditions that could affect you. However, Genome Sequencing does not test for all conditions that exist.

We want to learn if people prefer standard carrier testing or Genome Sequencing. We also want to know if Genome Sequencing is better for:

- Understanding your chance of having a baby with health issues based on carrier status
- Finding out about current or future health concerns for you or a future child
- Getting better medical treatment
- Identifying other family members who may have a higher risk for these health concerns.

We also want to learn how people understand and respond to the different types of genetic information they learn about before and after genetic testing.

How many people will be in this study?

About 400 women will take part in this study at Kaiser Permanente Northwest (KPNW). We will also ask about 100 male partners to take part in this study.

How long will the study last?

You will be enrolled for up to 4 years.

Which group will I be in?

If you agree to be in this research study, you will be assigned randomly (by chance), to one of the study groups:

Usual Care Group: standard carrier testing only (which is the way we usually provide care). About 250 women will be assigned to the Usual Care group.

Genome Sequencing Group: standard carrier testing plus Genome Sequencing testing. About 150 women will be in the Genome Sequencing group.

It is important to remember that neither group is known to be better than any other. You should be willing to be in either group before you agree to be in this study.

Study Procedures

In both groups you will get the standard clinical test for carrier status for the condition you requested as part of your usual medical care. This test has already been ordered by your regular doctor, and the results will be or have already been returned to you.

For both groups, we will:

- Put the test results into your medical record, so that any Kaiser Permanente provider can use the information to help provide you medical care.
- Have you complete a survey on your thoughts about genetic testing (about 30 minutes).
- Contact you 6 months after you get your results to complete a survey about your experience and about the testing and how you used the test result (about 30 minutes). We will send a link to complete the survey to your personal email account.
- Collect data from your medical record about how you use health care after this testing.

If you have a male partner, we will ask you to give him information about being in the study so we can ask him to get the same testing that you had. He will only be eligible if you were found to be a carrier. He does not have to be tested or be in the study for you to be eligible. If he chooses to be tested, he does not need to be a Kaiser Permanente member in order to get the testing. The testing will be provided to him at no charge.

For the Usual Care Group

In this group, you will need to provide a blood sample for the standard genetic test if you haven't already done so. No additional blood is taken as no added testing will be done.

For the Genome Sequencing Group

- You will need to provide two tubes of your blood (about 3 teaspoons) for the Genome Sequencing. In rare cases we may need to ask you back for a second blood draw (about 2 teaspoons) to double

any other personally identifying information.

The researchers in this study will be looking at your personal health information and may need to disclose it to others. Whenever possible, your samples and data will be labeled with a code and not your name, SSN, or other easily identifiable information. However, we cannot promise total privacy.

Information about you and your health, which might identify you, may be given to:

- National Institutes of Health (NIH) (funder who maintains dbGaP repository of de-identified genetic information)
- Commercial laboratory vendor who performs DNA sequencing
- University of Washington (collaborators who perform DNA testing and analysis)
- Oregon Health & Sciences University (collaborators who will confirm DNA testing and analysis of laboratory tests completed by University of Washington)
- The Institutional Review Board (IRB), a committee of scientific, nonscientific, and community members who review research to protect the rights and welfare of participants.

Kaiser Permanente has agreements with other organizations to protect your health information. If this information is given to an organization not covered by these policies and laws, Kaiser Permanente can no longer guarantee the privacy and confidentiality of your personal health information. By signing this consent form you agree to let us use and disclose your personal health information. If you do not agree to this, we cannot include you in the study. This agreement will not expire.

How long will my blood and health information be stored?

If you decide to be in this study, your blood and health information will be stored and possibly used in future approved research. If you decide now that your blood and health information can be used for research, you can change your mind at any time and we would remove your blood and health information from our research database. You can do this even if you are no longer a Kaiser Permanente member by contacting the investigator at the end of this consent form.

May I withdraw or cancel (revoke) my permission?

Yes. You do not have to be in this research study and you can quit at any time. If you decide not to be in this study or to withdraw from it will not affect your regular medical care or health care benefits, and your doctor's attitude toward you will not change. If you do not want to be in the study, the alternative is to receive usual care from your doctor.

If at any time you want to withdraw this agreement, you must notify

Katrina Goddard, PhD in writing or by phone at the Center for Health Research, 3800 N. Interstate Avenue, Portland, OR 97227 or 503-335-6361.

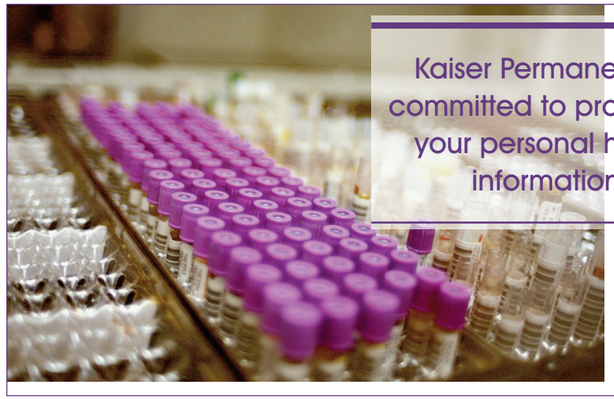
After we receive your request, only data that has already been looked at or disclosed will continue to be used, unless we need to monitor your data for your safety. No further blood or data will be collected, and we will destroy any remaining samples at your request.

Reasons why you might want to participate in this study:

1. Research is important before introducing new technologies, such as genome sequencing, in clinical practice.
2. Learning about carrier status before pregnancy is an important topic to you.
3. Participation in research allows others to benefit from your experience.

Reasons why you might not want to participate in this study:

1. Participation in this study could negatively impact your relationship with your partner.
2. You are concerned about the privacy risks of your genetic information in your medical record.
3. You or your male partner may learn about a genetic risk that you were not expecting.



on your Kaiser Health Plan coverage, including any co-pays. It is possible that this study will identify genetic risk of disease and additional medical medical tests for those diseases will be suggested. You will choose if you want any extra tests or procedures after learning your test results. You will be charged for this follow-up based on your Kaiser Health Plan coverage, including any co-pays. For example, if you are at higher risk of breast cancer, this study will not pay for a mammogram. Your health insurance might not pay for extra care to follow-up on genetic risks.

While you are in this study, you will continue to get regular medical care. All office visits, standard tests, and other standard medications you get while taking part in this study will be charged to you based on your Kaiser Health Plan coverage, including any co-pays. If you leave the Kaiser Health Plan, all study-related genetic counselor visits and other visits will be covered by the study; however, you will be charged for any other medical care at the rate charged to non-Kaiser members.

Will any commercial products be developed as a result of this study?

Research findings from this study may lead to the development of products of commercial value. If this happens, you will not be paid and you will not be compensated in any way. KPNW will not sell or trade any material or data gathered for the study for profit.

No KPNW employees will benefit financially from commercialization efforts. Any royalties or similar financial benefits received by KPNW will be used for research or non-profit public benefit.

Payment

We will give you a $10 gift card for each completed survey. If you complete all surveys, we will send you an additional $20, for a total of up to $60 depending on which group you are in.

What if we learn new information during the study?

We will give you any new information we learn during the study that might affect your medical care or your willingness to continue participation.

Medical Records Information

After the testing is performed, you can refuse to receive the results at any point; however, the results will still be placed in your medical record and can be viewed by any of your care providers.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you by prohibiting health insurance companies and group health plans including Kaiser Permanente, from using your genetic information when making decisions regarding your eligibility or premiums. Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment. For Oregon, all employers are subject to this requirement. This Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Confidentiality

Kaiser Permanente is committed to protecting your personal health information. State and federal laws also require Kaiser Permanente to maintain privacy and security of your information in this study. In order to do this study we will be looking at or collecting information about you and your health, including reviewing your medical record.

To protect your confidentiality we will use a study assigned number whenever possible and use only secure computers or locked files. If you receive genetic testing through the study, those tests will include your name, date of birth, and health record number so the results can be returned to your medical record. If information from this study is presented publicly or published in a medical journal, you will not be identified by name, picture, or

check the results.

- **The carrier status testing process on about 700 conditions** takes about 3 months. **We think that up to 20-50% of the people who have this test will learn that they are a carrier of a genetic condition, but very few of the couples will both be carriers of the same condition.** If the test finds you are a carrier, you will receive these results at an in-person meeting with a genetic counselor.

  This meeting will take about an hour. If the test does not find anything, we will tell you by phone or mail and you will not need to meet with a genetic counselor. A genetic counselor is someone who can tell you about genetic conditions, about what they might mean for you and your future children, and about resources to help manage those conditions. Our genetic counselors work as providers in the Kaiser Permanente system.
- We will give you any results that suggest that you carry a mutation for a condition that is life-shortening. The rest of the results are optional. We will ask you to tell us what types of optional results you want returned to you.

  You can decide to get all, some, or none of the optional results. If you choose to not receive some types of results before the test is performed, they will not be placed into your medial record.

  If you change your mind about what results you want after the testing is performed, you can refuse to receive the results; however, the results will still be placed in your medical record and can be viewed by any of your care providers.
- We will have you complete a second survey about your experience and opinions after you get your carrier status results (about 30 minutes). We will send a link to complete the survey to your personal email account.
- If there are any **results about disease that could affect you,** we will return them to you at an in-person meeting with a genetic counselor about a month after your visit to get your results on carrier status. We call these results "incidental findings" because they are not related to the reason you asked for genetic testing. We will only analyze and confirm information from your genome about certain conditions.

  We will only give you information that is "medically actionable," which means that it is about a medical condition you have that can be treated OR it is about a condition you may develop that can be prevented. For example, we would not give you information about a mutation for Alzheimer Disease, because there is no treatment.

  We would give you information about a mutation that makes you more likely to get breast cancer, since you could get early screening or choose to have surgery before you would possibly get cancer. **We don't think it is likely that your test will find this type of information.** If the test does not find anything, we will notify you by phone or mail and you will not need to meet with a genetic counselor.
- We will ask you to complete a survey about your experience and perceptions after your medically actionable incidental findings results are returned (about 30 minutes). We will send a link to complete the survey to your personal email account.
- We will look again at the mutations in your sequence about once a year until the study ends in 2017. Your genetic information will ***not*** have changed over time, but there may be new ways to interpret it that we want to share with you. What we know about genomics is changing all the time, and new, medically actionable incidental information may become available during the study. If there are changes that would affect your medical care, you will be contacted for a follow-up visit as part of the study.

If you have a meeting with a genetic counselor, our study staff would like to observe that meeting. This will help us learn how you understand

the results, what you plan to do with the results, and how we can improve the way these results are communicated to patients. We will ask you about your satisfaction with the study process and the test results in an interview. This interview will take about 30 minutes. We will also interview you and your partner 1-2 years after you meet with the genetic counselor to see what you have done with the information. The meetings with the genetic counselor and the interviews will be audio recorded.

Risks and Discomforts

Privacy

Although we are very careful and will do everything we can to protect your privacy, we cannot promise that there will never be a breach of your personal information collected in this study. You may wish to share your results with family members since your results could also affect them. But your family members may also share those result with others.

There is a small chance that your genetic information could be shared with others by mistake. Your genetic information will be part of your medical record. Anyone who has access to the medical record may see your genetic results. **In the unlikely event that your information was mistakenly shared, and if it were linked with a medical condition, this could affect your ability to get some kinds of insurance.** If family members were to see this information, it could also affect them, and it could hurt family relationships. It is possible that you could be identified from the sample if someone has another DNA sample from you or a relative. The two samples could be matched to identify you from the sample given for this study.

Your samples and information will be shared with researchers from KPNW and elsewhere (such as universities, companies, or non-profit organizations) for research studies that have been approved by an Institutional Review Board. Your coded (anonymous) genetic and other health information may be disclosed to these approved researchers to increase the chances of new discoveries. You will not get any genetic results from these other research studies.

There are many safeguards in place to protect your information while it is stored in repositories and used for research. The National Institutes of Health (NIH) has developed a federally funded database called dbGaP that collects the genetic test results of research studies. Qualified researchers from government, academic, or commercial institutions worldwide can access the databases. Your coded genetic and health information will be posted in an NIH database without your name or other information that could identify you. We do not think there are further risks to your privacy and confidentiality by sharing your genetic information in these databases; however, we cannot predict how genetic information will be used in the future.

To help us protect your privacy, we have applied for a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

However, you or the researcher may choose to voluntarily disclose the protected information under certain circumstances. For example, we may disclose medical information in cases of medical necessity, or take steps (including notifying authorities) to protect you or someone else from serious harm, including child abuse.

Additionally, if you request the release of information about you in writing (through, for example, a written request to release medical records to an insurance company), the Certificate does not protect against that voluntary disclosure. This Certificate does not prevent the researchers from releasing information about you to prevent serious harm to you or someone else. Moreover, federal agencies may review our records under limited circumstances, such as a Department of Health and Human Services request for information for an audit or program evaluation.

Pregnancy

A small percentage of women (7-8%) may become pregnant while the testing is underway and if this happens to you, this may cause you some anxiety. There are fewer options available for reproductive decision-making once you become pregnant. You can still be in the study if you get pregnant, and you can decide not to learn the results of your carrier status after becoming pregnant. Before each study visit, we will ask if you have become pregnant, and give you the chance to not get your test results. However, if the testing has been performed, the results will still be placed in your medical record and can be viewed by any of your care providers. If you decide that you want to get your carrier status results after becoming pregnant, standard genetic counseling will be made available to you.

Upsetting Information

Learning about your risks for a genetic disease or carrier status could be upsetting. Not knowing exactly how the genetic risk will affect you or your offspring may be stressful to you. Learning that a condition runs in your family might cause some tension among family members. Genetic counseling will be available to help you understand what this genetic information means to you and your family. If at any point we think that you are having too much anxiety or stress, we will offer you a referral for mental health counseling through Kaiser Permanente. Talking about private matters and feelings may make you feel uncomfortable. You can choose not to answer any question or stop an interview at any time.

Blood Draws

The risks of the blood drawing procedures may involve pain or bruising from the insertion of the needle, fainting, and very rarely, swelling or clotting of the vein, or infection where the needle enters the skin. Should you experience any discomfort during the blood draw, please inform the staff member working with you.

Unknown Risks

There may be unknown risks, stresses, or discomforts that we don't know about in this new research. You should tell us about any concerns that you have.

Potential Benefits

You may or may not personally benefit from participating in this research. Your participation will help us understand how to use these new genetic tests in the future and help us learn how people respond to receiving different kinds of information from this kind of genetic testing. We hope that future generations may benefit from the scientific and medical knowledge we gain from your participation. Knowledge we gain about better methods to predict, prevent, or treat disease may help society by advancing medical science.

Costs

Costs covered by the research study

The sponsor of this study, the National Human Genome Research Institute, will pay for any study procedures, including Genome Sequencing, conducted for research purposes. You or your health insurance including Kaiser Permanente will not be billed for any extra visits that are part of the study.

Costs not covered by the research study

The initial genetic testing that you requested and was ordered by your provider for carrier status before getting pregnant, such as for cystic fibrosis, will be charged to you based