Learning assigned at time of consent/enrollment:

SouthSeq Overview

Key Points:

- **SouthSeq is a study that will enroll newborns in NICUs from across the Southeastern United States.**
- **Each newborn will receive a genetic test called Whole Genome Sequencing to look for possible causes of the newborn's medical problems**
- **Results of the study may include a reason for a newborn's medical problems.**
- **Results may also include information about the chance the newborn or other family may develop other medical problems in the future.**

Read more...

You are being told about the SouthSeq study because your baby has medical problems that may have a genetic cause.

This study uses a new kind of genetic test, called genome sequencing that looks at your baby's entire genetic code.

Doing this test in a NICU may allow a diagnosis to be made earlier and may help your baby's doctors provide better care and treatments.

The goal of this study is to enroll about 1,500 newborns in the southeastern US. We want to learn if this test is helpful in a NICU and to understand the impact this impact has on patients and their families.

Results from the genome sequencing test will be given back to you and your baby's doctors. It may take 2-4 months to get the results.

Results may include:

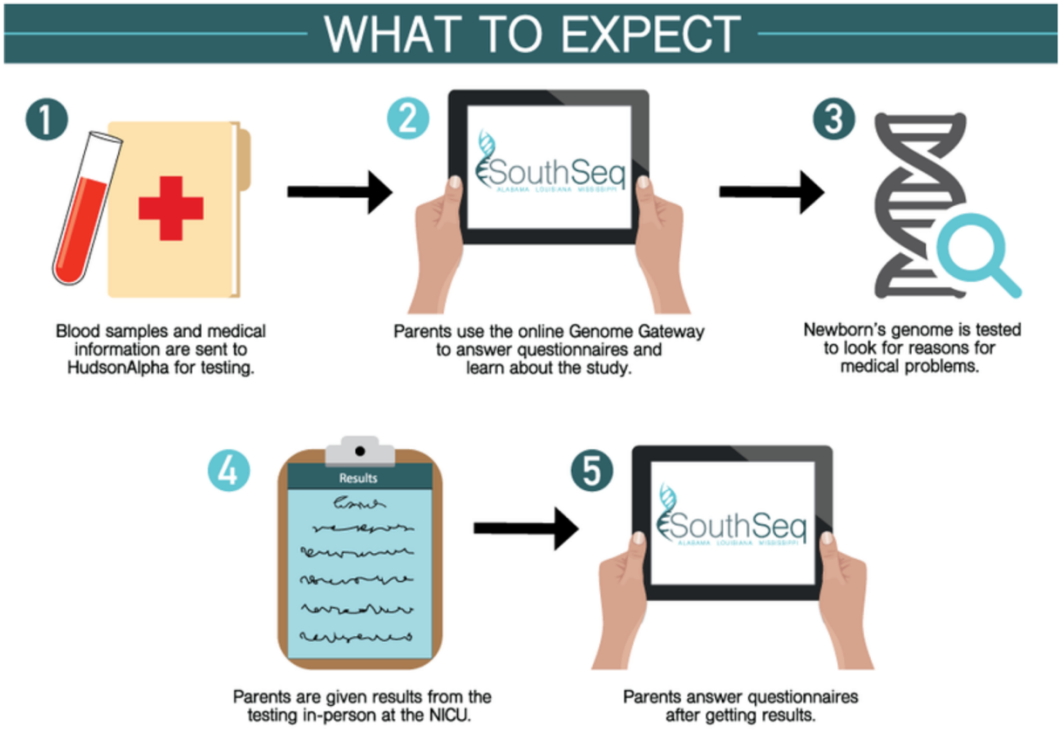
1. If the test was able to find the reason for your baby's medical problems
2. Genetic changes that may be important for your family's medical care

The learning topics here in Genome Gateway will give you more information about the study.

What to Expect

Key Points:

- **A blood sample will be collected from your newborn for genome sequencing. Samples will also be collected from parents if possible.**
- **Results from the genome sequencing test should be available in 2-3 months.**
- **You will be asked to complete online questionnaires at several different times. These questionnaires will ask questions about your experience with genome sequencing and the SouthSeq study.**
- **You will be followed by the study staff for up to one year. The study team may continue to look at information in your child's medical record for up to 8 years.**



Read more...

Here is a look at what you can expect from your participation in the SouthSeq study.

Through the SouthSeq study, a genetic test called genome sequencing will be done for your baby who is in NICU. A blood sample will be collected from your baby as well as the biological parents if possible. Genome sequencing will not be done on parent samples, rather these samples will be used for follow-up testing depending on the baby's results.

Blood samples and information about your baby's medical history will be sent to a lab at the HudsonAlpha Institute for Biotechnology, in Huntsville, AL for testing. You will be asked to complete several questionnaires, complete your baby's family history, and read educational information inside Genome Gateway.

The lab will look at your baby's DNA sequence and look for any genetic changes that could be the reason for medical problems. Results from the genome sequencing test will take 2-4 months to complete. You will be notified when results are ready and a time will be scheduled for you to discuss your results with a healthcare provider in the NICU.

After you receive results from the study you will be asked to complete several additional questionnaires and new educational information in Genome Gateway. Questionnaires help us learn more about how this type of testing can be used in a NICU and the impact genomic results have on patients and their families. We appreciate your participation in this study and willingness to share your family's experiences with us.

Throughout the study you will have access to Genome Gateway. Within Genome Gateway you will have access to files such your study consent form and your baby's results once they they have been discussed with you. You are also able to communicate with your SouthSeq study team using the message feature within Genome Gateway.

You will be sent an email and/or text message whenever there is a new questionnaire or new educational topic to complete.

You may be contacted by your child’s healthcare team or study staff to ask follow-up questions. You will be actively involved in the study up to one year.

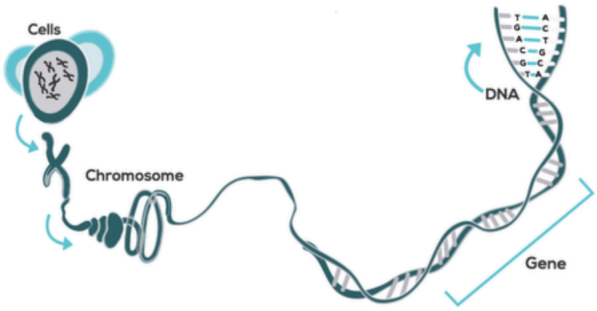
It is important for you to know that you can withdraw your consent to participate from the SouthSeq study at any time. To withdraw, please contact the study coordinator at the NICU where your baby was enrolled. If you choose to withdraw from this study, your child’s medical care will not be affected.

Genetics 101

Key Points:

- **A human body is made up of trillions of cells. Inside nearly all of our cells is a complete set of DNA.**
- **DNA contains genetic "instructions" that our bodies use and that we can pass to our children.**
- **A gene is a section of DNA that tells our body how to do a specific task.**
- **A person's entire set of DNA is called the genome. The human genome contains about 22,000 genes and about 3 billion letters of DNA.**

Read more...



Our understanding of genetics is increasing rapidly. We are learning more and more about how changes in a person's genetic makeup can impact health and risk of developing disease. Newspapers, TV, and the Internet are frequently announcing the discovery of new genes or genetic tests that are related to certain medical conditions. Genetics can be complicated, and it is often difficult to separate fact from what is not true. The first step, however, begins with a basic understanding of our genes and the human genome. Understanding these can increase a person's ability to make informed decisions when faced with genetic questions.

A cell is the basic building block of all living things. Adults have an estimated 10 trillion cells that make up their bodies. Inside a cell there is a command center, called the nucleus, that contains the cell's genetic information. This genetic information is in the form of DNA.

DNA (deoxyribonucleic acid) contains the genetic instructions that pass information from one generation to the next. DNA is found in long strands called chromosomes and is very tightly wound to fit inside the nucleus of a cell. The shape of DNA is similar to a twisted ladder (also known as a double helix). The "rungs" of the ladder are made up of four building blocks: Adenine, Thymine, Cytosine, and Guanine, abbreviated A,T,C, and G.

The term genome refers to all of the genetic information present in a cell – an organism's entire genetic makeup. There are nearly 3 billion DNA letters in a human's genome.

A gene is a specific stretch of DNA that provides instructions to the cell. Often, but not always, these instructions tell the cell how to put together a certain protein. For example, the human genome includes an insulin gene that tells a cell how to produce insulin – a protein that is important for digesting sugar. Some genes help determine whether a person is brown or blue-eyed, tall or short. Other genes determine the chance that a person will develop a wide variety of diseases. The human genome contains about 22,000 genes, which makes up only a small part of the total DNA sequence (about 2%). The rest of the DNA is made up of sections that control how genes work and sections that are not yet well understood.

Genome Sequencing

Key Points:

- **Genome sequencing looks at all of a person's DNA.**
- **Genome sequencing looks for changes or differences in a person's DNA sequence.**
- **DNA changes are common and most changes in DNA do not cause a problem. However, sometimes a change in DNA can cause a disease.**
- **Finding out whether a disease is caused by a genetic change can be important for patients, families and doctors.**

Read more...

Genome sequencing is a test that reads all of our DNA. Every person's DNA is made up of four letters (A, T, C, G). We all have about 6 billion of these letters - 3 billion that were inherited from each parent. Your baby's genome contains a lot of information!

Most often, genome sequencing is done using a blood sample, where DNA is taken from blood cells and put into a machine that reads the DNA letter sequence. The test looks at the order of DNA letters and compares it to a standard human genome sequence. Then the lab looks for changes in your baby's DNA that may be causing current medical problems or those that may happen in the future.

Having changes in DNA is not necessarily a bad thing; in fact, all people have millions of changes. Most DNA changes do not affect health. However, sometimes a DNA change can lead to disease.

The test may help doctors make a diagnosis that would not be possible using other tests. The information can help doctors and patients make a better decision about treatment.

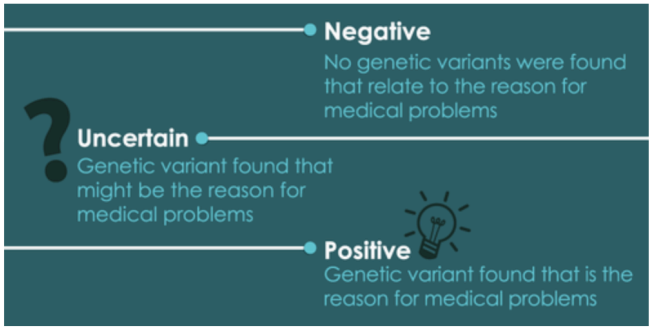
The genome sequencing test is very powerful, but it still has limits. We are not yet able to find and make sense of all the changes in DNA.

Types of Results

Key Points:

- **Results related to why the genome test was done are called primary results. There are 3 types of primary results: positive, negative, and uncertain.**
- **A positive result means that a genetic change has been found that is thought to be the cause of your child's medical problems.**
- **A negative result means that no genetic changes were found that are thought to be the cause of your child's medical problems**
- **An uncertain result means that a genetic change was found that might be the cause of your child's medical problems, but the lab is not sure.**

Read more...



Genome sequencing results that have to do with the reason the testing has been done are called "primary findings." In this study, results that explain why your child is having medical problems in the NICU would be primary findings. There are three possible types of primary results you may receive: positive, negative, or uncertain.

A positive result means that the lab found a genetic change that is believed to be the cause for your baby's medical problems. A positive result can lead to a diagnosis that has clear treatment and support resources. In other cases, a baby may be diagnosed with a new or less understood condition.

A negative result means that the lab did not find any genetic changes thought to be the cause of your baby's symptoms. A negative test result does not mean that your baby's symptoms are not due to a genetic change. It is possible that your baby has a genetic change that is not yet well understood or able to be found. In some cases, negative results can be looked at again in the future and a diagnosis may be possible at that time.

An uncertain result means that the lab found a genetic change that is not currently able to be understood. This genetic change may be the cause for your baby's symptoms but there is not enough proof to be certain. This genetic change may also not be the cause of symptoms and just part of typical DNA differences between people. Your baby's healthcare provider should not treat an uncertain result as a diagnosis, and should not make medical decisions based on this kind of result alone. Over time, many of these uncertain results will be better understood and changed to either a positive or negative result.

Possible Unexpected Results

Key Points:

- **Secondary results, or changes not believed to be associated with your child's medical problems may be found during the study.**
- **Secondary results may or may not lead to a change in a person's medical care.**
- **You will be given a choice as to whether you would like to learn about any secondary results that are found**
- **SouthSeq will not provide information about paternity or other family relationships.**
- **I wasn't sure if it was worth splitting hairs here about medically actionable.**

Read more....

Secondary results
During genome sequencing, the lab might find a genetic change that is not related to your baby's medical problems, but may still impact the health of your family. These types of results are called "secondary results."

An example of a secondary result is finding a genetic change that puts a person at an increased risk of future disease. This kind of result may explain a known family history of a disease. For example, the lab may find a genetic change related to breast cancer risk in an individual who has a strong family history of breast cancer. In other cases, a secondary result may increase risk for a disease that is not in the family history.

Based on a secondary result there may be steps that can be taken to lower the risk for the disease. This is also called a 'medically actionable' result. For example, finding an increased risk for cancer could lead to more cancer screening. In the SouthSeq study, only medically actionable disease risks are going to be returned as secondary findings. In addition, you are given a choice whether you would like to receive secondary results or not.

Family relationships
In some cases, whole genome sequencing may reveal unexpected information about family relationships. For example, genetic information may reveal that a child is not biologically related to his or her father or that the parents of a child are related to each other. However, this type of unexpected information will not be reported as part of the SouthSeq study.

Implications of Results

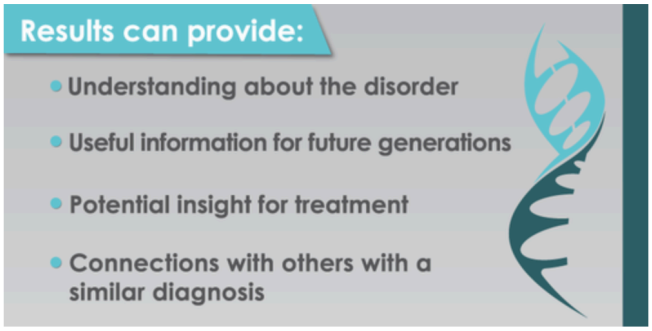
Key Points:

- **The most common result in SouthSeq will be a negative result.**
- **A negative result does not mean that there is no genetic cause for your baby's medical problems, just that we aren't able to find one with current technology.**
- **A variant of unknown significance (VUS) result means a genetic change has been found, but we need more information before we can be certain it is the cause of your baby's medical problems.**
- **A positive result means a genetic change has been found that explains the reason for your baby's medical problems.**
- **In many cases, a positive result does not change how a doctor will manage medical care of your baby.**

Read more....

Negative results

The most common result from this test is a negative result. This means that genome sequencing did not find any reason for your baby's medical problems. This does not mean that your baby's symptoms are not genetic. There is no perfect test that can find and understand all genetic changes. Your baby's doctor may choose to do other types of tests to continue looking for a reason for symptoms. In the future, your doctor may also ask that scientists re-read your child's genome sequence. As scientific knowledge grows, the test results may be better understood and a diagnosis may be made in the future.



Variant of uncertain significance results

Sometimes, a genetic change is found that might be the cause of your baby's symptoms. This is called a variant of uncertain significance (VUS). More information is needed to find out if the change is actually the cause of the symptoms or a harmless genetic change. Because it is uncertain, this type of result should NOT be used to help doctors make decisions about medicines or other care for your baby.

Positive results

In some cases, whole genome sequencing will find a genetic change that explains the reason for your baby's symptoms and gives your family a diagnosis. This means that doctors can stop looking for why your baby has medical problems. Sometimes, it also allows family members to learn the chance that someone else in the family could have the same symptoms.

Sometimes, getting a genetic diagnosis for your baby can help their doctors better care for them. For example, it may tell doctors they should think about using a certain medicine or therapy to treat your baby's symptoms. The result may also help doctors decide to stop using medicines or therapies that are not working, or inform them about treatments that are unlikely to work. Some results may even tell doctors that they should be on the lookout for other problems your baby does not currently have. This hopefully keeps more problems from happening later.

In many cases getting a genetic diagnosis does not change how doctors treat a baby's symptoms. It is possible to receive a diagnosis for which there are no approved medications or therapies. However, families can sometimes use the result to connect with other families that have children with the same diagnosis. This can help the families feel supported in caring for their child. It can also lead to the chance to be a part of more research, which may at some point help doctors learn how to better care for children with the same diagnosis.

Potential Impact on Family Members

Key Points:

- **It is important to consider the impact of any findings from SouthSeq on you and your family.**
- **A primary result may provide a diagnosis for other family members with similar medical problems.**
- **A primary result may provide information about the chance that current or future children may have similar problems.**
- **A secondary result can inform both the participant and their close relatives about health conditions.**

Read more....

The impact that genetic test results may have on family members is important to consider when thinking about whole genome sequencing. Unlike most other medical tests, whole genome sequencing can reveal health information about both the patient and their family members. This is because people share DNA with their family.

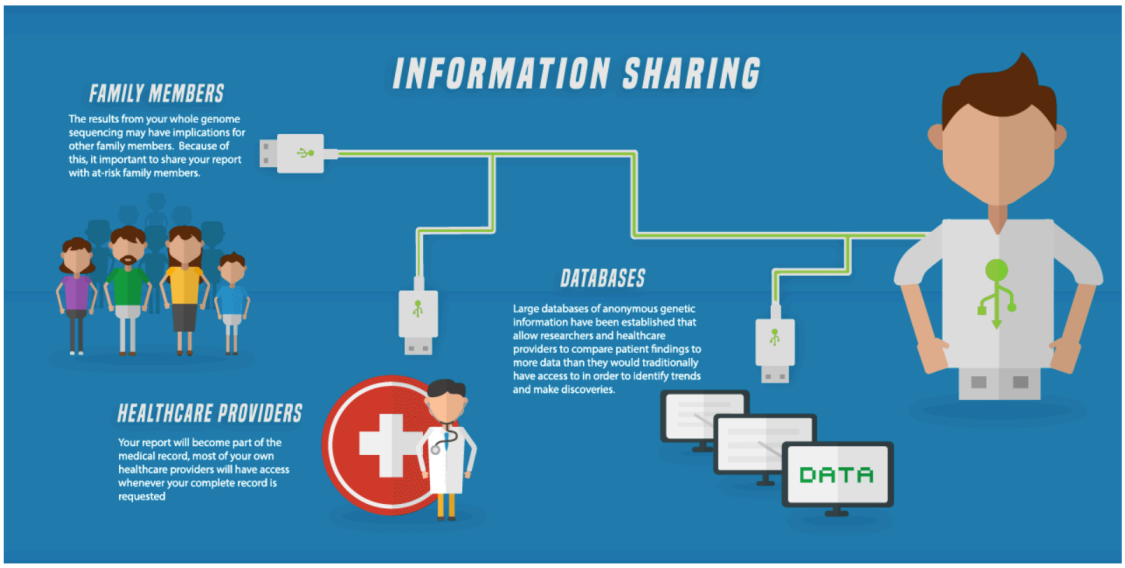
Primary result
Finding a diagnosis for one person may provide a diagnosis for other family members who have similar medical problems. In addition, finding a genetic cause for a person's medical problems may also tell us about the chance for other family members, such as current or future children and siblings, to have the same condition.

Secondary result
Secondary results can have important family impacts as well. For example, finding a strong genetic risk factor for certain types of cancer in a person means that some of his or her close relatives likely share the genetic variant and also have an increased cancer risk. Learning some of these results can be emotionally charged for patients. This is especially true if the results impact both the health of the person being tested, as well as the health of their siblings, parents, and other family members.

Data Access and Storage

Key Points:

- **You have choice in how you much information you want shared with others in the science community.**
- **or all participants in SouthSeq, the consent form and any results from this study will be included in your child's medical record.**
- **For all participants in SouthSeq, small parts genetic sequence, along with information about your child's symptoms (but not name, address or other identifying information) will be shared with public genetic databases and published in scientific journals.**
- **You have the option to share your child's whole genetic sequence with a private database for scientists called dbGAP. Your choice has no impact on your results or medical care.**
- **You have the option to allow your child's genetic sequence data and left over blood sample to be used in future research on disease. Your choice has no impact on your results or medical care.**



Read more....

As part of this research study, some of your private information may be shared with different people and databases. Some of these are not required for you to take part in the study, and you can decide which ones you feel comfortable having information shared with.

Everyone who agrees to take part in this research study allows their signed consent form to be put into their child's medical record. This means that everyone who can see your child's medical chart will know your family agreed to take part in this study. This may include healthcare providers, as well as school systems, insurance companies, and anyone else that has access to your child's chart. Results you receive from the research study will also be put into their medical chart.

The information from a genome sequencing test may also be shared with others outside of this research study. Everyone who agrees to take part in this research study allows small parts of their unique genetic sequence to be shared to public databases and published in scientific journals. Along with these parts of genetic code, details such as your child's age and a list of their symptoms may also be shared. This is to help other doctors and researchers learn what this study finds out about genetic changes and how they play a role in illness. These small amounts of genetic information cannot be used to identify someone, so no one outside of the research study looking at these databases or journals will know that it was your family.

In addition, everyone who agrees to take part in this research study allows their blood sample and the genetic information contained in their blood sample to be stored at the laboratory. These samples are used to help researchers better understand any results that come from this test. An example of this is using the genetic information stored at the laboratory to see if a genetic change in a child's blood is also present in their parent's blood.

There are two more places where samples or genetic information can be shared, but neither of these are required in order to take part in this study. The first is a private database called dbGaP. If you agree to have your information shared to dbGaP, your child's complete whole genome sequence and some information about their medical problems will be included. No names or dates of birth are included, and this is not a public database. The only people that can use this database are researchers who have applied for access and agreed to keep it private. However, because it is an entire genome sequence, which is unique to a person just like a fingerprint, there is a small chance this could someday be used to identify a specific person. If you are not comfortable with this, you can say "no" to dbGaP and still take part in the research study.

The second place where your sample or information may be used is in the laboratory where the testing is done. As mentioned above, you are required to have your sample kept there to better understand the results of this test. However, researchers are also interested in using these blood samples to perform other types of genetic research on human disease. If you are not comfortable with your or your child's sample being used for any other research outside of this specific study, you can say "no" to sample storage and still take part in the research study.

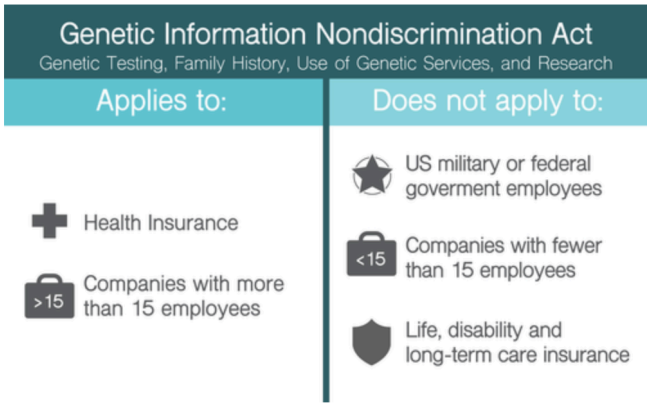
Genetic Discrimination

Key Points:

- **Some people are concerned about how their genetic information could be used to make it harder to get a job, insurance or other service.**
- **The Genetic Information Nondiscrimination Act (GINA) ensures that health insurance companies cannot decide if someone can have coverage or what amount they will be charged to get that coverage based on genetic testing.**
- **GINA prevents many employers from using this information in making hiring, firing, or promotion decisions.**
- **GINA does not always apply and has exceptions, including members of the US military and in decisions made by life, disability, or long-term insurance policy providers.**

Read more...

Some patients who are thinking of having genetic testing may be concerned about genetic discrimination, or how the results might be used against them in the future. They fear that that certain people or groups would use a patient's genetic information to make employment, insurance, or other services harder or impossible to get. "Genetic information" in this case means genetic test results, family health history, or the fact that a person has seen a genetics doctor or been a part of genetic research.



In 2008, the Genetic Information Nondiscrimination Act (GINA) was signed into law to reduce genetic discrimination. GINA ensures that health insurance companies cannot decide base on genetic information if someone can have coverage or how much they pay for coverage. GINA also prevents insurance companies from requiring patients to have genetic testing or asking for the results. This act also keeps many companies from using genetic information against a current or potential employee in making hiring, firing, or promotion decisions. However, GINA does not apply in all cases. For example, companies with fewer than 15 employees do not have to follow GINA. GINA also does not apply to the US military or to federal government employees (however, these groups often have separate policies in place). Also, life, disability, and long-term care insurance policies are not protected by GINA. These companies could still use genetic information to make decisions about coverage and/or cost.

Because of these exceptions, someone thinking about any type of genetic testing (clinically or as part of a research study) should ask their doctor or genetic counselor about the chance of genetic discrimination. Some questions that could be asked include:

- "What type of test am I having?"
- "What are the possible results?"
- "Who is able to see my results?"
- "What is my chance to get the illness you are testing for?"

A person thinking about genetic testing may want to apply for life, long-term care, and disability insurance policies before testing, in case the results show an increased risk to develop an illness. However, sometimes people are thought to already have a higher risk for an illness based on their family history. In some cases, a genetic test result could actually show a person does not have a high chance to have the same illness that is in their family. In this case, the genetic test result could actually help the person applying for these insurance policies.

If you have additional questions or concerns about the possibility of genetic discrimination, we encourage you to ask your healthcare provider or visit www.ginahelp.org.

If You Have Questions

Contact Us:

We understand that you may have questions that come up that are not addressed in these learning topics. Use the information below as a guide to the best person to contact depending on your specific question or need.

- If you have questions or concerns about your child's health and medical care, please contact your child's healthcare providers.
- If you have questions about the status of your whole genome sequencing test or your results, please contact the study coordinator where you were enrolled into the study.
  - University of Alabama at Birmingham Medicine: Kelli Hagood (205-934-6452)
  - Woman's Hospital in Baton Rouge: Hillary Wienpahl (225-924-8310)
  - University of Mississippi Medical Center: Heather Williams (601-815-3070)
- If you have questions, concerns, or complaints about the research project, please contact Dr. Bruce Korf at 205-934-9411.
- If you have questions about your rights as a research participant, you may also contact the UAB Office of the Institutional Review Board (IRB) at 205-934-3789.

Learning assigned at time of result return:

Review of the Study

Key Points:

- **SouthSeq uses a new test called whole genome sequencing.**
- **The purpose of SouthSeq is to determine the impact whole genome sequencing has on patients and their families.**
- **Results will vary but may include a genetic reason that explains your newborn's medical problems and how genetic changes may be important to your family's medical care.**

Read more...

You are enrolled in the SouthSeq study because your baby has medical problems that may have a genetic cause.

This study uses a new kind of genetic test, called genome sequencing that looks at your baby's entire genetic code.

Doing this test in a NICU may allow a diagnosis to be made earlier and may help your baby's doctors provide better care and treatments.

The goal of this study is to enroll about 1,500 newborns in the southeastern US. We want to learn if this test is helpful in a NICU and to understand the impact this impact has on patients and their families.

Results from the genome sequencing test will be given back to you and your baby's doctors. Results may include:

1. If the test was able to find the reason for your baby's medical problems
2. Genetic changes that may be important for your family's medical care

The learning topics here in Genome Gateway will give you more information about the study, possible results, and important things to consider.

What to Expect Next

Key Points:

- **You will be notified when your results are ready and a genetic counseling session will be scheduled**
- **New questionnaires and learning articles will be available to you after your results have been returned.**
- **You will be actively enrolled in the trial for up to one year.**
- **We will continue to review your records for up to 8 years and update you with any new information if you give permission to be re-contacted.**

Read more...

By taking part in SouthSeq, a genetic test called whole genome sequencing will be done for your baby. When results are ready, you will be notified and a time will be scheduled for you to discuss the results with a healthcare provider in the NICU. A healthcare provider will go over whether any genetic changes were found that are thought to be the cause of your baby's symptoms. The provider will also discuss any medical recommendations based on the test result and answer any questions that you may have. You will be provided with a copy of the test results as well.

Questionnaires

When you first enrolled in SouthSeq you were asked to fill out several online questionnaires. There are additional questionnaires we will ask you to fill out now that results are ready and again in several months. These questionnaires will be filled out online in Genome Gateway. You will be sent an email and/or text message whenever there is a new survey to complete.

Learning

Educational topics, like this one, will continue to be available to you in Genome Gateway until the study closes. We encourage you to come back and review this information in the future as needed. You will also continue to have access to the shared files (including your consent form and test results) and messaging features within Genome Gateway.

Future Contact

You may also be contacted by your child's healthcare team or study staff to ask follow-up questions. You will be actively involved in the study for up to one year. It is possible that new information will be discovered about genetic variants that were found in your newborn, even after you have received results from the SouthSeq study. You may be contacted by your child's healthcare team or study staff with updated information about your child's genetic test result, if you have given permission to be re-contacted.

The study team will continue to look at information in your child's medical record for up to eight years to understand the impact of this kind of testing on your child's medical care. After that, the data will be kept for further research but personal identifiers will be removed.

It is important for you to know that you can withdraw your consent to participate from the SouthSeq study at any time. To withdraw, please contact the study coordinator at the NICU location where your baby was enrolled. If you choose to withdraw from this study, your child's medical care will not be affected.

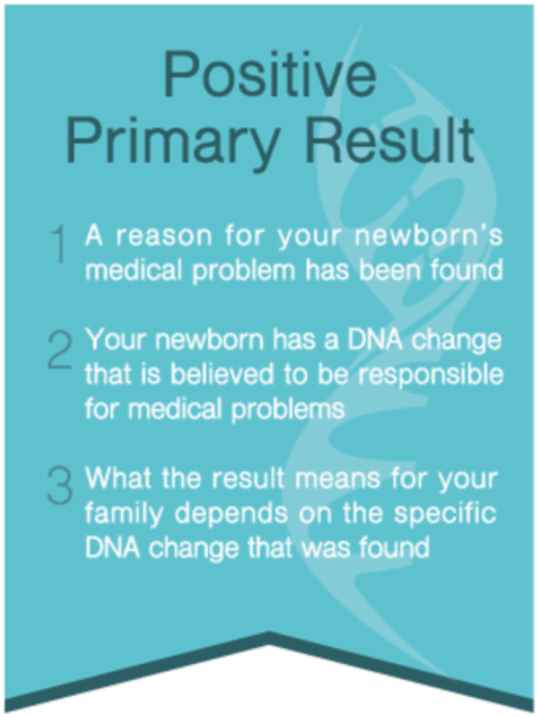
Positive Primary Result

Key Points:

- **A positive primary result means we have identified a genetic change that is the likely cause of your newborn's medical problem.**
- **A positive result may help guide medical care, but in many cases there are no specific treatments or cures known for genetic conditions.**
- **A positive result may impact your or your newborn's future family planning.**
- **A positive result may allow you to connect with support groups, other families, or with organizations that may have useful resources.**

Read more...

Primary results are those related to your newborn's medical problems and the reason behind the WGS testing was done. A positive primary result from a whole genome sequencing test means that a genetic change was found that is likely to be the cause of your newborn's symptoms.



How are positive results used?
Receiving a positive result may help doctors better understand your newborn's medical needs. This information could lead to changes in how your newborn is cared for. However, many genetic conditions do not have specific treatments or cures. Sometimes having a genetic diagnosis can provide a better picture of what the condition might be like in the future. Keep in mind that it is not possible to know the exact symptoms that will occur and how severe they will be.

Receiving a positive result could have an impact on your or your family's future family planning. Some genetic changes are new in an individual and not present in other relatives, while other genetic changes are inherited and passed down through a family. Knowing whether the genetic change found in your child was new or passed down can help your healthcare provider give you a more specific estimate of the chance that other family members, such as future children, may have the same condition or symptoms.

When you discuss with the healthcare provider your newborn's WGS results you will also receive a copy of the test results and a letter explaining the results in detail. If you receive a positive result, the healthcare provider will go over the specific genetic change that was found and what it means for your newborn's medical care and your family.

Finding Support

For some families, receiving a positive result allows them to connect with specific support groups, resources and/or research studies specific for the genetic condition that their newborn has. Your result report will include information about currently available resources specific to your child's condition. In addition, the following resources for the larger, rare disease community may also be of interest to you:

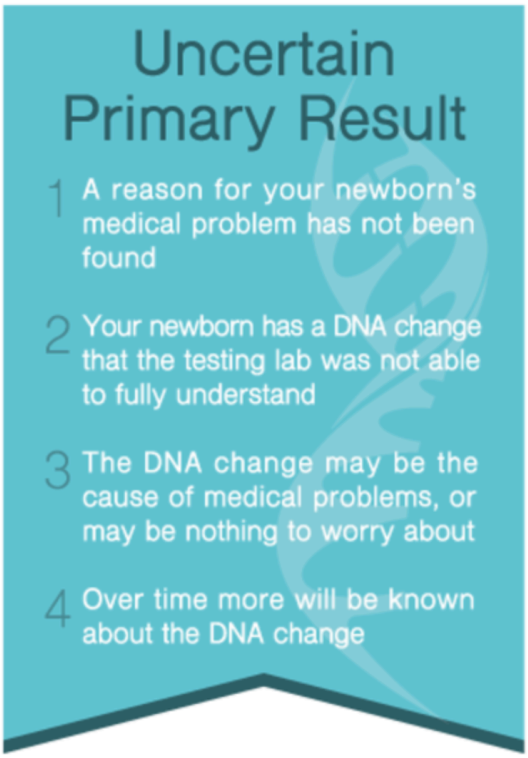
- The National Organization for Rare Disorders (NORD)
- Global Genes: Allies in Rare Disease
- Alabama Rare

Uncertain Primary Result

Key Points:

- **An uncertain primary result means that we found a genetic change that may be responsible for your newborn's medical problem.**
- **There is simply not enough information available to know if the genetic change is causing your newborn's medical problem or not.**
- **If more information becomes available about an uncertain primary result, you may be contacted by your healthcare provider or SouthSeq staff.**

Read more...



Primary results are those related to your newborn's medical problems and the reason the WGS testing was done. An uncertain primary result means that the study found a genetic change that is not yet well understood. This is because there is not enough information available to be able to decide if the change is actually the cause of symptoms or if it is a harmless genetic change. This kind of result is called a variant of uncertain significance (VUS).

Because it is uncertain, this type of result should not be viewed as a definite diagnosis and may not help doctors make decisions about care for your child. Our hope is that over time more will be learned about the genetic change and the experts will be able to decide whether it is, or is not, the cause of symptoms. Our knowledge of genetics and how it relates to diseases is constantly improving.

When you discuss your newborn's results from the SouthSeq study you will receive a copy of the test results and a letter explaining the results in detail. If you receive an uncertain result, the healthcare provider will go over the specific genetic change that was found.

During the SouthSeq study, if the testing laboratory is able to better understand the variant of uncertain significance and decide whether it is the likely cause of symptoms, you may be contacted by your healthcare provider or study staff with new information about your test result. We encourage individuals who have an uncertain result to stay in touch with their healthcare team regularly to find out if new information has been learned about the genetic variant that was found.

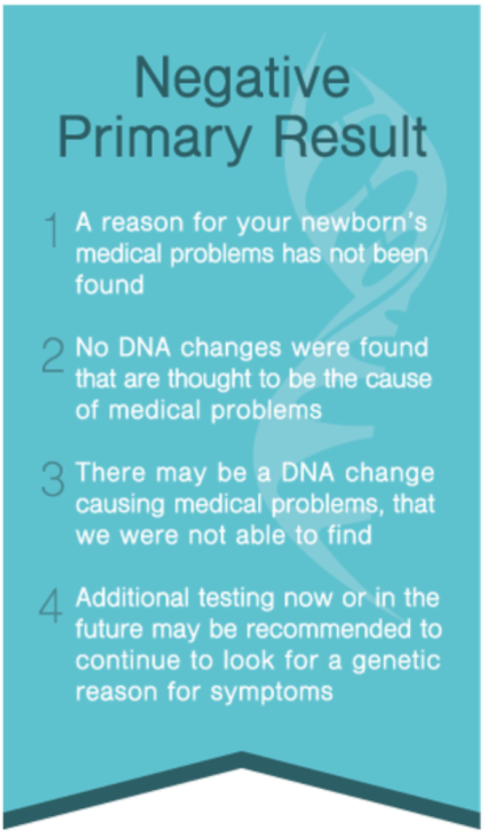
Negative Primary Results

Key Points:

- **A negative primary result means that we did not find a genetic change that is the cause of your newborn's medical problem**
- **It is possible that your newborn's medical problem is caused by more than one genetic change and/or environmental factor - these cases are very difficult to diagnosis.**
- **It is possible that your newborn's symptoms are caused by a single genetic change that we are not able to find with current testing.**
- **It is still possible to find a genetic cause if a new genetic test becomes available or if the SouthSeq laboratory looks at your results again in the future.**

Read more...

Primary results are those that are related to your newborn's medical problems and the reason that the testing was done. A negative primary result means that no genetic changes were found that are thought to be the cause of your newborn's symptoms. It would be easy to think that this means the symptoms are not caused by a genetic disorder. However, this is not the case. There are many reasons that a person might receive a negative result.



Reasons for a Negative Result
It is possible that your newborn's symptoms are not caused by a single genetic change. In some cases, symptoms are caused by multiple genetic and environmental factors. These cases are very difficult to diagnose with the types of testing available today.

It is also possible that your newborn's symptoms are caused by a single genetic change that is not able to be found with current testing options. There are certain types of genetic changes that are very difficult to find and a lot of genetic changes that we do not yet fully understand.

Over time, we will continue to learn more about how genetic changes cause symptoms and human disease. Sometimes, a person who had a negative result when they were first tested will later receive a genetic diagnosis. This could happen through a new genetic test that might be ordered, or by the laboratory taking another look at the whole genome sequencing data in the future. It is important for you to keep in touch with your child's healthcare providers to stay up to date on testing options and new information.

Secondary Results

Key Points:

- **A secondary result is a genetic change that is not causing your newborn's medical problems, but is associated with risk for other diseases in the future.**
- **SouthSeq only reports secondary findings where steps can be taken to prevent or reduce disease risk.**
- **It is possible the genetic change is new in your newborn, but more likely that it was inherited from a parent.**
- **We may be able to determine which side of the family the secondary findings came from.**

Read more...

A secondary result or finding is a genetic change that is not related to the reason for testing but may still be important to know about.

What kinds of secondary results does SouthSeq look for?
In addition to searching for a reason for your newborn's medical symptoms, the SouthSeq study also looks for changes in a small list of other genes. These genes are related to the possibility of developing other diseases in the future, like cancer or heart disease. The study only reports secondary results that are considered actionable, meaning steps can be taken to prevent or reduce risk of disease. Knowing that someone has a risk to develop a certain disease in the future may mean that they need to see a certain kind of doctor or have special tests to check for symptoms.

What does it mean to receive a secondary result?
Receiving a secondary result means that a genetic change was found that is known to cause an increased risk of a particular disease in the future. Sometimes getting a secondary result can explain a person's family history of disease. Other times a secondary result is surprising, and found in a person who does not have any family history of the disease. Based on the specific result there may be medical changes recommended that lower risk or detect disease at an earlier stage.

While it is possible that a secondary result is a brand new genetic change in your newborn, it is more likely that it was passed down from a parent. If the study received blood samples from both parents' samples, we may be able to tell you which side of the family the secondary finding came from. It is important to talk with your child's genetics team or with your own doctor about this finding and whether you and your relatives may need testing as well.

Sharing Your Results

Key Points:

- **Your newborn's genetic results will be included in their medical record and small, unidentifiable parts of your newborn's genetic code will be shared on public databases.**
- **It is your choice if you would like to share your newborn's entire genetic sequence on a private research database called dbGaP.**
- **It is your choice if you would like a small sample of your newborn's blood to be kept for future research that may help children like yours in the future.**
- **You should think carefully about what other medical providers and family members you might like to share your results with.**

Read more...

By participating in SouthSeq, some of your private information may be shared with different people and databases. Some of these are required for all SouthSeq participants. Others are optional and you get to decide what types of information you feel comfortable having shared and with whom.

Where will my data automatically be shared?
Everyone who agrees to take part in SouthSeq will have their signed consent form put into their child's medical record. In addition, the genetic test results you receive from the study will also be automatically put into their child's medical record. Everyone who agrees to take part in this research study also allows small, unidentifiable parts of their unique genetic sequence to be shared to public databases and published in scientific journals. This information cannot be used to identify your child or your family.

What choices do I have for more data sharing?
When you consented to participate in the SouthSeq study you were given the option to share your family's genetic information with two other places. The first is a private database called dbGaP to which only researchers have access. The second is the laboratory where the genetic testing was done. For more information about these places that your data may be shared, review the prior section on Data Access [make live link].

Who should I share my study results with?
Depending on the type of genetic results you get from the SouthSeq study, there may be others with whom you would like to share your results. As you think about who else might need or want to see your child's results, it is important to remember that their genetic test results are private health information to use and share as their parent desires. While there may be benefit to your child, yourself and others in knowing this information, there could also be risks and implications in having your child's information shared with others. For more information about these risks and implications, see the prior section on Genetic Discrimination.

Sharing with Healthcare Providers

Participants may choose to share their child's results with other healthcare providers besides the study physician. The results you receive may impact multiple aspects of your child's medical care and it may be helpful for providers in multiple specialties to see the test results.

Sharing with Family Members

Results from a whole genome sequencing test may have implications for you and your family members. In some cases, a genetic test result may explain medical symptoms in family members. In other cases, a result may indicate that family members are at risk of developing a disease in the future or being a carrier for a genetic condition which they could pass on to their children. There may be genetic tests that your relatives are interested in having themselves based on your family's test results. Your child's healthcare provider will go over any potential impacts on family members during your result discussion.

Dominant Inheritance

Key Points:

- **For most genes, each person has two copies; one they inherited from their mother and one they inherited from their father.**
- **A condition or disease with a dominant inheritance pattern happens when a change in one of these genes is enough to cause a problem.**
- **A person with a dominant condition has a 50% chance to pass on the changed gene to a child.**
- **It is important to keep in mind that not all people with the same gene change will have the same severity of symptoms.**

Read more...

Dominant inheritance is one way that a genetic trait or condition can be passed down in a family. For most genes, each person has two copies. One gene copy is inherited from mom and the other is inherited from dad. A condition is inherited in a dominant pattern when a disease-causing (pathogenic) change in just one copy of a gene is enough to cause the condition, even though the other copy of the gene is working.

How are dominant conditions inherited?
A person with a dominant condition has a 50% (1 in 2, like the flip of a coin) chance to pass on the changed gene copy to a child. The child that gets this copy will have the condition. There is also a 50% (1 in 2, like the flip of a coin) chance that the parent with the condition will pass the typical copy of the gene to a child. The child that gets this typical copy will not have the condition.

It is important to keep in mind that two people with the same condition may not have the same exact symptoms. Even in the same family, people with the gene change may have no symptoms, mild symptoms, or severe symptoms. A mildly affected adult with a dominant condition may have a child with serious medical problems related to the condition. A person with more serious symptoms may also have children that have milder symptoms.

Sometimes a patient is the first person in their family with a dominant condition. For these people, the change was present in either the egg or sperm from which they developed. This random change in a gene is called a new (also called de novo) variant.

Recessive Inheritance

Key Points:

- **For most genes, each person has two copies; one they inherited from their mother and one they inherited from their father.**
- **A condition or disease with a recessive inheritance pattern is only present when both copies of a person's gene have the same harmful change.**
- **A person with one working copy of the gene and one copy with a harmful change usually will not have symptoms, but is considered a carrier of the condition.**
- **When both a mother and a father carry the same recessive condition, they have a chance of having a child with the disease.**

Read more...

Recessive inheritance is one of the types of inheritance that causes a genetic trait or condition. For most genes, each person has two copies in every cell of their body. When a condition is recessive, both copies must have harmful changes to cause the condition. A person with one working copy of the gene and one copy with a disease-causing (pathogenic) change is considered a carrier of the condition. Carriers of a recessive condition usually do not have any symptoms.

How are recessive conditions inherited?
When both a mother and father are carriers of the same recessive condition, they have a chance of having a child with the disease. If both parents happen to pass on their "changed" copy, the child will have symptoms of that condition.

When each parent has a "working" copy and a "changed" copy in a gene of a recessive condition, three different outcomes are possible:

1. The child *is affected* and *has symptoms* of the condition. This occurs when the child inherits a "changed" copy from each parent. Each child has a 25% chance (1 in 4) of having the condition.
2. The child *is not affected* but *is a carrier*. This occurs when the child inherits one parent's "working" copy and the other parent's "changed" copy. Each child has a 50% chance (2 in 4) of being a carrier of the condition but not being affected. This child does not have to worry about having the disease, but may be concerned about passing their "changed" copy on to their own children in the future.
3. The child *is not affected* and *is not a carrier*. This occurs when the child inherits a "working" copy from each parent. Each child has a 25% chance (1 in 4) of not being affected and not being a carrier. This child does not have to worry about having the condition or passing the condition on to future generations.

X-linked Inheritance

Key Points:

- **Our sex is determined by two of our 46 chromosomes; women normally have two X chromosomes and men typically have an X and a Y chromosome.**
- **Sometimes genetic changes are linked to the X chromosome, these are called X-linked conditions.**
- **Men only have one X chromosome, so if a male inherits a disease-causing change in his X gene, he will have the condition.**
- **Women inherit two X chromosomes, so if the woman inherits only one changed X gene and one working X gene she will usually not have the disease, but will be a carrier.**

Read more...

X-linked inheritance, also called sex-linked inheritance, is one of the types of inheritance that causes a genetic trait or condition. Two of the 46 chromosomes found in each cell of the body are called the sex chromosomes. One of these is called the X chromosome and the other is called the Y chromosome. These chromosomes determine our sex. Women normally have two X chromosomes and men normally have an X and a Y. Women pass an X chromosome to each of their children. Men pass either the X or the Y chromosome and therefore determine a child's sex.

X-linked Genetic Conditions
A medical condition caused by a change in a gene on the X chromosome is called an X-linked condition.

Males have only one X chromosome. This means that a male has only one copy of each of the genes that are on the X chromosome. If he has a disease-causing change on his X chromosome, he will have the condition.

Females have two X chromosomes. This means that a female has two copies of each gene on the X chromosome. If one of her X chromosomes has a disease-causing change, she will usually not have the condition. This is because her other X chromosome contains a "working" copy of the gene. However, she would be however, a carrier for the condition.

How are X-linked Conditions Inherited?

When a mother is a carrier for an X-linked condition, four different outcomes are possible:

1. The child *is a boy* and *is affected* and has symptoms of the condition. This occurs when the male child inherits the "changed" gene copy from the mother. Each son has a 50% chance (1 in 2) of having the condition.

2. The child *is a boy* and *is not affected*. This occurs when the male child inherits the "working" gene copy from the mother. Each son has a 50% chance (1 in 2) of not being affected. This child does not have to worry about having the condition or passing the condition on to future generations.

3. The child *is a girl* and *is a carrier (but likely not affected)*. This occurs when the female child inherits the "changed" gene copy from the mother. Each daughter has a 50% chance (1 in 2) of being a carrier.

4. The child *is a girl* and *is not a carrier (and is not affected)*. This occurs when the female child inherits the "working" gene copy from the mother. Each daughter has a 50% chance (1 in 2) of not being a carrier. This child does not have to worry about having the condition or passing the condition on to future generations.

Because males pass their X chromosome on to all female children, all daughters of a man with an X-linked condition will be carriers of that condition. Because males do not pass on an X chromosome to any male children, none of the sons of a man with an X-linked condition will have the condition.

Can girls be affected with an X-linked condition?

Early in a female's development, one of her two X chromosomes is randomly and permanently "turned off" in each of her cells. This is a process called X-inactivation. Because X-inactivation is random, the X chromosome from the mother is active in some cells, and the X chromosome from the father is active in other cells.

Most females who are carriers of an X-linked condition do not have any symptoms of the condition. However, some do have symptoms, usually in a mild form. This is a result of uneven, or skewed, X-inactivation. Sometimes, the "working" copy of the gene will be "turned off" in so many cells that the female will have symptoms of the condition. The severity of her symptoms depends on the amount of cells where the "working" copy of the gene remains active.

New (de novo) Genetic Changes

Key Points:

- **Sometimes genetic changes are not inherited from either parent but occur for the first time in an individual, these changes are called de novo.**
- **De novo changes happen when an egg or sperm cell have a genetic change that the rest of the parent's cells do not.**
- **A person with a de novo change can pass this change to their children.**
- **The chance for a parent with a child that has a de novo dominant change to have additional children with the same change is less than 1 in 100.**

Read more...

In some cases, genetic changes are not inherited (transmitted) from either parent but instead occur for the first time in an individual. De novo variants are these new genetic changes that happen for the first time in a person are called. The word de novo is a Latin word for "new."

How do new genetic changes happen?
De novo changes happen when an egg or sperm cell has a genetic change that the rest of the parent's cells do not. These new genetic changes occur due to random chance as egg and sperm cells are made. If a de novo change happens in a gene that causes a dominant disorder, the person will have that disease while the rest of the family will not. This is because in a dominant disease, having a single disease-causing change in one copy of the gene is enough for someone to have the disease.

How does a new genetic change affect risk in family members?
Even though a person with a de novo change did not inherit the change from a parent with the disease, they do have a chance to pass the change on to their children. Each child of a person with a de novo dominant genetic condition has a 50%, or 1 in 2, chance to have the same disease as their parent.

For parents of a child with a de novo dominant inherited condition, the chance to have another child with the same condition is very low. In rare cases, other eggs or sperm may have the same change as the child with symptoms, which would increase the risk for another affected child. We are not able to test all the cells in a parent's body to find out if other cells may carry the change. Therefore, we usually say that the chance for a sibling of a child with a de novo dominant condition to be affected is less than 1%, or 1 in 100. This means that if you have additional children, the chance for them to be born with the same condition as your child is less than 1 in 100.